Functional Mapping of Learning Disabilities

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MASTERS

2019 Neuro Summit
San Diego

Neural circuitry for vision and reading

Brian A. Wandell
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QUANTITATIVE MEASUREMENTS

∞

COMPUTATIONAL MODELS

∞

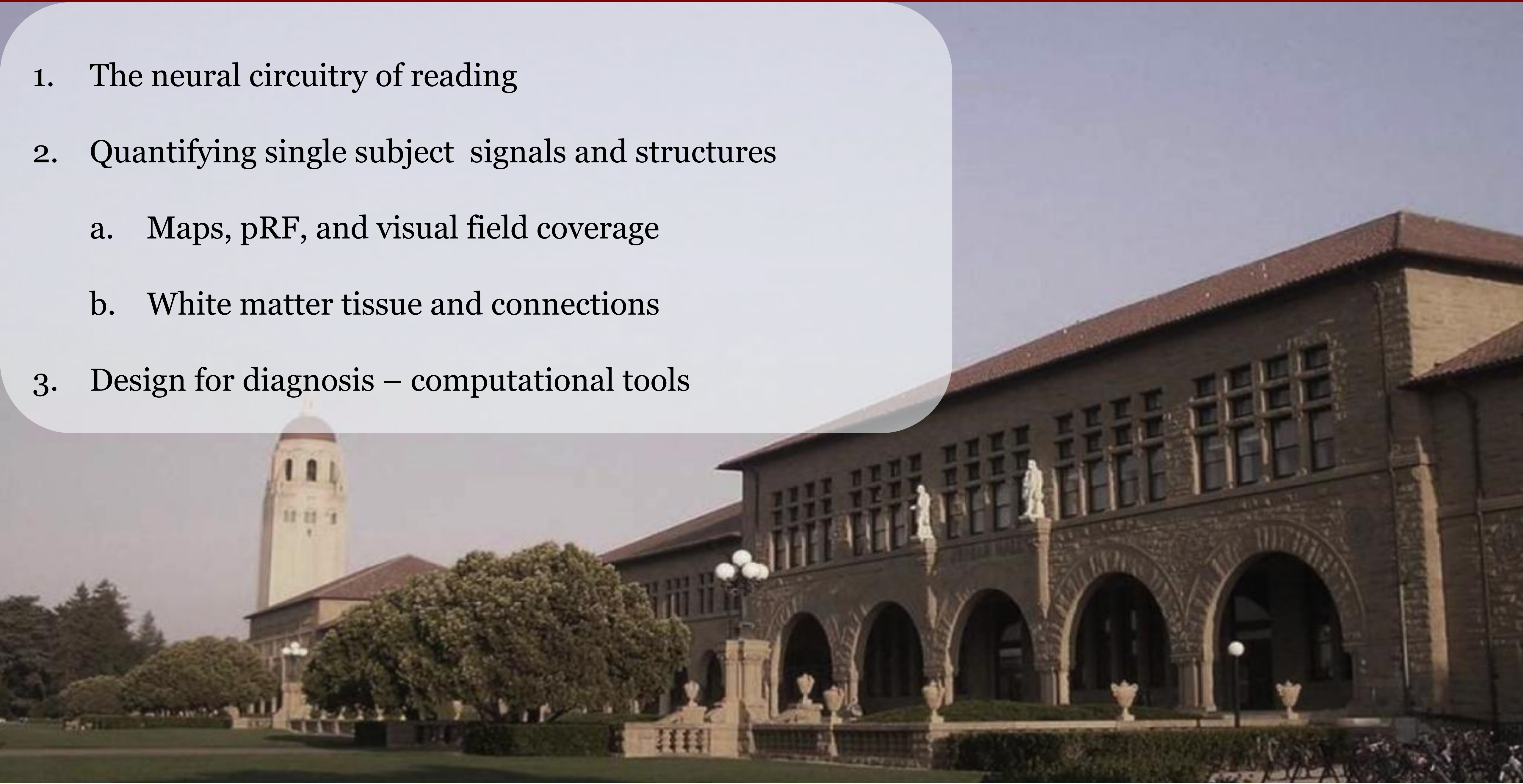
CHECK AND SHARE

Slides: available at
https://www.stanford.edu/~wandell/talks-and-tutorials

Disclosure: I am a co-founder of Flywheel.io a commercial venture supporting cloud scale collaborative science

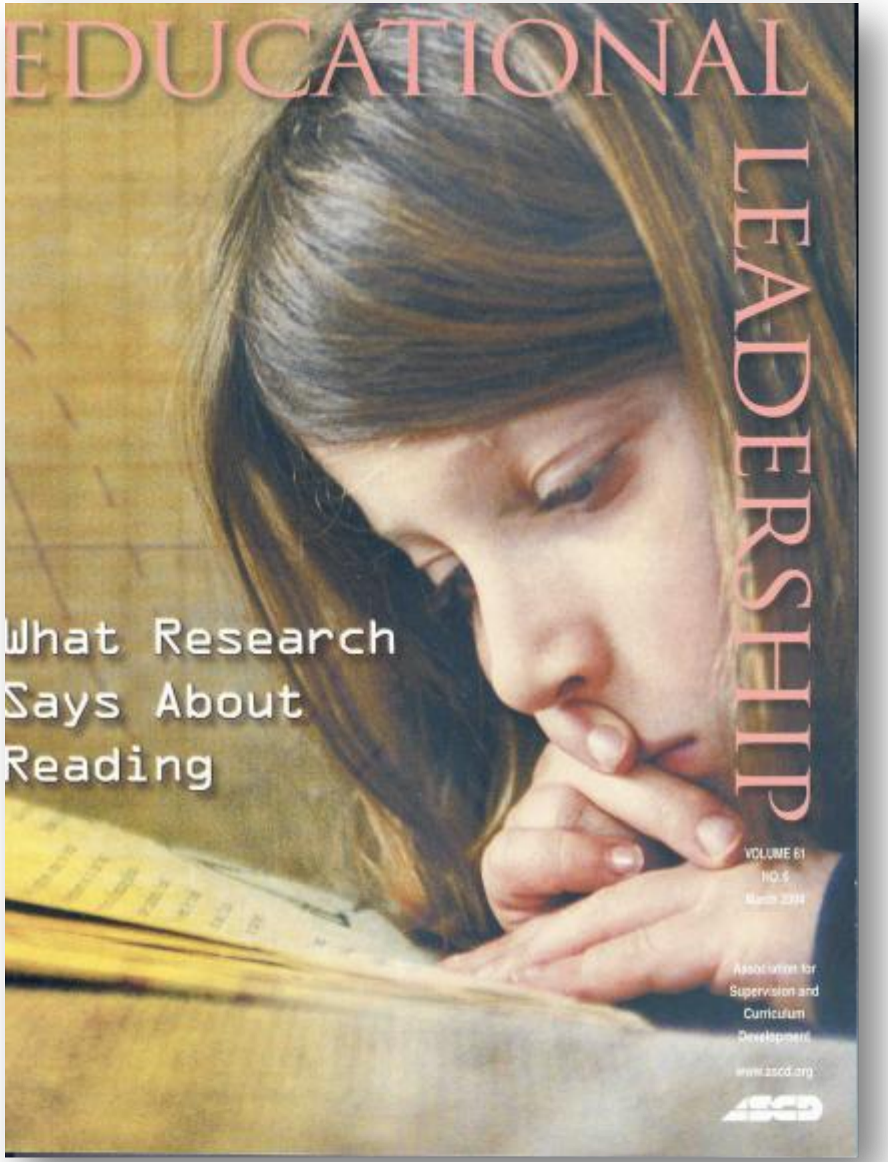
Talk plan: Neural circuitry for vision and reading

1. The neural circuitry of reading
2. Quantifying single subject signals and structures
   a. Maps, pRF, and visual field coverage
   b. White matter tissue and connections
3. Design for diagnosis – computational tools



Reading and the Educational Community

- In the US and Western Europe between 5-17% of children struggle to learn to read
- We would like to diagnose whether or not a particular child will ultimately succeed
- We are searching for neural measures that help make this prediction, with better accuracy than behavioral testing

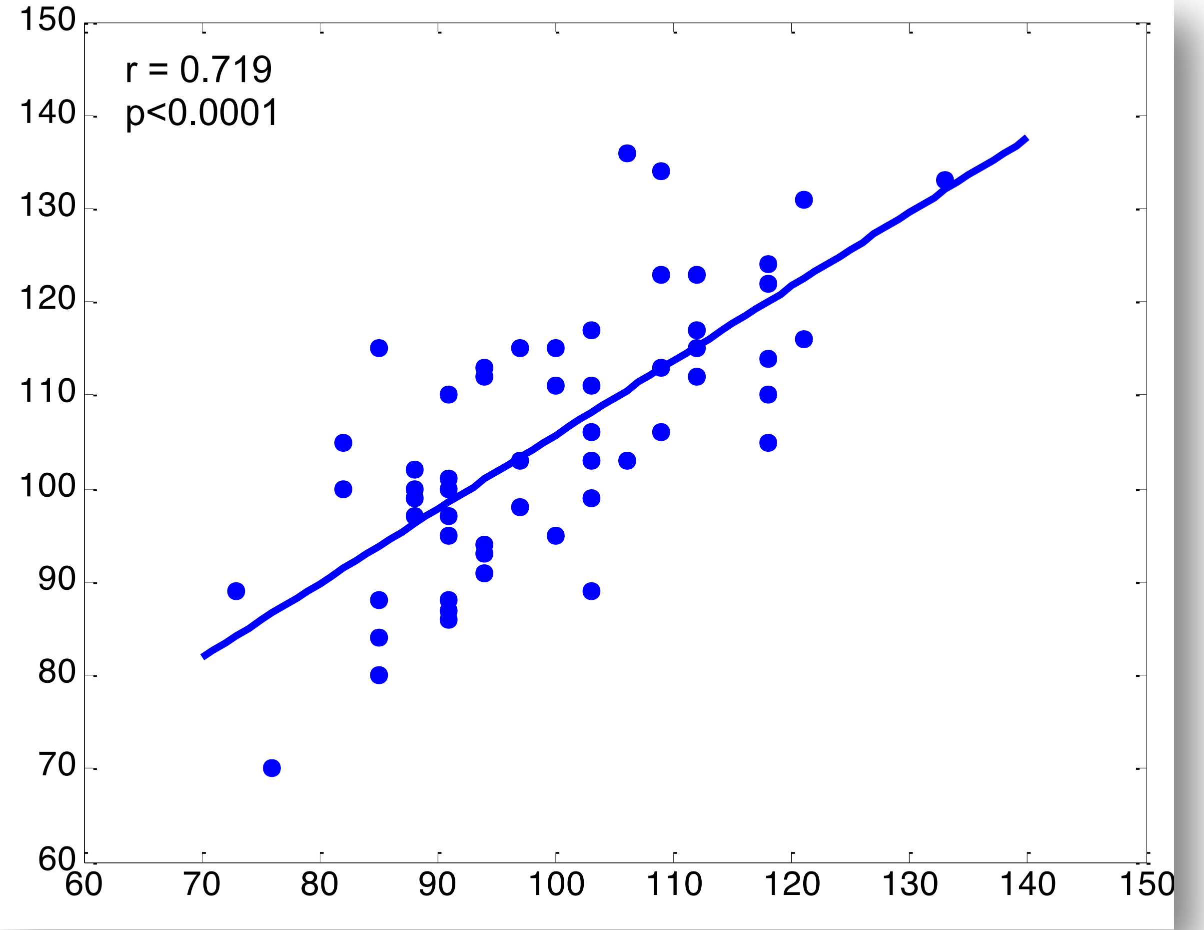


Reading letter-based systems and phonemic awareness

elision (strain-/r/ = stain)
blending (/t/+/oi/ = toy)

- Hearing, distinguishing and manipulating the sounds in words (also phonological awareness)
- Claimed to be the chief causal factor in early reading achievement
- **Hope**: If we train phonemic awareness, children will become better readers (also skills-training, decoding)

Reading (Word ID)
read aloud:
'..together,.. enough, ..'



Phonological Awareness (elision, blending)

Bradley and Bryant, 1978, 1983
Wagner & Torgesen, 1987
Stanovich, 1991

Education community consensus: Visual circuitry is not the problem

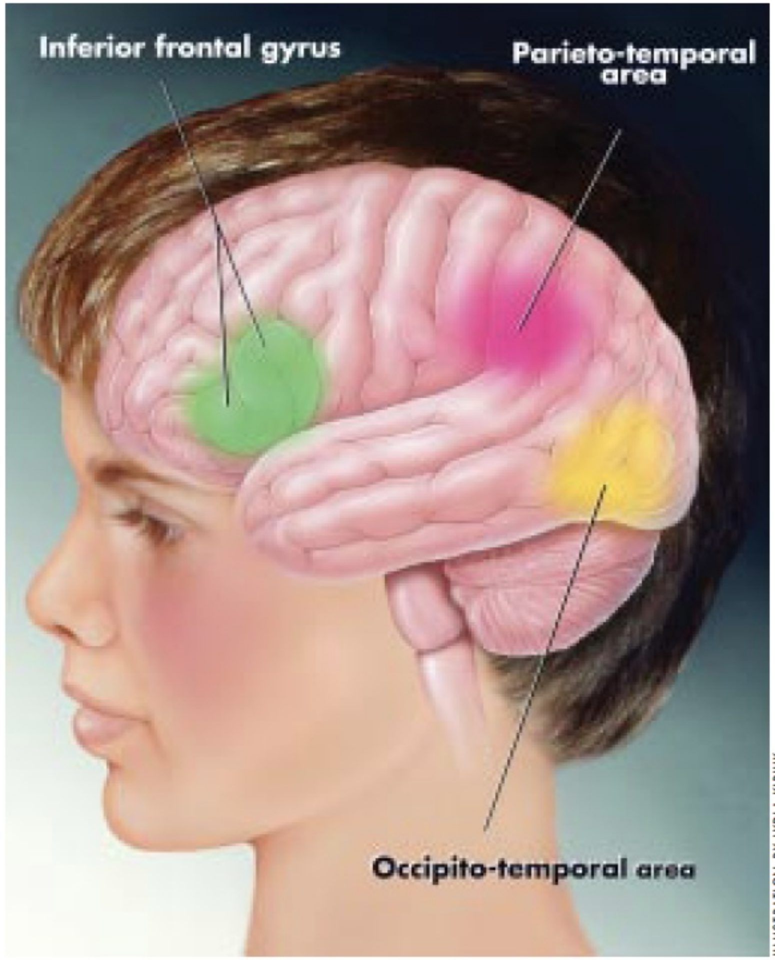
To my mind, the discovery and documentation of the importance of phonemic awareness … is the single most powerful advance in the science and pedagogy of reading this century. (Adams, 1990)

… the specification of the role of phonological processing in the earliest stages of reading acquisition is one of the more notable scientific success stories of the last decade. (Stanovich, 1991, p. 78)

… perhaps the most important single conclusion about reading disabilities is that they are most commonly caused by weaknesses in the ability to process the phonological features of language. (Torgesen et al., 1999, p. 579)

Many hypotheses about the biology of reading disability

- **Interhemispheric transfer** (Damasio, Simos, Henderson)
- **Magnocellular deficit** (Lovegrove, Stein, Livingstone)
- **Auditory processing** deficits (Tallal, Merzenich, Goswami)
- **Attention** and short term memory (Ahissar, Pammer)
- **VWFA** circuitry doesn't develop (many)



Summary 1: Biological basis of reading disability

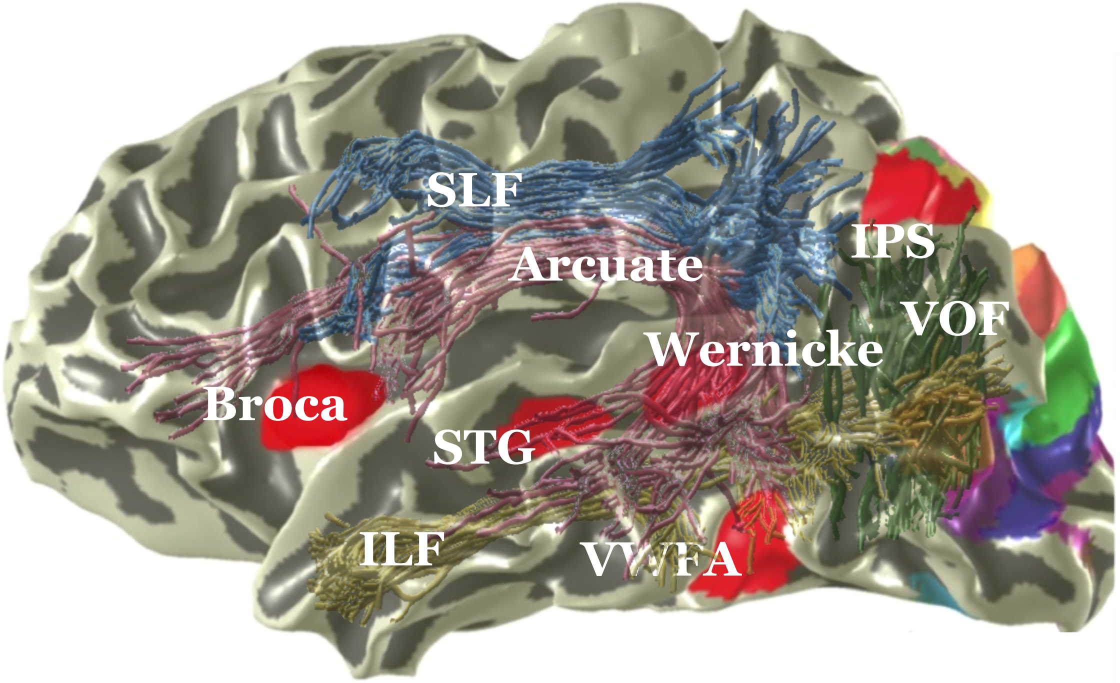
There are many competing ideas about the biological basis of reading disabilities. Different biological impediments may affect different people. We should systematically explore the likely causes.

