Speech, Language and Hearing Sciences
Western Michigan University

Considerations for the Use of Neuroimaging for Predicting Recovery of Speech and Language in Aphasia

Linda I. Shuster, Ph.D., CCC-SLP

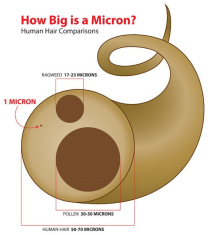
Overview of the Talk

- Important aspects of neuroimaging technology
- Neuroimaging technologies being used to predict aphasia outcome, their limitations and advantages
- Biomarkers
- Overview of the biomarkers for predicting recovery from aphasia that have been identified to date
- Using neuroimaging as a clinical test for predicting aphasia recovery
  - Qualitative aspects of clinical testing
  - Clinical utility
  - Ethical, legal, social implications
- Recommendations and Summary

Important Aspects of Neuroimaging Technology

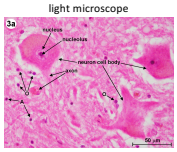
- spatial resolution
- temporal resolution
- contrast
- artifact
- signal-to-noise ratio (SNR)

Spatial Resolution



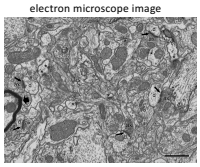
µm = micron, micrometer
1 µm = 0.001 mm, 0.0001 cm

light microscope



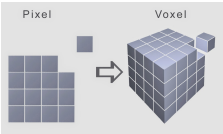
nerve cell body = 15µm - 25µm (0.015-0.025mm)

electron microscope image



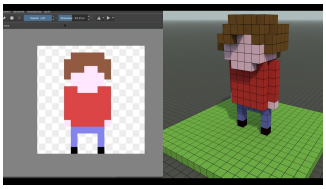
synapses = <0.1µm – 0.5µm

Spatial Resolution (cont.)

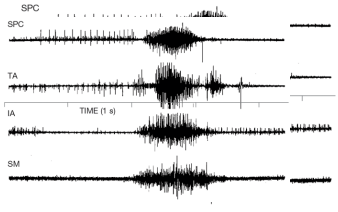


pixel (picture element) = 2D sample of an image

voxel (volume element) – 3D pixel

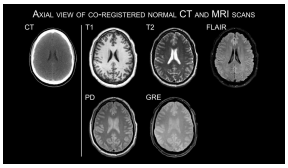


Temporal Resolution

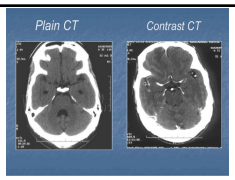


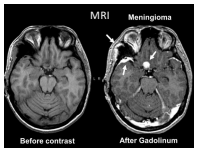
time

Contrast – endogenous vs. exogenous



intrinsic (endogenous)

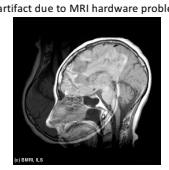


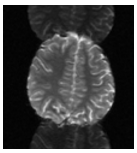


extrinsic (exogenous)

Artifact

artifact due to MRI hardware problems

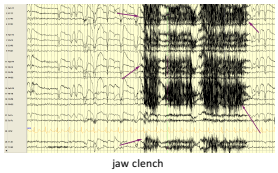




artifact due to patient movement

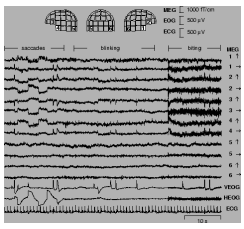
ghosting artifact in MRI can arise from different sources

Artifact (cont.)



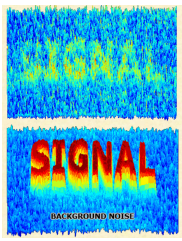
jaw clench

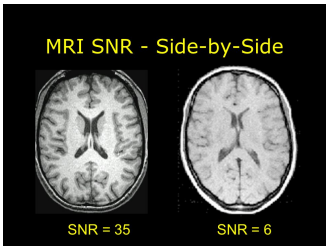
EEG



magnetoencephalography

Signal-to-Noise





Overview of Imaging Technologies and the Biomarkers Being Used to Predict Recovery from Aphasia

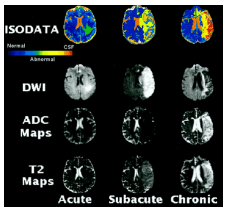
Biomarker (biological marker)

- a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, patho-genic processes or pharmacological responses to a therapeutic intervention (Biomarkers Working Group, 2001)
- important to determine relationship between biomarker and relevant clinical endpoint, e.g., language recovery after a stroke
- invasive and non-invasive
- neuroimaging data are one kind of biomarker

Structural Magnetic Resonance Imaging (MRI)

- images brain *structure*
- typical biomarker – lesion site and size
- magnet field strength measured in Tesla (T)
- stronger magnetic field provides:
  - better spatial resolution
  - better SNR
- temporal resolution – N/A
- spatial resolution
  - depends on hardware and software
  - <1 – 2 mm voxels

