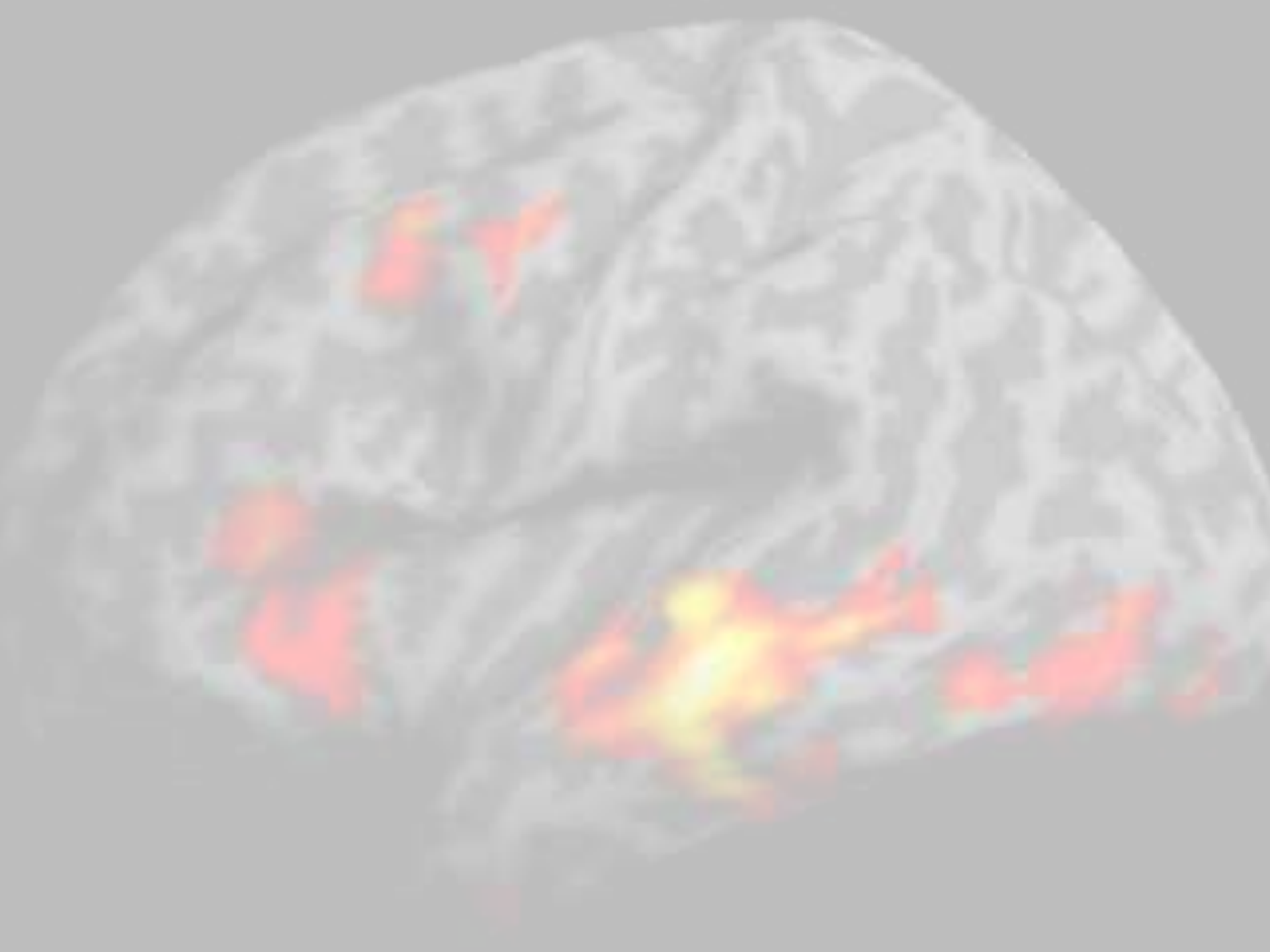
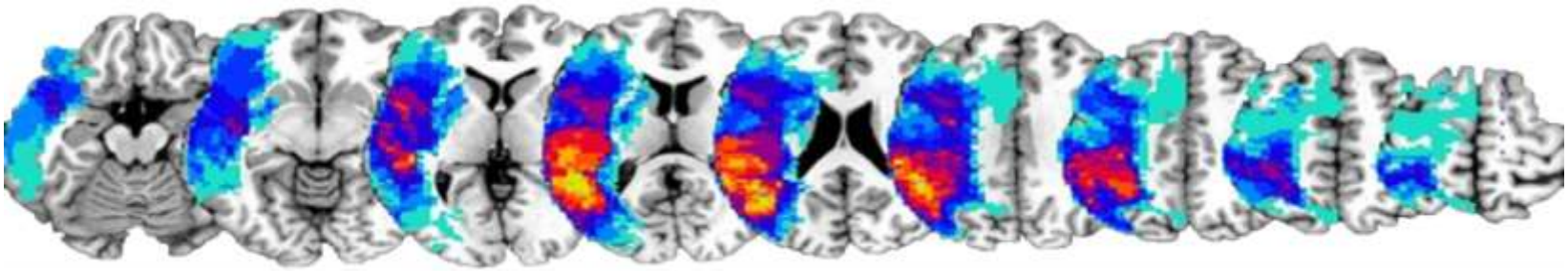


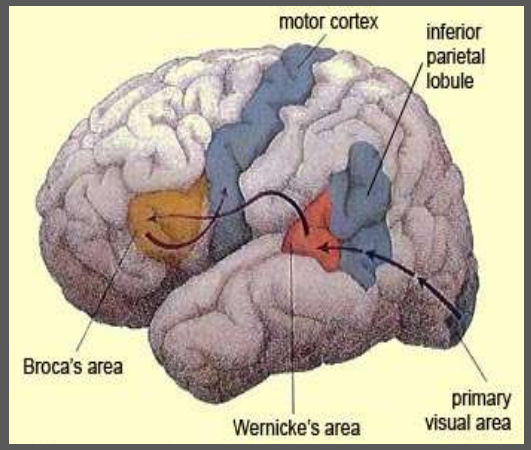
Neural dynamics of language-related and spontaneous activity in aphasia

Aneta Kielar Ph.D.
Assistant Professor
Speech, Language and Hearing Sciences
University of Arizona

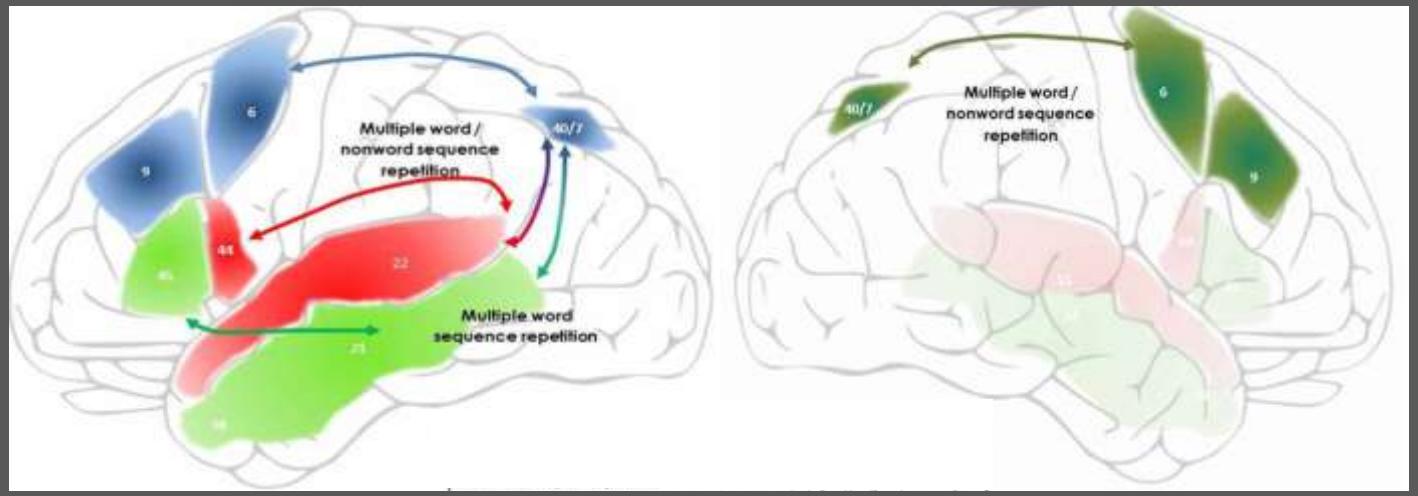


Neural Basis of Language

Classical Model

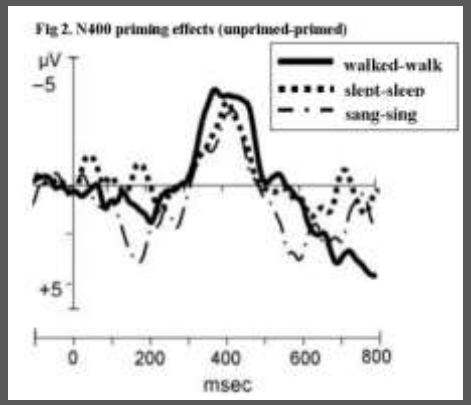


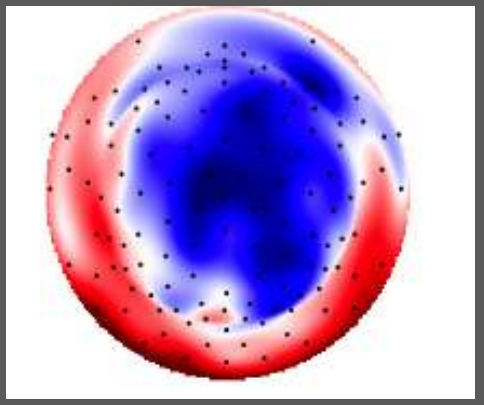
Network Models



Majerus 2013

Electroencephalography

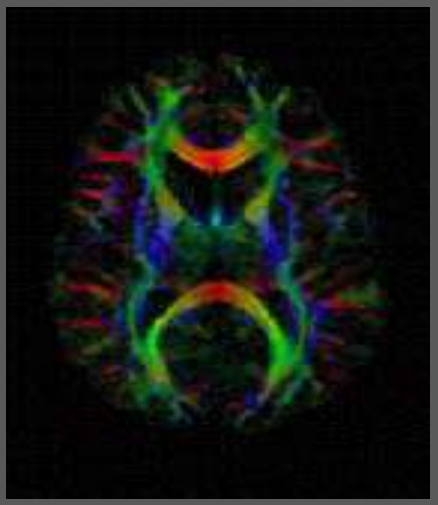




f/MRI

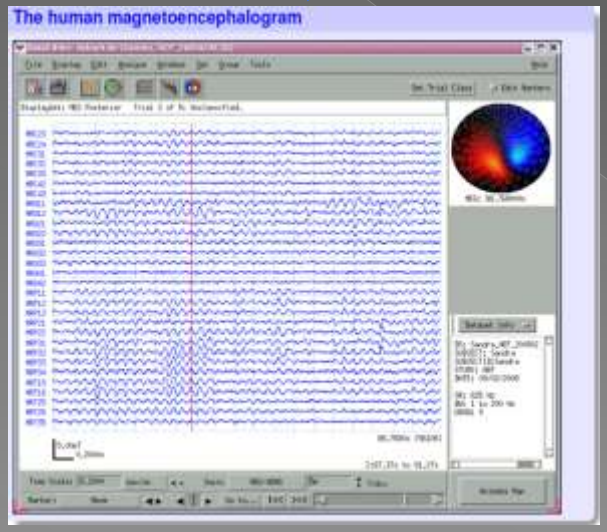
Lesion Studies

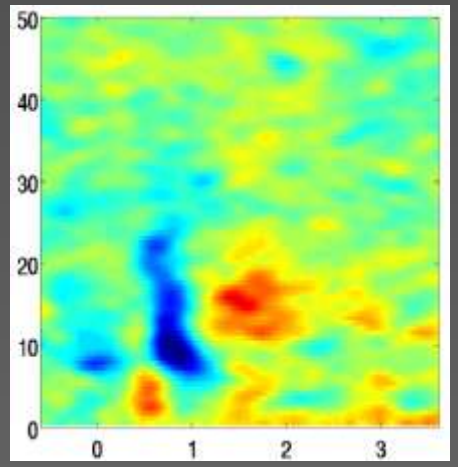
White mater

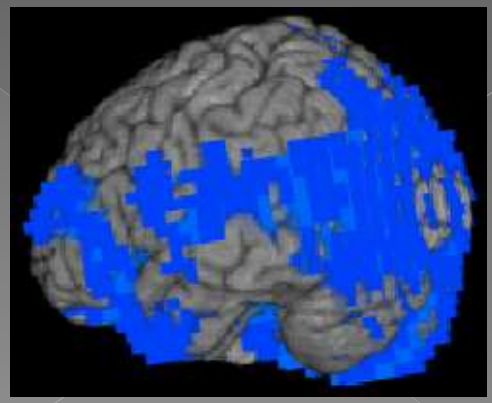


Magnetoencephalography (MEG)

http://research.baycrest.org/meg

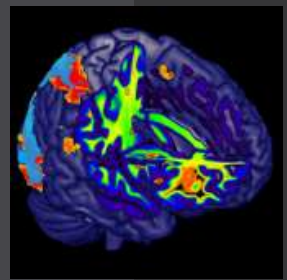






Overview

- Background: Neural pathways for semantics and syntax
- Mapping language responses: MEG & EEG methods
- Plasticity of language responses in post-stroke aphasia
- Spontaneous neural dynamics in stroke and aging



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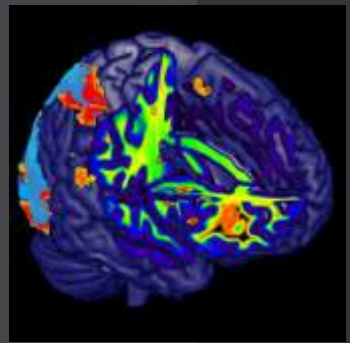