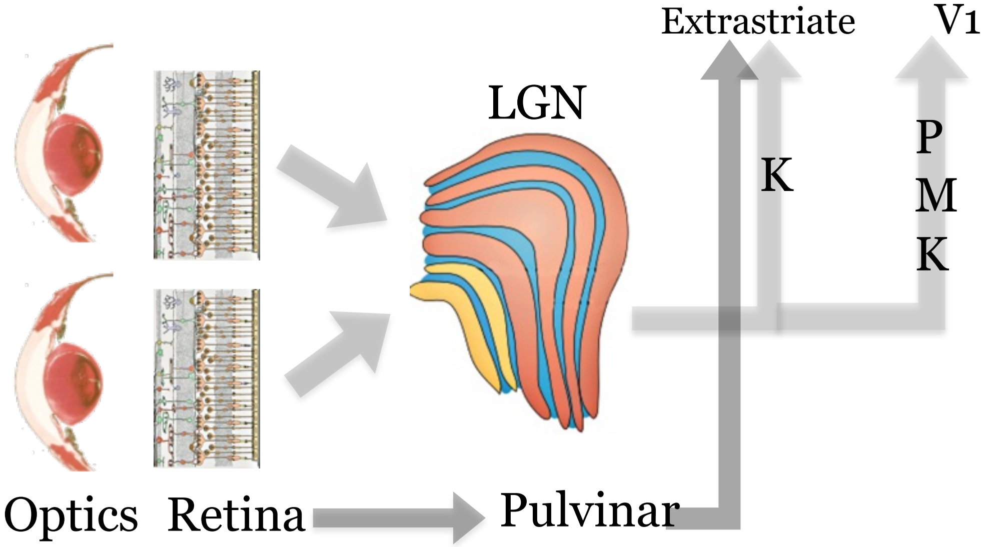
Major components of the reading pathway

Rosemary Le

The goal: Diagnosis

- Identifying the locations and responses in a poor reader that differ significantly from measurements in good readers
- Developmental issues



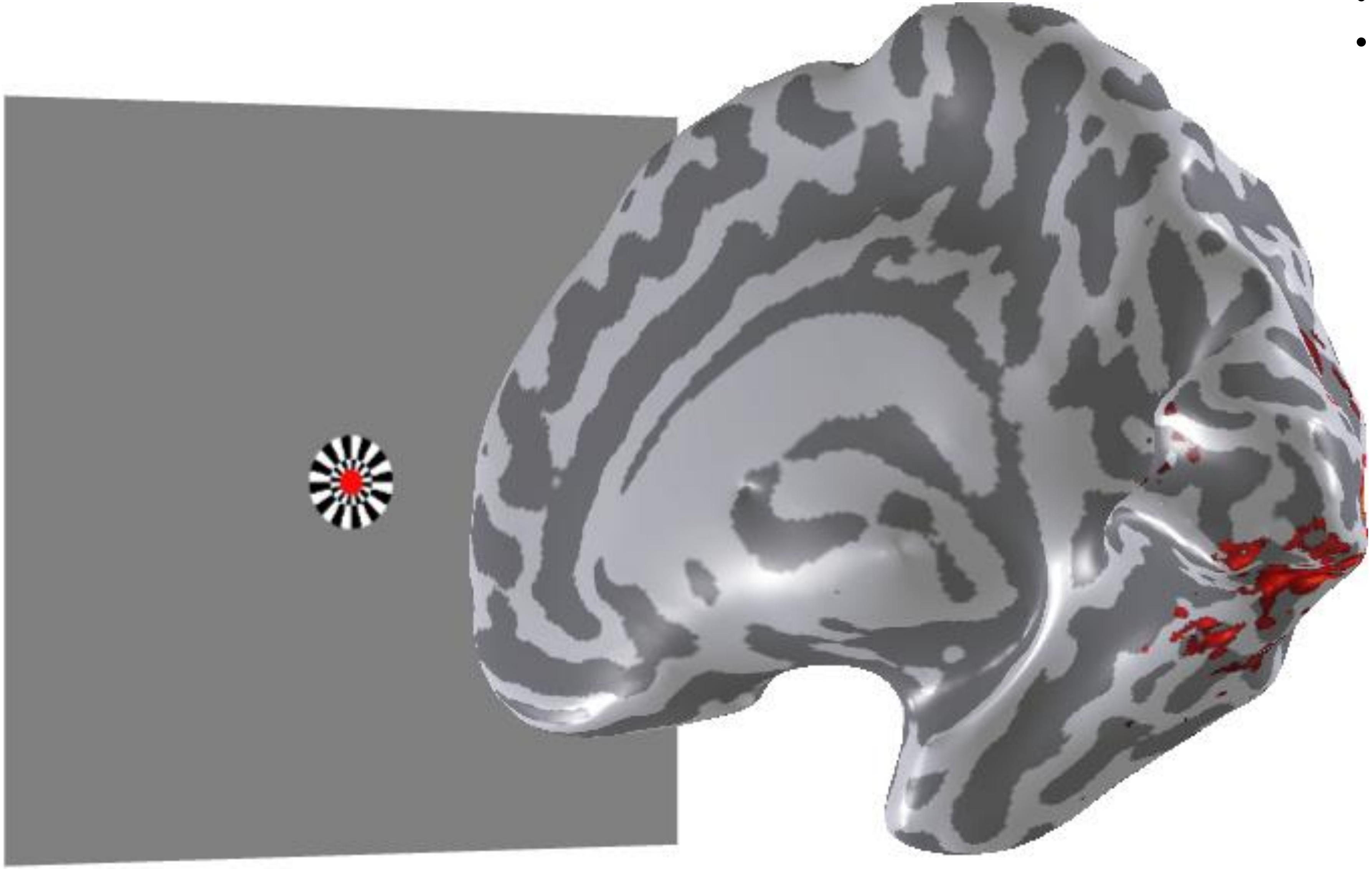


Diagnosing the Neural Circuitry of Reading (2017) Brian A. Wandell and Rosemary K. Le **Neuron** V. 96, Issue 2, October 11, 2017

Learning to See Words B.A. Wandell, A. Rauschecker and J. Yeatman (2012). **Annual Review of Psychology** Vol. 63, pp.31-53.

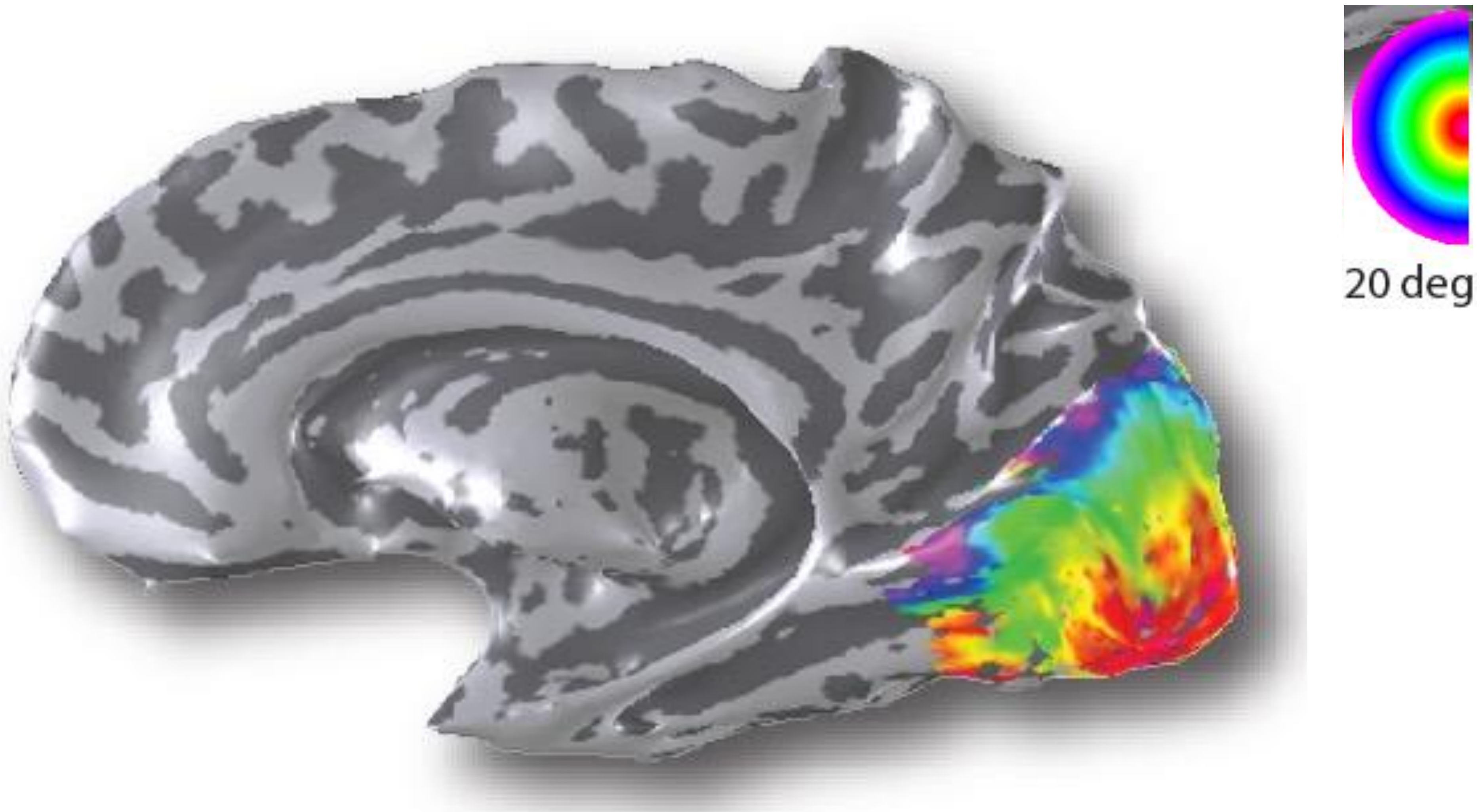
Advances in cortical mapping: eccentricity map

(Engel et al., 1994,1997; Sereno; Tootell, DeYoe; Others)

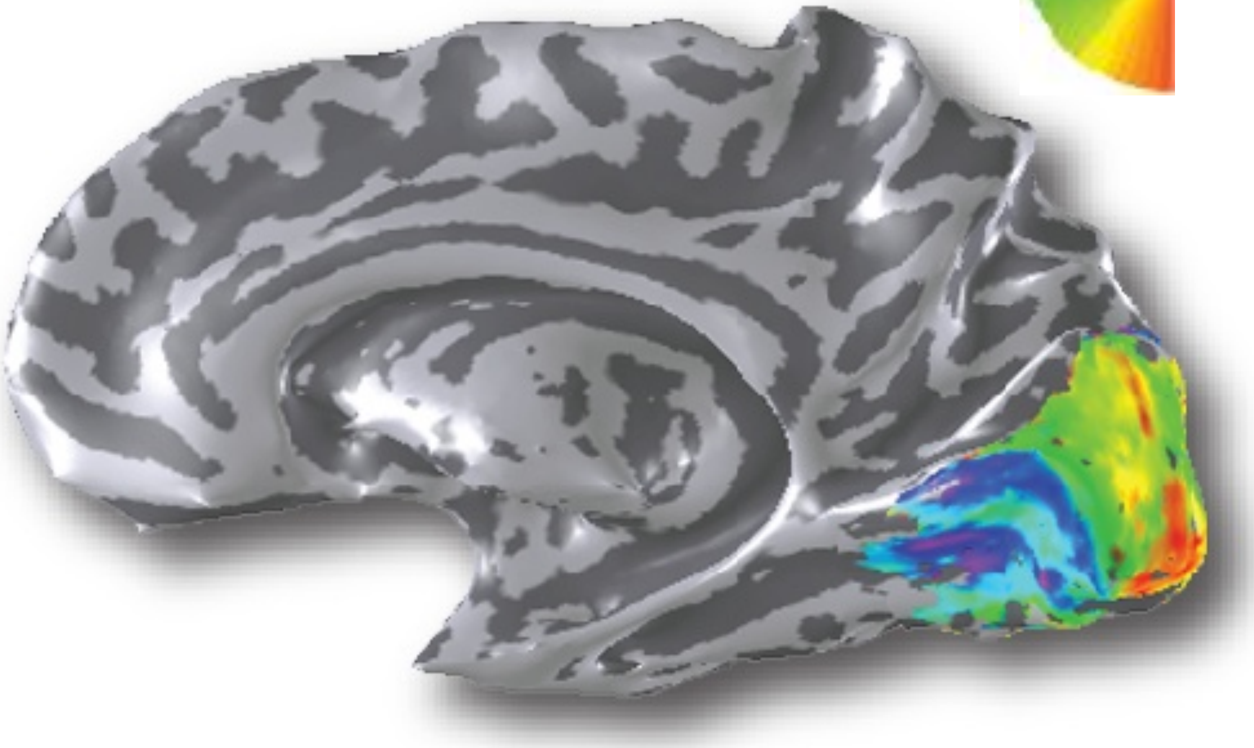


- Inflated brain
- Gray/white are sulci/gyri

Advances in cortical mapping: eccentricity map



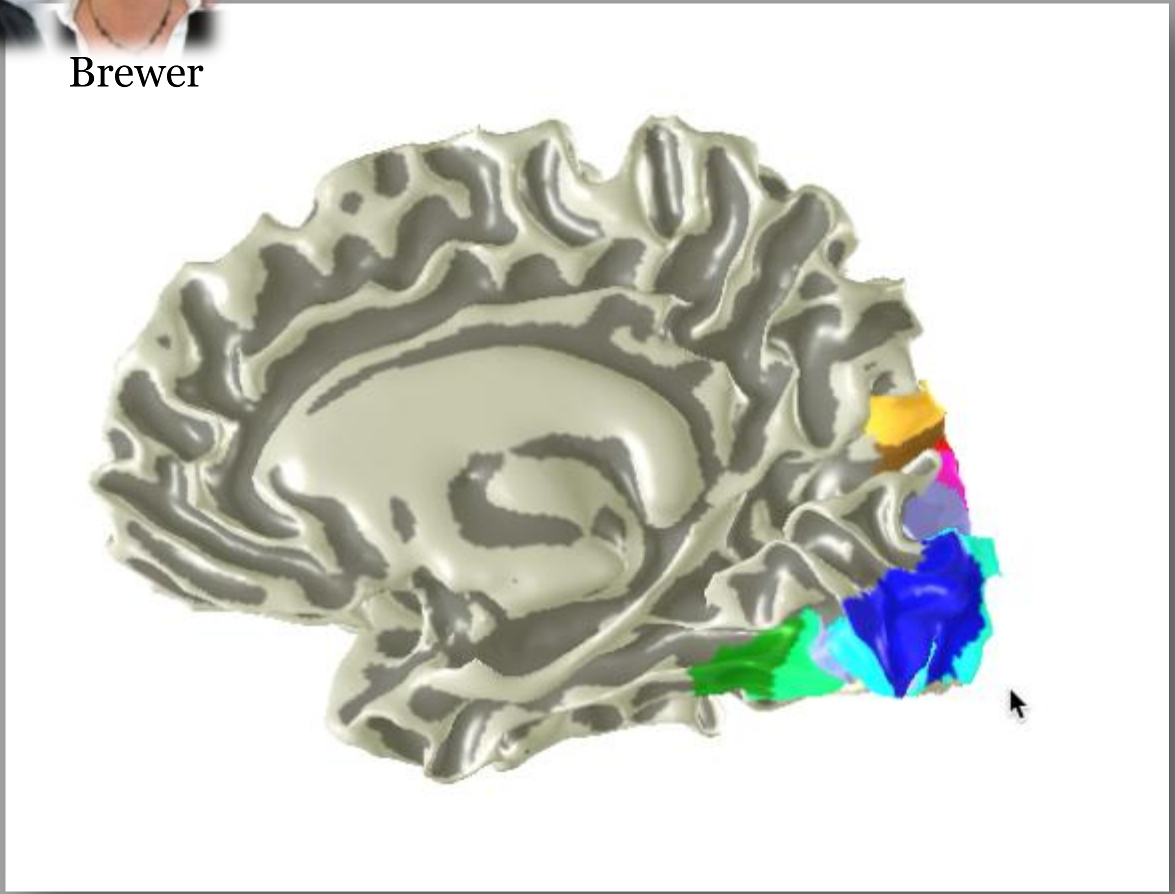
Advances in cortical mapping: angular map



Visual field maps can be measured in individual subjects

Winawer

Brewer



366 Neuron 56, October 25, 2007

Cell Press
Neuron
Review

Visual Field Maps in Human Cortex

Brian A. Wandell,[1,*] Serge O. Dumoulin,[1] and Alyssa A. Brewer[2]
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[2]Department of Cognitive Sciences, University of California, Irvine, Irvine, CA 92697, USA
*Correspondence: wandell@stanford.edu
DOI 10.1016/j.neuron.2007.10.012

Much of the visual cortex is organized into visual field maps: nearby neurons have receptive fields at nearby locations in the image. Mammalian species generally have multiple visual field maps with each species having similar, but not identical, maps. The introduction of functional magnetic resonance imaging made it possible to identify visual field maps in human cortex, including several near (1) medial occipital (V1,V2,V3), (2) lateral occipital (LO-1,LO-2, hMT+), (3) ventral occipital (hV4, VO-1, VO-2), (4) dorsal occipital (V3A, V3B), and (5) posterior parietal cortex (IPS-0 to IPS-4). Evidence is accumulating for additional maps, including some in the frontal lobe. Cortical maps are arranged into clusters in which several maps have parallel eccentricity representations, while the angular representations within a cluster alternate in visual field sign. Visual field maps have been linked to functional and perceptual properties of the visual system at various spatial scales, ranging from the level of individual maps to map clusters to dorsal-ventral streams. We survey recent measurements of human visual field maps, describe hypotheses about the function and relationships between maps, and consider methods to improve map measurements and characterize the response properties of neurons comprising these maps.

Vision Research 51 (2011) 718-737

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Review

Imaging retinotopic maps in the human brain

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ABSTRACT

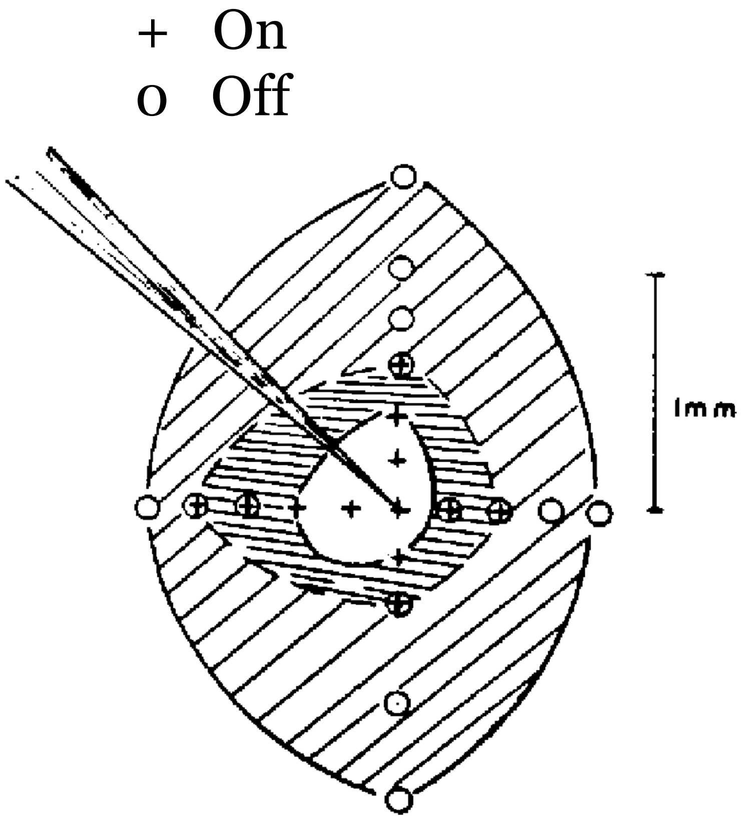
A quarter-century ago visual neuroscientists had little information about the number and organization of retinotopic maps in human visual cortex. The advent of functional magnetic resonance imaging (MRI), a non-invasive, spatially-resolved technique for measuring brain activity, provided a wealth of data about human retinotopic maps. Just as there are differences amongst non-human primate maps, the human maps have their own unique properties. Many human maps can be measured reliably in individual sub-

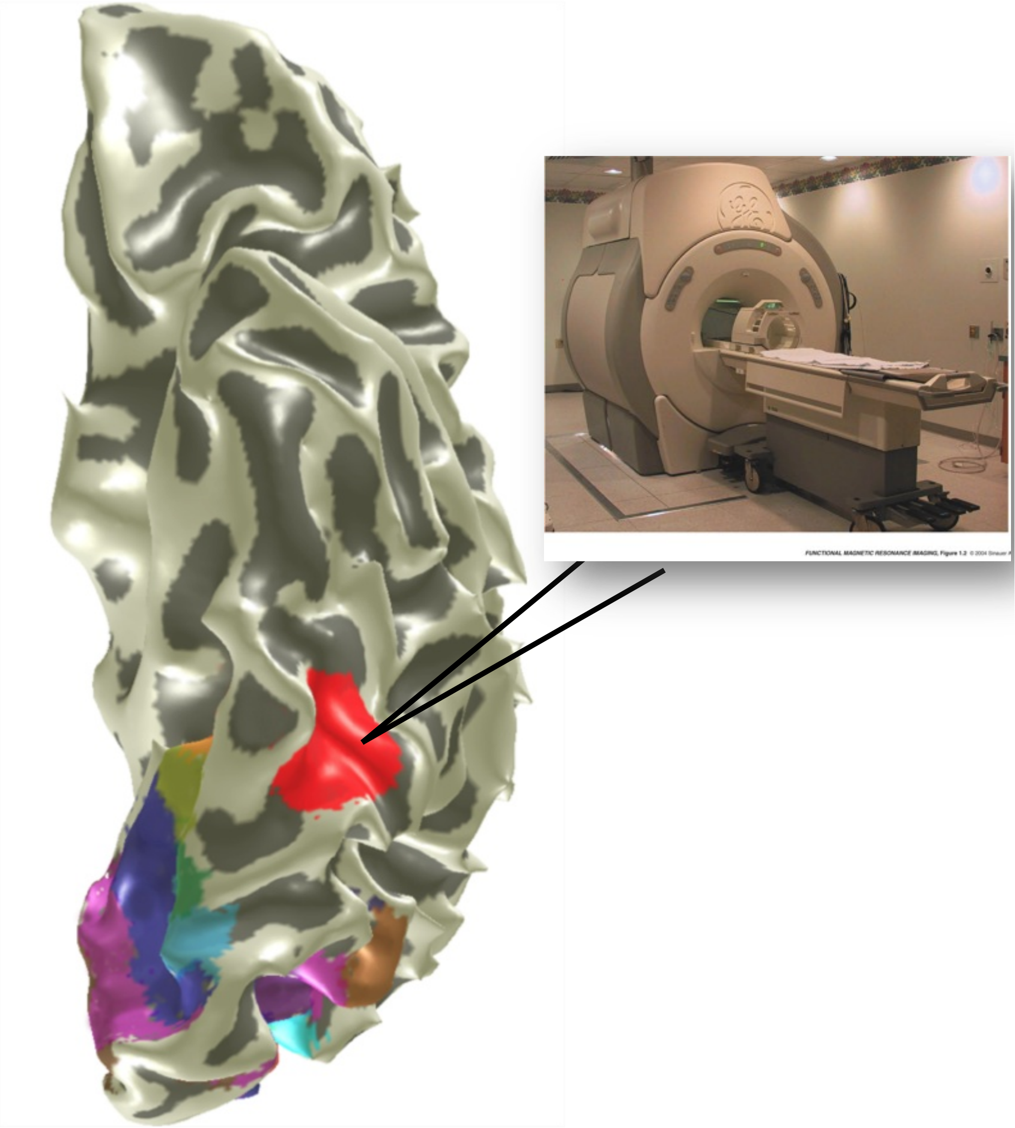
Modeling visual cortex responses

- Population receptive fields

Quantitative modeling: the population receptive field (pRF)

‘Responses can be obtained in a given optic nerve fiber only upon illumination of a certain restricted region of the retina, termed the receptive field of the fiber (Hartline, 1936)’.





