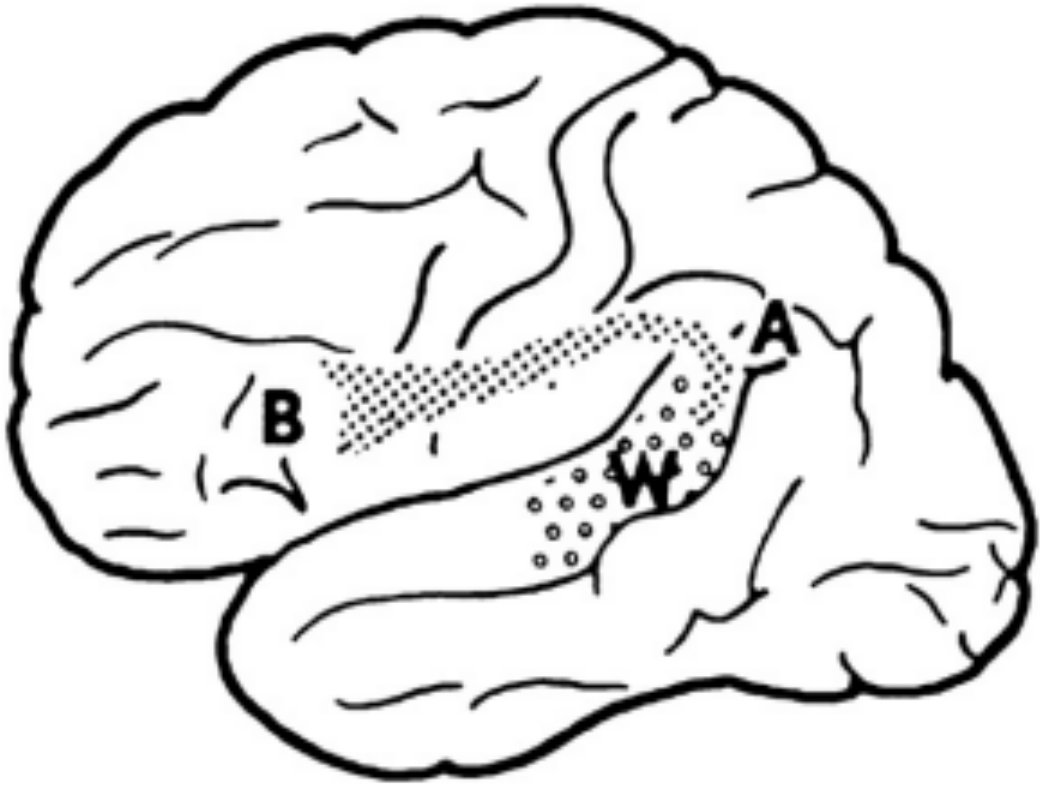
Arcuate Fasciculus



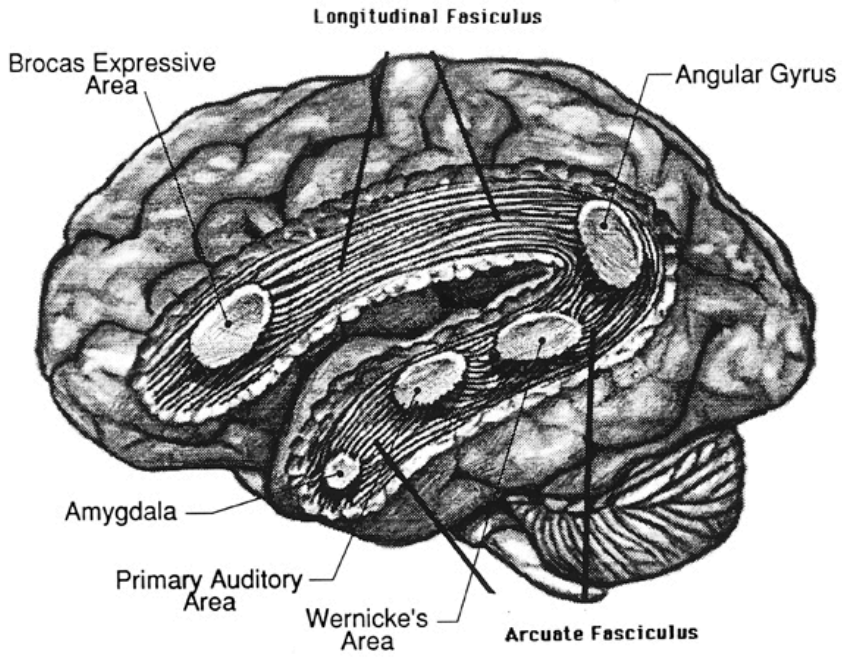
From Geschwind, Science, 1970

Outline

- 1. Background
- 2. Afferent & Efferents
- 3. Neurophysiology
- 4. Neurochemical systems
- 5. Behavioral correlates
- 6. Physiological correlates
- 6. Clinical Pathologies

Background

- Provides connectivity between regions involved in language processes



- Phonological processing during speech perception and production

Phonological processing: involves detecting and discriminating differences in phonemes or speech sounds

Two Distinct Language Pathways: Dorsal and Ventral

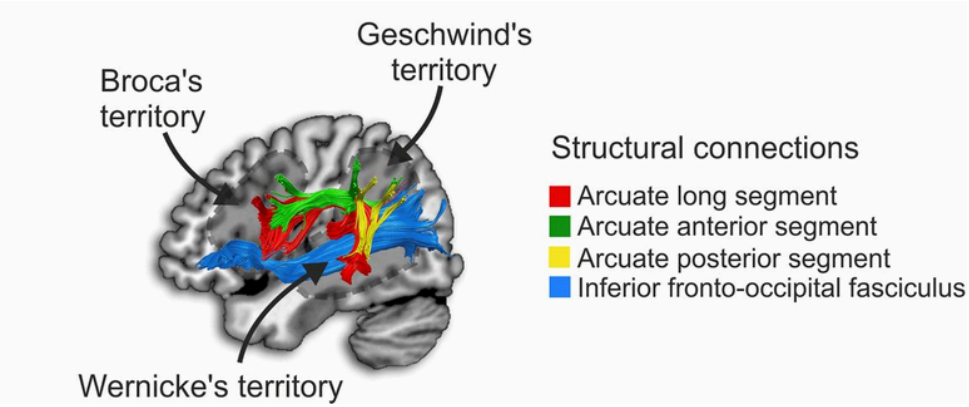
Dual Stream System

Dorsal

- Mapping of auditory speech sounds to articulatory (motor) representations
- Processing complex syntactic structures

Ventral

- Mapping of auditory speech sounds to meaning
- Processing less complex syntactic structures



Lopez-Barroso et al., PNAS. 2013.