Elements of Language

Orthography

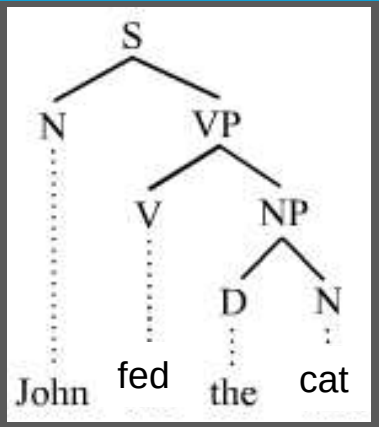
C A T

Semantics

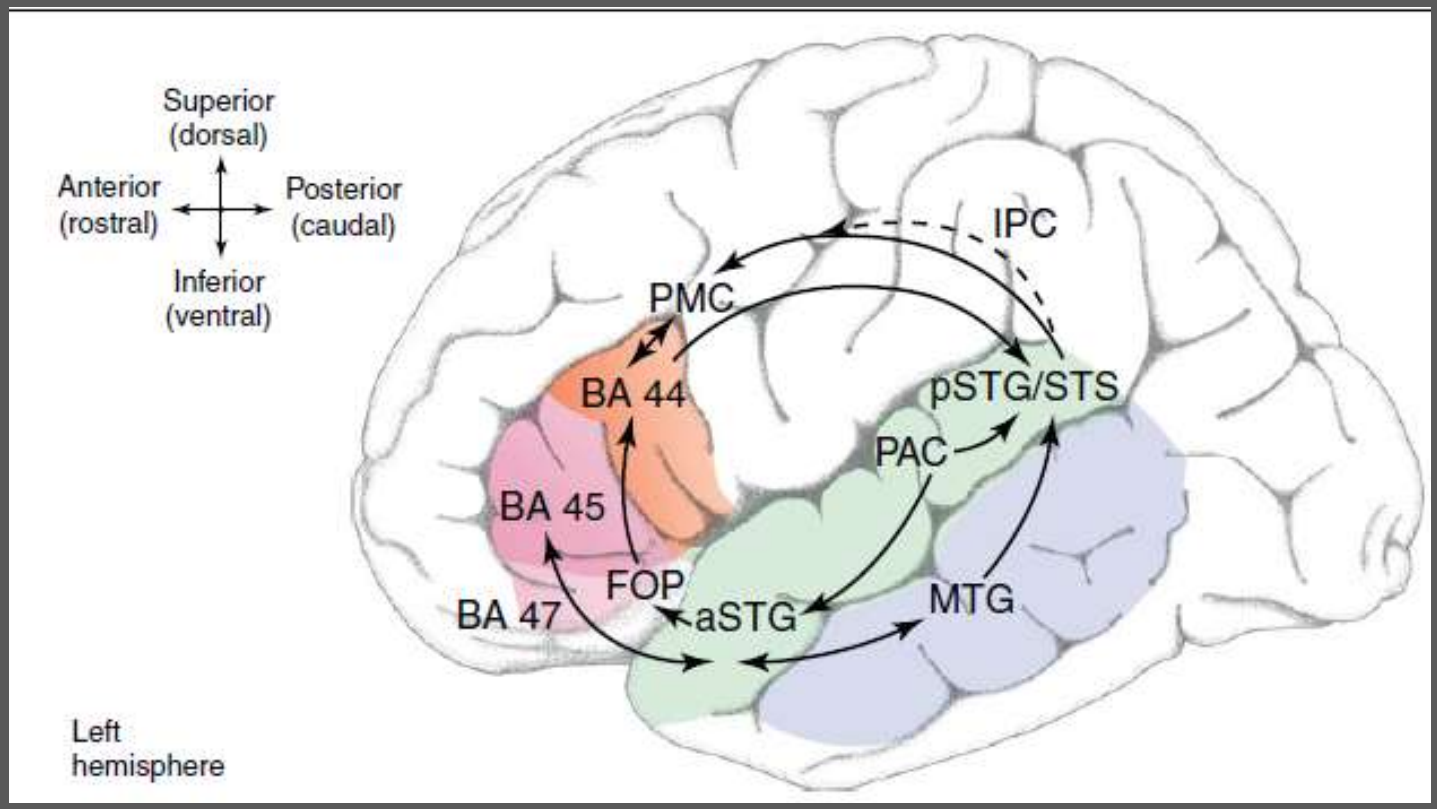
Phonology

/kaet/

Syntax



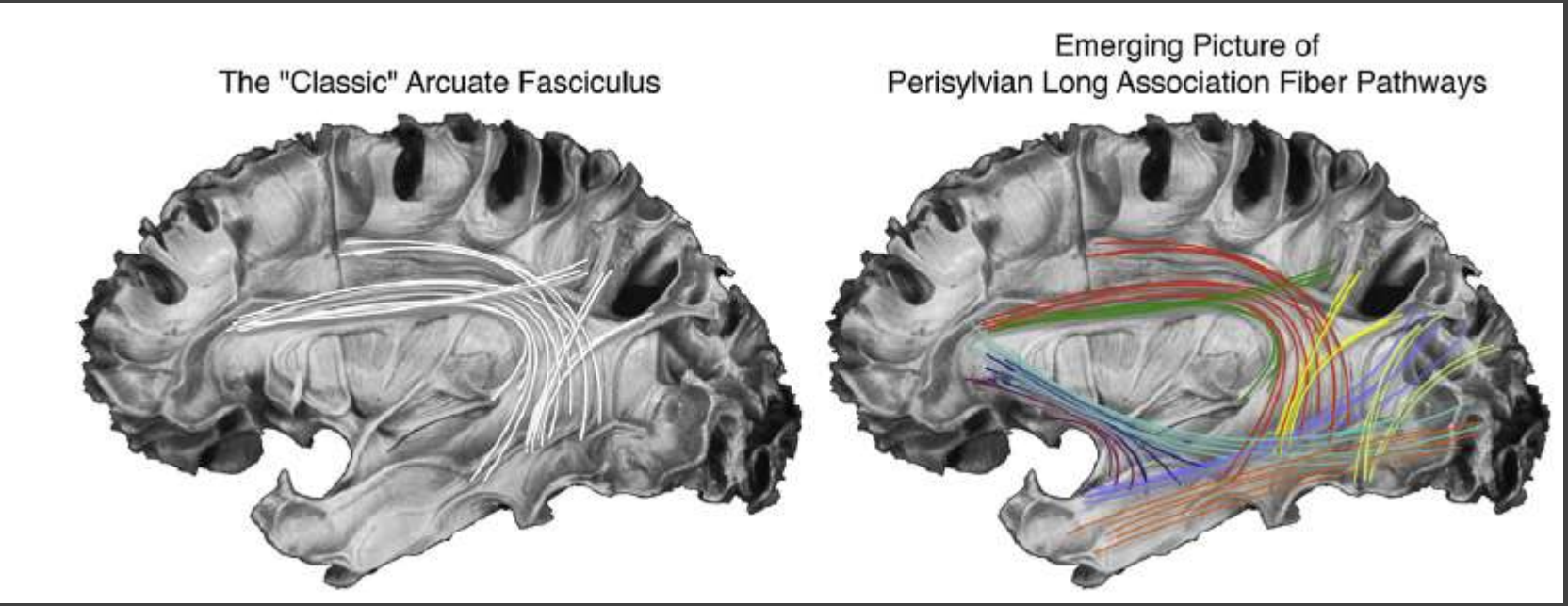
Neural Basis of Language



from Friederici 2012

The integration of the semantic and syntactic aspects of language depends on the dynamic interactions between anterior and posterior brain regions (Hagoort, 2014; Klingbeil et al., 2018; Poepel, 2014)

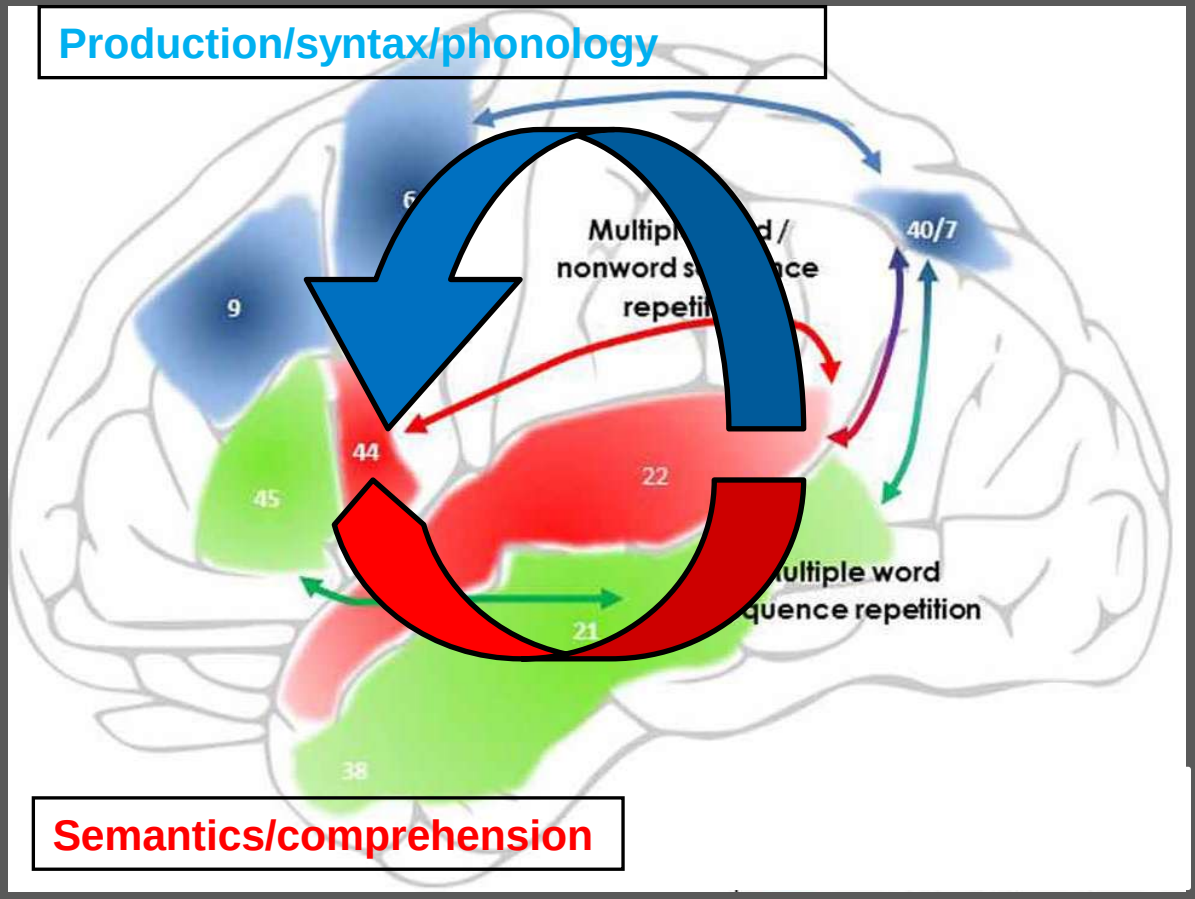
Neural Basis of Language



Tremblay et al., 2016

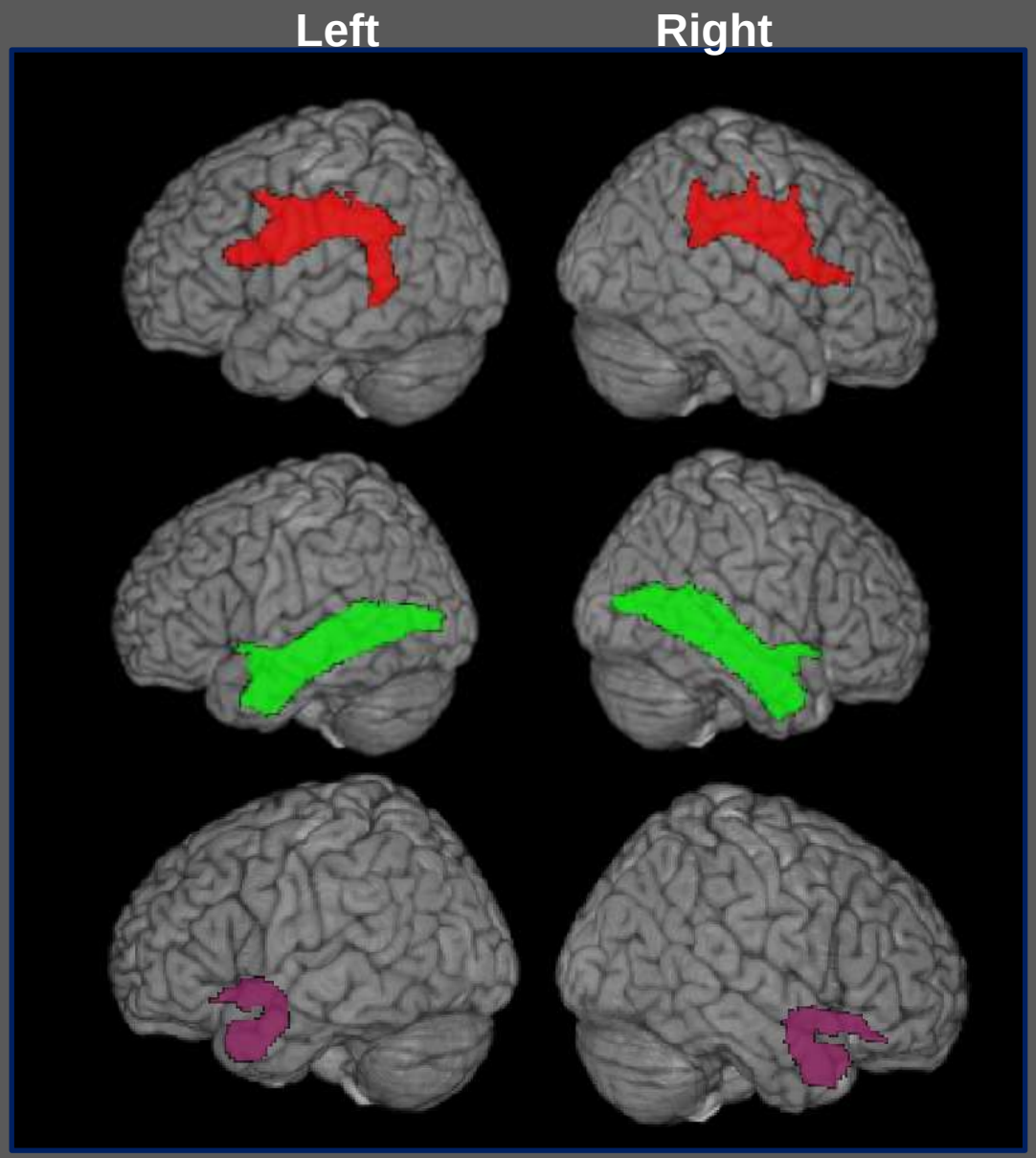
White matter tracking: Interactions are mediated by at least two major white matter pathways (Griffiths et al., 2012; Saur et al., 2008, 2010; Catani & Mesulam, 2008; Tremblay et al., 2016)

Dorsal Pathway:
From pSTG/AG/SMG to dIFG via arcuate and superior longitudinal fasciculus