- limitations
  - magnetic field not safe for all
  - must lie still
  - claustrophobia
  - noisy
  - session length (~30 min)
  - machines with stronger magnetic fields have smaller bores
- advantages
  - no radiation involved
  - relatively good spatial resolution

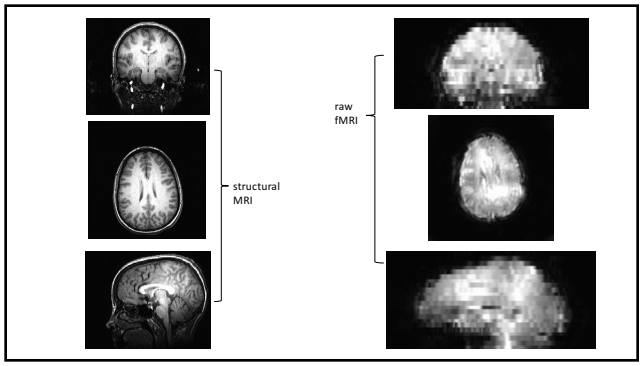


stroke imaging

Functional MRI (fMRI)

- images brain *function*
- uses same hardware as MRI
- biomarker – site(s) of activation correlated with task performance
- temporal resolution – ~5-8 seconds post-stimulus
- spatial resolution
  - depends on hardware and software
  - 2-3+ mm

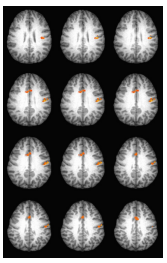
- limitations
  - same as MRI
  - indirect measure of neuronal function (blood volume/flow)
  - complicated process of image analysis
  - must be registered (aligned) with structural image for localization
  - typically, only pre-surgical planning covered by insurance (e.g., brain tumor)
- advantages
  - assesses function
  - no radiation involved



fMRI

R L

Brain activation during word repetition

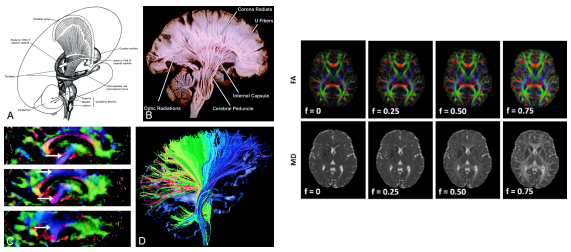


From: Shuster, L., Moore, D., Chen, G., Ruscello, D. & Wonderlin, W. (2013)

Diffusion Tensor Imaging/Fiber Tractography

- images brain structural connections
- uses same hardware as MRI
- spatial resolution - millimeters
- temporal resolution – N/A
- biomarker – structural integrity of neural pathways
- limitations
  - same as MRI, e.g., magnetic field, movement
  - potential for missing fibers due to sensitivity issues
  - not yet used routinely in clinical practice

- advantages
  - provides information about brain connectivity
  - non-invasive



Electroencephalography (EEG)

- images brain electrical signals
- good temporal resolution - milliseconds
- poorer spatial resolution
- biomarkers – synchrony of brain activity, strength of brain connections
- limitations
  - sensitive to movement – no speaking
  - spatial resolution
  - cannot image deep brain structures
  - time for set-up

Shuster WVSHA 2018

- advantages
  - temporal resolution
  - measure of brain function
  - non-invasive

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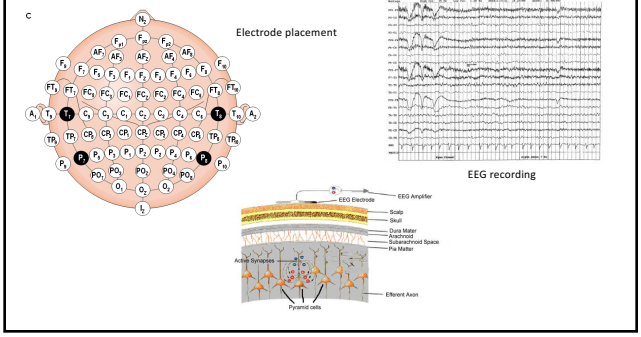
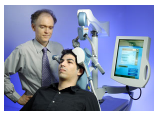
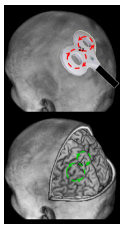


Transcranial Magnetic Stimulation (TMS)

- uses a electromagnetic field to generate current in nerve cells
- nerve cell activity can enhance or negatively affect behavior
- electromagnetic field applied in pulses
- pulses can be varied in intensity and frequency
- biomarker - brain "lesions" in neurotypicals
- limitations
  - cannot assess deep brain structures
  - risk for seizures, particularly in those prone to seizures

  - auditory, sensory stimulation by pulse
  - potential peripheral nerve stimulation
- advantages
  - non-invasive
  - ability to simulate brain lesions