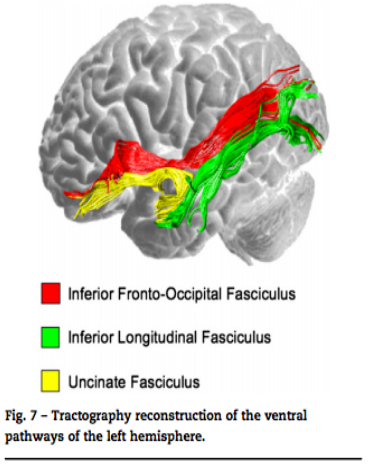
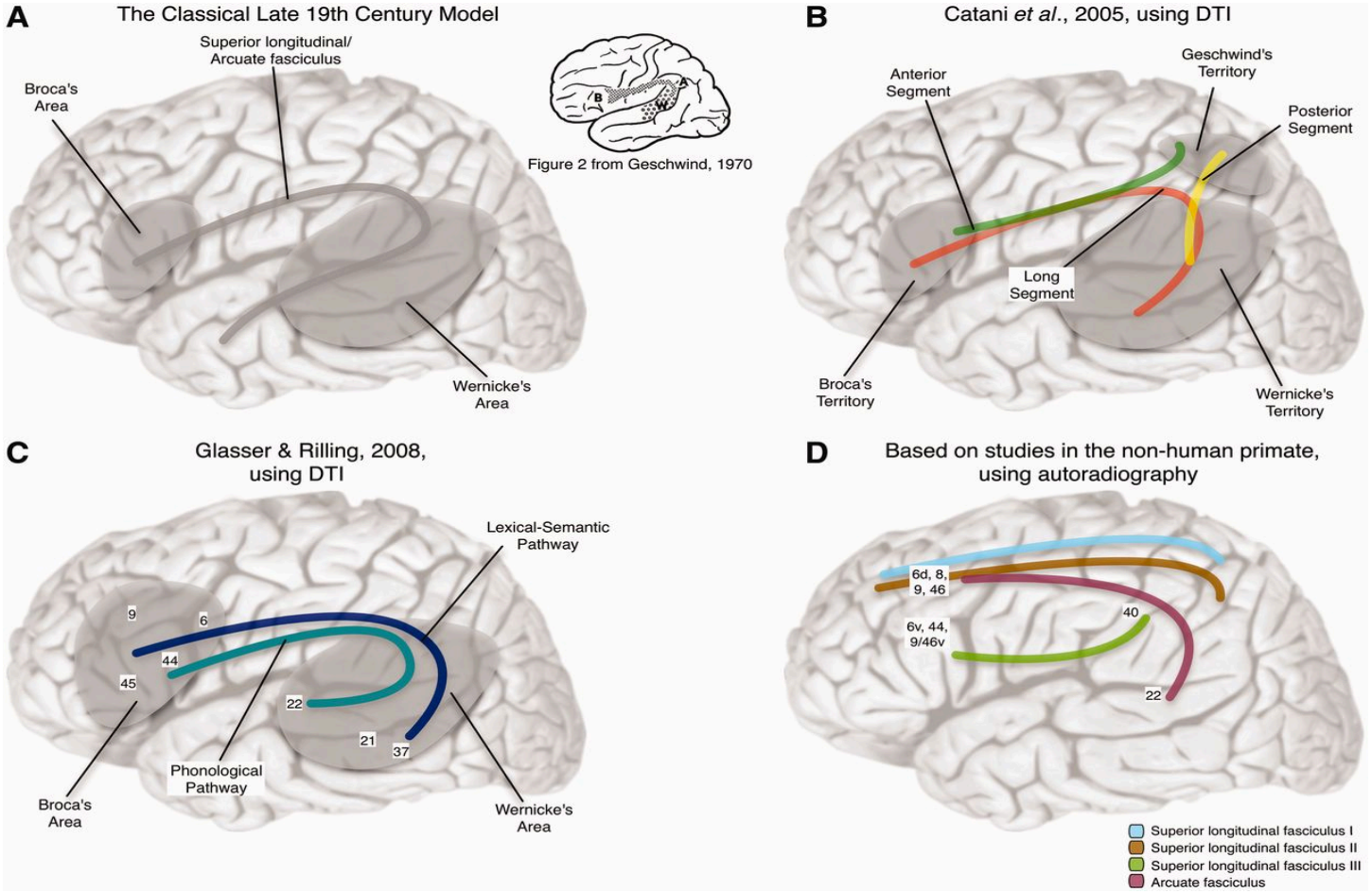


Fig. 7 – Tractography reconstruction of the ventral pathways of the left hemisphere.

Catani and Mesulum, Cortex. 2008

Diverging Theories

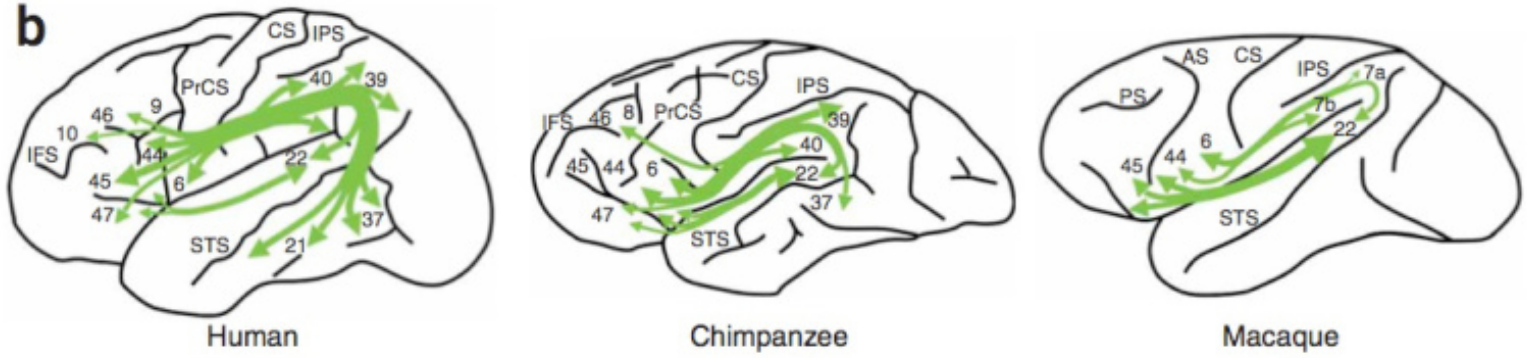
Connectivity profile of the AF is still not fully understood



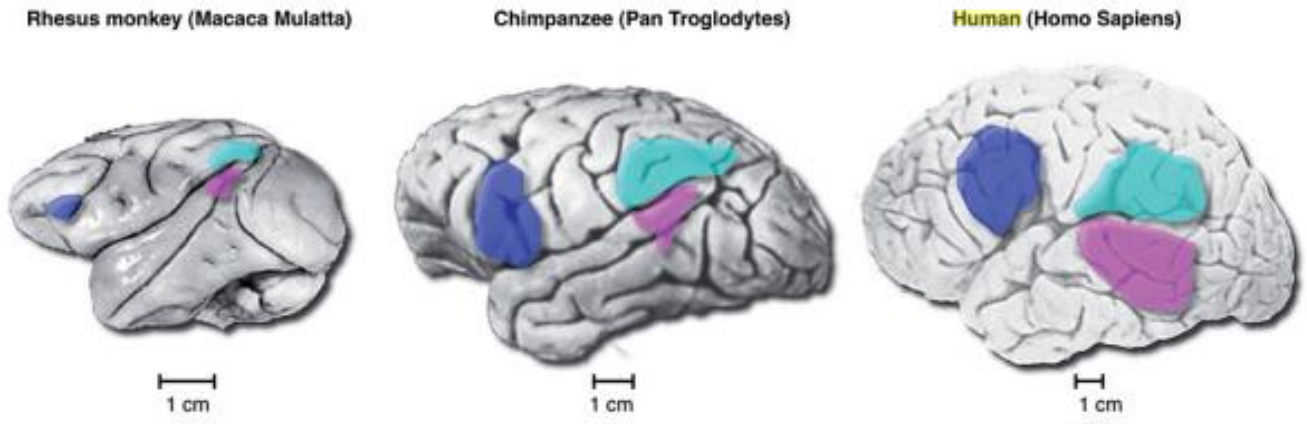
Dick and Tremblay. Brian. 2012

Humans vs. Non-Human Primates

- Organization and cortical terminations of the AF modified in human evolution

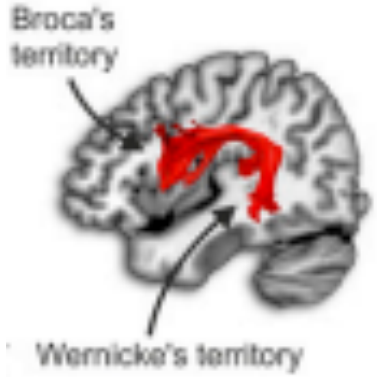


- Increase in size from monkey to man of cortical areas corresponding to Broca's and Wernicke's areas (according to cytoarchitecture)

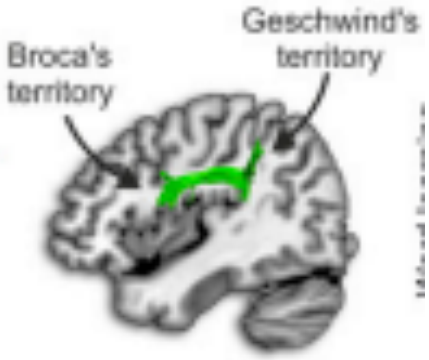


From Catani, Atlas of Human Brain Connections. 2012; Rilling et al., Nature Neuroscience. 2008

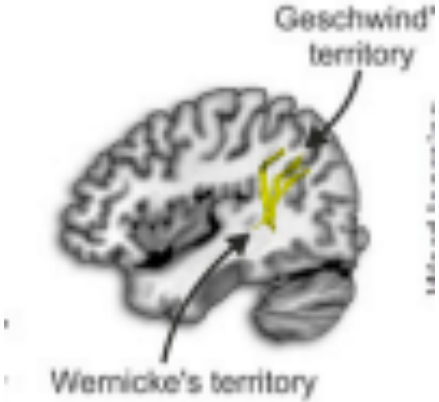
Divisions



1) **Long, direct segment** – connects posterior superior temporal gyrus (Wernicke's) inferior frontal gyrus (to Broca's)