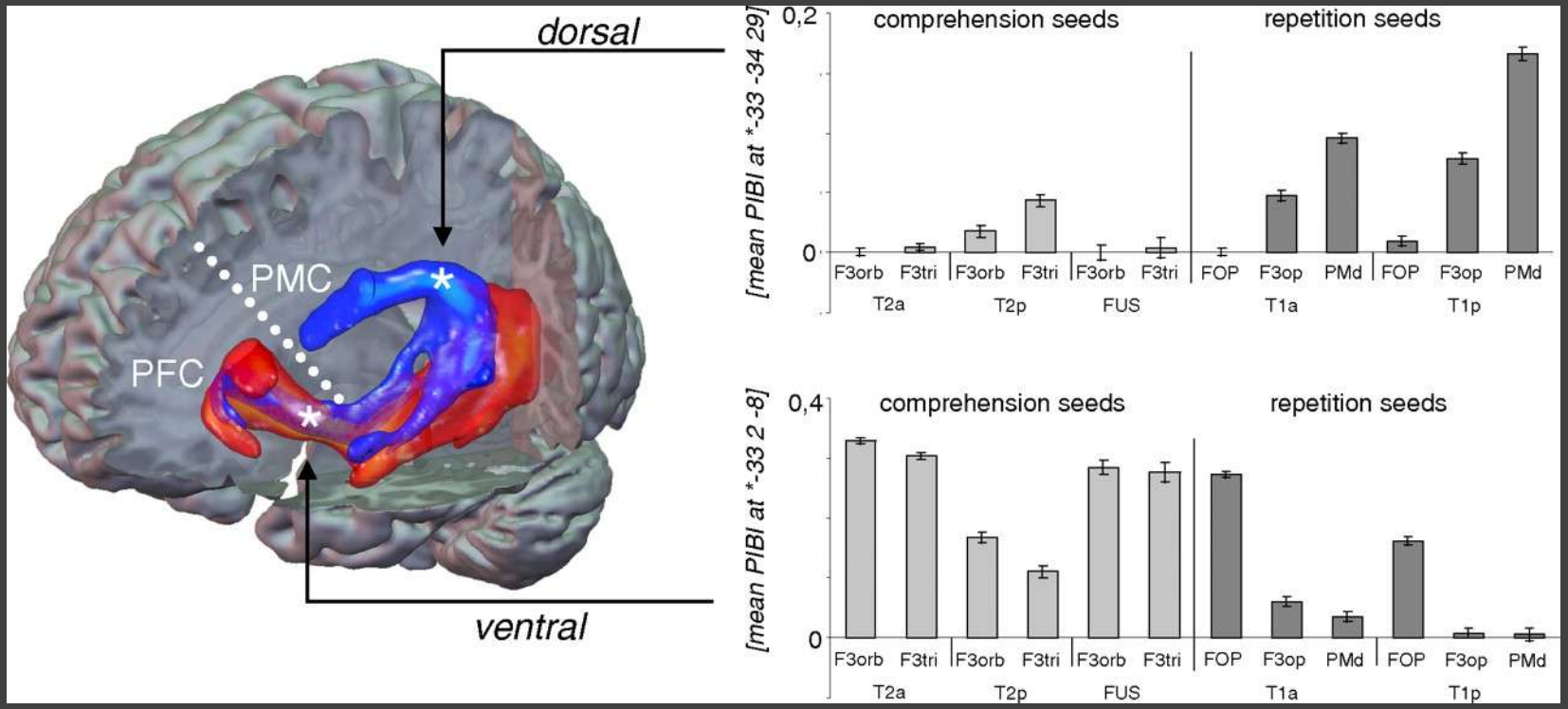
Ventral Pathway:
From pSTG/MTG/ via inferior longitudinal fasciculus, crosses into the vIFG via the extreme capsule and the uncinate fasciculus

Diffusion Tensor Imaging (DTI data)



Kielar, Deschamps, Panamsky, & Meltzer, et al. *in preparation*

Pathways for language

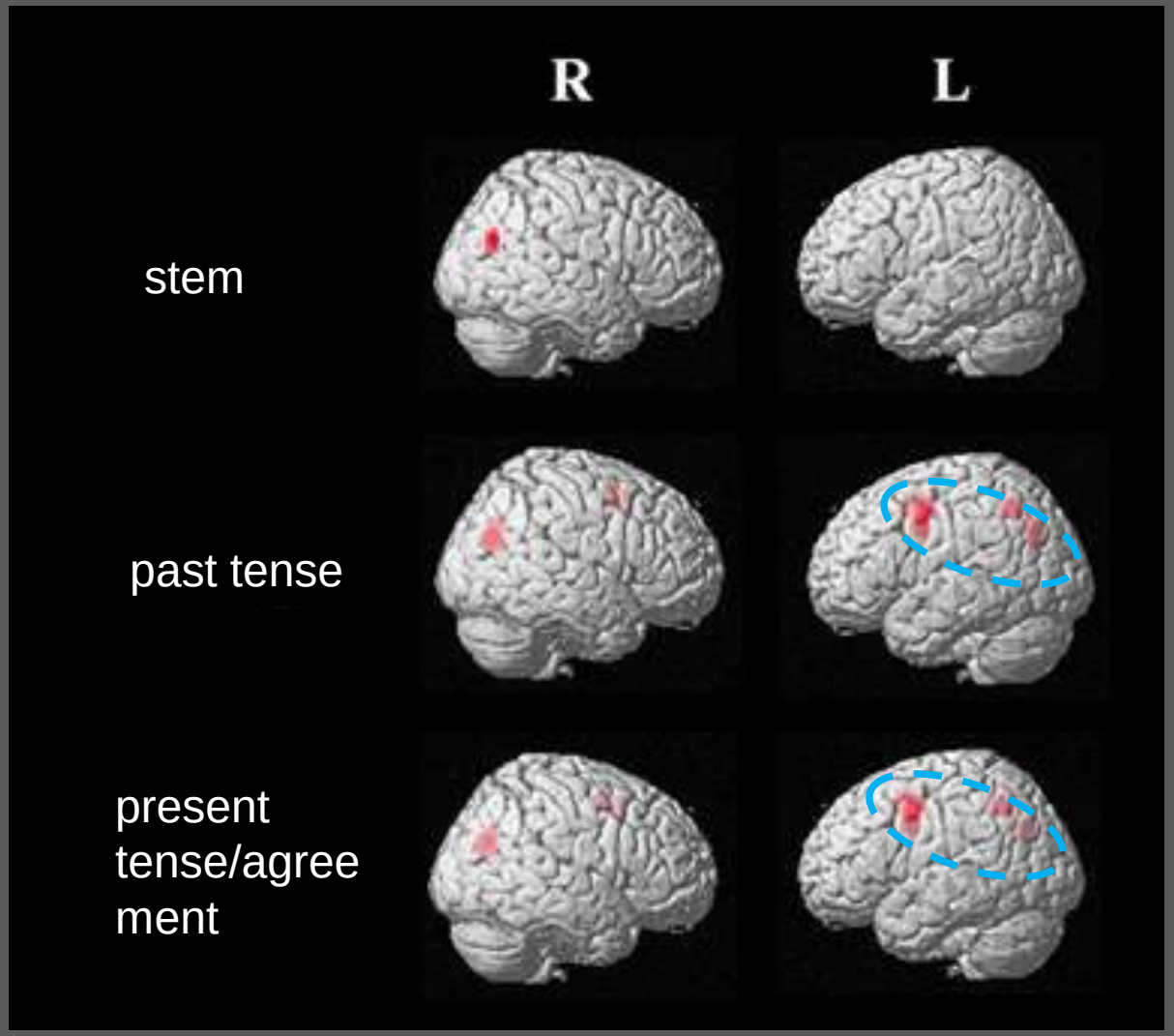


Saur D et al. PNAS 2008;105:18035-18040

Production of Verb Inflection: fMRI

Tense Inflection

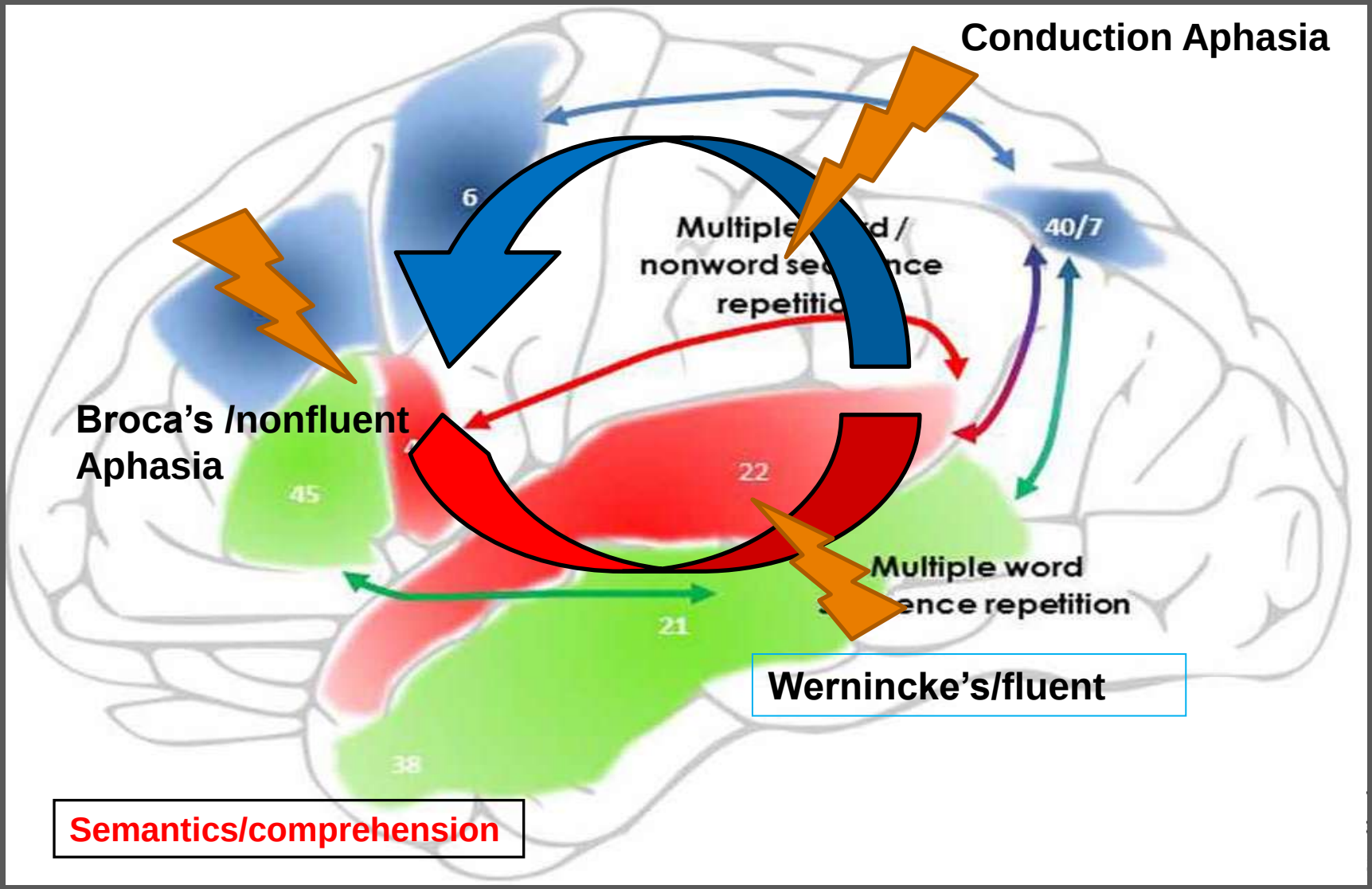
Tense:
Yesterday: saved
Nowadays: saves
Stem: save



Kielar, Milman, Bonakdarpour, & Thompson. (2011). *Journal of Neurolinguistics*

Relationship to Stroke Aphasia

Production/syntax/repetition/phonology/working memory



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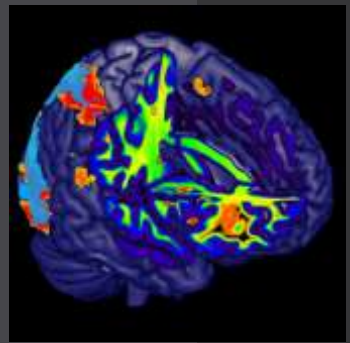
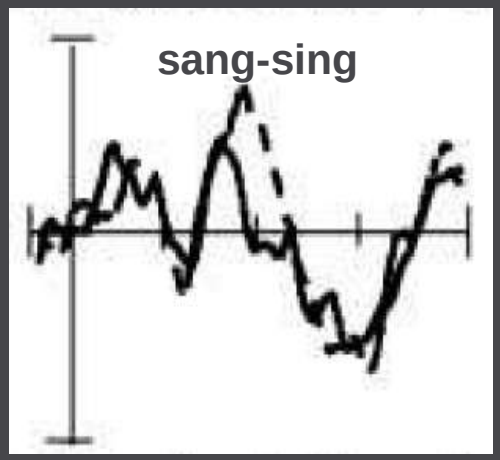
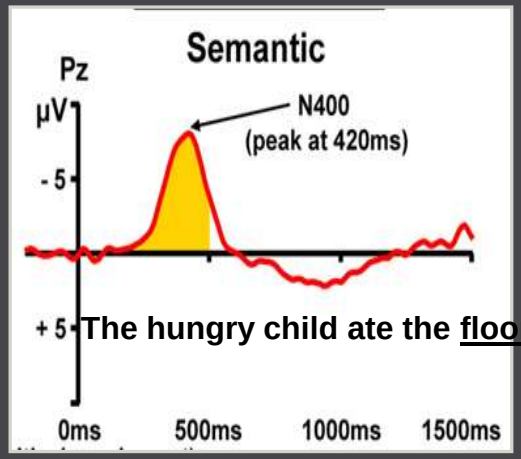