Sherrington, 1910
Kuffler, 1953

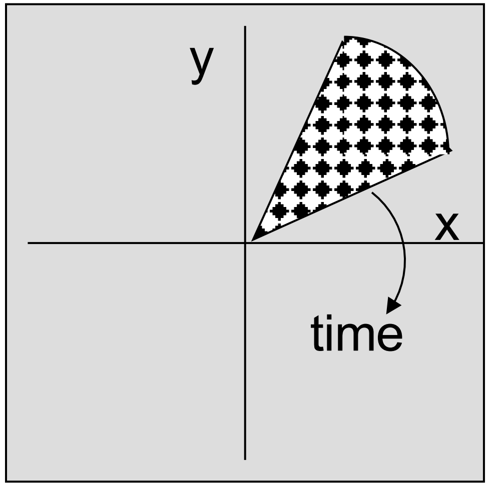
- Functional description
- Stimulus-referred

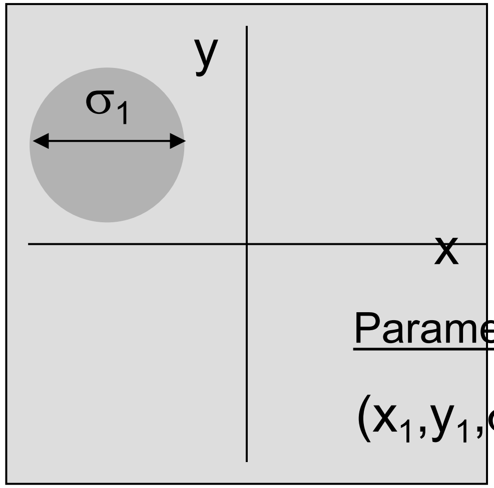
Population receptive field idea

Serge Dumoulin

- For each voxel, find a spatial receptive field that explains the fMRI measurement.
- The spatial RF model is the object of interest.
- Minimally, the model is linear in contrast and has an (x,y) location in the visual field and a spread
- More complex models are also being studied (e.g., CSS)

Stimulus

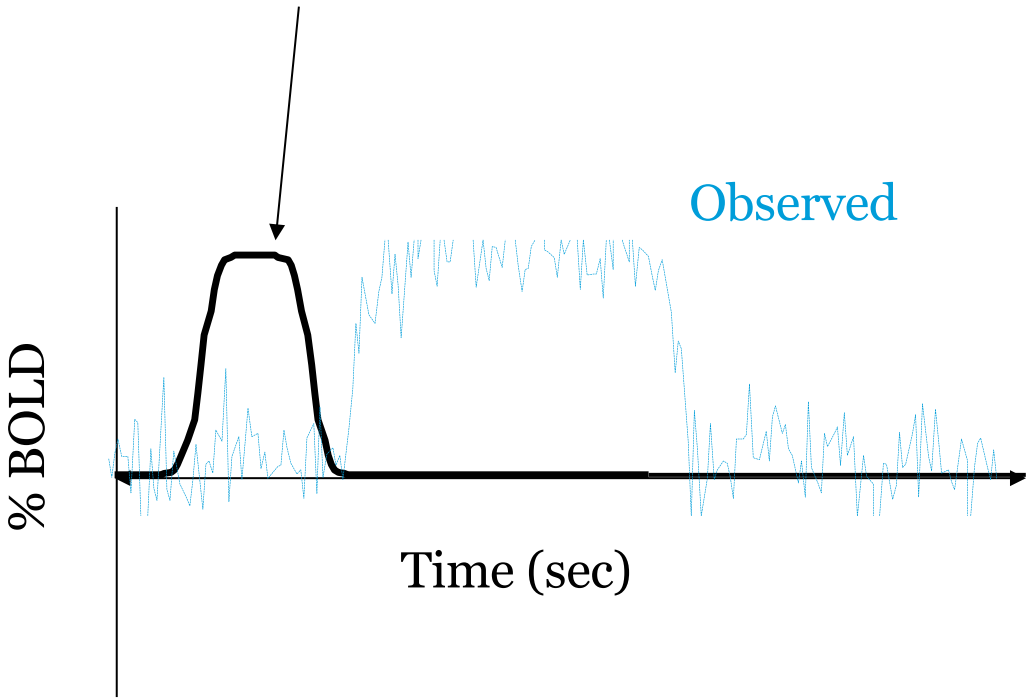




Parameters

(x_1, y_1, σ_1)

Predicted BOLD (including HRF)



Population receptive field idea

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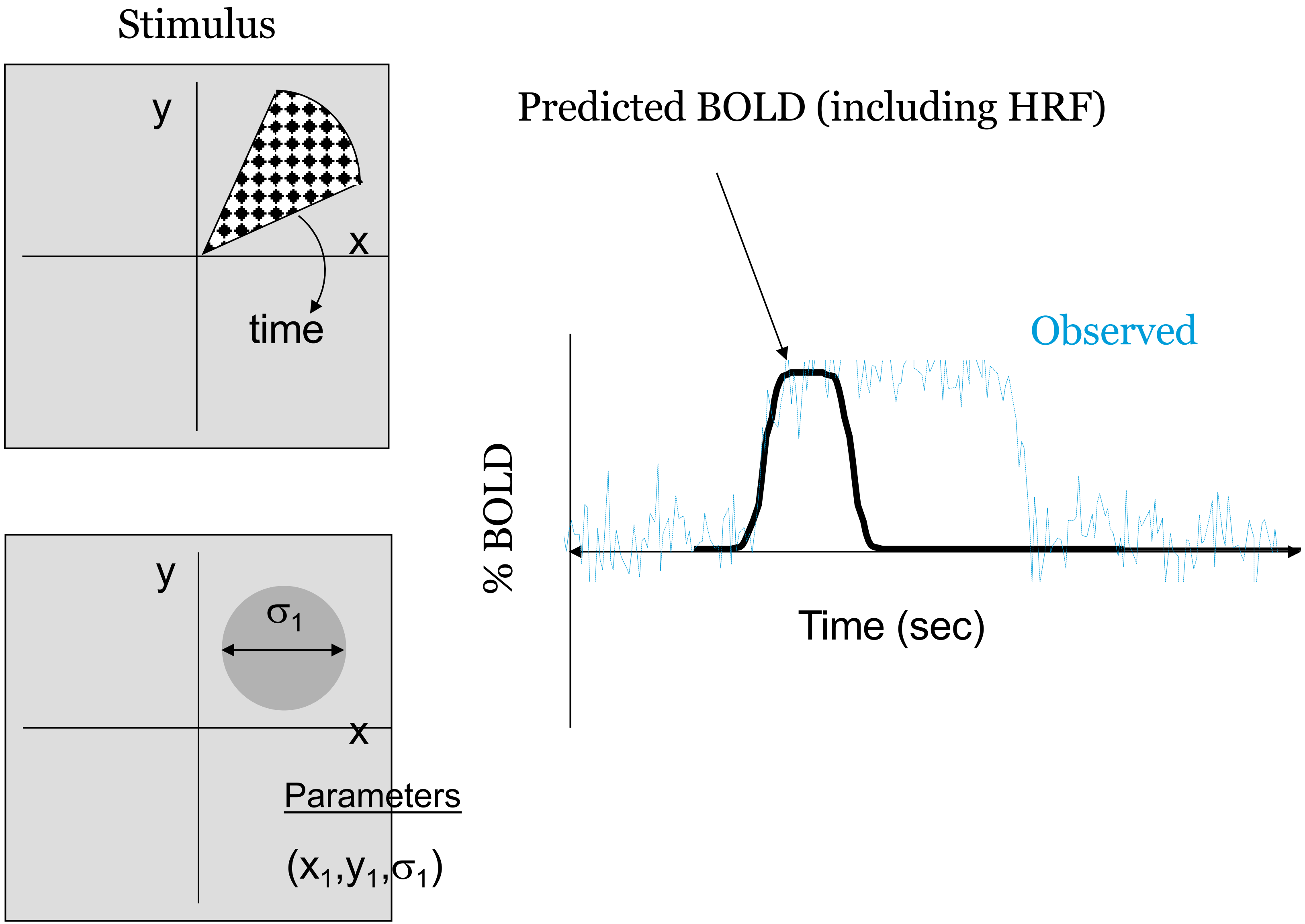

Population receptive field idea

Stimulus

- For each voxel, find a spatial receptive field that explains the fMRI measurement.
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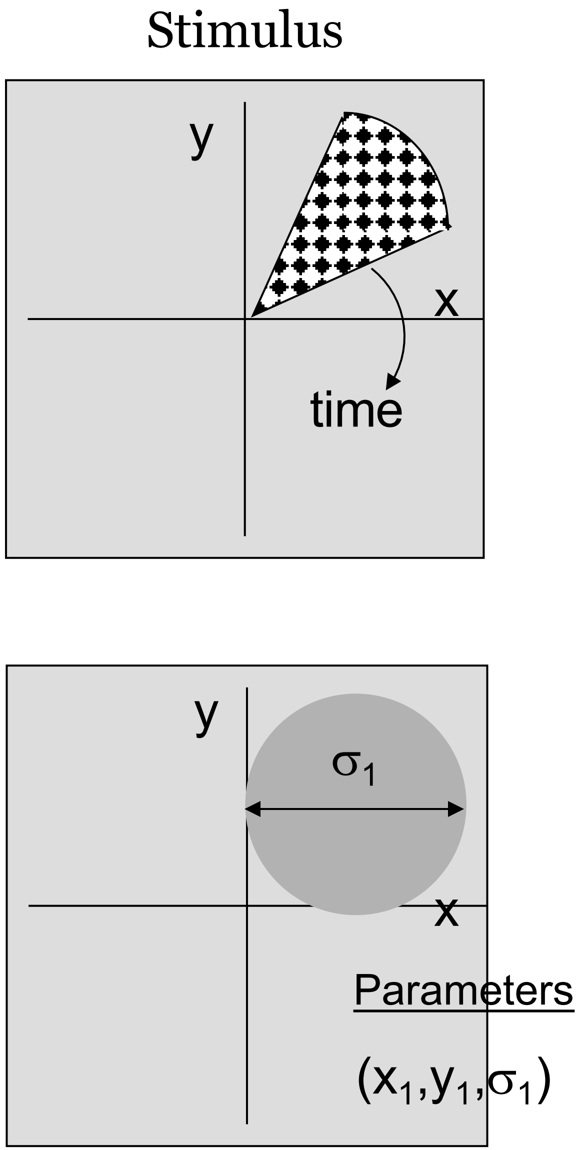
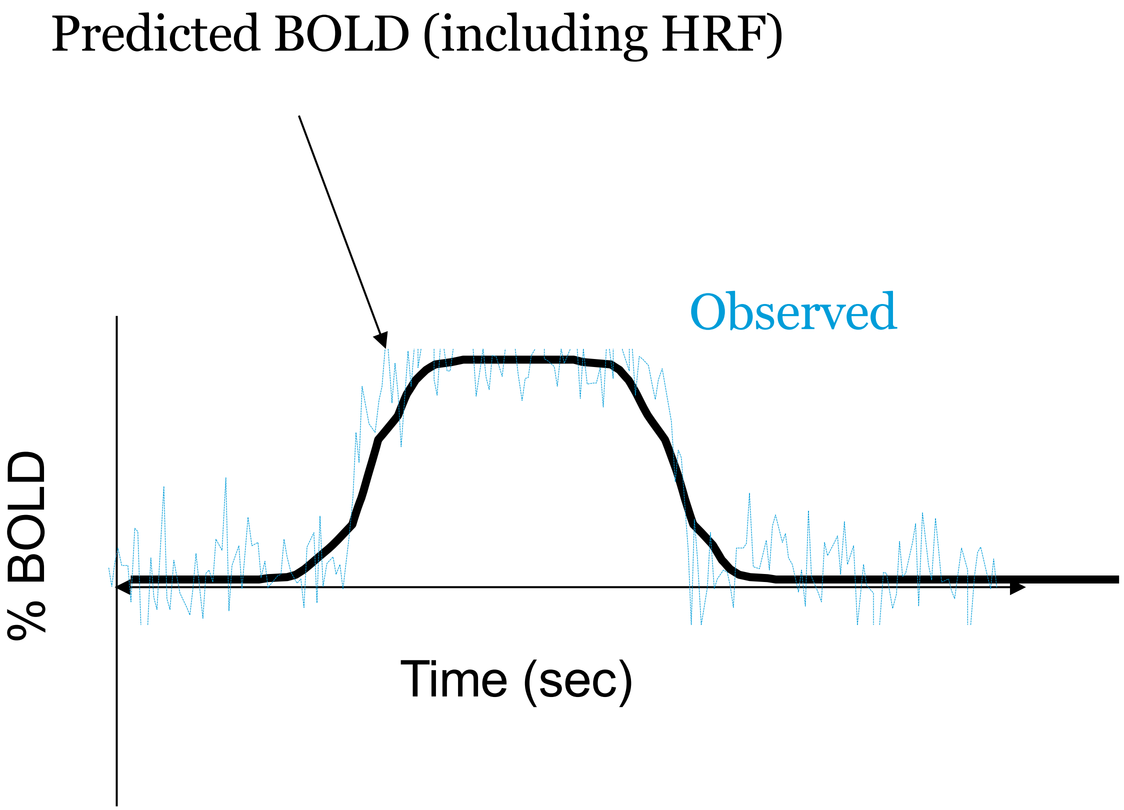
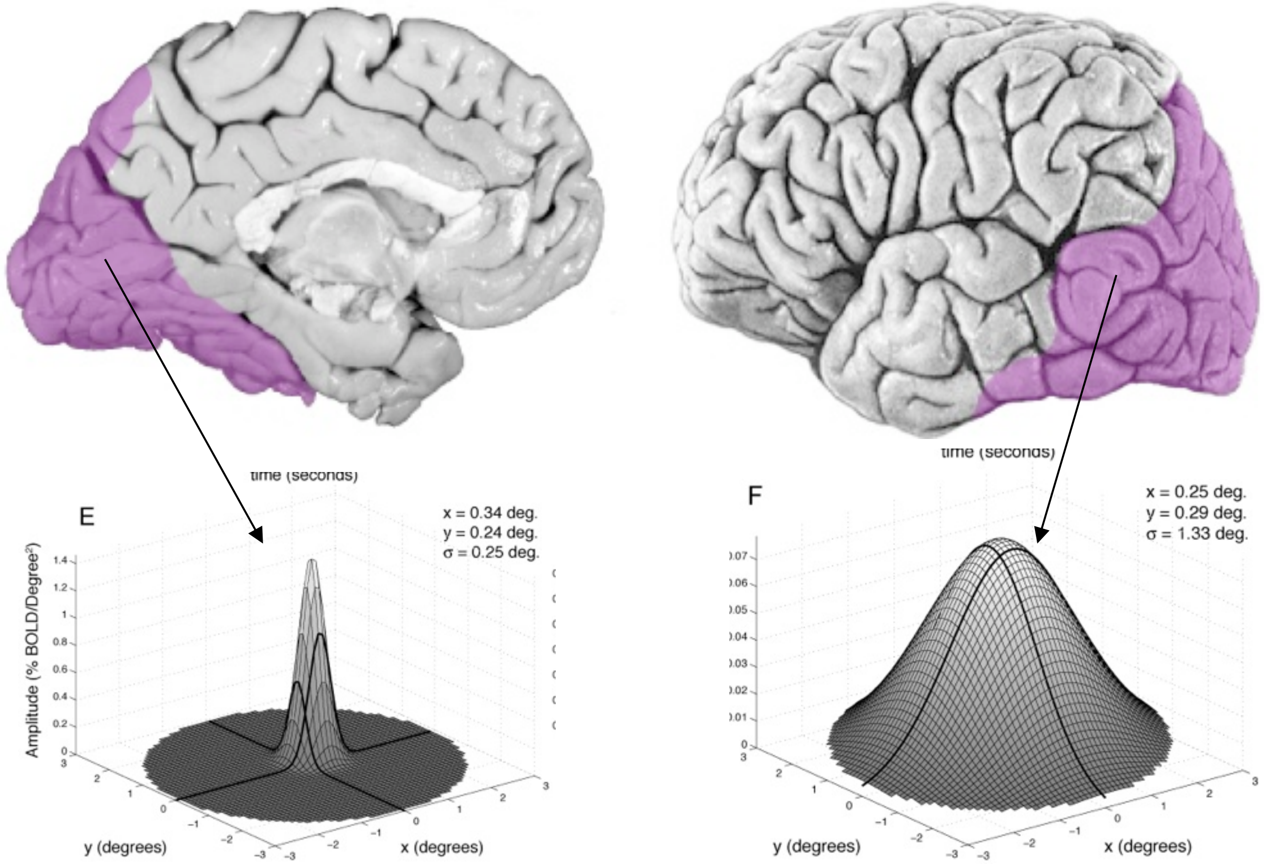