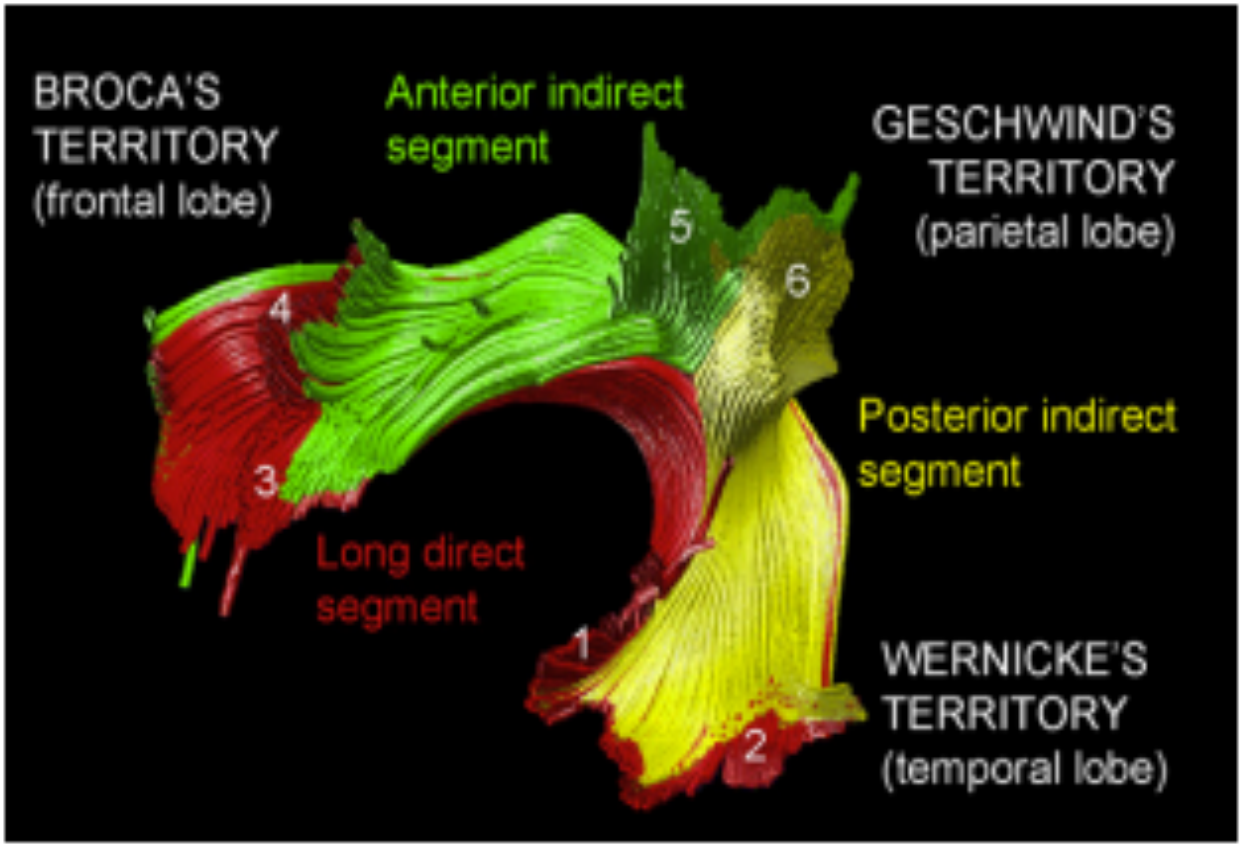
2) **Anterior, indirect** – connects inferior frontal gyrus (Broca's) with inferior parietal cortex (Geshwinds)



3) **Posterior, indirect** – connects inferior parietal lobule (Geschwind's) with posterior superior temporal gyrus (Wernicke's)

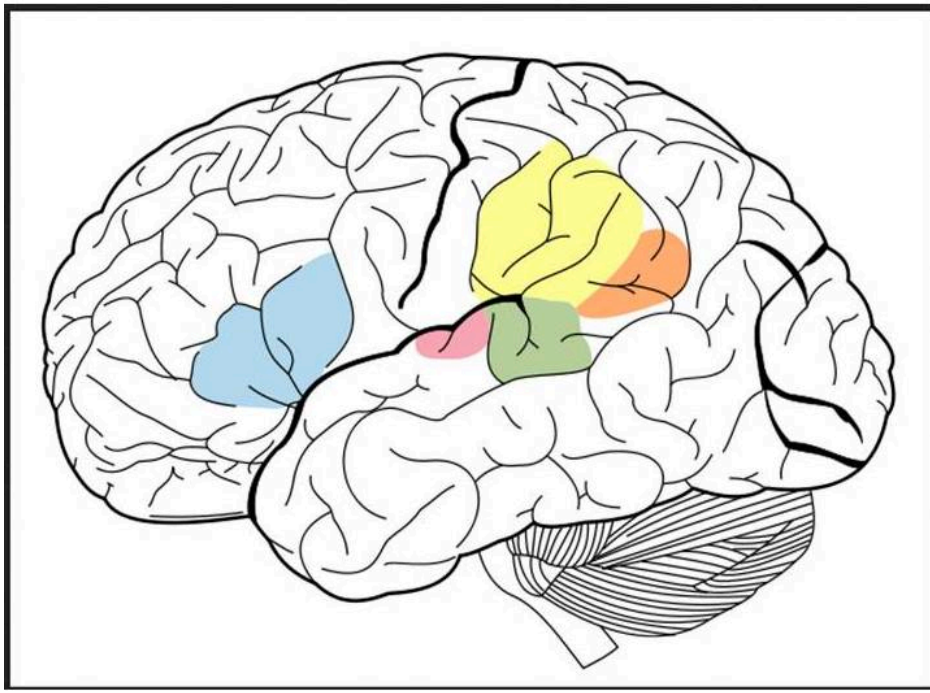
Catani et al. Ann Neurol. 2005

Divisions



1. Superior temporal lobe; 2. middle temporal lobe; 3. inferior frontal and precentral gyrus; 4. middle frontal and precentral gyrus; 5. supramarginal gyrus; 6. angular gyrus

Language Regions



Broca's area *(blue)*

pars opercularis (B44)

pars triangularis (B45)

Wernicke's area *(green)*

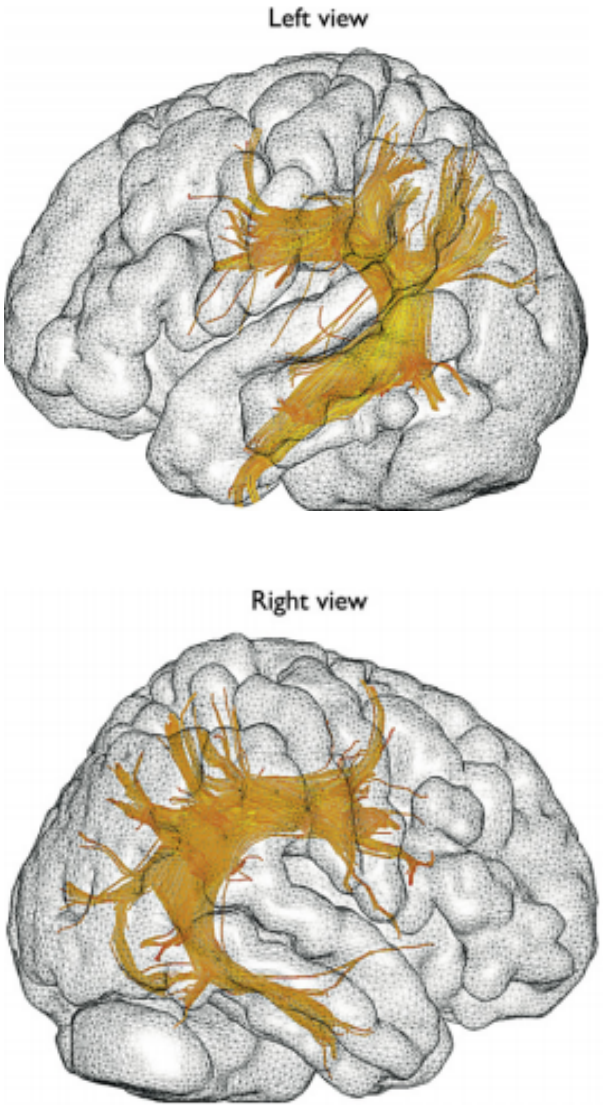
posterior superior temporal gyrus

Geschwind's area *(yellow, orange)*

inferior parietal cortex (supramarginal gyrus, angular gyrus)