ERP responses

N400: semantic processing *The pizza was too hot to sing*/eat*



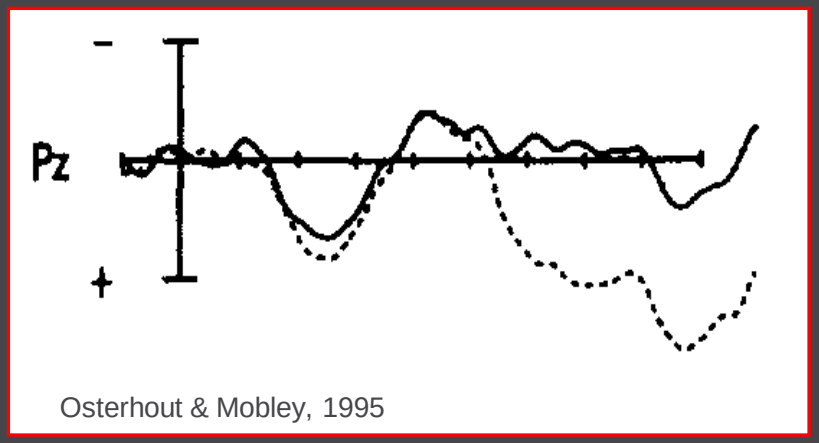
Kielar & Joanisse, 2009, *JOCN*



Tse et al., 2007, PNAS

P600: syntax

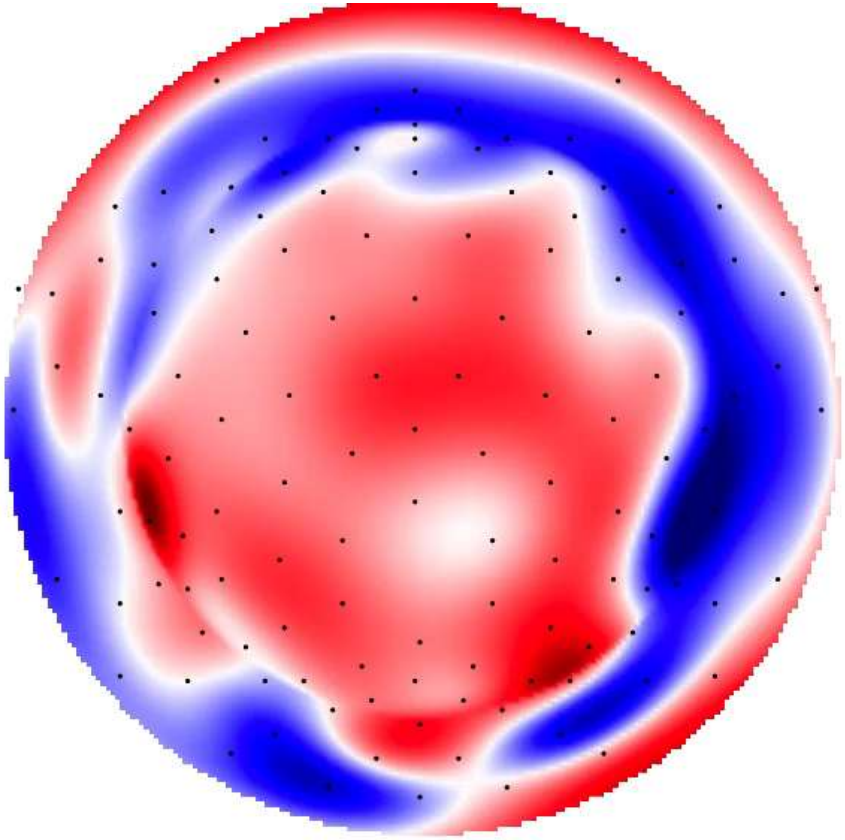
Many judges hopes to become Supreme Court Justices



Osterhout & Mobley, 1995

N400 response

*e.g., The pizza was too hot to sing**



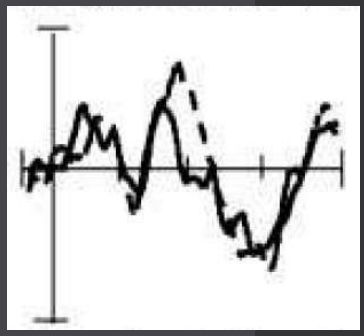
ERP Responses

- Are ERP responses related to different neural processing networks in the brain?

- Does recovery from aphasia correlate with expression of these responses?

ERP Responses in Aphasia

- ERPs have been used as an index of the integrity of semantic and syntactic processing in *aphasia*



- ERP and violation paradigm

- Factors which impact on-line sentence processing in agrammatic aphasia?

Kielar, Meltzer-Asscher, & Thompson. (2012) ,*Neuropsychologia*

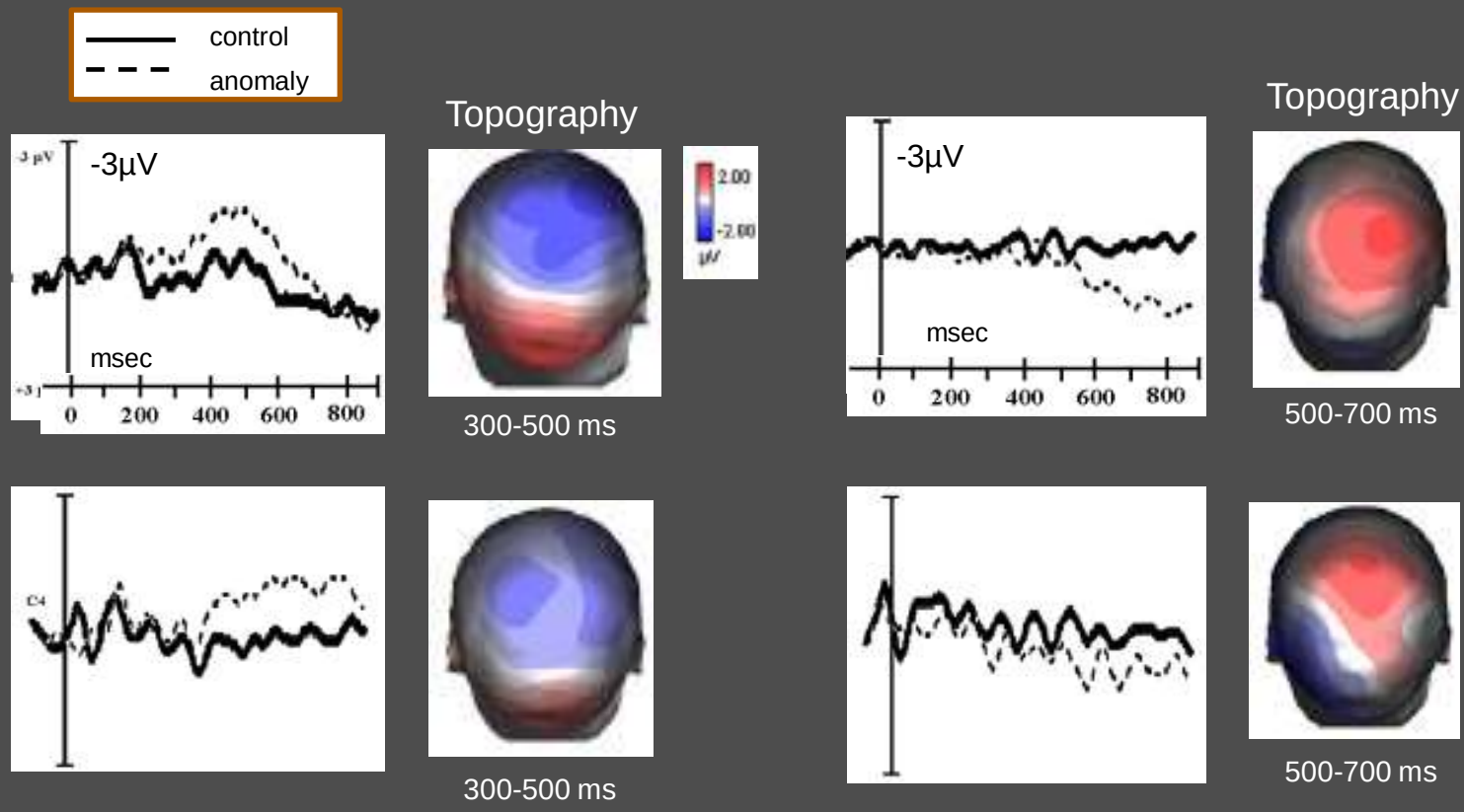
Semantic Anomaly

Anne visited the doctor and the socks

Syntactic/Argument Anomaly

Anne sneezed the doctor and the nurse

Control Sentence: *Anne visited the doctor and the nurse*

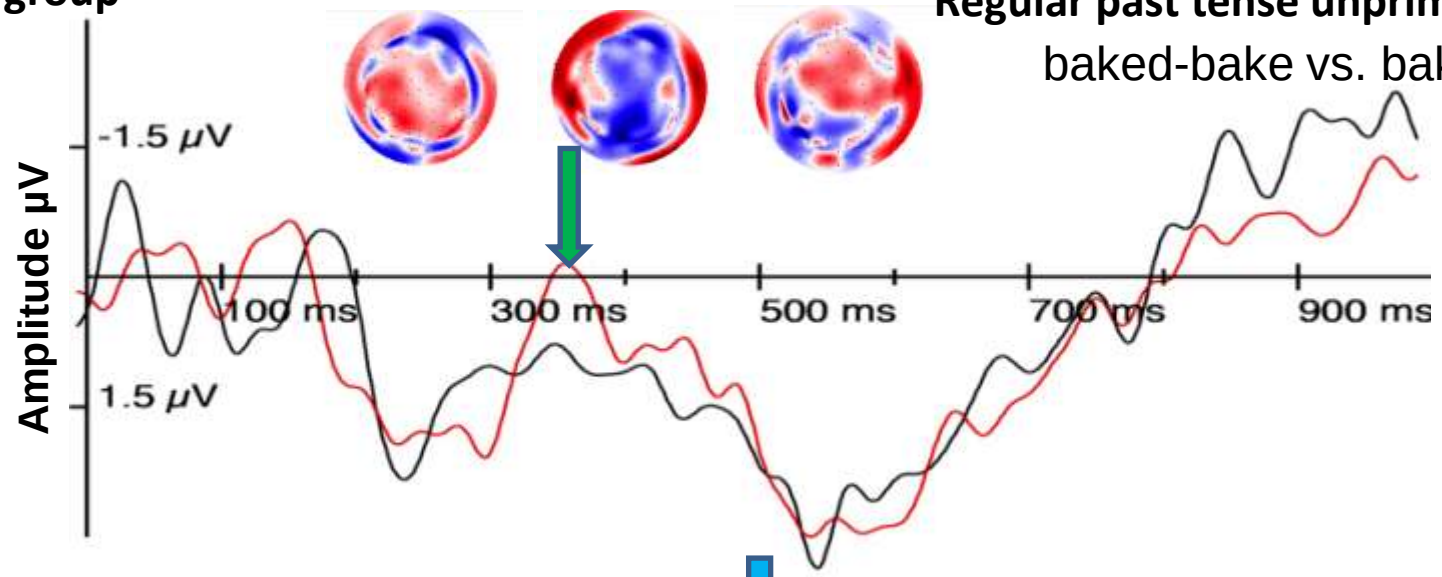


Kielar, Meltzer-Asscher, & Thompson. (2012). *Neuropsychologia*

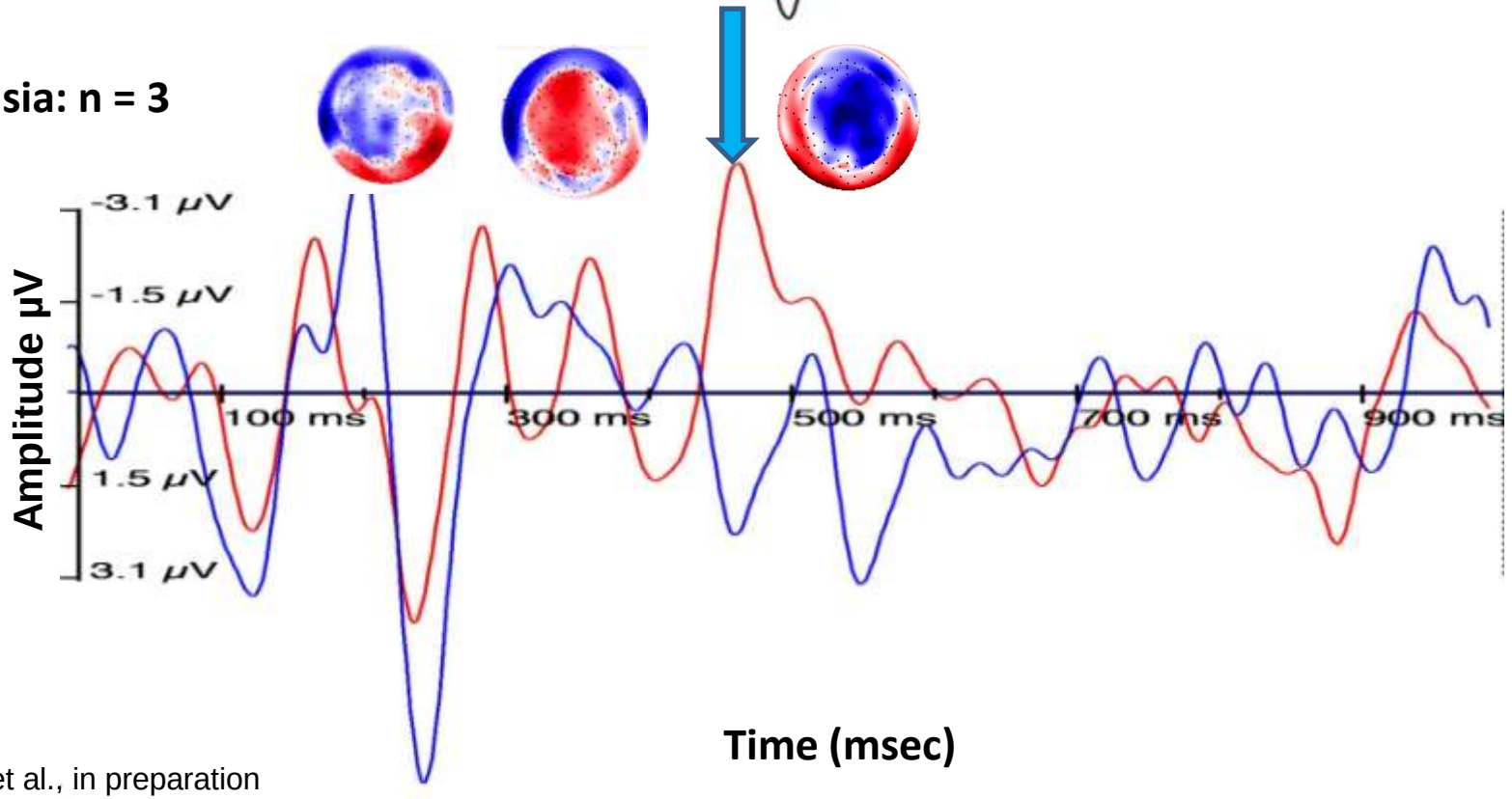
Control group

Regular past tense unprimed vs. primed

baked-bake vs. baked-walk



Aphasia: n = 3



Time (msec)

Kielar et al., in preparation

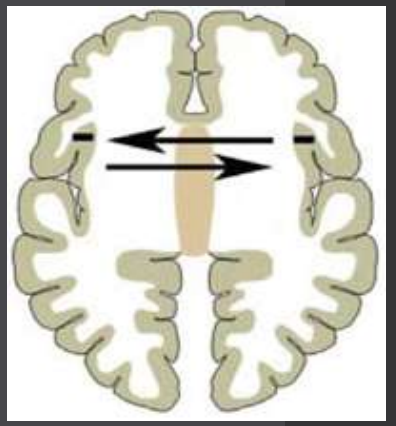
- **Semantic processing seems relatively well preserved in agrammatic aphasia**

- **Syntactic processing is impaired**

- **Questions:**
  - Are semantic responses more preserved because the system that generates them is less affected?