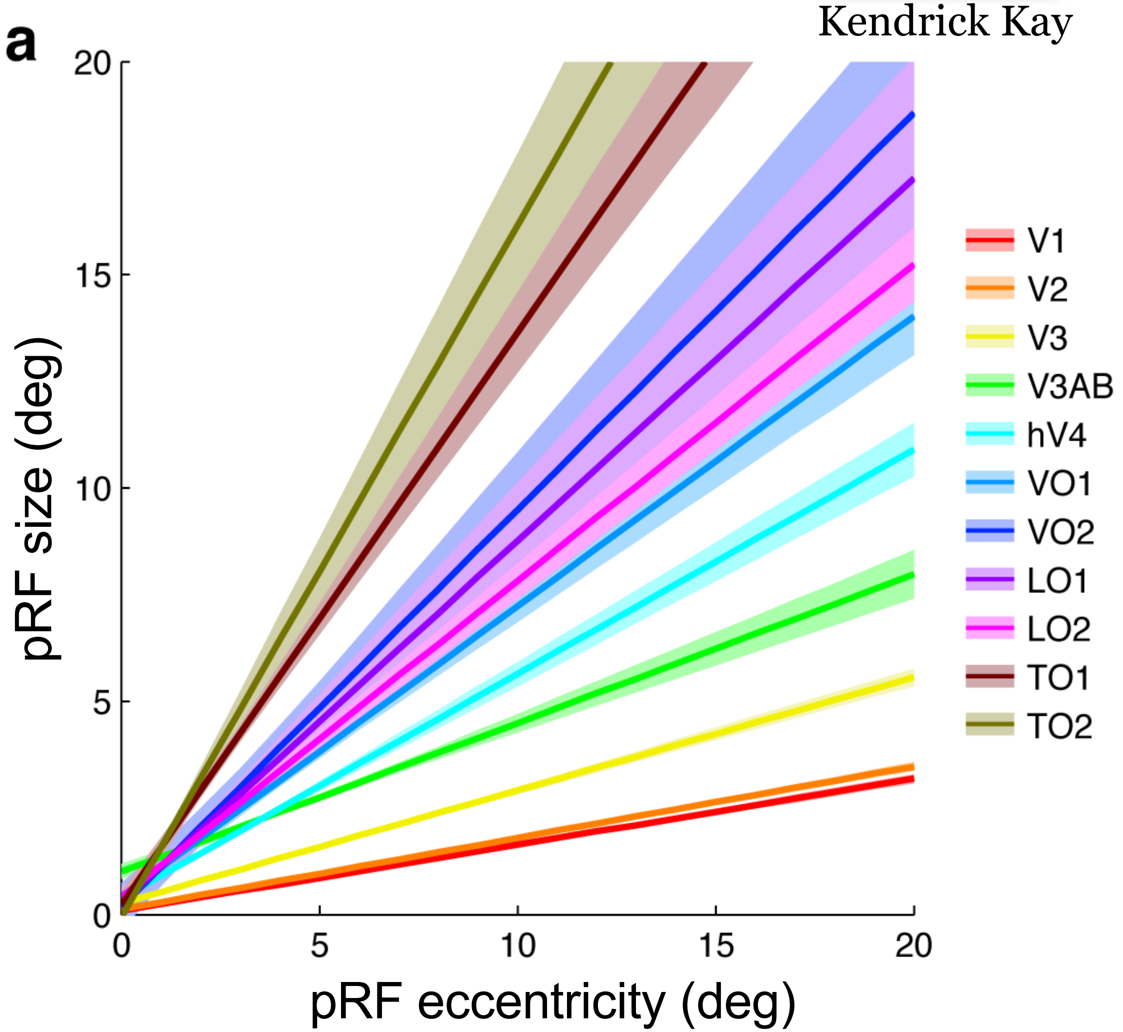


PRF size varies substantially and regularly across visual cortex

- At common eccentricities, different maps have different pRF sizes
- PRF size increases with eccentricity for all maps
- Bands are bootstrap estimates of the standard error

Kendrick Kay

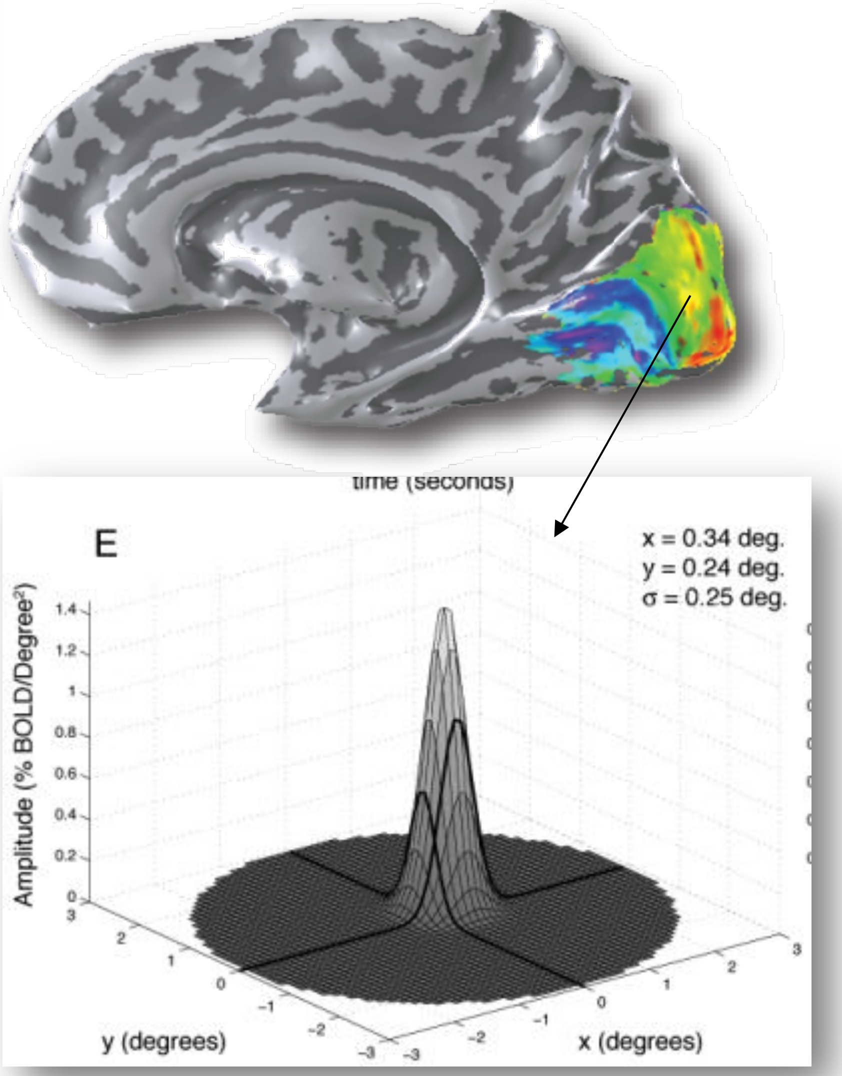




Advances in cortical mapping - the field of view

Amano et al. 2009

- A single voxel within, say V1, responds to a small part of the visual field and thus has a small **field of view**

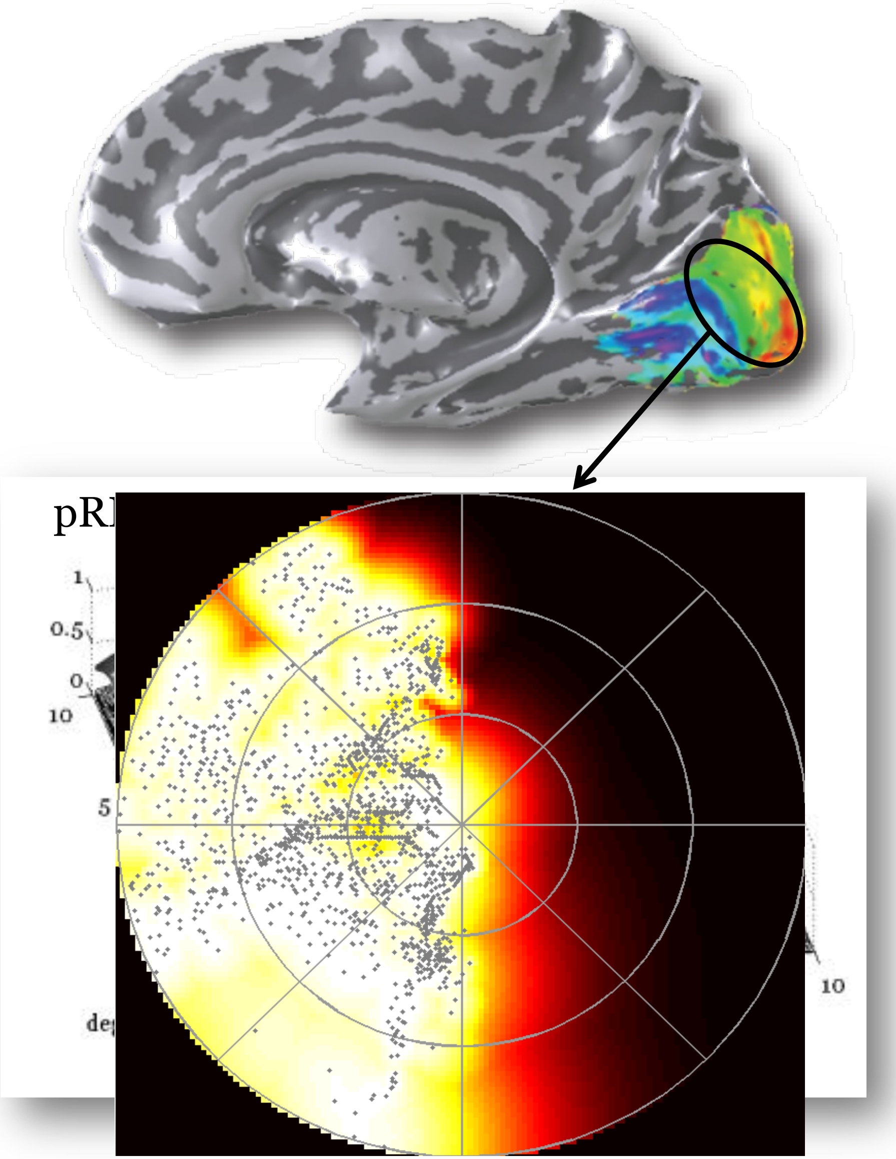


2. Advances in cortical mapping – the field of view of V1

Amano et al. 2009

- A single voxel within, say V1, responds to a small part of the visual field and thus has a small **field of view**

- Combining the pRFs from the voxels in a region, say all of V1, describes the region's field of view



Summary 3 – pRFs are widely used in individual subjects

- Attention
- Stability and Plasticity
- Prosopagnosia
- Development and aging
- Autism
- Alzheimer's disease

Trends in Cognitive Sciences, June 2015, Vol. 19, No. 6 349

Review

CellPress

Computational neuroimaging and population receptive fields

Brian A. Wandell[1] and Jonathan Winawer[2]

[1] Psychology Department and Neurosciences Institute, Stanford University, Stanford, CA, USA
[2] Psychology Department and Center for Neural Science, New York University, New York, NY, USA

Functional magnetic resonance imaging (fMRI) noninvasively measures human brain activity at millimeter resolution. Scientists use different approaches to take advantage of the remarkable opportunities presented by fMRI. Here, we describe progress using the computational neuroimaging approach in human visual cortex, which aims to build models that predict the neural responses from the stimulus and task. We focus on a particularly active area of research, the use of population receptive field (pRF) models to characterize human visual cortex responses to a range of stimuli, in a variety of tasks and different subject populations.

Understanding sensory circuits

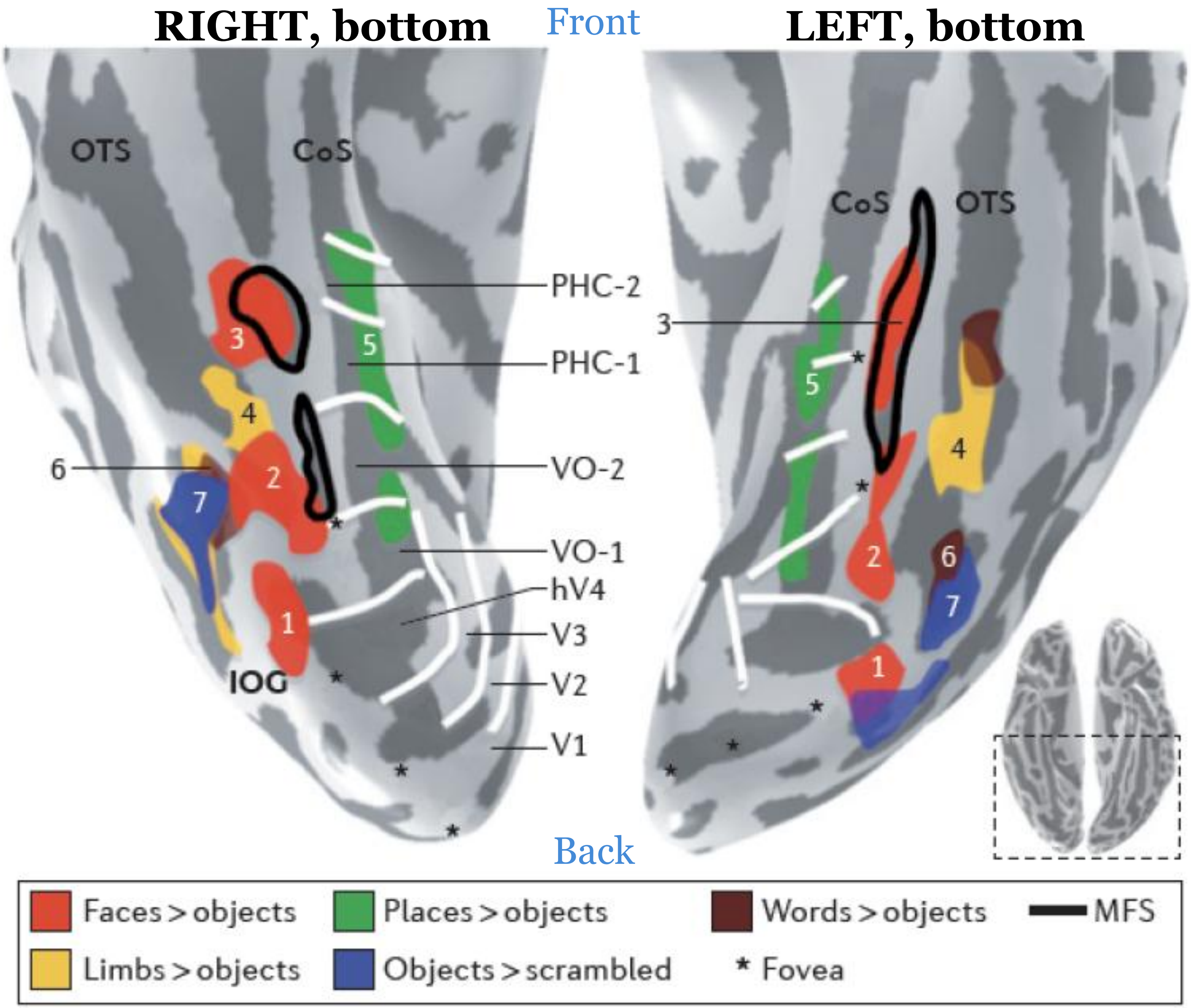
A mark of understanding a sensory system is the ability to predict how it will respond to stimulation. In the case of human visual cortex, we would like to accurately predict how each part of the system responds to any visual input. Such predictions are beyond current capabilities, but progress has

Receptive field models

For more than 75 years, visual neuroscientists have relied on the receptive field concept to make progress in the face of limited knowledge of the neural circuitry [3]. Sherrington [4] coined the phrase 'receptive field' to describe the region of skin from which a scratch reflex could be elicited: 'The "receptive field" may be conveniently applied to designate the total assemblage of receptive points whence by suitable stimuli a particular reflex movement can be evoked' ([4], p. 32). Hartline applied the concept to visual neurons [5]. Hartline's initial definition, similar to Sherrington's, emphasized the spatial extent of the receptive field: 'No description of the optic responses in single fibers would be complete without a description of the region of the retina which must be illuminated in order to obtain a response in any given fiber. This region will be termed the receptive field of the fiber' ([5], p. 410). Over the years, the receptive field concept has expanded to include stimulus features (e.g., orientation, motion, or contrast) and to be based on explicit

Advances in cortical mapping: functional specializations

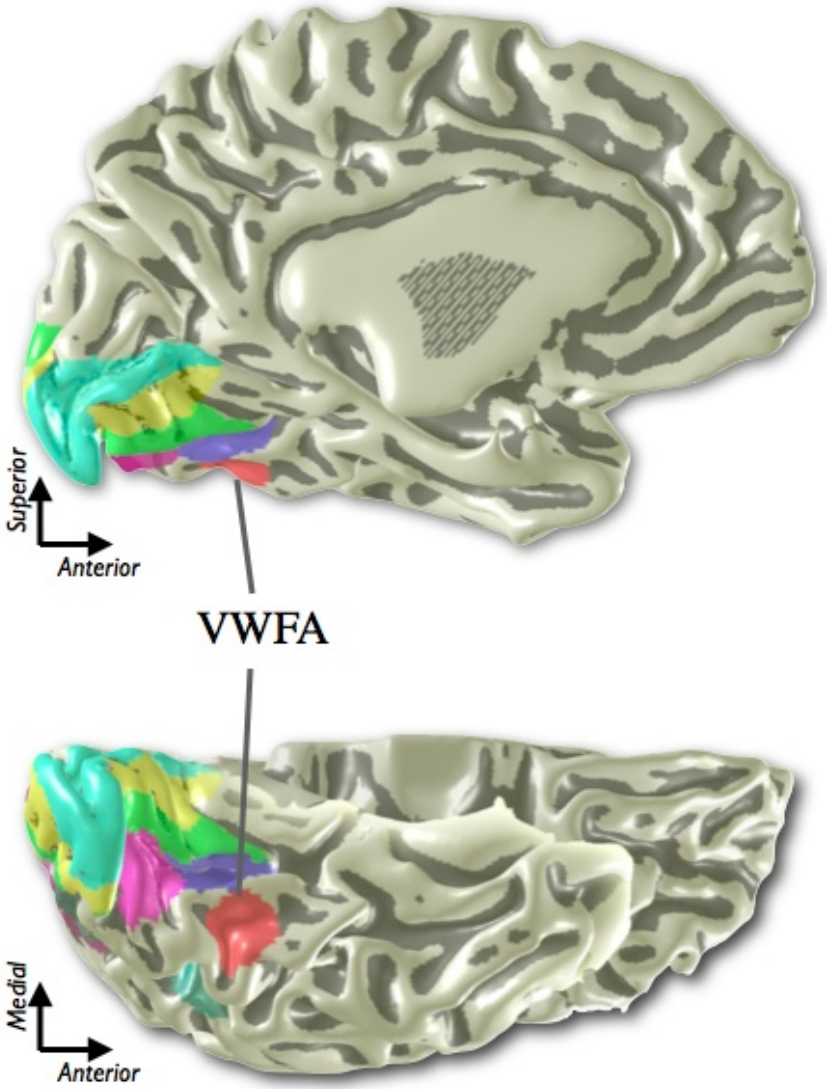
- Ventral occipito-temporal cortex (VOTC), near the visual field maps, contains several specialized processing regions
- Each region responds better to some class of stimuli than others (functional specialization)
- The visual word form area (VWFA) is one of these specializations