Hemispheric Asymmetry

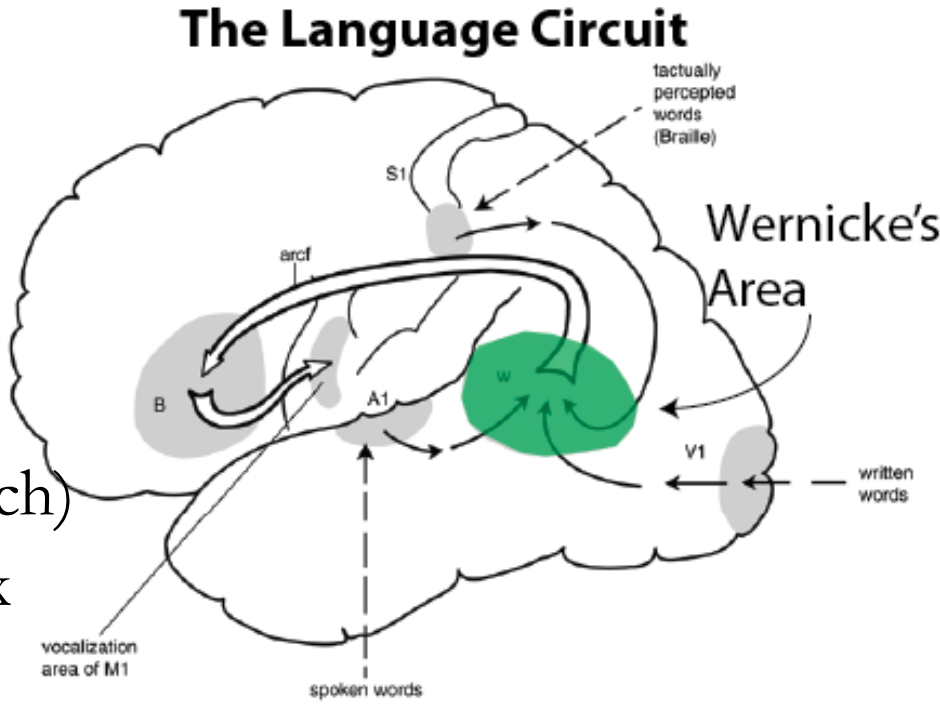
- Left-right differences in perisylvian aanatomy
- Greater proportion of arcuate fibers on left
- Very heterogenous
- extreme degee of heterogeneity
  - 60% extreme leftward lateralization
  - 20% mild leftward lateralization
  - 20% bilateral, symmetrical pattern
- Gender
  - 40% females extreme left
  - 85% males extreme left
- Starts early in development
  - infants aged 1-4 mo. show some leftward lateralization



Catani et al. 2007

Afferents and Efferents

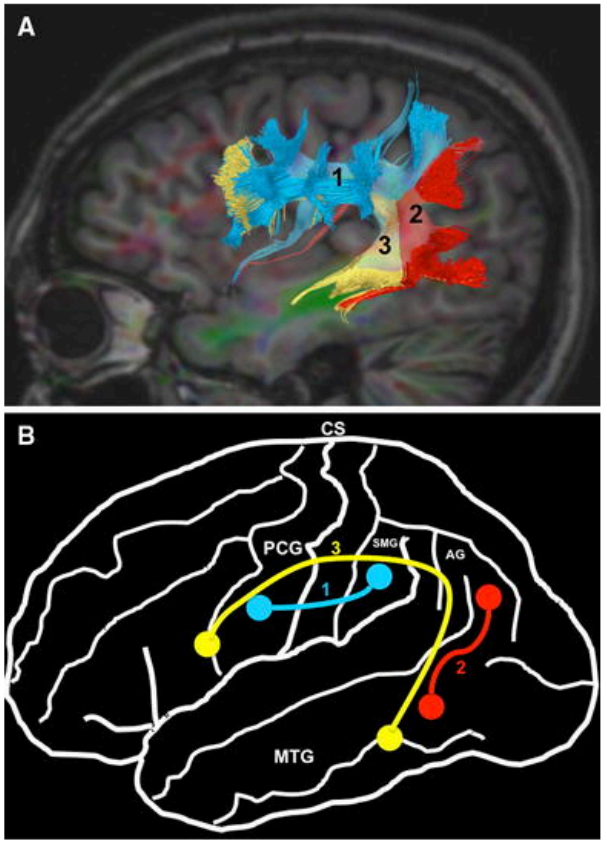
- Originates in posterior temporal gyri
- Posterior superior temporal gyrus (Wernicke's) receives input from
  - Primary auditory cortex (speech)
  - primary somatosensory cortex (Braille)
  - primary visual cortex (reading)
  - angular gyrus (mediates input from visual and and somatosensory areas)



From Verstynen. *Zombie Brains*.

Terminations: Parietal

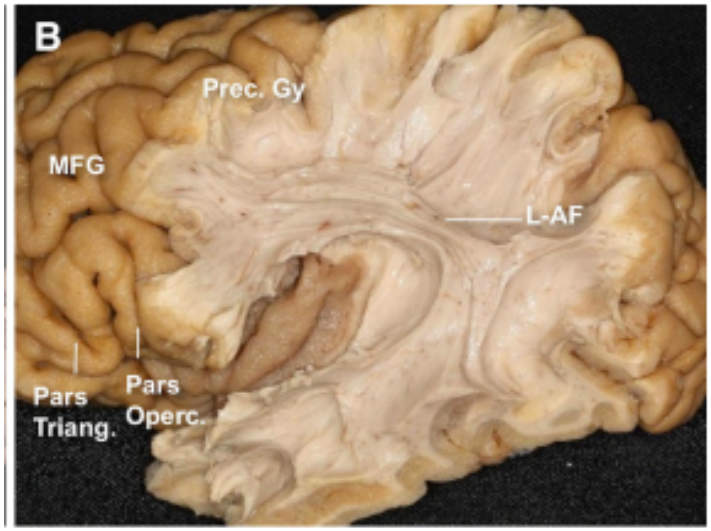
- Inferior parietal lobule (Geschwind's)
  - supramarginal gyrus
  - angular gyrus

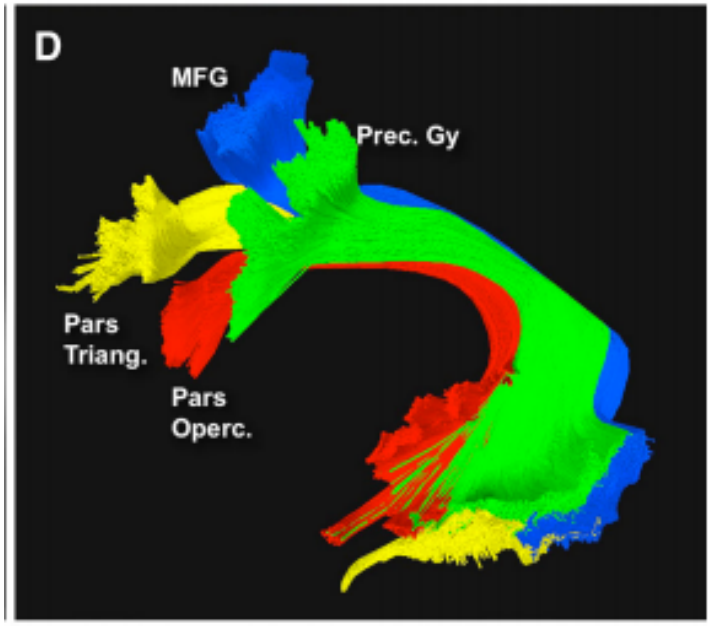


From Martino et al., Brain Struct Funct. 2012

Terminations: Frontal

- Inferior frontal gyrus (posterior)
  - Pars opercularis (B44)
  - Pars triangularis (B45)
- Caudal middle frontal gyrus
- Ventral precentral gyrus
- May be bi-directional



