



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY

The Human Connectome Project Mapping Brain Networks With MRI

Randy L. Buckner, PhD

Sosland Family Professor of Psychology and of Neuroscience,
Harvard University

Director of Psychiatric Neuroimaging, Massachusetts General Hospital

Disclosures

My spouse/partner and I have the following relevant financial relationship with a commercial interest to disclose:

Consultant Pfizer, Roche, Alkermes

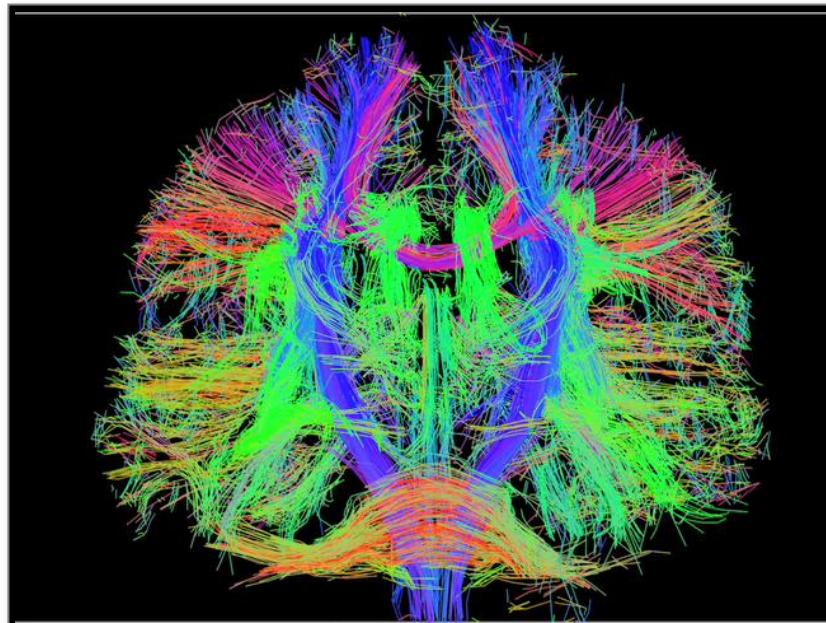
Learning objectives

- To understand how MRI methods can map organization of brain networks.
- To understand limits of available techniques.
- To review recent discoveries that map the organization of brain networks important to higher-level brain function.

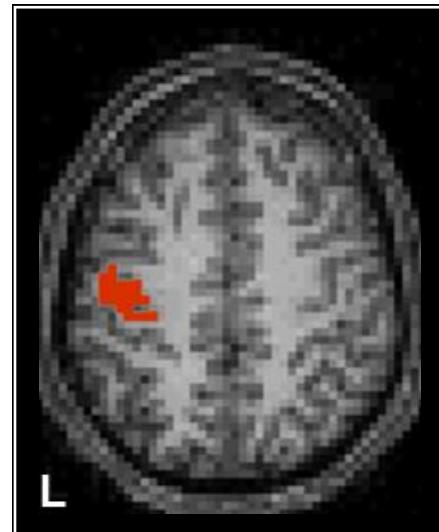
Measuring Brain Networks in the Human

Intrinsic Activity

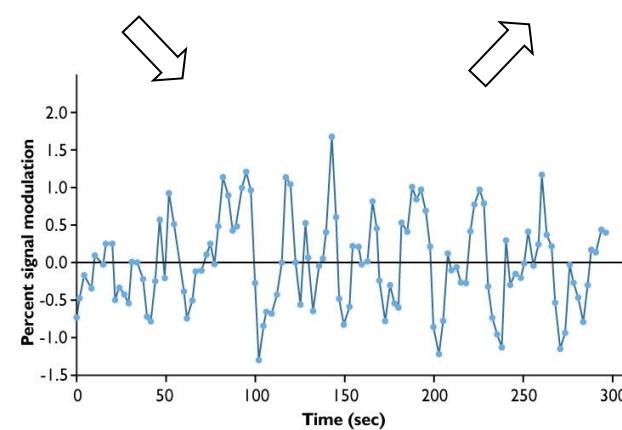
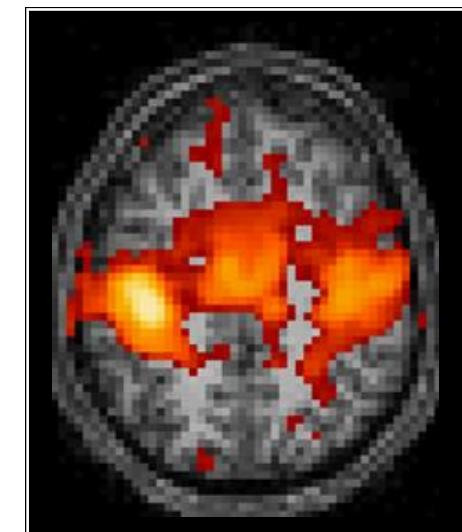
Diffusion