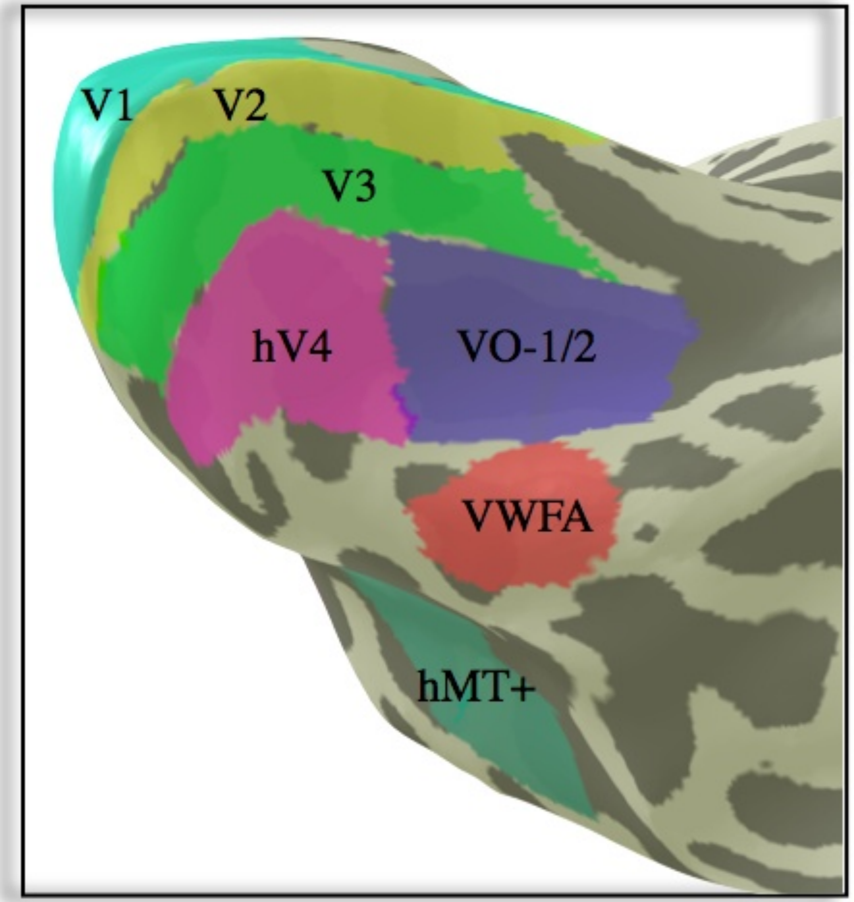
Grill-Spector and Weiner
Nature Reviews Neuroscience, 2014

Locating reading circuits and maps

Andreas Rauschecker



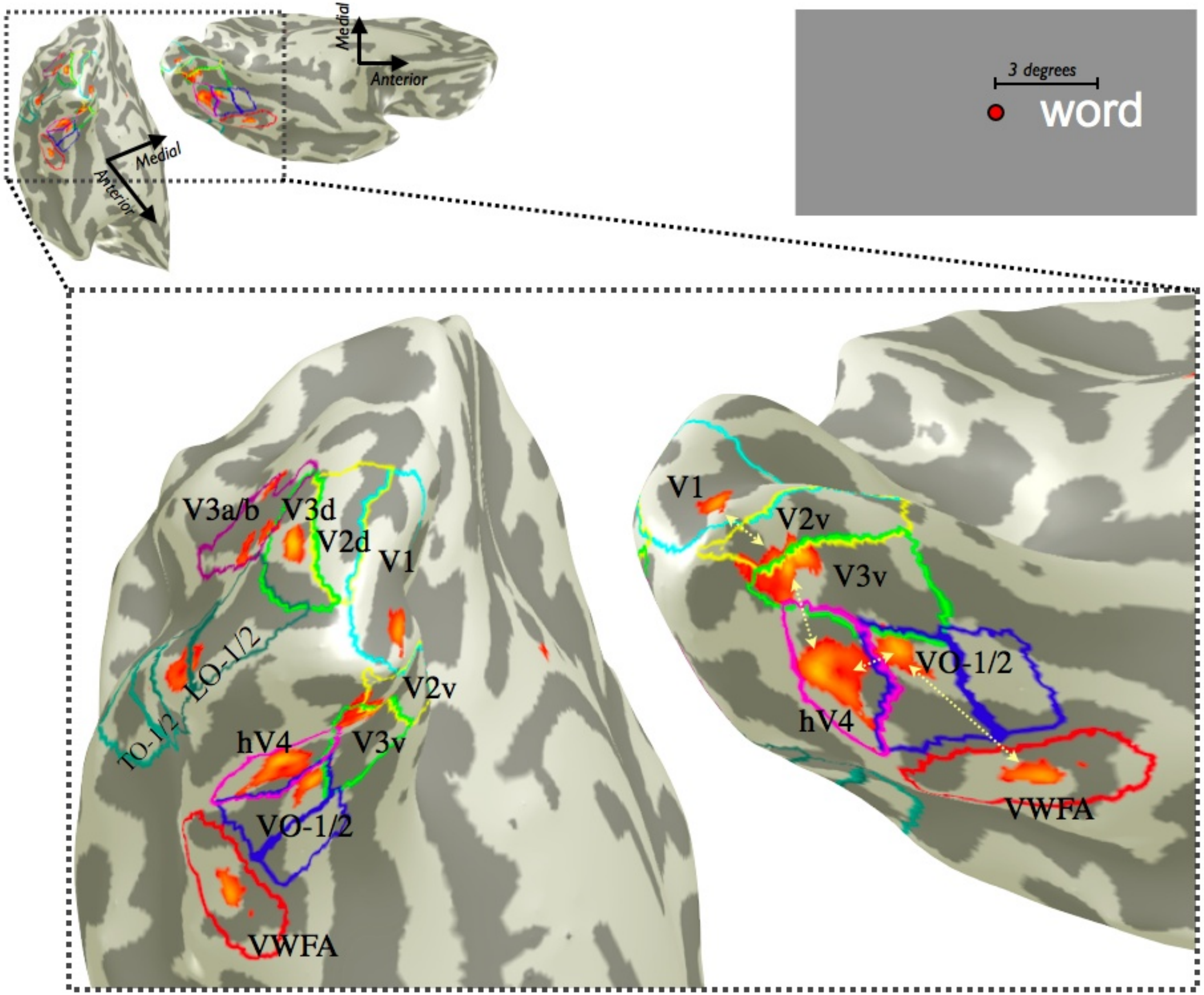
VWFA - essential for reading, but not unique to reading



Measuring the activity while reading (fMRI)

- We can see the locations of the cortical activations during reading

- Through the maps and on to the VWFA



Field of view in reading circuitry of a single subject

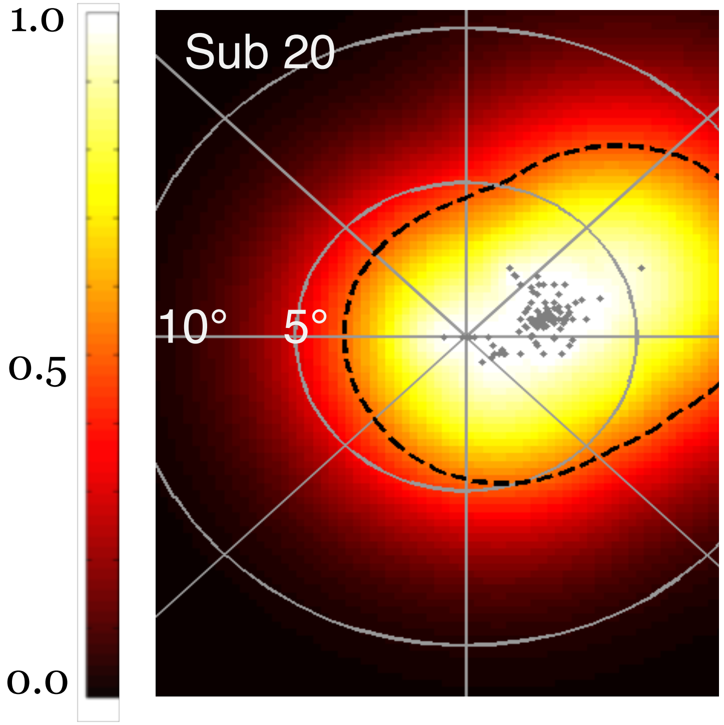
Kaoru Amano

- Using these methods, we have learned that the portion of cortex engaged in reading only sees a small part of the visual field – it has **a small field of view**
- We can measure these in individual participants
- Note words as contrast

Bottom, left

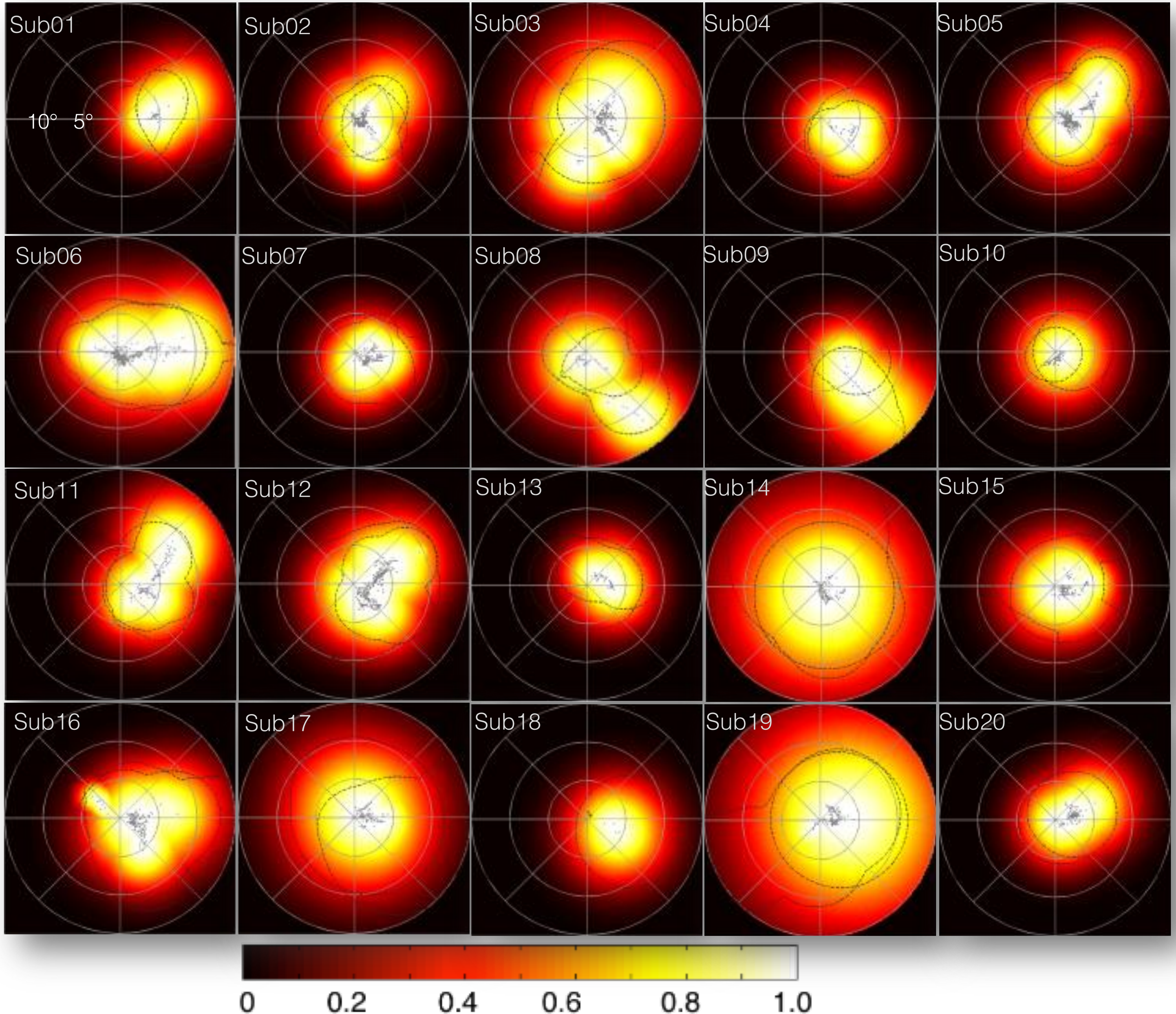
Measure the VWFA region

Sub 20



2a. Advances in cortical mapping –VWFA field of view in different subjects

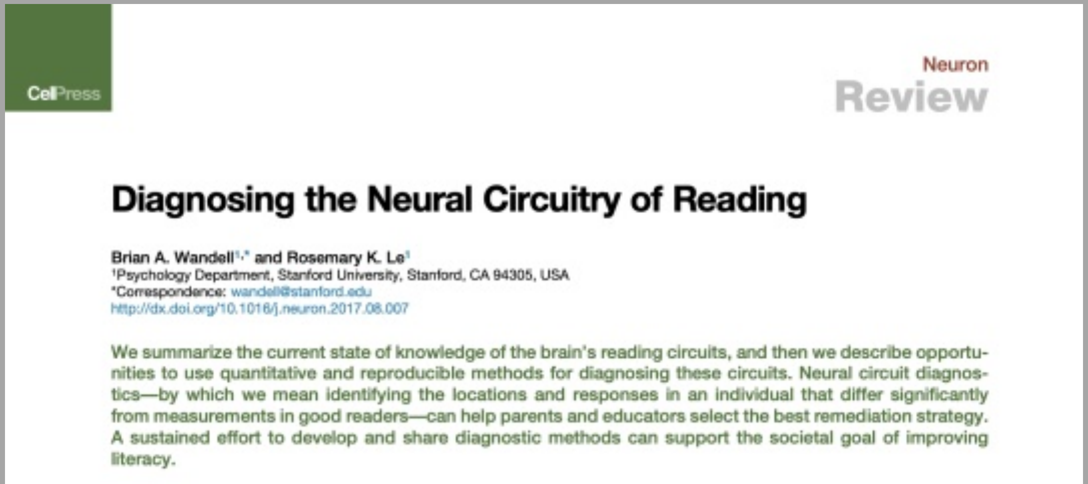
- There are significant differences between participants
- We will correlate these differences with measures of word recognition and eye movement patterns



Left hemisphere only

Summary 2: Advances in cortical mapping

Portions of the visual circuitry for seeing words can be identified. Certain functional responses, such as the field of view, can be reliably estimated in single subjects. These quantitative measures might help diagnose part of the reading circuitry.


CellPress

Neuron
Review

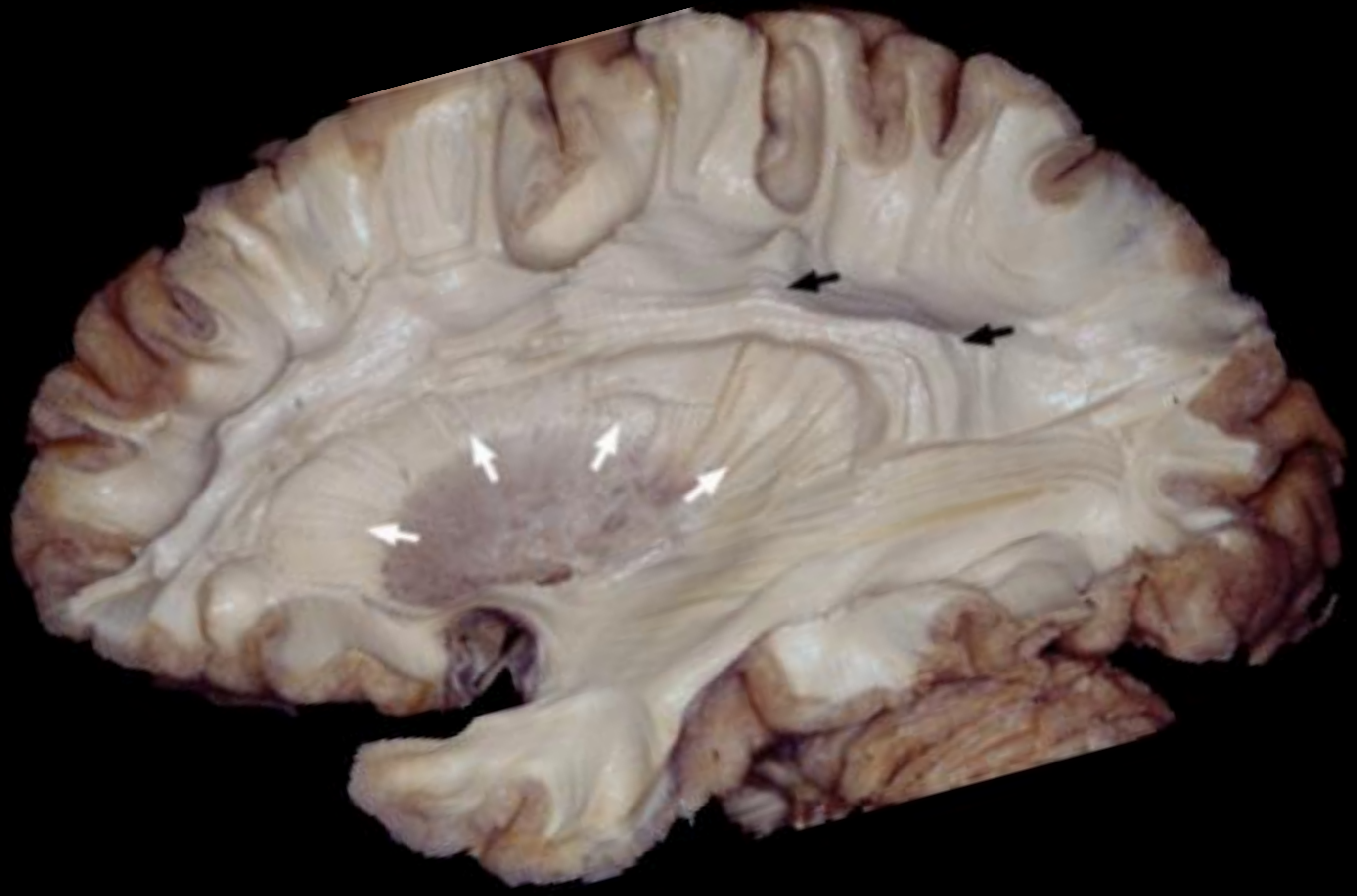
Diagnosing the Neural Circuitry of Reading

Brian A. Wandell[1,*] and Rosemary K. Le[1]
[1]Psychology Department, Stanford University, Stanford, CA 94305, USA
*Correspondence: wandell@stanford.edu
http://dx.doi.org/10.1016/j.neuron.2017.08.007

We summarize the current state of knowledge of the brain's reading circuits, and then we describe opportunities to use quantitative and reproducible methods for diagnosing these circuits. Neural circuit diagnostics—by which we mean identifying the locations and responses in an individual that differ significantly from measurements in good readers—can help parents and educators select the best remediation strategy. A sustained effort to develop and share diagnostic methods can support the societal goal of improving literacy.