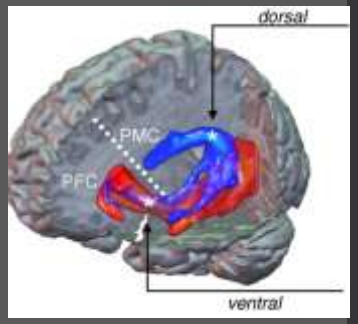
    or
  - Compensation: Shift to the preserved RH?

  - Is syntax and semantics reorganized/ compensated differently?



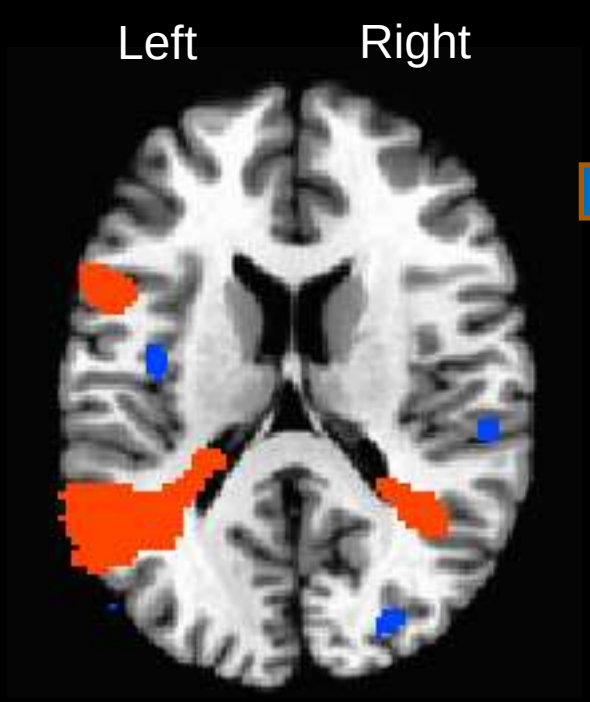
Aphasia and Language Pathways

- What is the role of pathways and overlying cortical regions in recovery from aphasia?
- Can alternative regions participate in compensation for brain damage?
- Role of spared LH/perilesional regions?
- Role of RH function after stroke?

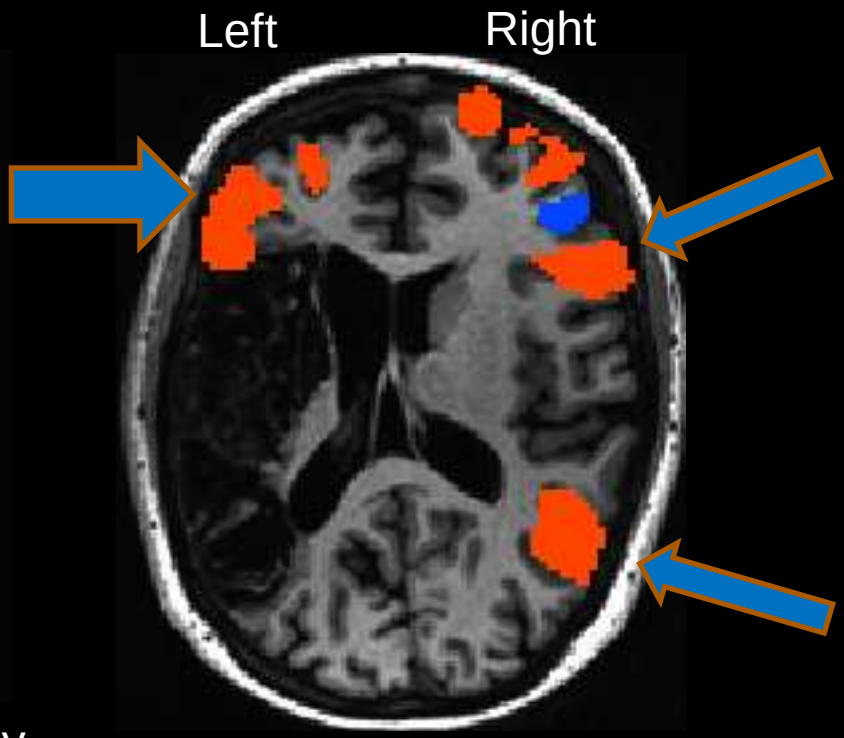


Neural Correlates of Recovery

- Recovery of function in *perilesional* areas has been associated with best clinical outcome (e.g., Heiss et al. 1999, Heiss & Thiel, 2006; Saur et al. 2006; Vitali et al., 2007)

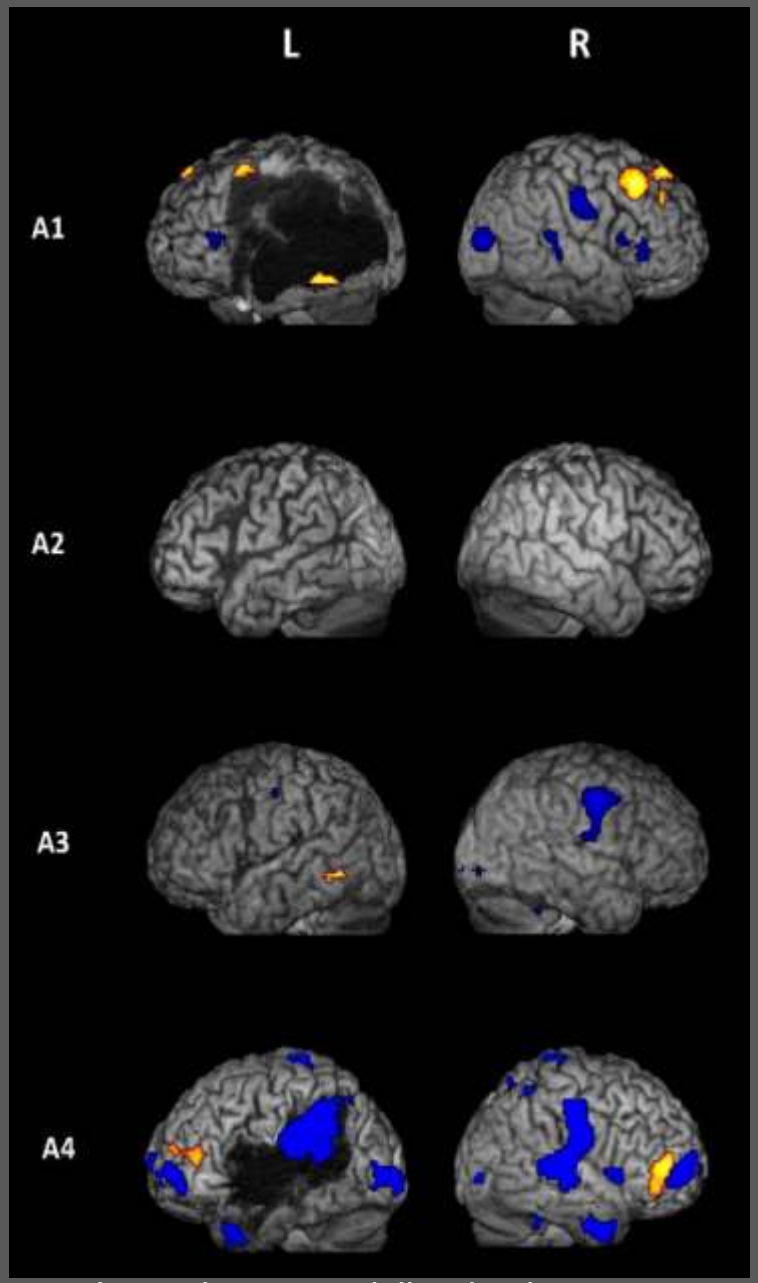


Language activation in healthy participant on the left



Activity in well recovered aphasia patient

Verb Inflection Treatment



Pre Tx > Post Tx

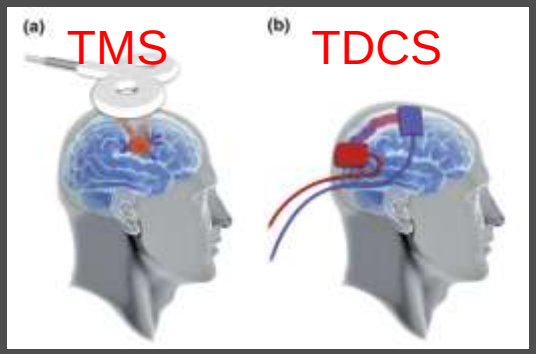
Post Tx > Pre Tx

no changes

Kielar, Milman, Bonakdarpour, Fix, & Thompson (pilot data)

What is the role of RH in language recovery ?

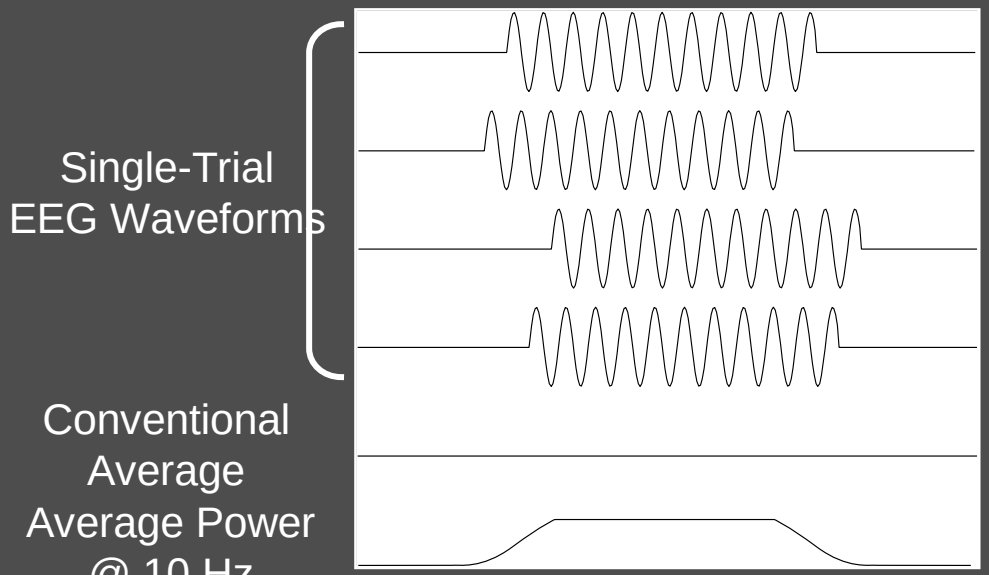
- RH activation represents adaptive plasticity or compensatory mechanisms? (Blasi et al., 2002; Kiran, 2012; Meltzer et al., 2013; Muddo et al., 1999; Thulborn et al., 1999)
- RH recruitment may be maladaptive
- Interfere with language recovery, by precluding reactivation of spared LH areas (Belin et al., 1996; Heiss & Thiel, 2006; Thiel et al., 2015)



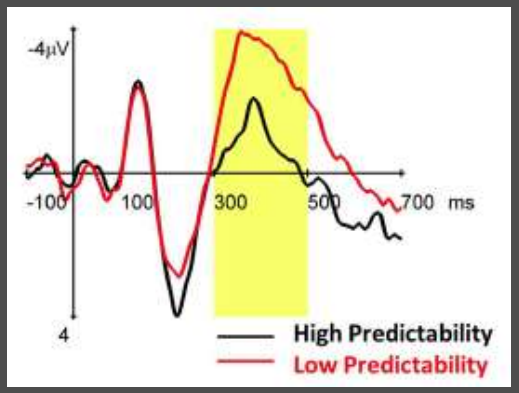
- **Event Related Potentials (ERPs)**
  - **ERPs** are powerful tools in dissociating semantic and syntactic aspects of language processing in time
- **Magnetoencephalography (MEG)**
  - **MEG** signal utilized for language research:
  - MEG signals are not distorted by passing through the skull to the sensors, allowing for much more accurate source localization (vs.EEG)
  - The temporal properties of the signal are nearly instantaneous with respect to neural firing (like EEG)

MEG/EEG: Analysis

- The classical method of signal analysis is to derive event-related responses in time-domain:



Source: ERP boot camp, S. J. Luck



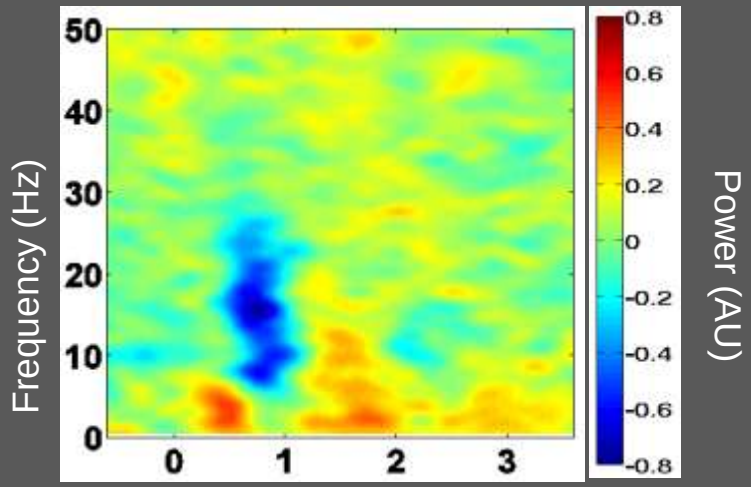
Lee et al., 2012
ERPs to expected and unexpected words
doi: 10.3389/fpsyg.2012.00285

Changes in the amplitude of ongoing oscillations induced by behavioral events

Time-frequency Representation

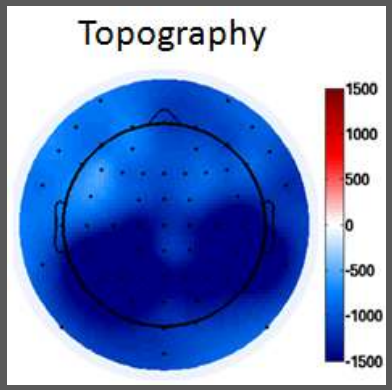
David Cohen, MEG recording of alpha rhythm in 1971