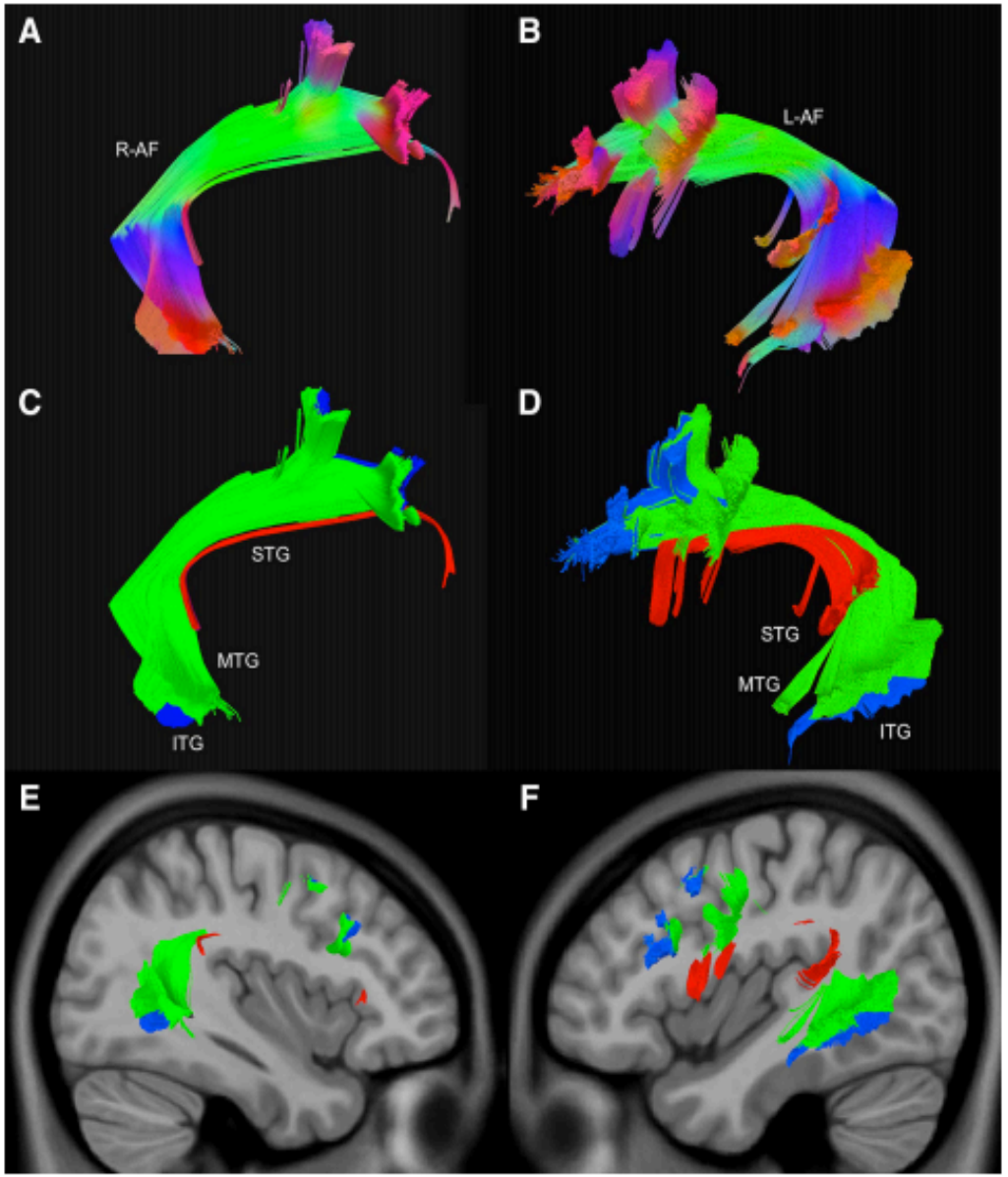


Fernandez-Miranda, Brain Struct Funct, 2014

Left vs. Right Terminations

Hemispheric variations in terminations

Fewer terminations in pars opercularis and precentral gyrus in right hemisphere



Connectivity of the AF

Posterior, indirect:
posterior middle and superior temporal gyrus → angular gyrus

Anterior, indirect:
inferior parietal cortex → inferior frontal gyrus and ventral precentral gyrus

Long, direct:
Supplementary:
Inferior and middle temporal gyrus →
ventral precentral, caudal middle, dorsal pars triangularis
Primary:
Superior and middle temporal gyrus →
pars opercularis and ventral precentral

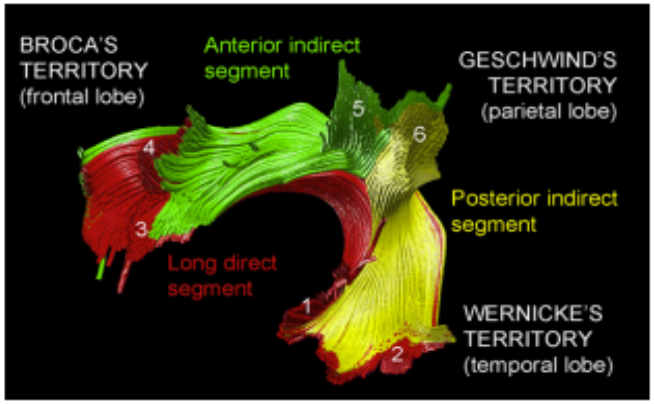
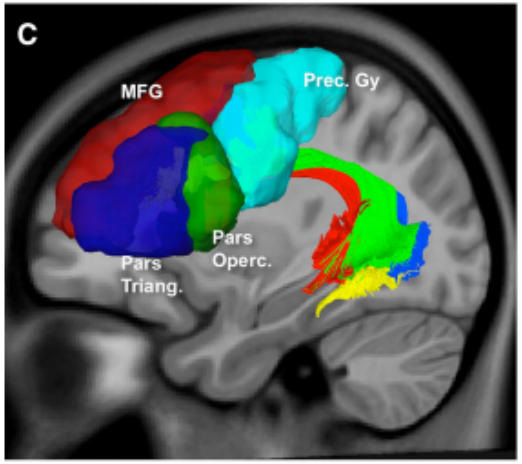


Fig. 5 – Tractography reconstruction of the arcuate fasciculus. Numbers indicate the cortical projections of the segments: 1, superior temporal lobe; 2, middle temporal lobe; 3, inferior frontal and precentral gyrus; 4, middle frontal and precentral gyrus; 5, supramarginal gyrus; 6, angular gyrus (mod. from Catani et al., 2005).

Fernandez-Miranda et al. Brain Struct Funct. 2014

Connectivity of the AF



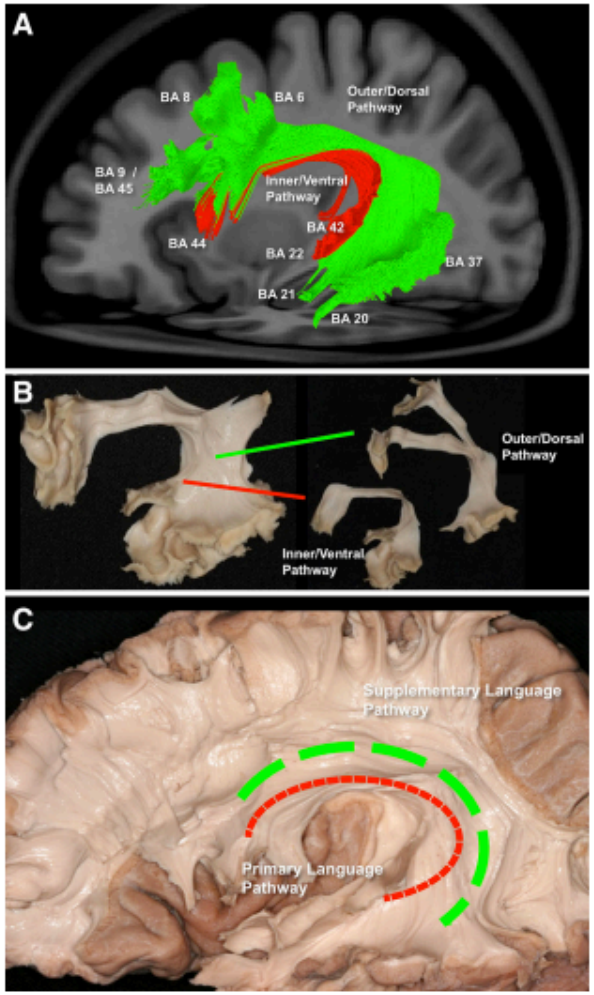
- **Long, direct:**

Supplementary (green):

- Inferior and middle temporal gyri → ventral precentral, caudal middle frontal, dorsal pars triangularis

Primary (red):

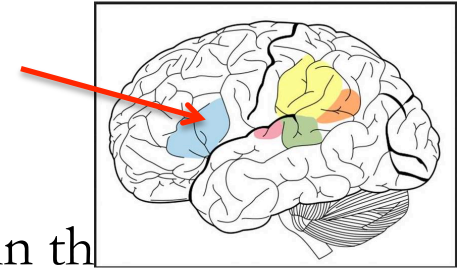
- Superior and middle temporal gyrus → pars opercularis and ventral precentral