Connections between brain regions

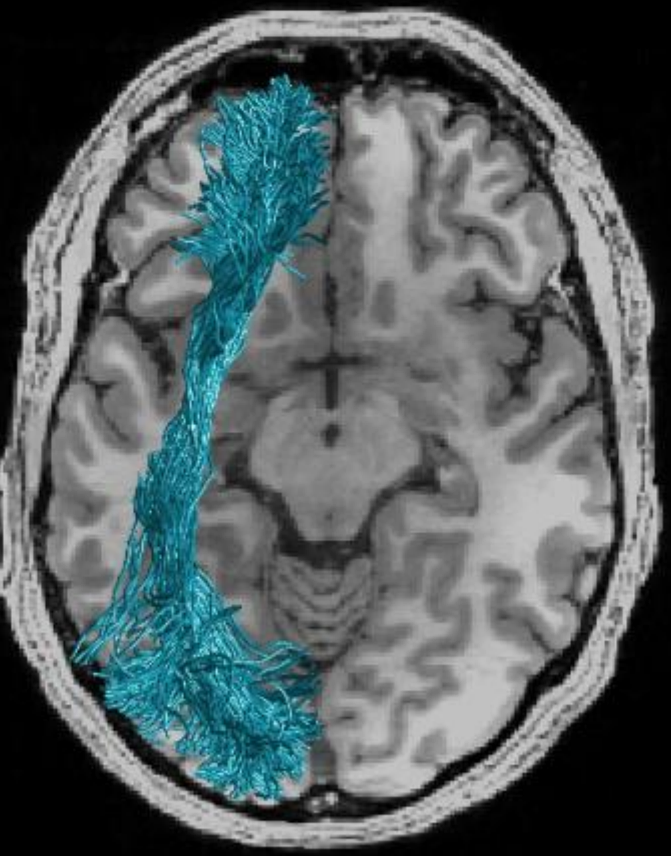
- There are many long-range connections
- These connections are not passive – they change their properties in response to use
- A system with active wires



Courtesy Professor Ugur Ture

Connections between brain regions - tracts

Left
IFOF



150 Directions, 2 mm^3, B=2000 projected on a 1 mm^3 T1 anatomical image

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NATURE METHODS | ARTICLE

Evaluation and statistical inference for human connectomes

Franco Pestilli, Jason D Yeatman, Ariel Rokem, Kendrick N Kay & Brian A Wandell

Introduction to LiFE

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RESEARCH ARTICLE

Ensemble Tractography

Hiromasa Takemura, Cesar F. Caiafa, Brian A. Wandell, Franco Pestilli

Published: February 4, 2016 • http://dx.doi.org/10.1371/journal.pcbi.1004692

Extension to ensemble method

Annual Review of Neuroscience
Vol. 39: 103-128 (Volume publication date July 2016)

Clarifying Human White Matter

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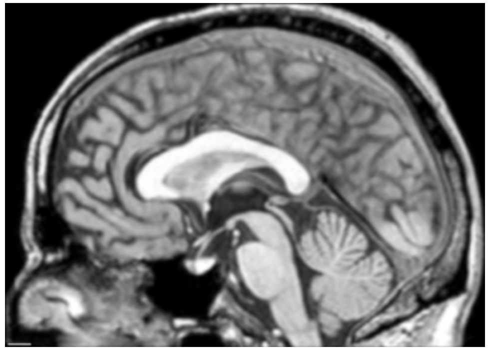
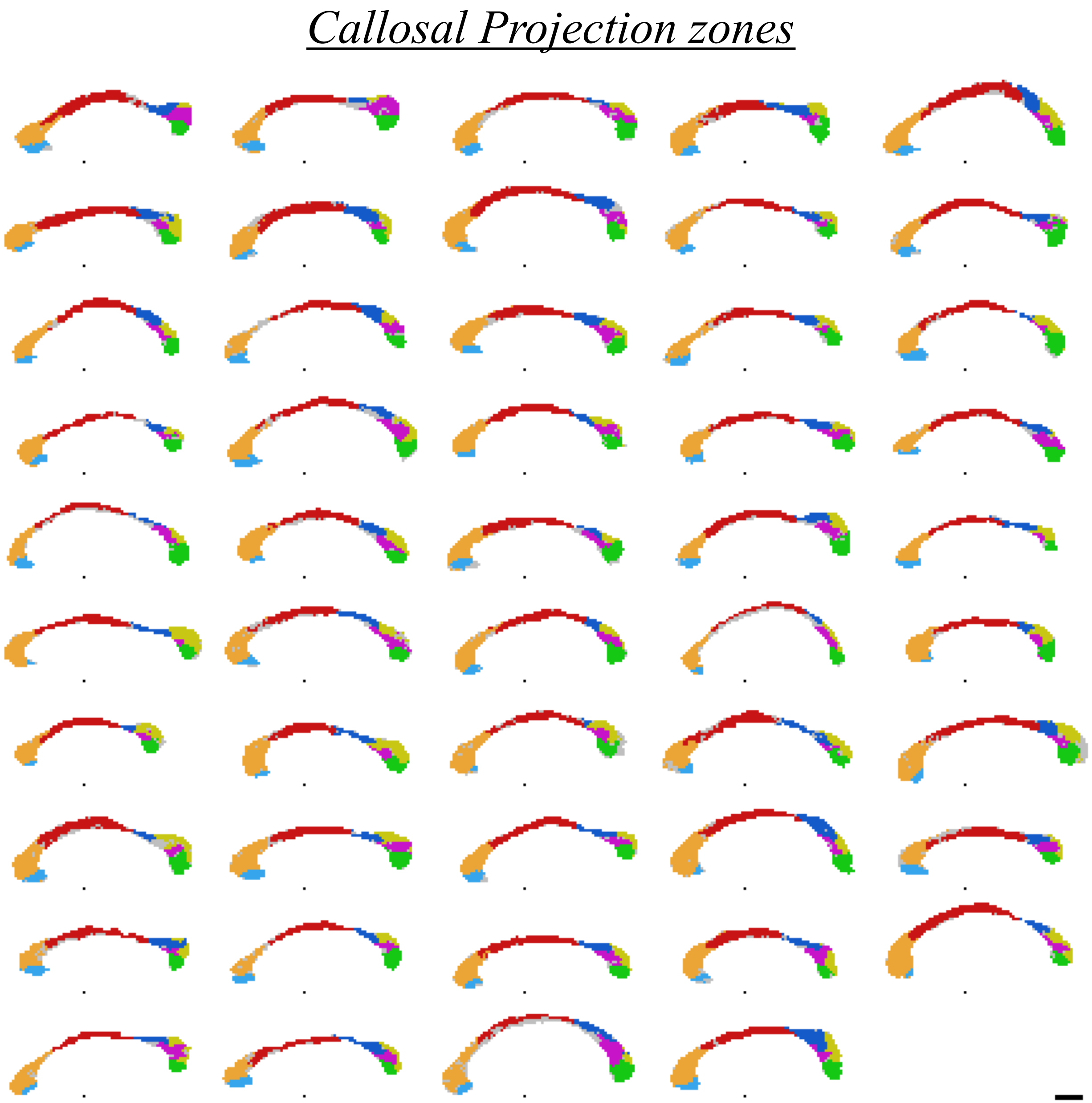
Review of diffusion imaging

Callosal shapes differ significantly – projection based segmentation

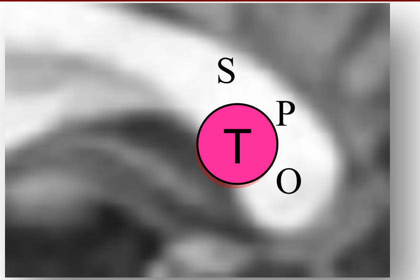
- We subdivide the corpus callosum into distinct regions that depend on where the tracts project

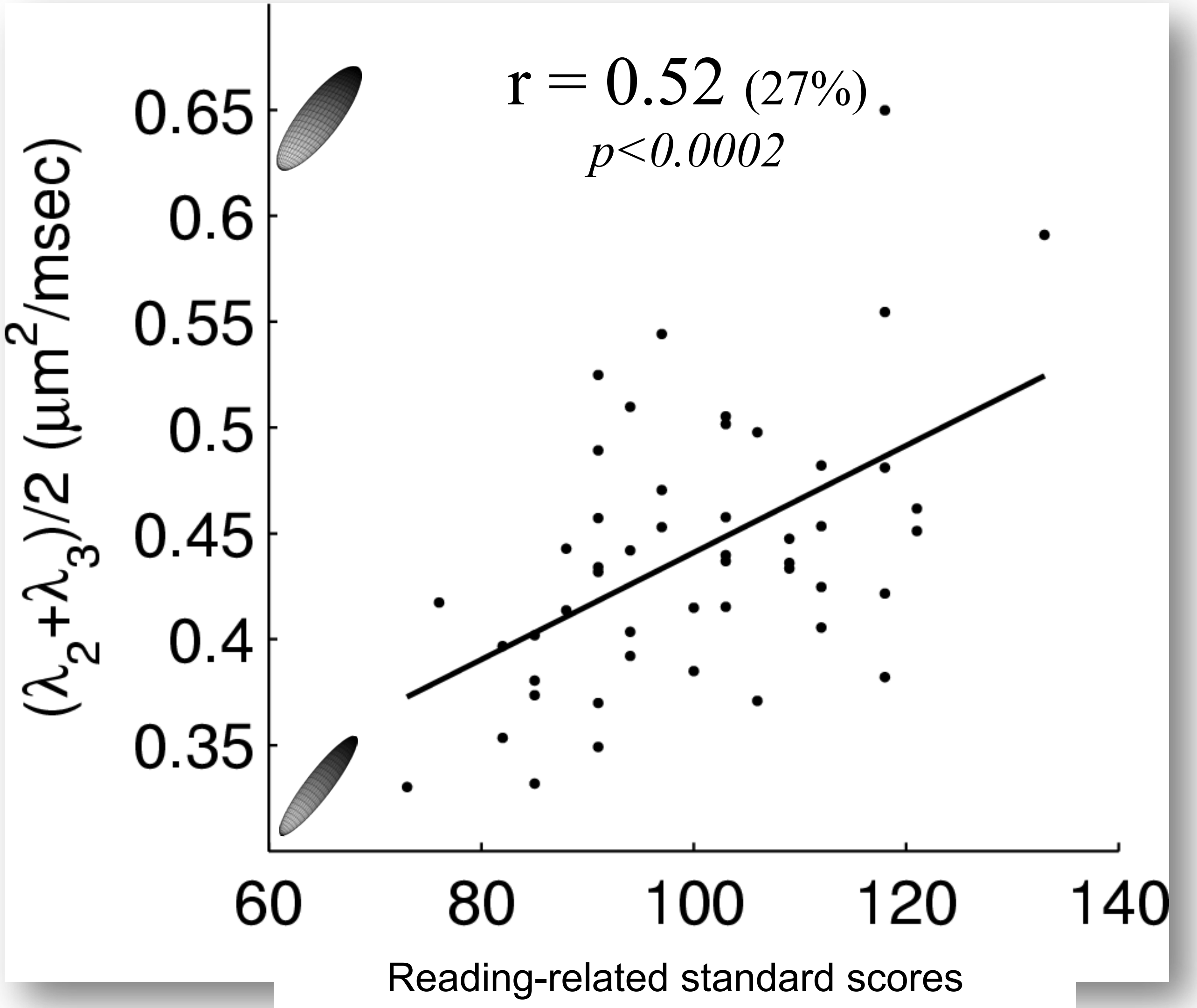
- Each subject is different





Radial diffusivity in callosal temporal lobe projections correlates with sounding out words





Bob Dougherty

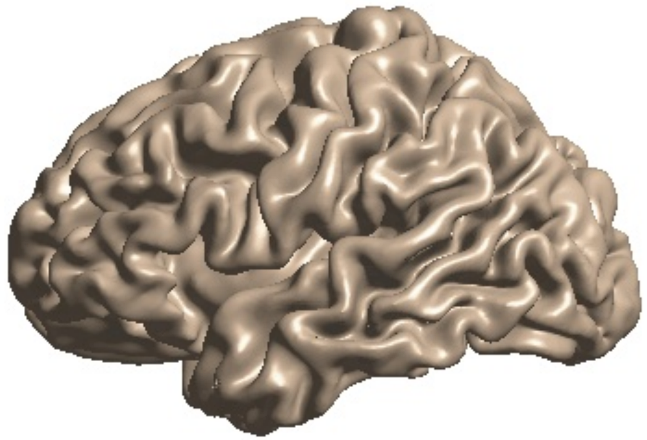
Michal Ben-Shachar

- Callosal tracts that project to the temporal lobe correlate with reading scores

Replications

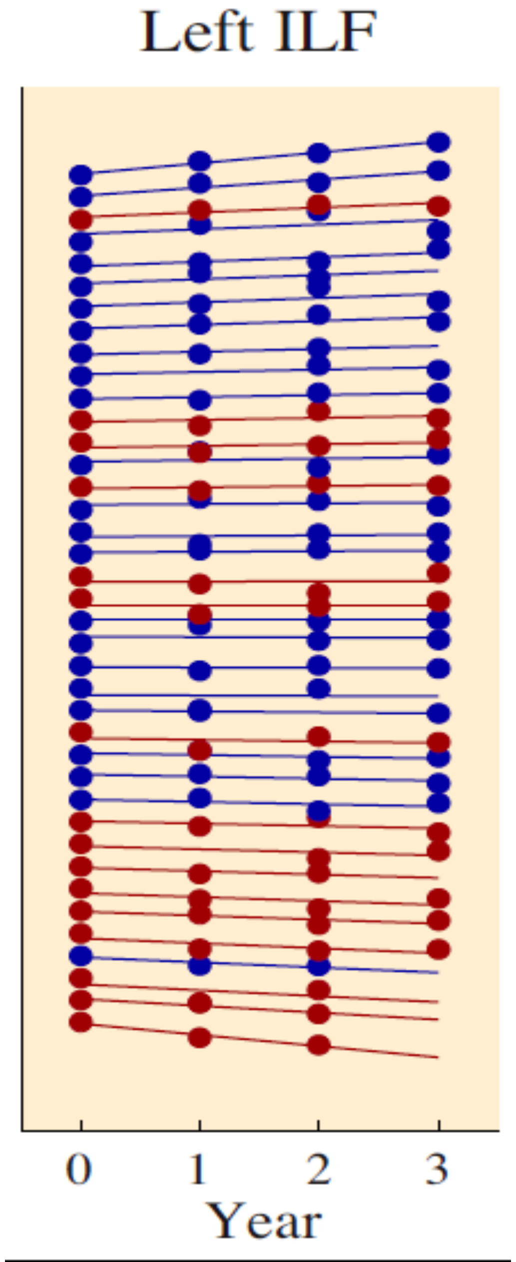
Dougherty et al., PNAS, (2007)
Odegard et al. (2009)
Frye et al. (2009)

2b. Connections between regions – good and poor readers develop differently



- Measured brain and behavior at 4 time points **(data management!)**
- The first measurements predict reading over the next few years
- The rate and direction of FA development differs between good and poor readers in the Arcuate and the ILF

- Fractional anisotropy (FA)
- Displaced vertically for each participant
- Ordered by slope
- Colored by reading score



Jason Yeatman

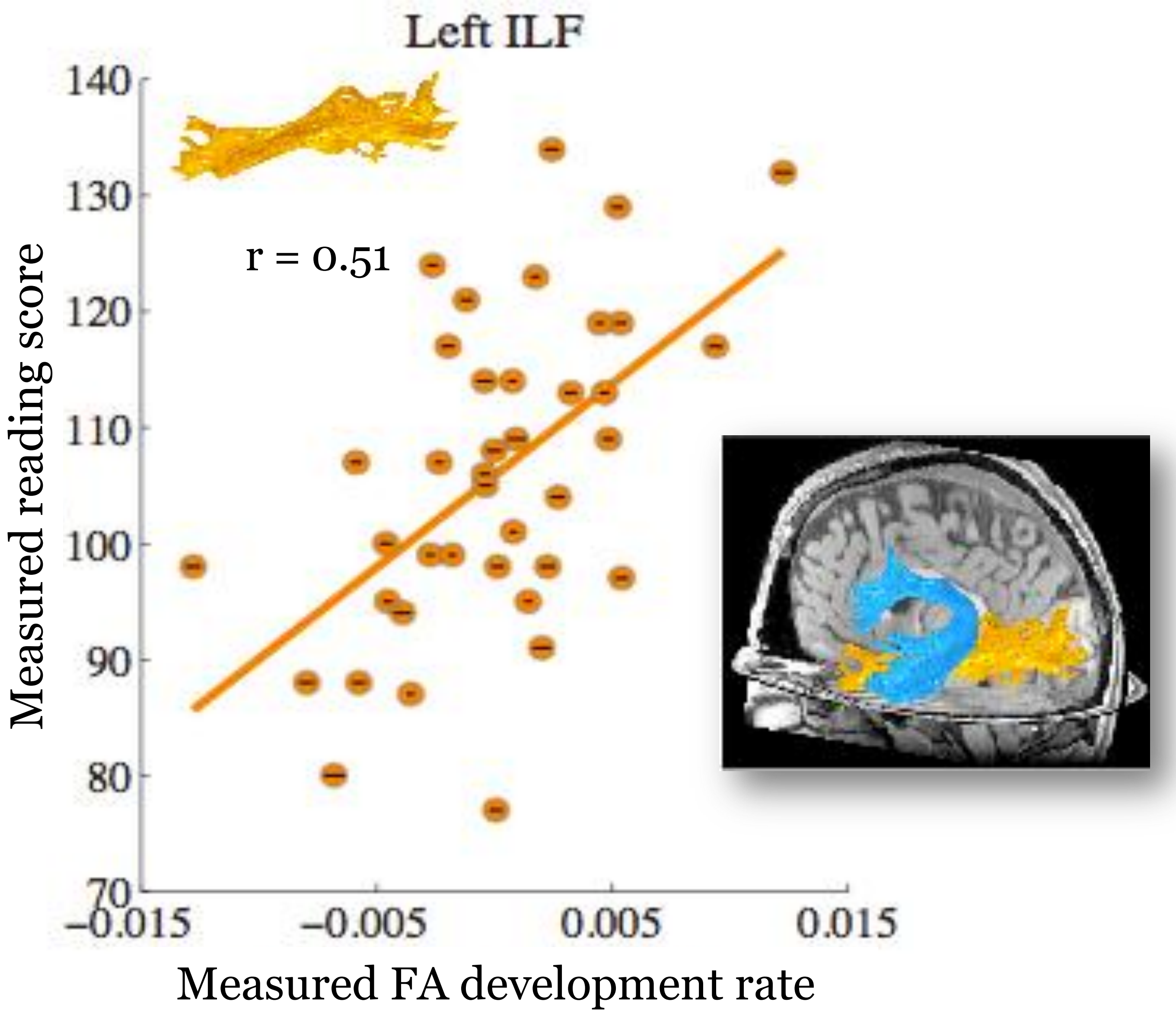
Blue: Good readers
Red: Poor readers

Connections between regions – good and poor readers develop differently

(Yeatman et al., 2012, *PNAS*)

- Development measured by dMRI in the ILF and Arcuate, but not others tracts, correlates with the ability to rapidly see words

- This is one reason we think that the wires are active, changing in response to learning and memory



Automated Fiber Quantification

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RESEARCH ARTICLE

Tract Profiles of White Matter Properties: Automating Fiber-Tract Quantification

Jason D. Yeatman, Robert F. Dougherty, Nathaniel J. Myall, Brian A. Wandell, Heidi M. Feldman