Responses to individual words in the sentence



*e.g., The girl ate the computer**

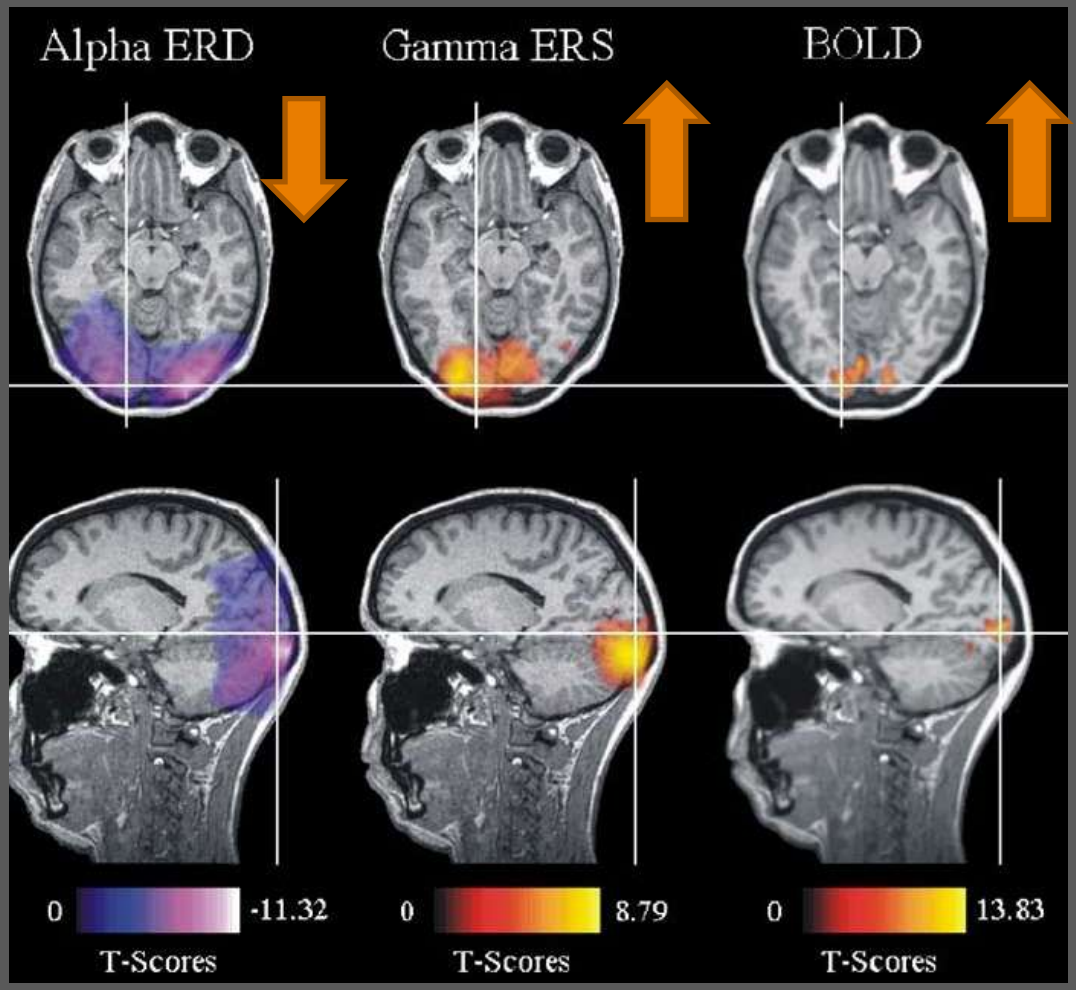
Time-frequency representation of relative power changes (ERP data) across timepoints and frequencies



Useful in assessing language processing in **aging & clinical populations**, which may show significant delays or variability in the latency of neural responses

From: Kielar, Panamsky, Links, Meltzer. (2015). *NeuroImage*

Relationship between Oscillations and BOLD responses



From: Brookes et al (2005). The spatial distribution of alpha band power change, gamma band power change and BOLD signals (p = 0.001) during viewing of static checkboard pattern. For alpha and gamma band images red = increase in power ; blue = decreases in power. The SPM or T scores relating to BOLD signal thresholded at corrected p = 0.05.

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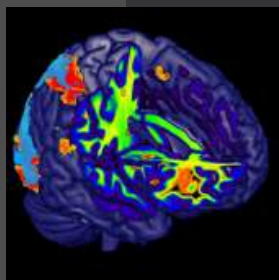
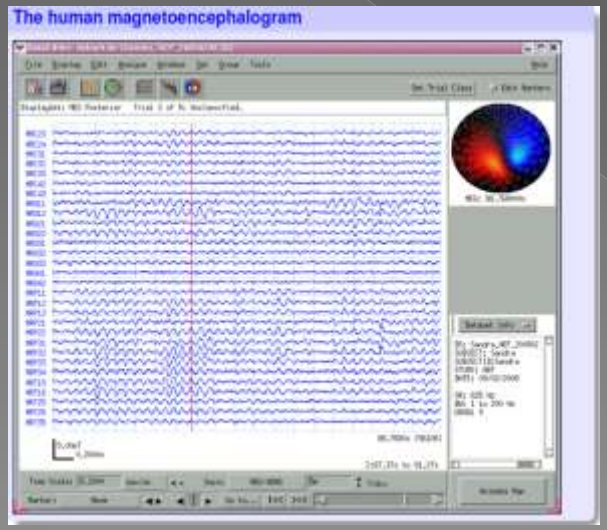
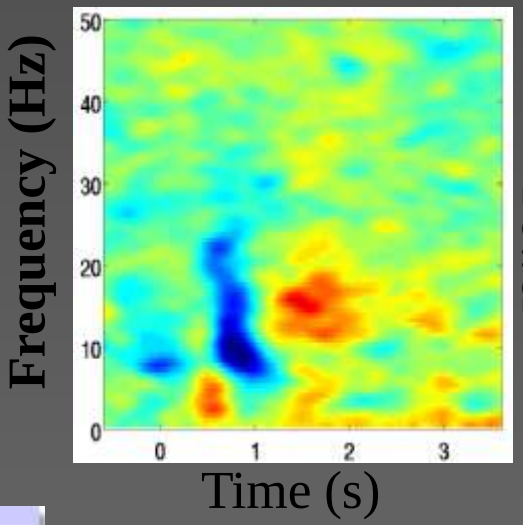
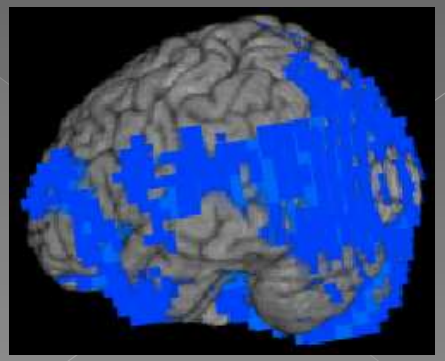


Magnetoencephalography (MEG)



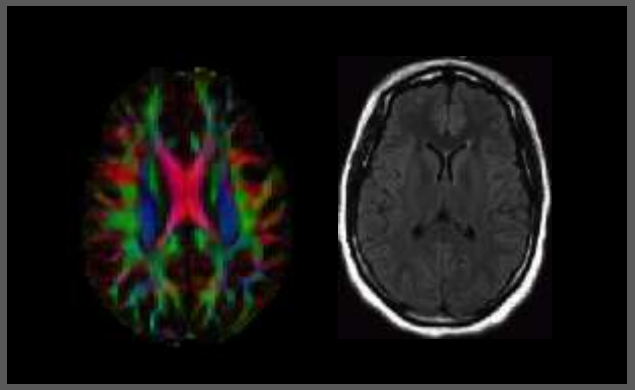




http://research.baycrest.org/meg

Method

- **MEG**
  - Sentence comprehension task
  - Resting MEG
- **MRI**
  - Structural scan, DTI, resting state BOLD, blood flow (pASL)



Method

- **Participants**
  - Native English speakers
  - LH lesion, single stroke, chronic stage
  - 8 nonfluent/expressive, 1 fluent, 5 conduction, 5 anomia

	Age (years)	Ed (years)	TPO
Stroke	n=19		
Mean (SE)	65 (2.49)	17	4.26
Older	n=19		
Mean (SE)	65 (2.57)	17	----

- **Stimuli:**
  - Semantic anomaly (N400)
    - She will go to the bakery for a loaf of books 
  - Syntactic anomaly (P600)
    - She will going to the bakery for a loaf of bread 
  - Control
    - She will go to the bakery for a loaf of bread 
    - Each anomaly was compared to a control word in the same position in the sentence
- **Task:**
  - Sentence acceptability judgement task

+

She

will

go

to

the

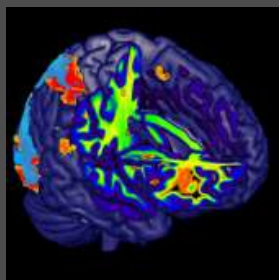
bakery

?

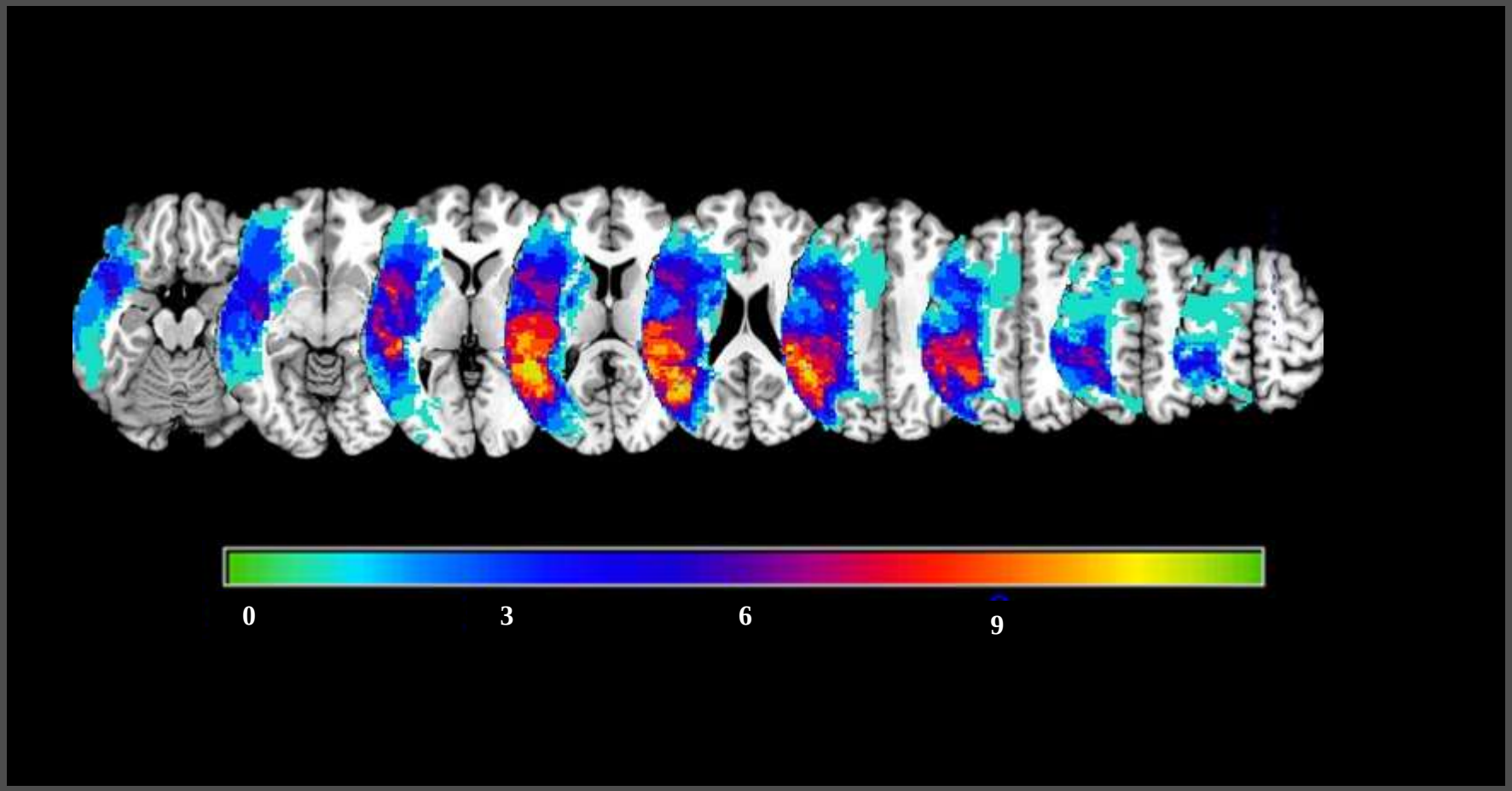
Predictions

Anomaly type	Frequency domain	Neuronal Networks Engaged
semantic	**8-30 Hz ERD**	**Ventral > Dorsal**
syntactic	**8-30 Hz ERD**	**Dorsal > Ventral**

Possibility of compensatory reorganization of language functions to the contralateral hemisphere ?