SEED REGION

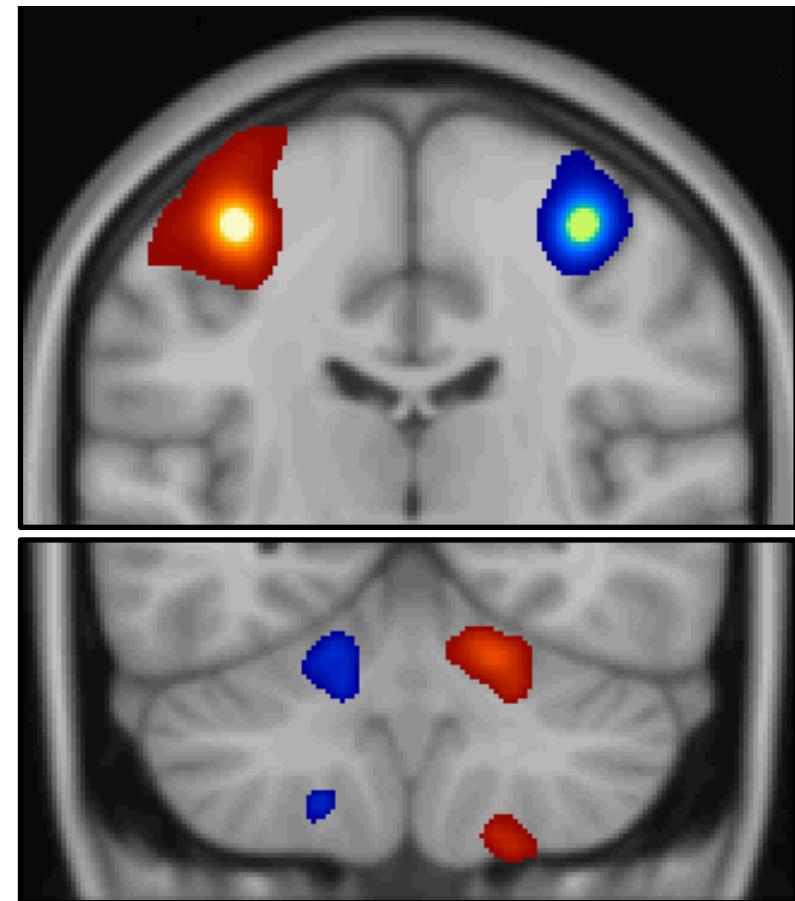
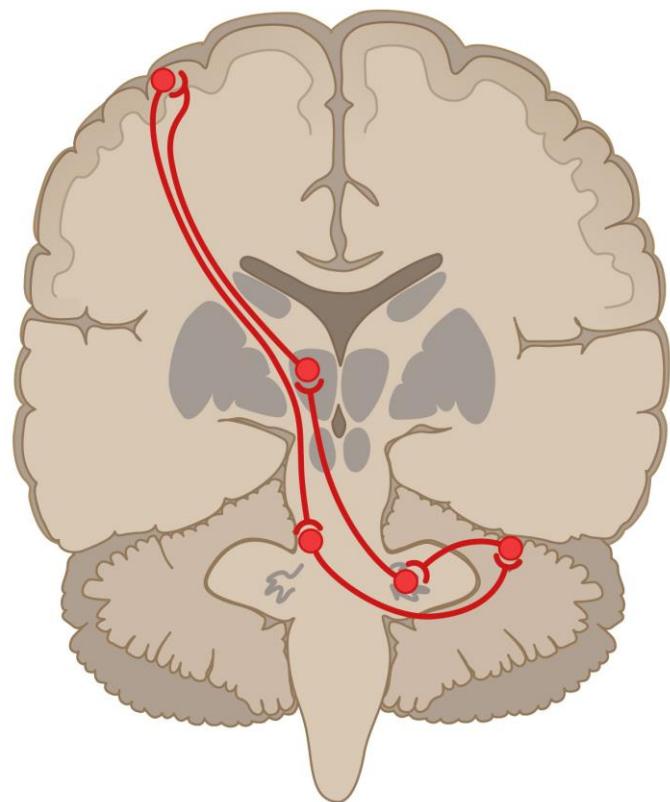