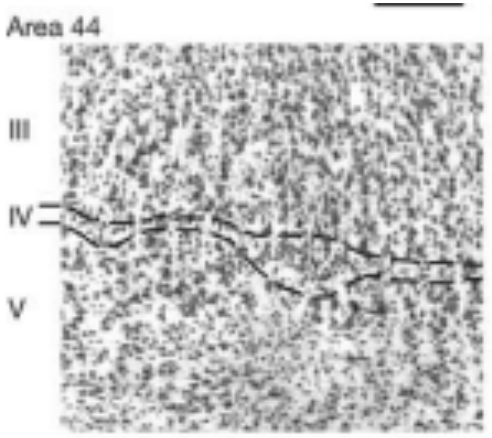
Fernandez-Mirando, Brain Struct. Funct. 2014

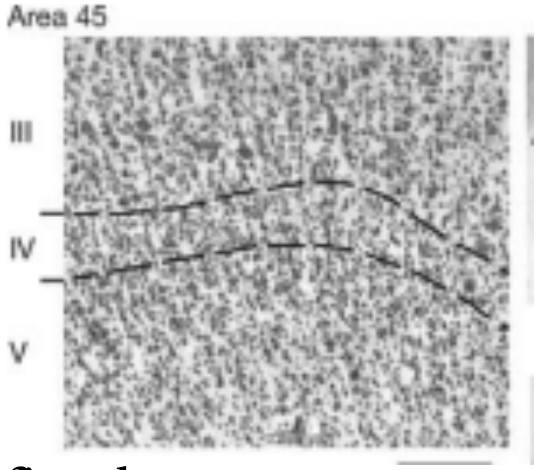
Neurophysiology

Topography: Broca's area



- Pars triangularis (B45) and pars opercularis (B44) differ in th cytoarchitecture
  - Both share very large pyramidal cells in deep layer III and layer V, low cell density in layer VI
  - Area 44 is "dysgranular" (containing a thin layer IV of small granular cells with pyramidal cells from deep layer III and upper layer V intermingled with those of layer IV), area 45 has densely packed granular cells in layer IV

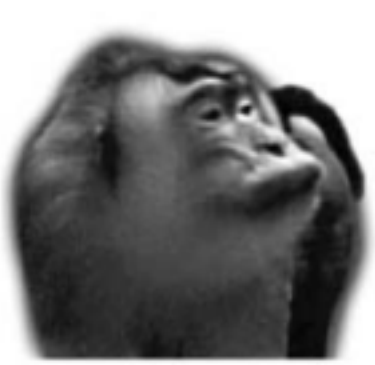


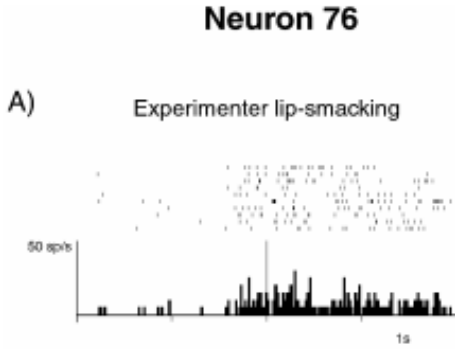


- Broca's area not unambiguously defined

Petrides et al., Nature. 2005

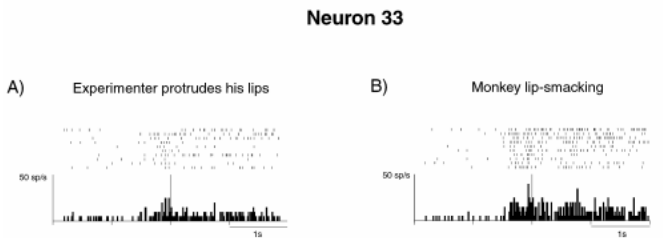
Mirror Neurons





Respond when performing an action and when observing others perform the same action

- mirror neurons in macaque area F5c (homolog of Broca's area 44 in humans)
- Responded when experimenter made communication-specific orofacial movements
- Same firing when monkey performed an action (lip-smacking) and when viewed experimenter perform action
- Broca's 44 may have evolved originally as area involved in high-level motor control over orofacial actions, including those involved in communication

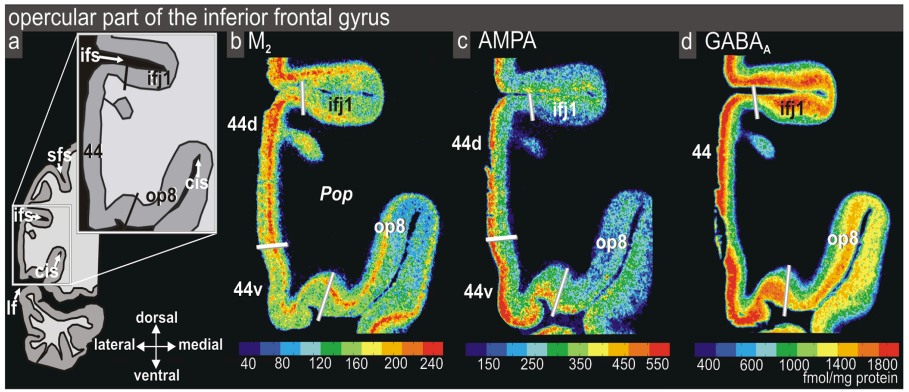


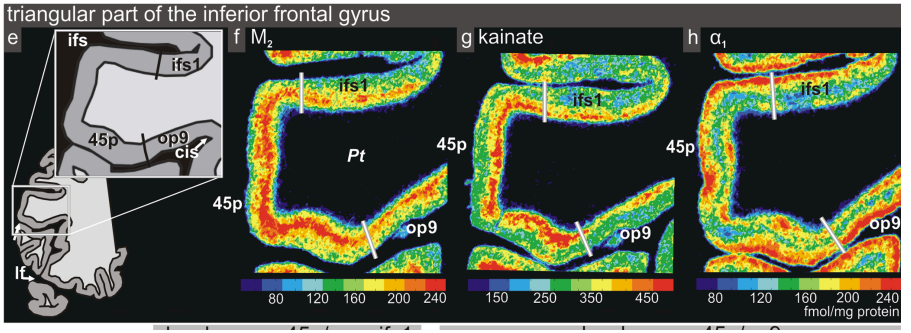
Ferrari et al., European Journal of Neuroscience. 2003

Neurochemistry

Broca's Receptor Architecture

- Glutamatergic, GABAergic, Cholinergic, Noradrenergic receptors
- Greater M1 receptor density on area 44
- Based on receptor architecture, divisions of ventral and dorsal B44 and anterior and posterior B45



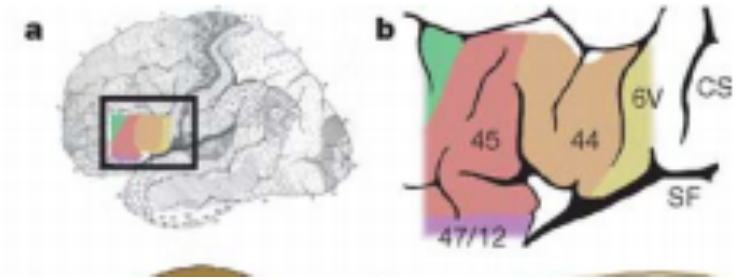


Amunts et al., Plos One. 2010

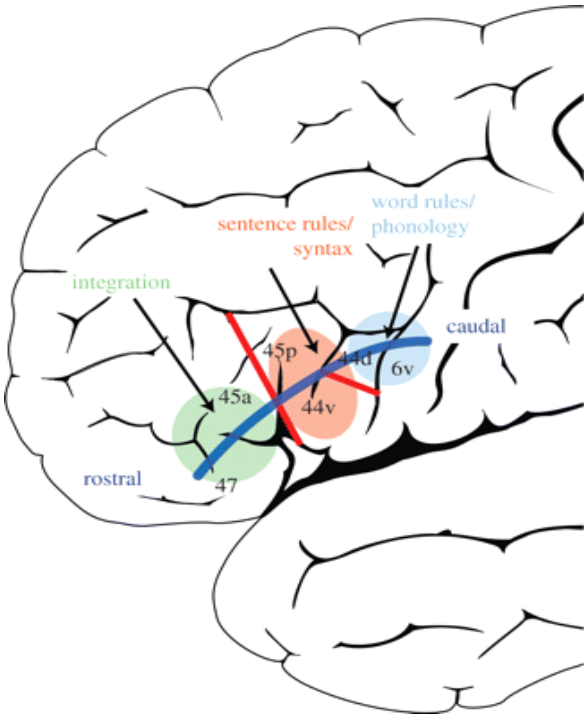
Behavioral Correlates

Broca's area

- Posterior portion of inferior frontal gyrus

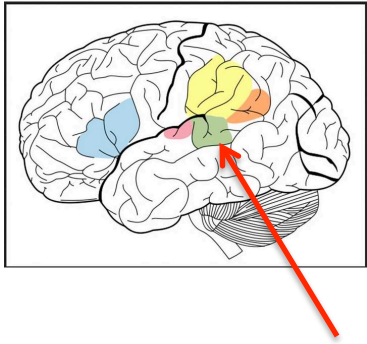


- Anterior ventral to posterior dorsal functional gradient in Broca's complex:
  - Anterior pars triangularis (BA 45) for semantic processing:
    - naming animals or objects
  - Ventral pars opercularis (BA44) and posterior pars triangularis (BA 45) for syntactic processing:
    - combining words according to correct grammatical language rules
  - Dorsal pars opercularis (BA 44) for phonological processing
    - saying words beginning with the letter f