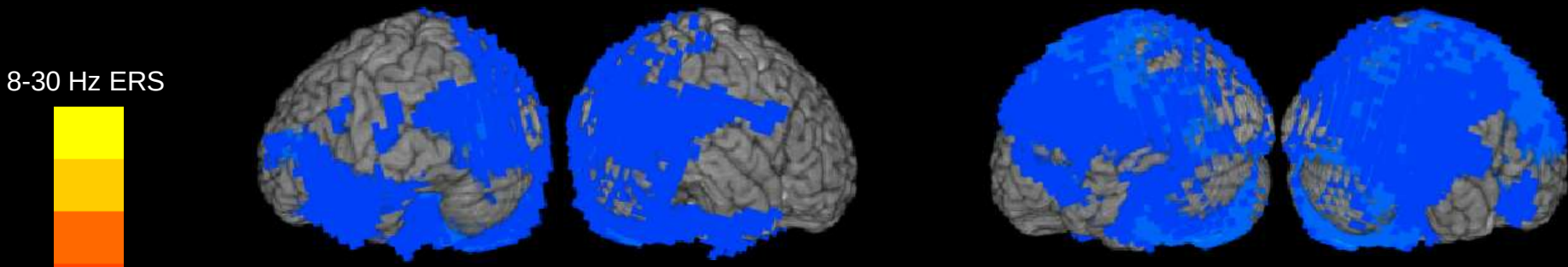
Stroke lesion extent



Older Adults

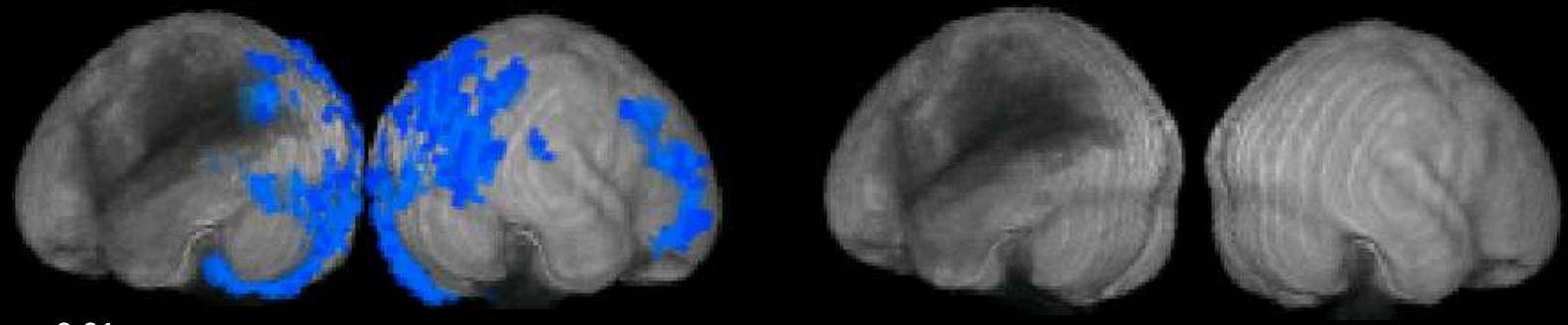
Semantic Violation - Control

Syntactic Violation - Control



p = 0.01

Stroke Patients

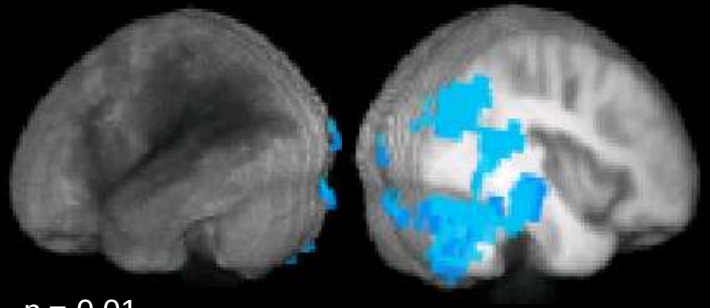


p = 0.01

Kielar, Deschamps, Jokel, & Meltzer, in revision

Correlation of 8-30 Hz ERD with task performance

Semantic 8-30Hz ERD vs. Accuracy



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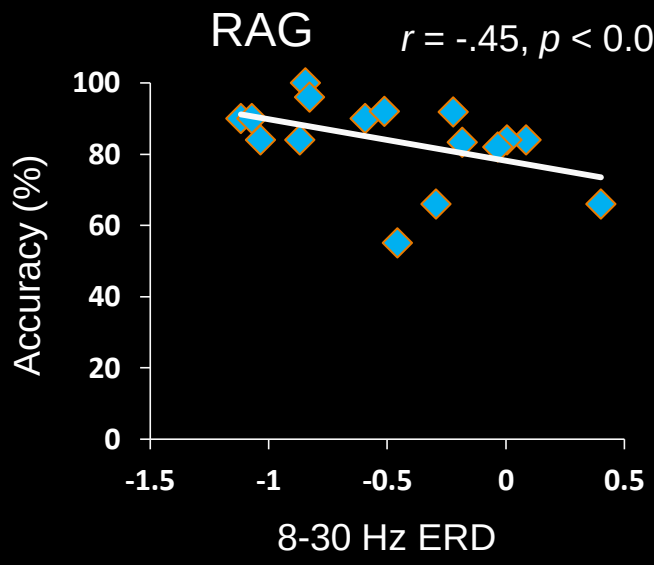
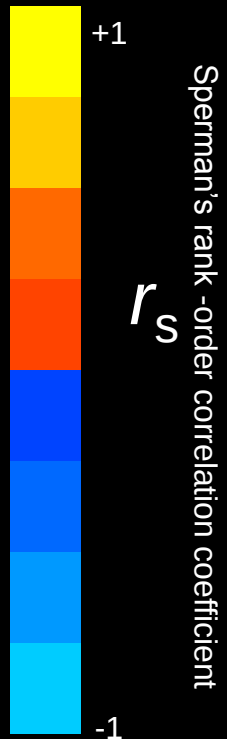
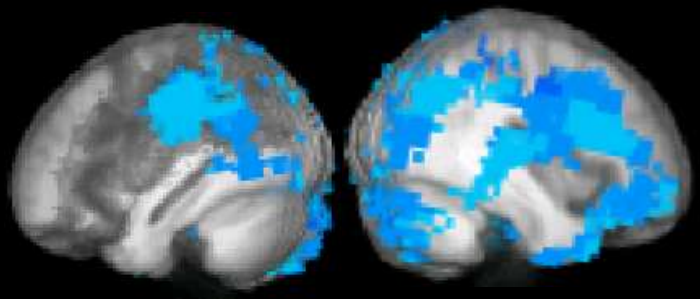
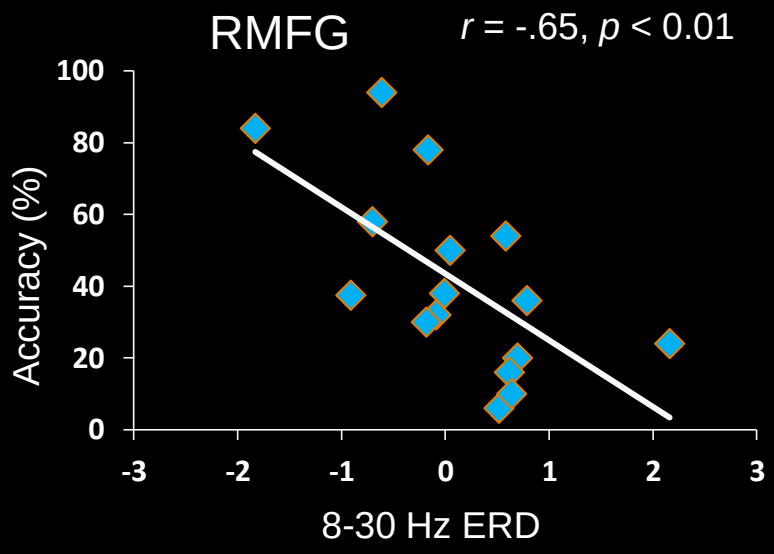




Syntactic 8-30Hz ERD vs. Accuracy

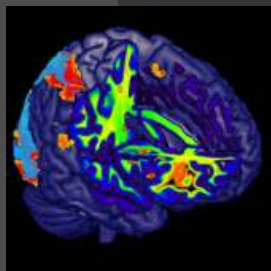




Kielar, Deschamps, Jokel, & Meltzer.(2016).

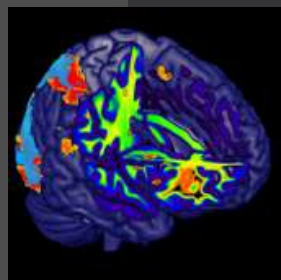
Neural Correlates of Recovery

- Semantic: recruitment of the RH & activation of LH perilesional cortex
- Syntactic: associated with bilateral dorsal & right frontal recruitment
- Recovery of semantic processing: shift to the right hemisphere components of the ventral network
- Recovery of syntax is mediated by bilateral dorsal regions



Neural Correlates of Recovery

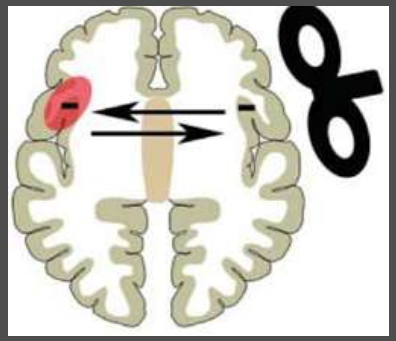
- Patients recruited RH dorso-lateral frontal cortex that was not activated in controls
  - But not significantly correlated with better performance
- Temporo-parietal regions more directly associated with successful sentence processing
  - Supports recovery/performance
  - Possibility of homologous recruitment



Clinical relevance

- Implications for treatment of comprehension impairment in patients with aphasia

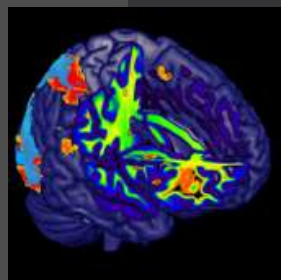
- RH activity may be adaptive for receptive semantics



- Inhibitory stimulation to the RH may not be optimal for the treatment of comprehension deficits

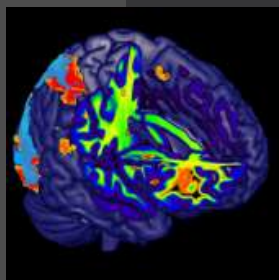
Neural Correlates of Recovery

- Compensation in the RH
- What is the role of preserved LH areas?
- Can we identify a *neural biomarker* of changes occurring in the preserved perilesional region?

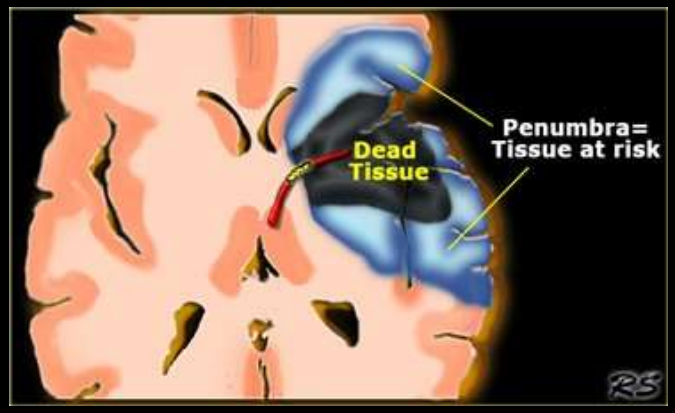


Overview

- Background: Neural pathways for semantics and syntax
- Mapping language responses: MEG & EEG methods
- Plasticity of language responses in post-stroke aphasia
- Spontaneous neural dynamics in stroke and aging

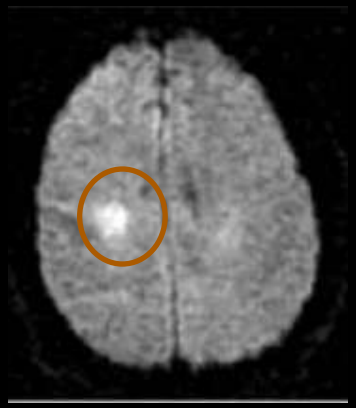


Role of functional lesion in stroke

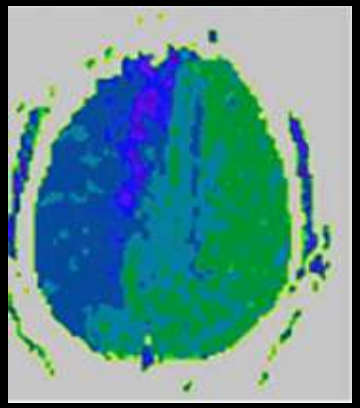


Area of reduced blood flow but not infarcted

Diffusion

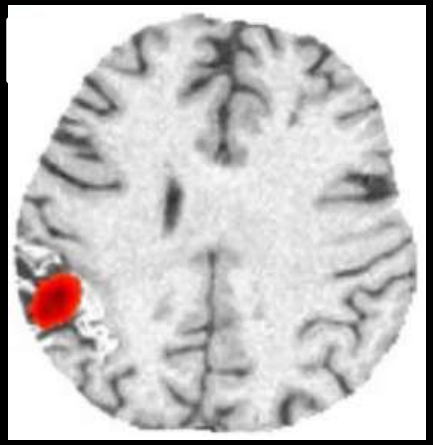


Perfusion



Hillis et al., 2007

High amplitude slow-wave activity

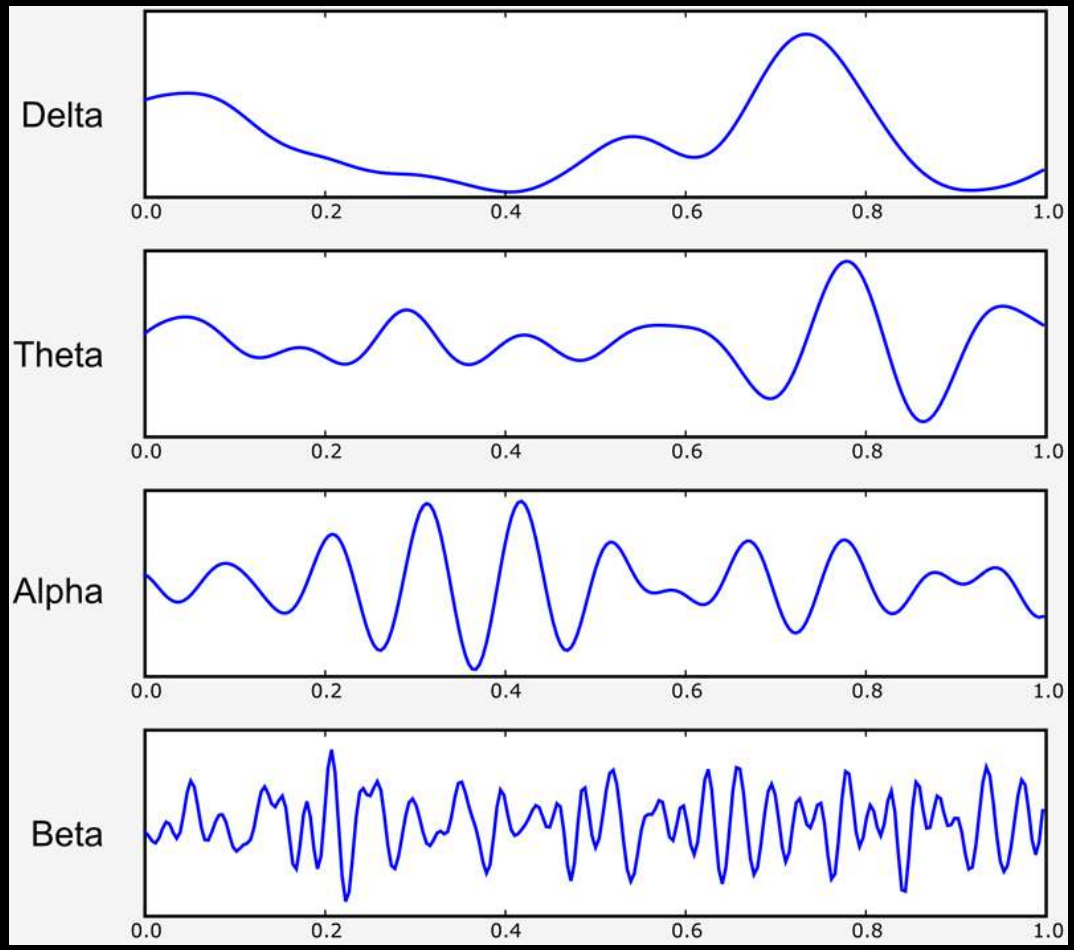


Localization of pathological oscillatory power
in the delta-band (0.5–3 Hz)