CORRELATED NETWORK



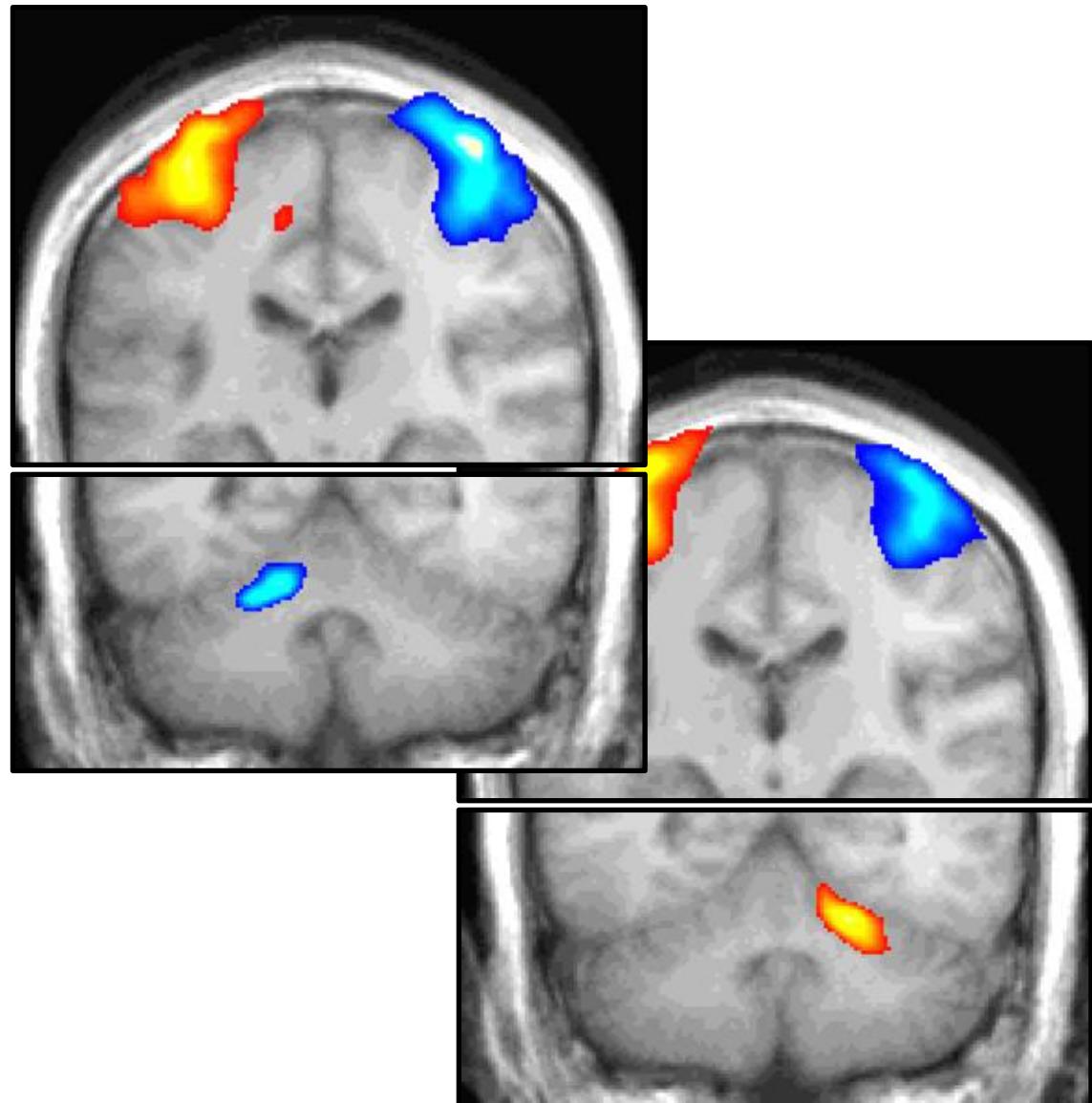
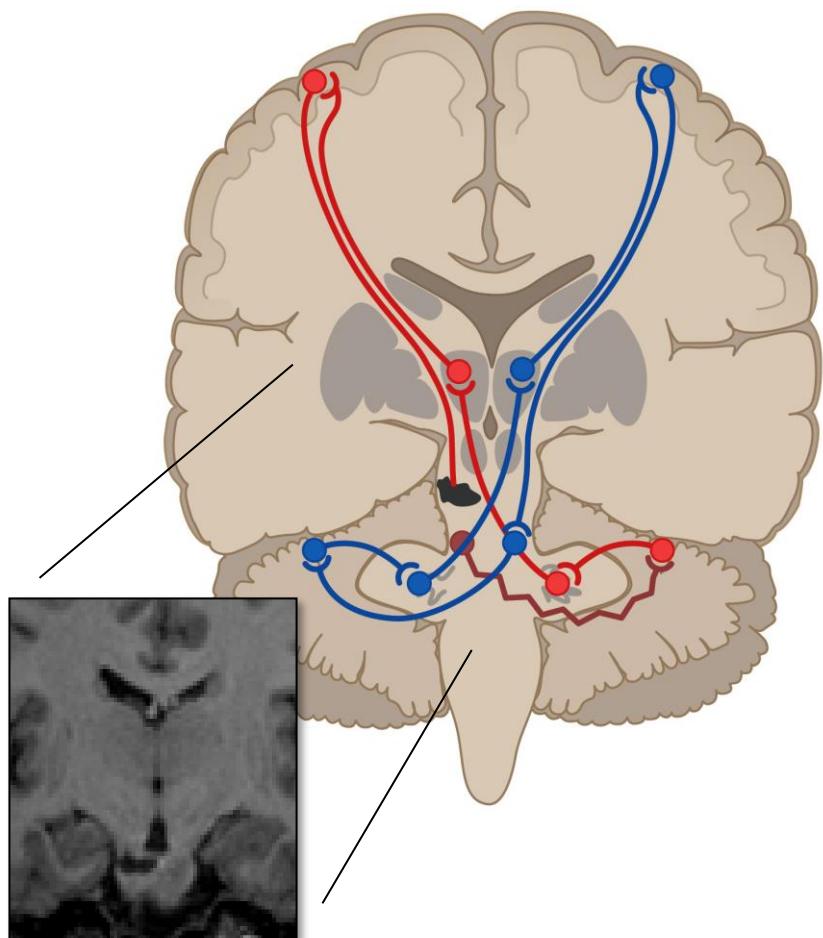
Example Validation