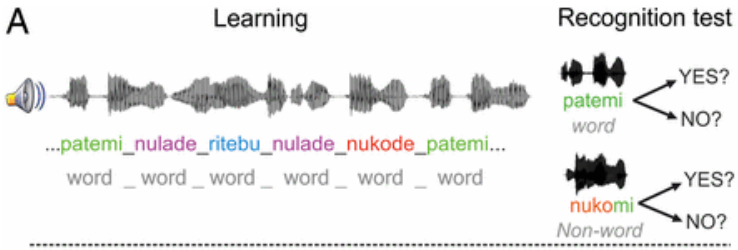
Petrides et al., Nature. 2005

Wernicke's area: Receptive Language Center

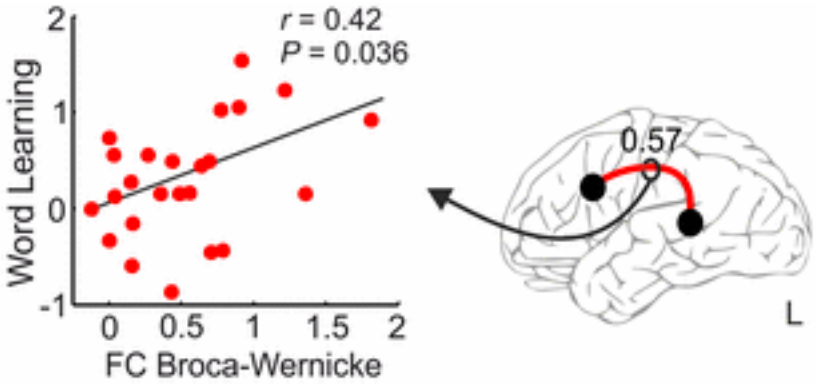


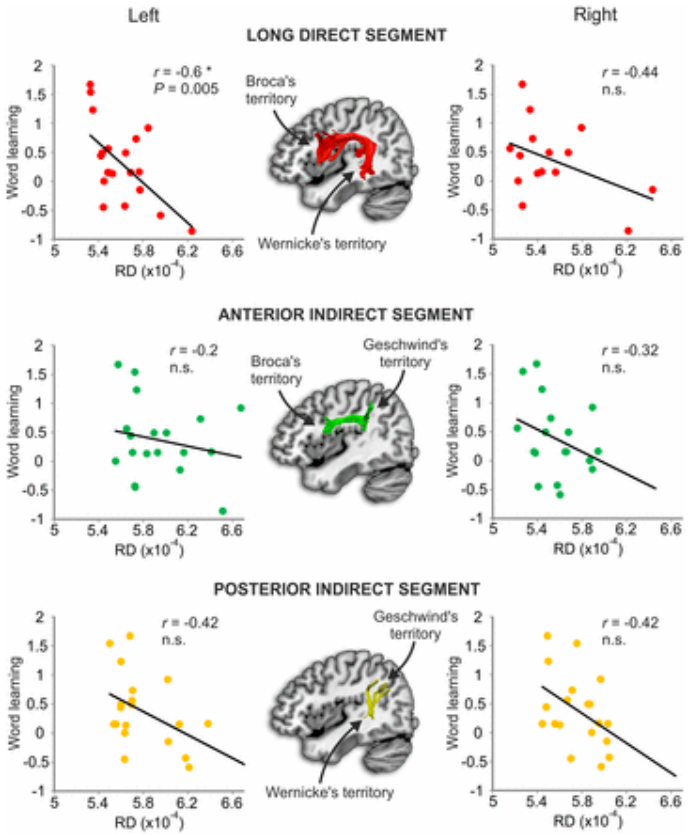
- Understanding of written and spoken language
- Verbal memory
- Lexical processing (reading, auditory)
- Sentence comprehension
- Retrieving meaning of words during semantic tasks
- Word generation
- Activated by movements of eyes, mouth, body
  - Component of perceptual motor systems

Word Learning



Word learning correlates with microstructural properties (AF) and strength of functional connectivity of the direct connections between Broca's and Wernicke's territories (long segment)





Lopez-Barroso et al., PNAS. 2013

Functional Asymmetry

Left AF

Language

Verbal working memory

Right AF

Visuospatial processing

Prosody

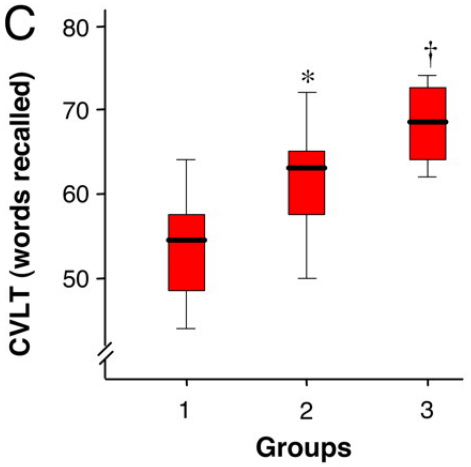
Process of articulating specific words (syntax, grammer) merged with emotional context (i.e., prosody), processed by the corresponding anatomical regions in the non-dominant (right) hemisphere

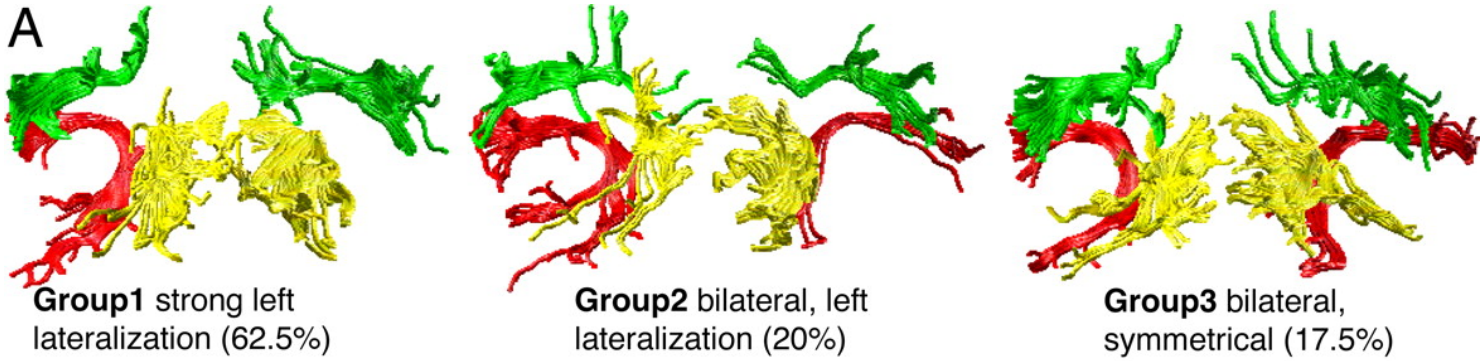
Catani and de Schotten, Cor

Functional Asymmetry

Bilateral representation, not extreme lateralization, might be advantageous for specific cognitive function

Individuals with more symmetric patterns of connections performed better on tasks involving remembering words using semantic association





Catani et al., PNAS. 2007

Physiological Correlates
(none found)