Butz et al. 2004

MEG: Spontaneous Activity

- Method: Data acquired during 5 minute resting scan in MEG
- Relative power



1-4Hz

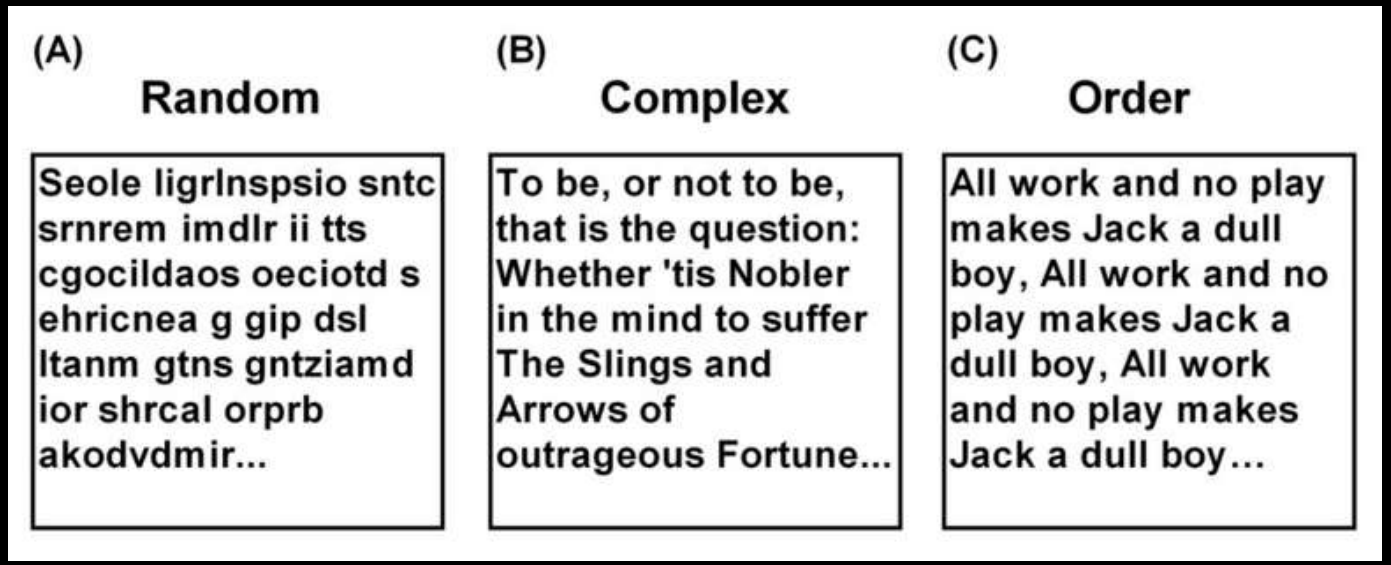
5-7Hz

8-12Hz

15-30Hz

MEG: Spontaneous Activity

- Signal Complexity
- Multiscale Entropy (MSE): Reflects complexity of neural signal/informational content



Low entropy **High entropy** Low entropy

http://www.psynetresearch.org/complexity-analysis-of-brain-signals.html

MEG: Spontaneous Activity

Signal Complexity

Slowing

Stroke vs. Older

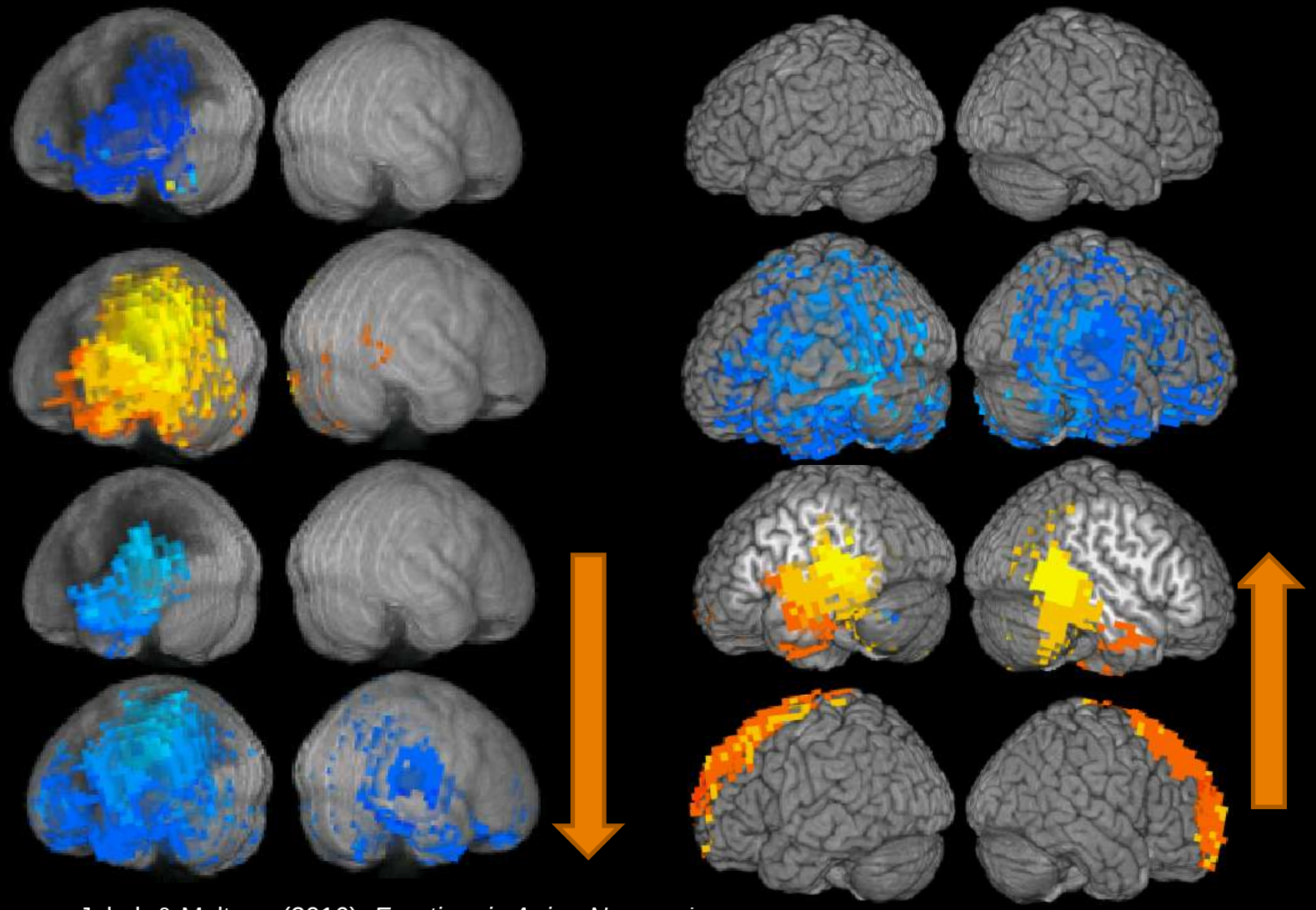
Older vs. Young

MSE: scales 1-5

Delta 1-4 Hz

Alpha 8-12 Hz

Beta 15-30 Hz

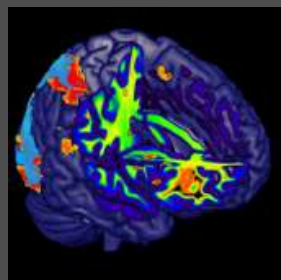


Kielar, Chu, Deschamps, Jokel, & Meltzer. (2016). *Frontiers in Aging Neuroscience*

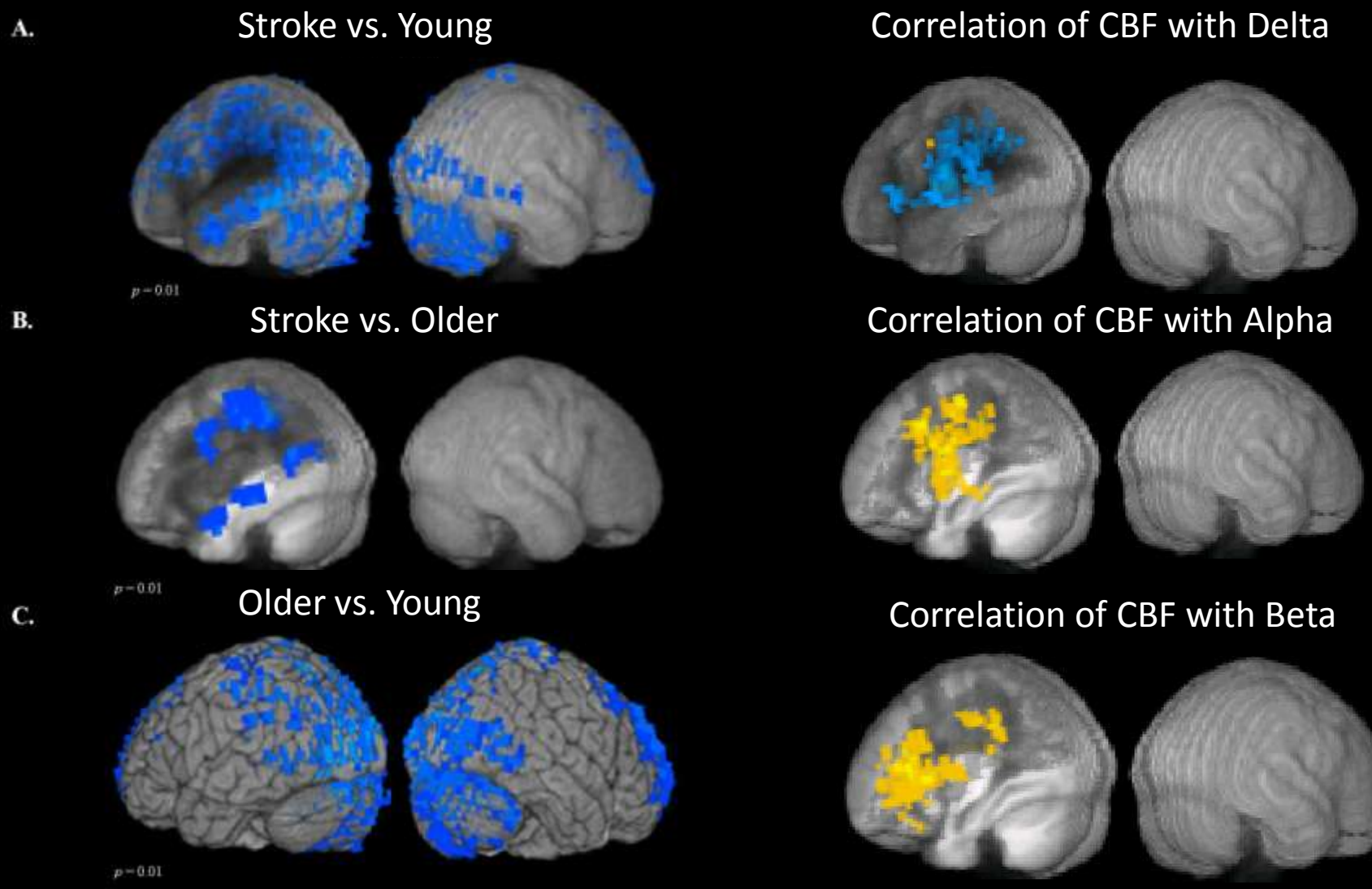
MEG: Spontaneous Activity

- Perilesional neural tissue:
  - Shows decreased entropy
  - Produced abnormal slow-wave activity
  - Decreased alpha/beta power
- **Clinical relevance:** identify cortical tissue that is preserved but not functioning efficiently
- Can be targeted for intervention

- Aging related changes



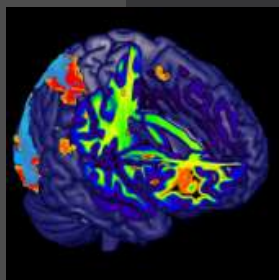
Relationship to Blood Flow



Kielar, Chu, Deschamps, Jokel, & Meltzer. (2016). *Frontiers in Aging Neuroscience*

Summary

- MEG spectral measures: sensitive to stroke
- Relationship between hypoperfusion and electrophysiological abnormalities
- MEG signal complexity: sensitive index of neural dysfunction in perilesional tissue in chronic stroke
- Distinguishable from healthy aging



Conclusions

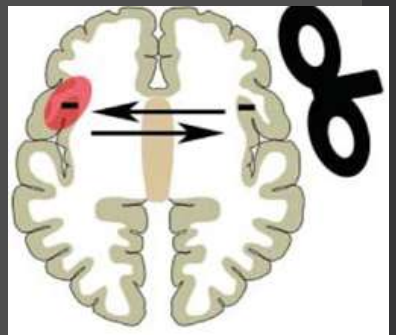
- In the presence of a lesion, language networks reorganize to brain regions in perilesional and contralesional cortex
    - Pattern of reorganization depends on the task
- Better capacity to recruit preserved RH for semantic compared to syntactic processing

Conclusions

- Perilesional neural tissue produced abnormal slow-wave activity and showed reduced blood flow, indicating the extent of *”functional lesions”*
- Neuronal slowing is associated with hypoperfusion
- Reduced task related responses in perilesional tissue and the degree of RH recruitment may be related to abnormal neuronal slowing

Implications

- Theoretical and clinical relevance:
  - Identify contribution of dorsal and ventral pathways to semantic and syntactic processing
  - Identified changes in the cortical representation of language in post-stroke aphasia
  - Noninvasive methods for identification of cortical function in stroke, aging, and neurodegeneration



People

- Collaborators

Pelagie Beeson, Ph.D.
SLHS

Dianne Patterson, Ph.D.
SLHS

Ying-hui Chou, Ph.D
Steven Rapcsak, MD
Kindle Rising, SLP

Jed Meltzer, Ph.D.
Regina Jokel, Ph.D. SLP
Priyanka Shah-Basak, Ph.D.

Students

Sara Mohr, SLHS
Leah Rice, Linguistics
Hanna Johnson, Physiology
Phoebe Lughes, SLHS, Spanish
Alexis Morrison, Neuroscience
Katie McConville, Neuroscience
Kimberly Skvarla, Neuroscience

HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

ORC ONTARIO RESEARCH COALITION


Thank you