Published: November 14, 2012 • https://doi.org/10.1371/journal.pone.0049790

yeatmanlab / AFQ

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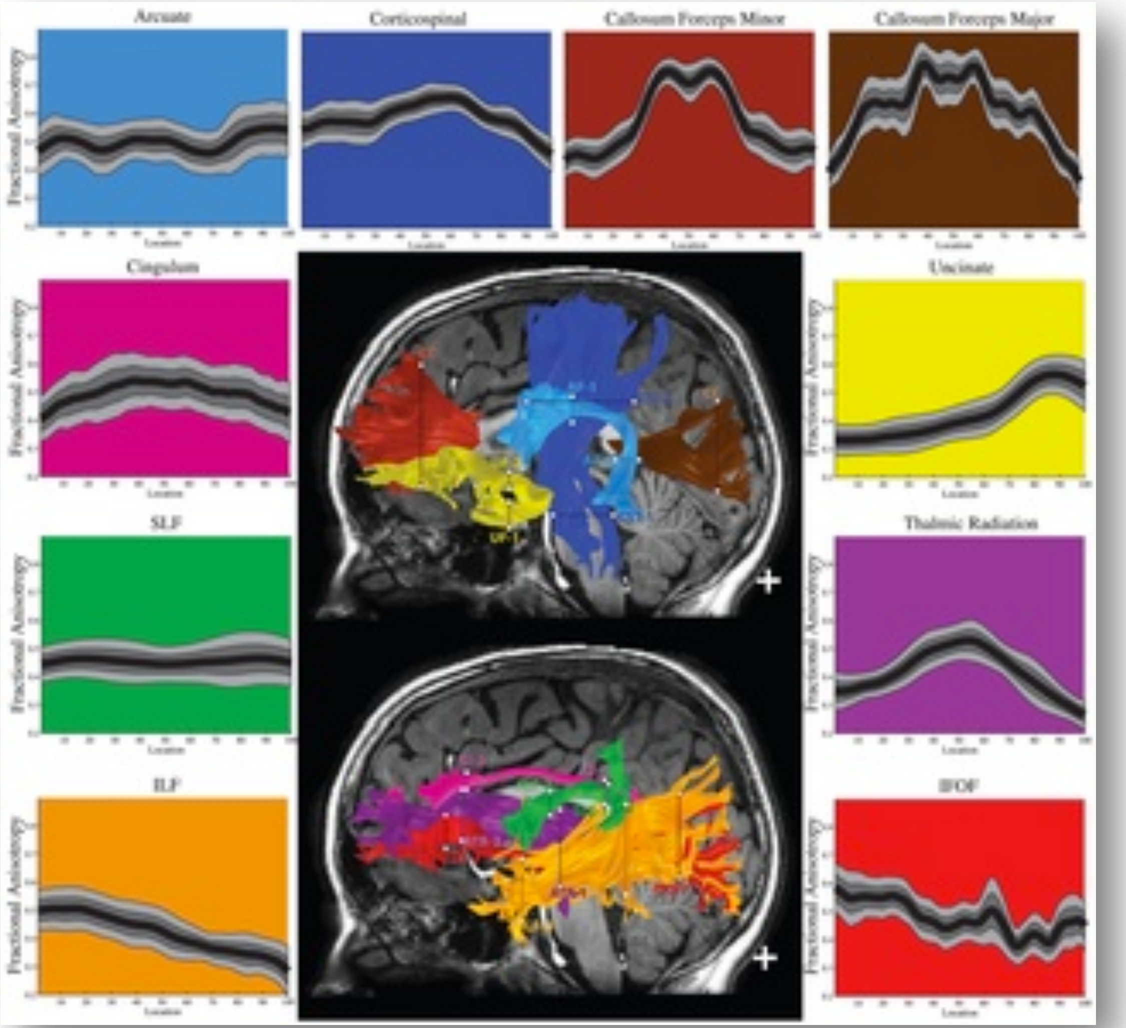
Jason D. Yeatman edited this page on May 9, 2017 · 34 revisions

Automated fiber quantification (AFQ)

AFQ automatically identifies the core of major fiber tracts and quantifies the tissue properties in the voxels near the tract cores. The analysis produces a set of "Tract Profiles" that measure the tissue property at sample positions from the start to the end of the tract core. There is one profile for each tract and tissue property combination. The tract profiles have been used to characterize white matter properties in healthy brains or quantify abnormalities in diseased brains. Through the use of neuroinformatics tools, we can automatically identify abnormalities in the profiles of an individual.

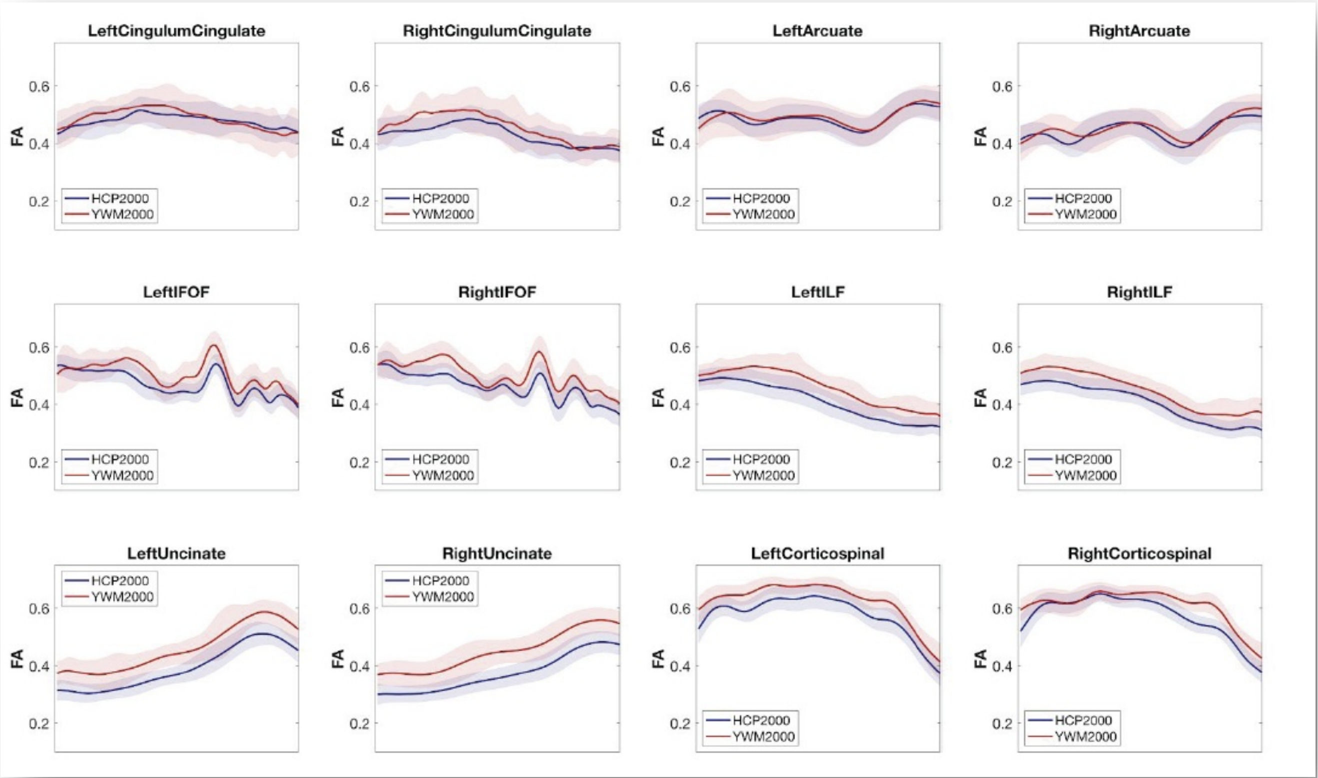
AFQ is described in

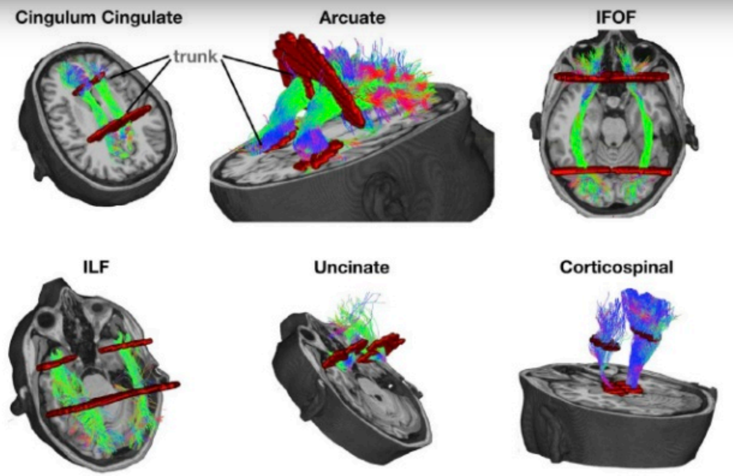
> Yeatman JD, Dougherty RF, Myall NJ, Wandell BA, Feldman HM (2012) Tract Profiles of White Matter Properties: Automating Fiber-Tract Quantification. PLoS ONE 7(11): e49790. doi:10.1371/journal.pone.0049790



Translating tools from lab to clinic

- Extending single subject diagnosis to tractography
- Comparisons across sites
- Work in progress with Lerma-Usabiaga, Mukherjee and others





NeuroImage

Replication and generalization in applied neuroimaging

Garikoitz Lerma-Usabiaga [a,b,*], Pratik Mukherjee [c,d], Zhimei Ren [e], Michael L. Perry [a], Brian A. Wandell [a]

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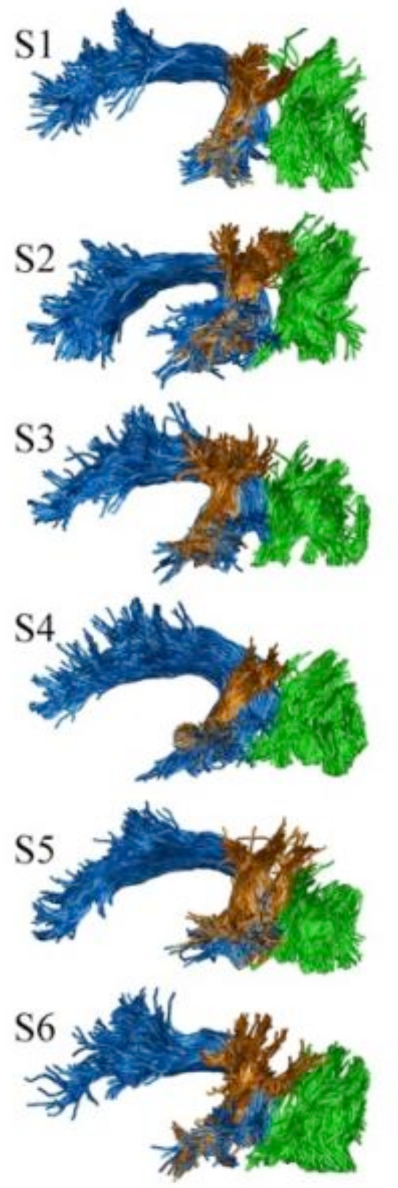
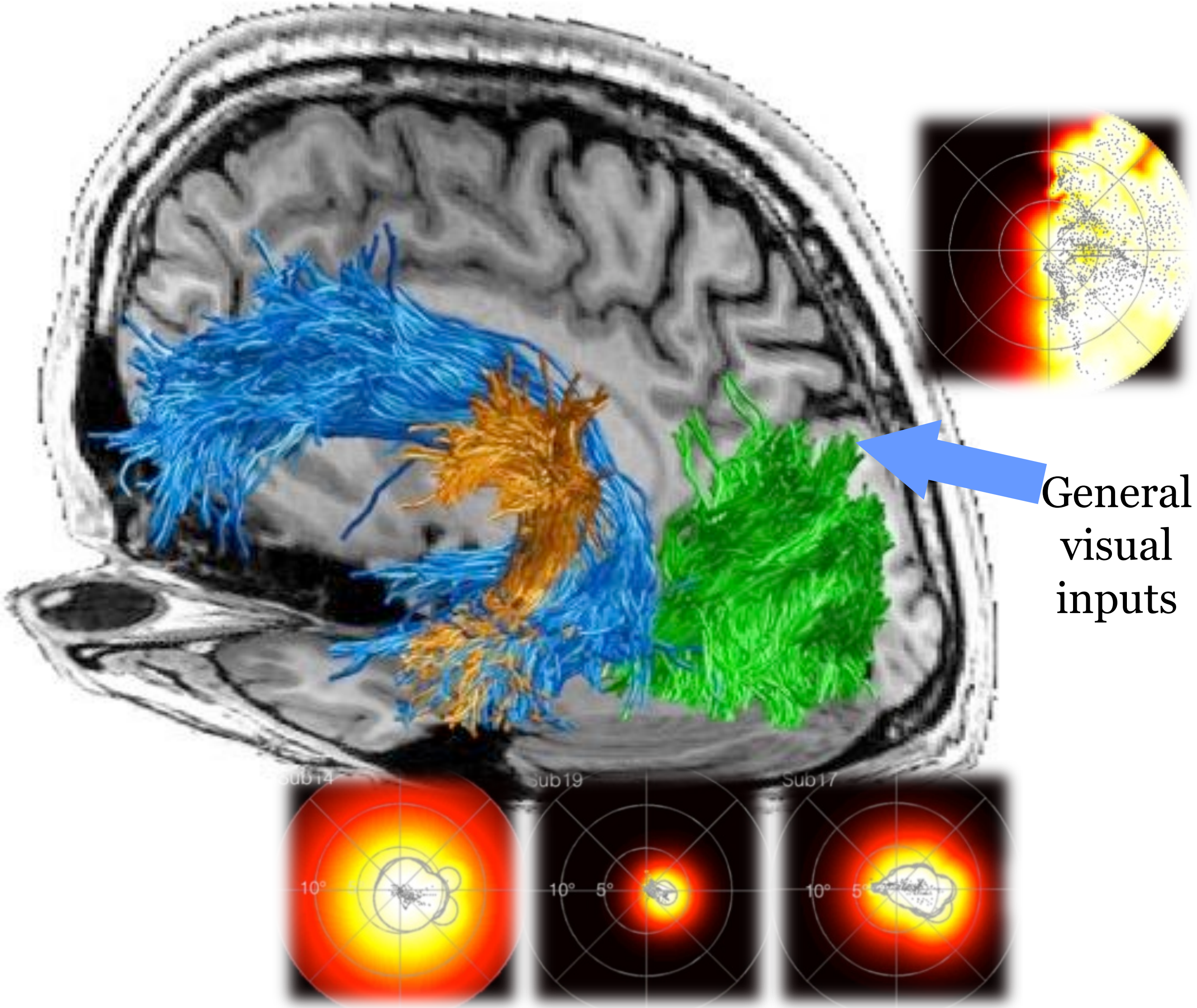
Connections between regions – can this difference be a factor in poor reading





Hiromasa Takemura

Summary 3: Advances in cortical mapping

Portions of the visual circuitry for seeing words can be identified. Certain anatomical properties, such as tract diffusivity and qMRI measures, can be reliably estimated in single subjects. These quantitative measures might help diagnose part of the reading circuitry.

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Current Opinion in Neurobiology

Biological development of reading circuits

Brian A Wandell and Jason D Yeatman

Human neuroimaging is expanding our understanding of the biological processes that are essential for healthy brain function. Methods such as diffusion weighted imaging provide insights into white matter fascicles, growth and pruning of dendritic arbors and axons, and properties of glia. This review focuses on what we have learned from diffusion imaging about these processes and the development of reading circuitry in the human brain. Understanding reading circuitry development may suggest ways to improve how we teach children to read.

Given the expanded opportunity to measure such processes, what might be learned from these measurements? Some behaviors, such as psychological tests of performance during brief trials, may be best understood by measuring synaptic activity or spikes. But other important behaviors, such as learning to read, acquiring a second language, or learning to regulate emotions, take place over longer time periods and may depend on biological processes such as cell development, growth and pruning of dendritic arbors, the proliferation and activity of glia

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Full text provided by www.sciencedirect.com
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White matter pathways in reading

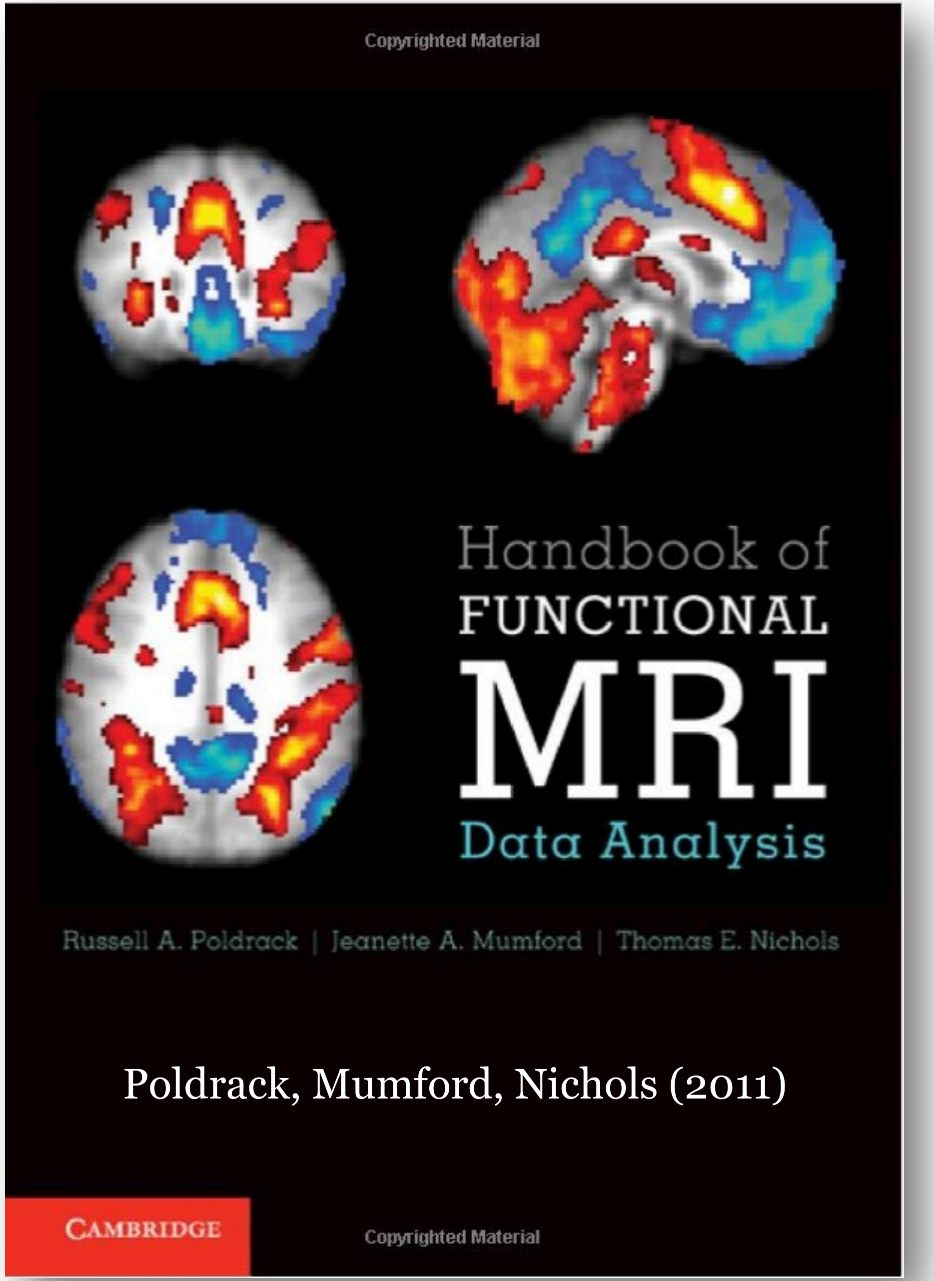
Michal Ben-Shachar, Robert F Dougherty and Brian A Wandell

Skilled reading requires mapping of visual text to sound and meaning. Because reading relies on neural systems spread across the brain, a full understanding of this cognitive ability involves the identification of pathways that communicate information between these processing regions. In the past few years, diffusion tensor imaging has been used to identify correlations between white matter properties and reading skills in adults and children. White matter differences have been

rely on the transmission of information from visual areas in the right hemisphere to language regions in the left hemisphere. There are also important examples in which white matter diseases lead to specific cognitive disabilities. Geschwind particularly emphasized the idea that acquired reading disorders are manifestations of a 'disconnection syndrome' in which damage to white matter disrupts communication between key cortical reading

Group comparisons and single subjects

- Many neuroimagers perform group comparisons
- A typical report will summarize response or structural differences between two groups; the cover of this well-known book is an example
- Group comparisons differ greatly from the designs for diagnosis (single participant methods), and the necessary tools differ as well