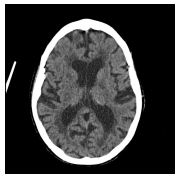


TMS

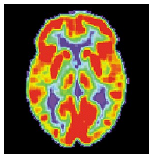
Other Potential Technologies (no studies of aphasia recovery to date)

- magnetoencephalography (MEG) – indirect measure of brain electrical signals
- computerized tomography (CT) – measure of brain structure
- positron emission tomography (PET)
  - measure of blood volume/flow
  - indirect measure of neural activity
- functional near-infrared spectroscopy (fNIRS)
  - monitors blood hemoglobin (similar to BOLD fMRI)
  - indirect measure of neural activity

MEG



CT



PET

fNIRS

Examples of Studies Investigating Biomarkers to Predict Recovery from Aphasia

How do you define "recovery?"

Price et al., 2010; 2017

- Patient Language Outcome and Recovery After Stroke (PLORAS) database
- outcome measure for recovery = Comprehensive Aphasia Test
- imaging biomarkers
  - lesion site using MRI
  - lesion size using MRI
- clinicians compare their clients to PWA in the database

Wang et. al. 2013

- outcome measure for recovery – speech fluency and naming assessed through conversation, picture description, Boston Naming Test
- imaging biomarker
  - arcuate fasciculus (AF) imaged with DTI
  - AF lesion site/size = AF lesion load (AF-LL); measured in cc
- results – AF-LL could stratify PWA into severe and non-severe outcomes

Yourganov et. al. 2016

- outcome measure for recovery – Western Aphasia Battery (WAB)
- imaging biomarkers
  - structural connectome - map of neural connections using DTI
  - lesion size using MRI
- results – combination of connectome and lesion data were able to predict performance on the WAB

Nicolo et. al. 2015

- outcome measure for recovery – Geneva Bedside Aphasia Score at two time points
- imaging biomarker
  - EEG weighted node degree (WND) and coherence
  - WND reflects strength of neural connections
  - coherence reflects synchronization of activity among brain regions
- results
  - PWA with good improvement demonstrated high WND
  - greater improvement in language when neural oscillations in Broca's area were coherent with the rest of the cortex

Lorca-Puls et. al. 2017

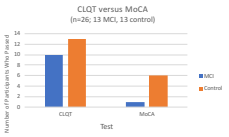
- outcome measure for recovery – Comprehensive Aphasia Test
- imaging biomarker – areas of the brain where function was disrupted by TMS in neurotypicals (simulated lesions)
- results
  - TMS-simulated lesions could explain phonological processing abilities in PWA
  - These included supramarginal gyrus and pars opercularis of the left inferior frontal gyrus

Using Neuroimaging as a Clinical Test for Predicting Aphasia Recovery

Qualitative Aspects of Clinical Testing

- sensitivity – the ability of a test to identify those people with the disease/problem (true positive)
- specificity – the ability of a test to identify those people without the disease/problem (true negative)
- positive predictive value (PPV) – the likelihood that a person who tests positive actually has the disease
- negative predictive value (NPV) – the likelihood that a person who tests negative for the disease does not have the disease

Data from Cox, Shuster, Chase, & Nelson (in progress)



	CLQT	MoCA
sensitivity	23%	92%
specificity	100%	54%
PPV	75%	67%
NPV	54%	88%

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- analytic validity – ability of the neuroimaging method to detect the biomarker
  - sensitivity – proportion of persons with aphasia (PWA) in whom the biomarker can be detected when present (true positive vs false negative)
  - specificity – proportion of PWA in whom the biomarker was not detected when it was not present (true negative vs false positive)
  - confirm non-invasive, indirect techniques with invasive, direct techniques
- clinical validity
  - sensitivity – proportion of PWA for whom there was a positive outcome when the positive biomarker for recovery was present
  - specificity – proportion of PWA for whom there was a negative outcome when the positive biomarker recovery was absent
  - need a lot of data from many PWA to look at individual variability
  - PPV – the probability that someone who does possess the positive biomarker will recover

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- NPV - the probability that someone who does not possess the positive biomarker will not recover
- role of social environment in recovery

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Clinical Utility

- effect on patient care
- available expertise in the technology
- quality assurances
- access to/expense of the technology
- financial costs

Ethical, Legal, Social Implications

- implications of a negative prognosis for recovery
- powerful influence of brain imaging

Recommendations

- consistently define recovery
- consider clinical applicability in the design of every research study
- collect MUCH MORE data on individuals
- consider other factors that influence recovery
- acknowledge the limitations of each neuroimaging technology
- consider the access to the technology
- study more people who have completely recovered

Summary

- many investigators are proposing the use of neuroimaging to predict recovery from aphasia
- there has been some progress, but many questions remain
- this has important implications for treating aphasia and other neurogenic communication disorders
- if this testing is implemented clinically, SLPs may be in the position of having to explain results