Clinical Pathologies

Symptoms	Clinical presentation	Tracts involved
Broca's aphasia	Non-fluent speech, impaired repetition, intact comprehension	Anterior and long segment
Wernicke's aphasia	Impaired auditory comprehension and repetition, fluent speech	Posterior and long segment
Conduction aphasia	Repetition deficits, paraphasias, relatively intact comprehension and fluency	Long segment
Transcortical motor aphasia	Impaired fluency but intact repetition and comprehension	Anterior segment
Transcortical sensory aphasia	Impaired comprehension but intact fluency and repetition	Posterior segment
Global aphasia	Severe deficit in language comprehension, production, and repetition	Anterior, posterior, and long segments
Pure alexia	Acquired reading impairment often associated with colour agnosia. Spontaneous writing and writing to dictation are preserved	Posterior segment
Dyslexia	Developmental reading difficulties	Anterior segment, posterior segment
Dysgraphia	Deficits in spontaneous writing and on dictation	Anterior segment
Working memory deficits	Impaired digit span	Anterior, posterior, and long segments
Apraxia	Loss of the ability to perform voluntary skilled movements without sensorimotor deficits	Anterior and posterior segments
		Right hemisphere
Unilateral spatial neglect	Failure to respond or reorient to novel or meaningful stimuli presented to the left hemispace	Anteior, posterior, and long segments, SLF II
Expressive amusia	Inability to sing or play a previously learned instrument. Loss of the ability to write musical annotations	Anterior segment, long segment
Receptive amusia	Difficulties to recognize out-of-tune notes, familiar melodies, or read musical annotations	Posterior segment, long segment
Anterior affective-aprosodia	Flatness of speech and loss of gestural abilities involving the face and limbs	Anterior segment, long segment
Posterior affective-aprosodia	Inability to comprehend or repeat emotional gestures and discern speech intonation	Posterior segment, long segment

Autism

Yellow = Left
Green = Right

Reversed hemispheric asymmetry in nonverbal autistic children

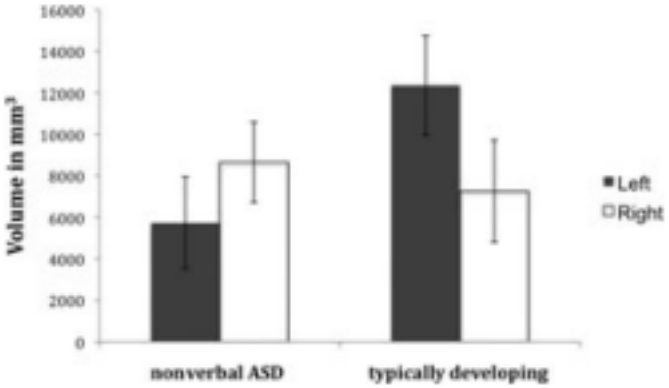
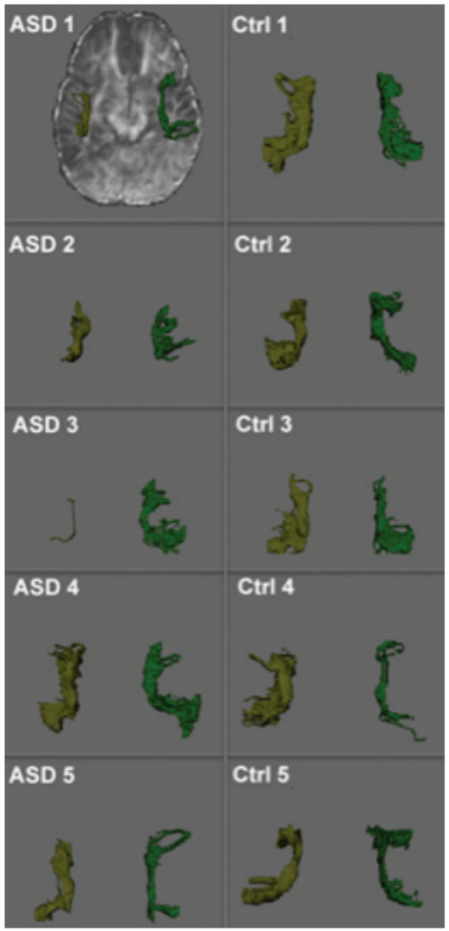


Figure 1. Total average volumes of the left and right AF of the nonverbal children with ASD and the typically developing children.



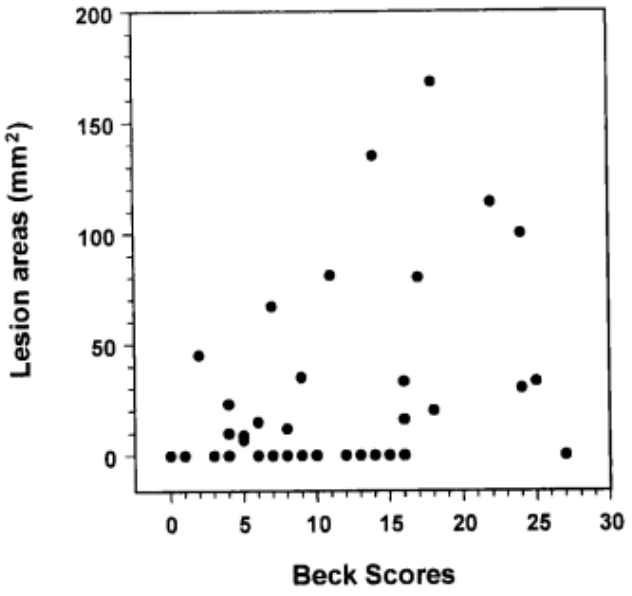
Wan et al., 2012

Depression in Multiple Sclerosis

- 50% lifetime risk of depression
- Total lesion area in left AF (mm^2) predicts greater BDI scores
- Accounted for 17% of BDI score variance

Table *Correlations of Beck Depression Inventory scores with lesion measurements*

	Lesion area (mm^2)		Pearson's correlation coefficient	
Area of analysis	Mean	(SD)	*r* Value	*p* Value
Axial analysis				
Uncinate fasciculus region				
Right	168	(157)	0.15	0.165
Left	167	(190)	0.13	0.198
Periventricular region				
Right	807	(693)	0.09	0.288
Left	918	(761)	0.11	0.235
Arcuate fasciculus region				
Right	44	(60)	0.13	0.201
Left	35	(47)	0.40	0.003



Pujol et al., Neurology. 1997.

Schizophrenia

- Paranoid schizophrenics with auditory hallucinations showed *lower* FA in prefrontal regions, external capsule, occipitofrontal fasciculus, inferior longitudinal fasciculi, CC relative to healthy controls
- Schizophrenics showed *higher* FA in *arcuate fasciculus*

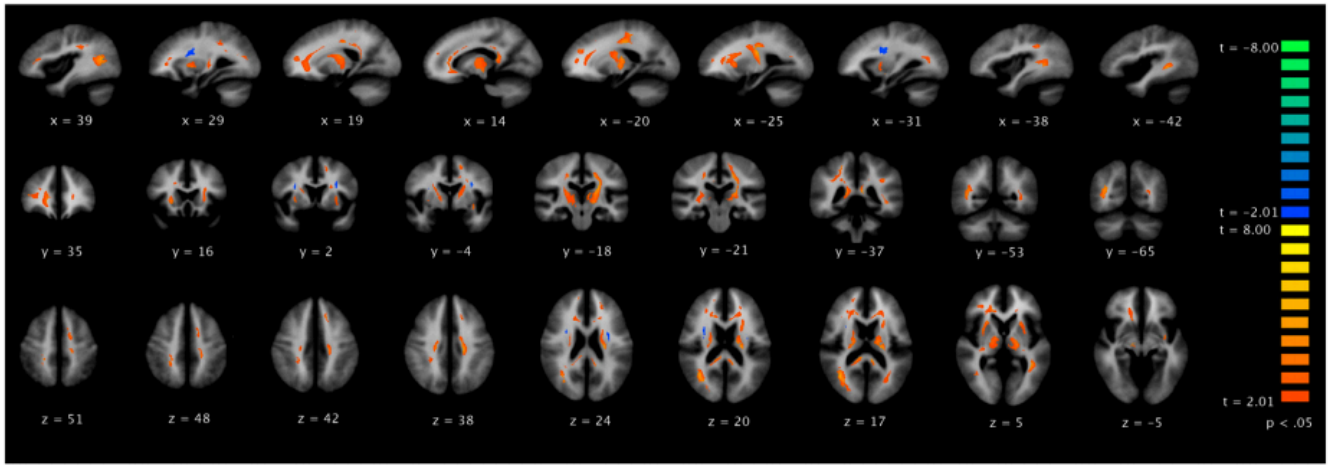


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Fig. 1. Results of a whole-brain voxel-by-voxel group comparison of FA values (blue—areas of higher FA values in patients, red—areas of higher FA values in controls) significant at $P<0.05$, two-tailed, corrected for multiple comparisons. The Talairach coordinates for the respective planes are indicated. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

- Also less leftward asymmetry found in adults with schizophrenia

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