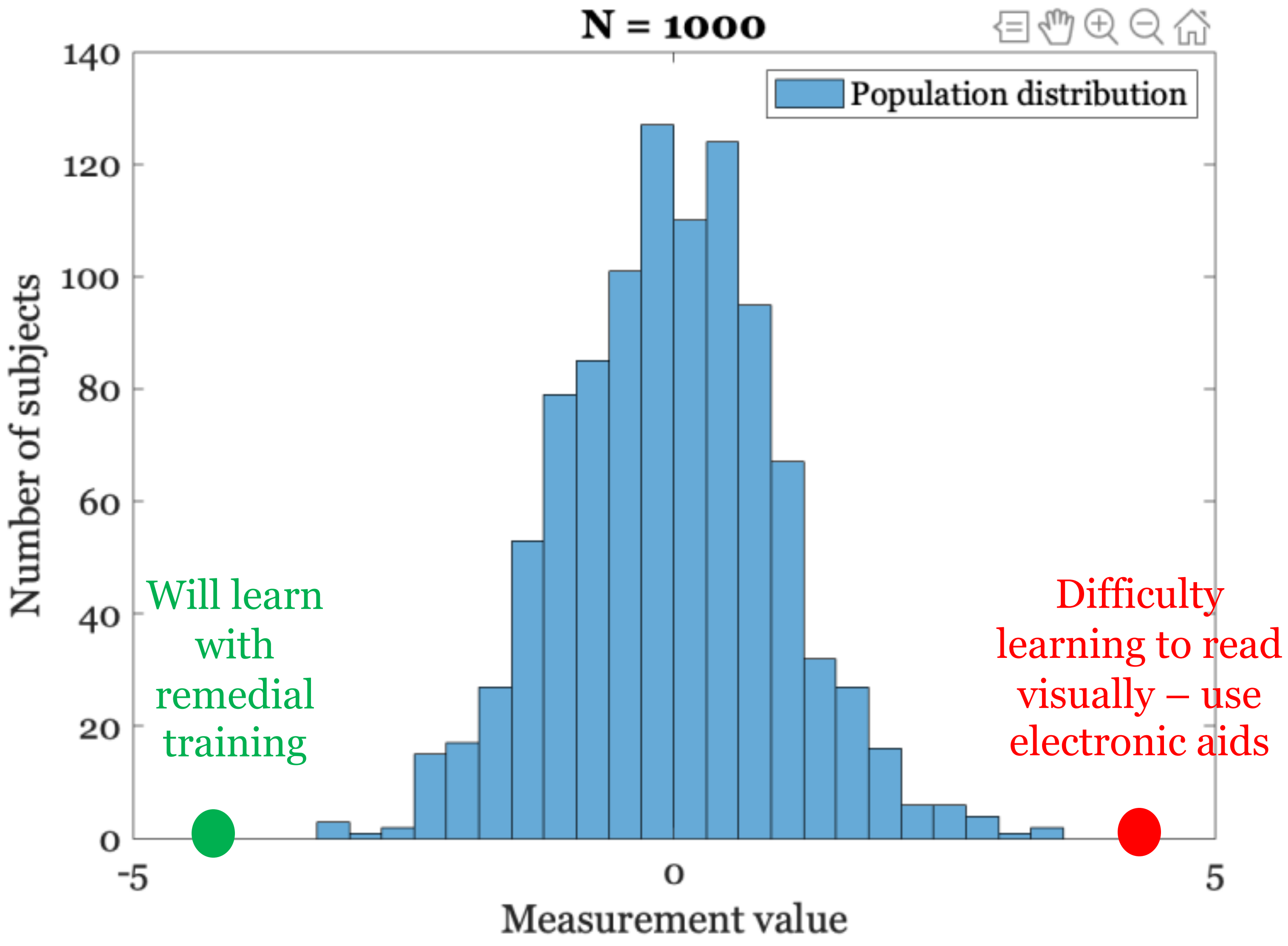
Poldrack, Mumford, Nichols (2011)

Design for diagnosis

- **Goal**: Determine the best way to help a particular child

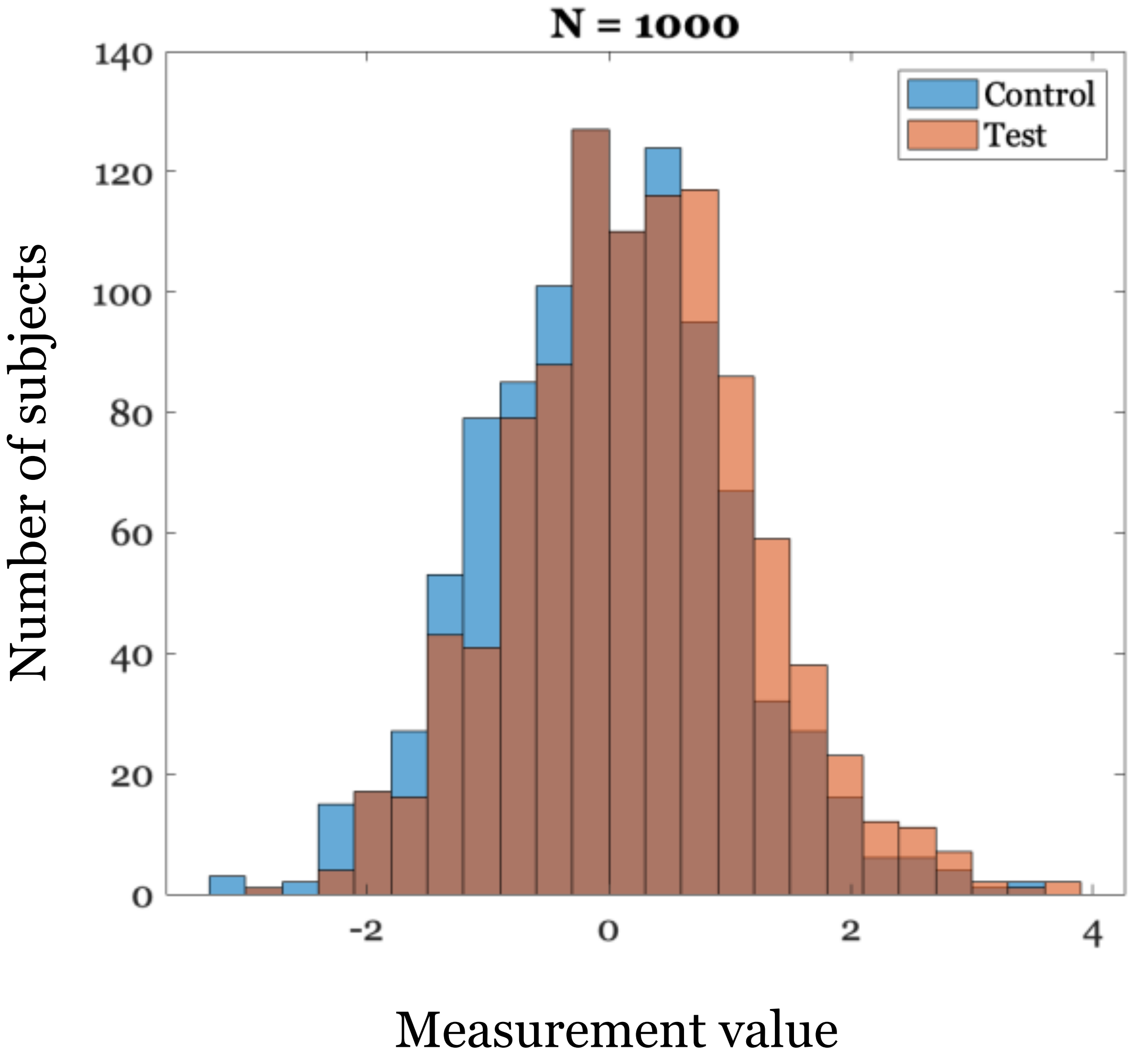
- The distribution (blue) at the right shows a population distribution of a potentially helpful diagnostic measurement

- The filled circles are measurements from two children; we would like to use the measurement to decide how to support the child



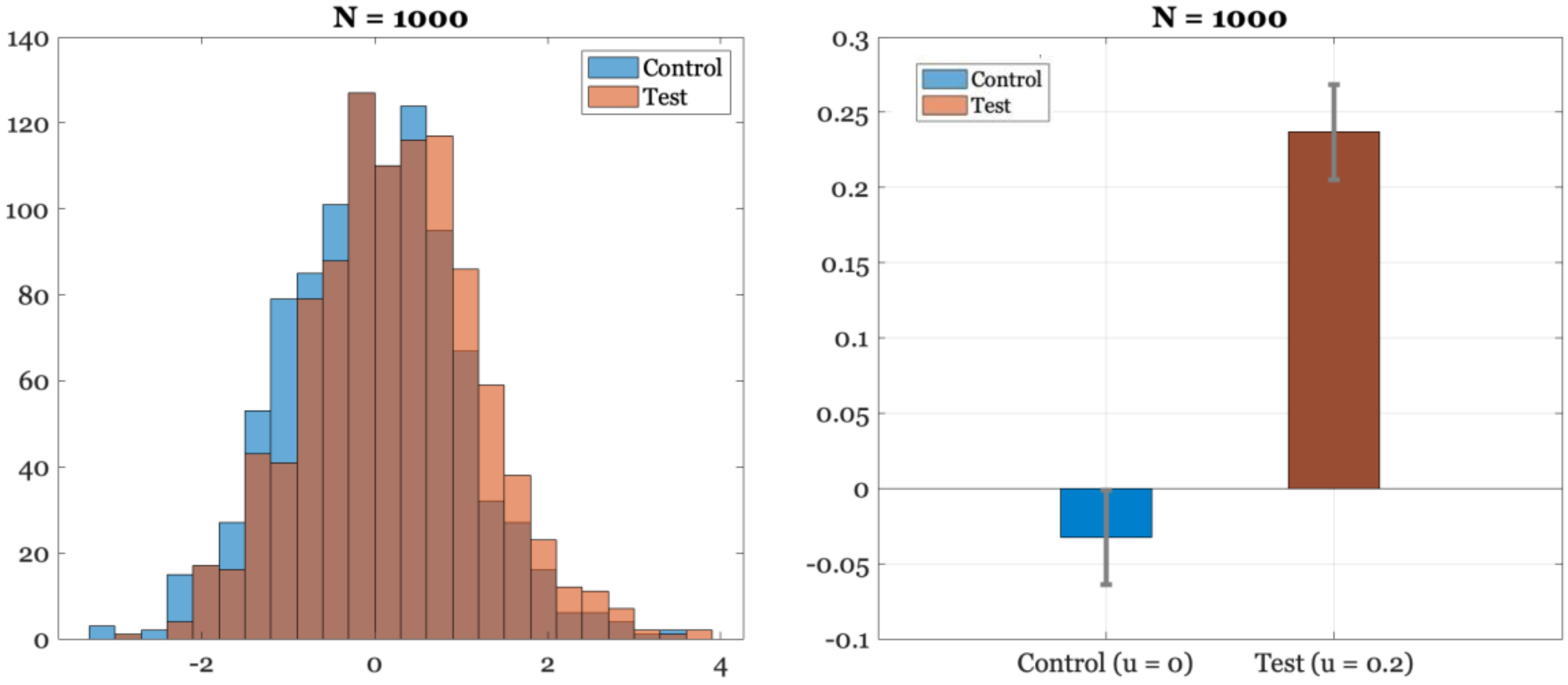
Design for diagnosis - the problem with group comparisons

- A group comparison can provide a misleading perception of how well a diagnostic works
- Suppose we compare a particular measure on controls and the test group of poor readers
- This measure does not help us with diagnosis



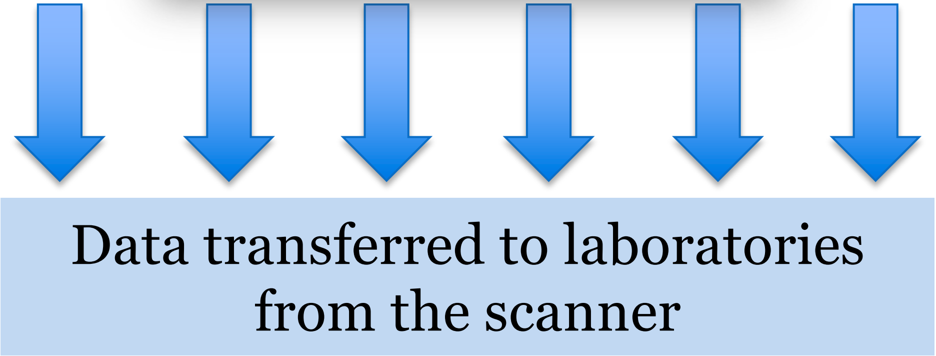
Design for diagnosis - the problem with group comparisons

- These are the same data as the histograms, but plotted as a group comparison
- The group means are very different and the paper would encourage us to consider this biomarker
- This issue becomes greater as N increases



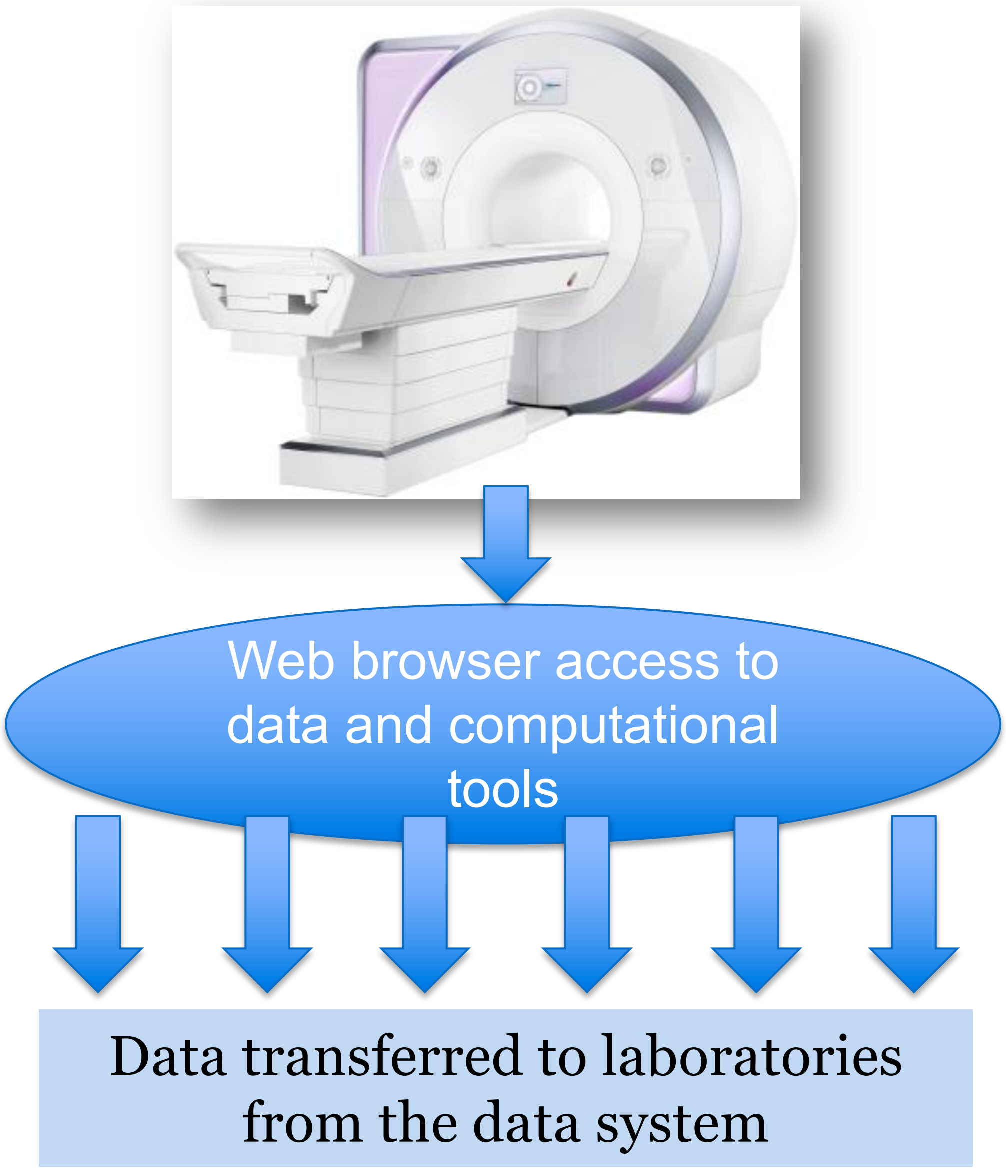
Data and computational management: both are important for diagnosis

- Most MRI Centers provide one of these data retrieval options from the MRI scanner
  - Copy data to CD, DVDs, USB hard drive
  - Copy to a server and remote login
- Data and metadata are transferred to a system controlled by a student or post-doc
- **Limitations** – reuse and sharing become burdensome; metadata and pre-processing information are frequently lost



Data and computational management: both are important for diagnosis

- Archiving MRI Center data eliminates the need for users to gather the data again for publication
- The data should be available through a platform-independent web browser to simplify access
- Basic tools, such as search, visualization, and pre-processing can be available through the browser
- The data are ready for sharing and reuse; metadata can be stored; pre-processing methods shared can be shared



Modern Informatics Platform for Biomedical Research and Collaboration

Cloud-Scale Research Solution

Clinical & Research Data

- Imaging Modalities
- PACS / VNA
- Any Research Data
- …

FLYWHEEL

Capture · *Curate* · *Compute* · *Collaborate*

- Imaging Research Centers
- Clinical Research
- Clinical Trials

Research Applications

- Machine Learning
- Imaging Research
- Multi Center Studies

Data Privacy & Regulatory Compliance

I am a co-founder of the company

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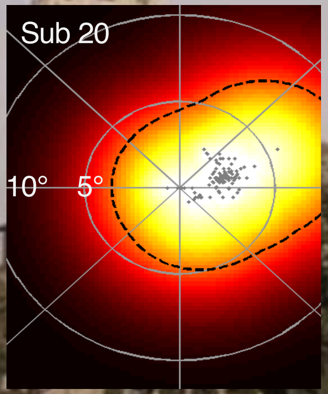
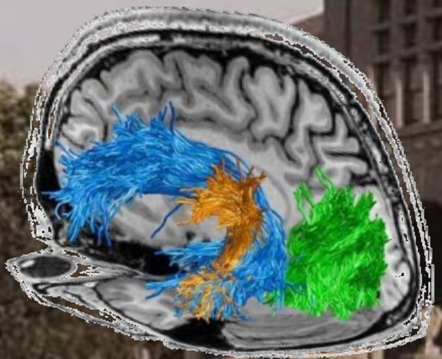
Summary 4: Experimental design for diagnosis – summary

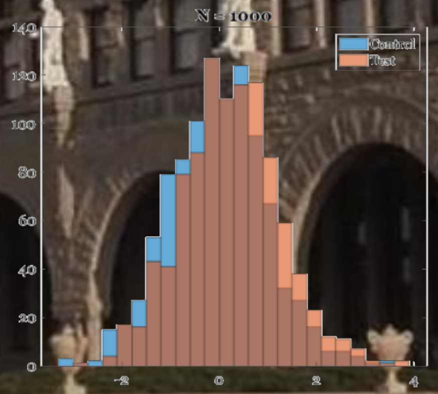
Use experimental designs and tools for single subjects and judge experimental measures by whether they can diagnose individuals, not groups

Talk review: Neural circuitry for vision and reading

1. The neural circuitry of reading
2. Quantifying single subject signals and structures
    a. Maps, pRF, and visual field coverage
    b. White matter tissue and connections
3. Design for diagnosis – computational tools







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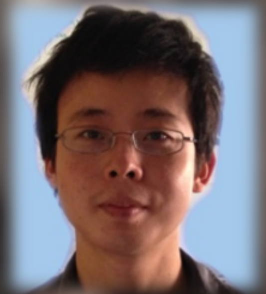

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