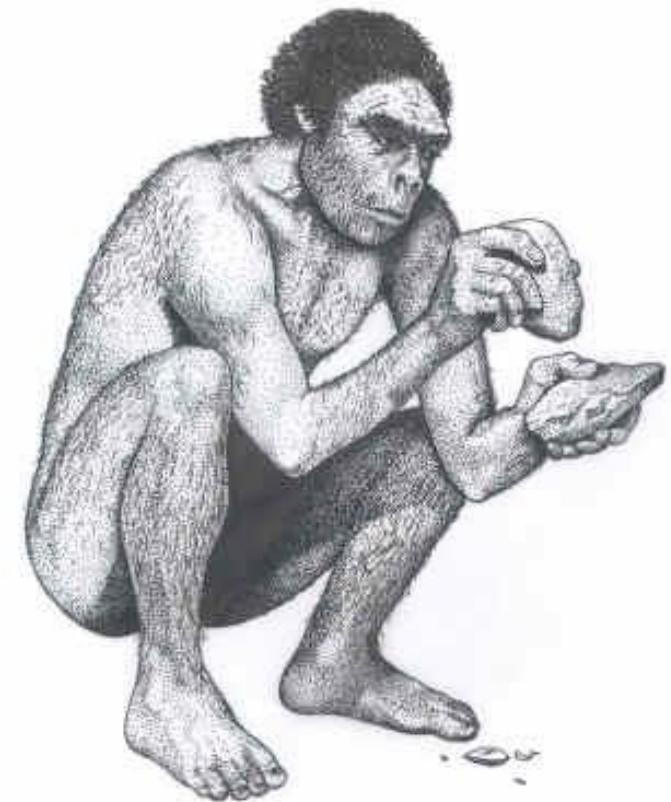
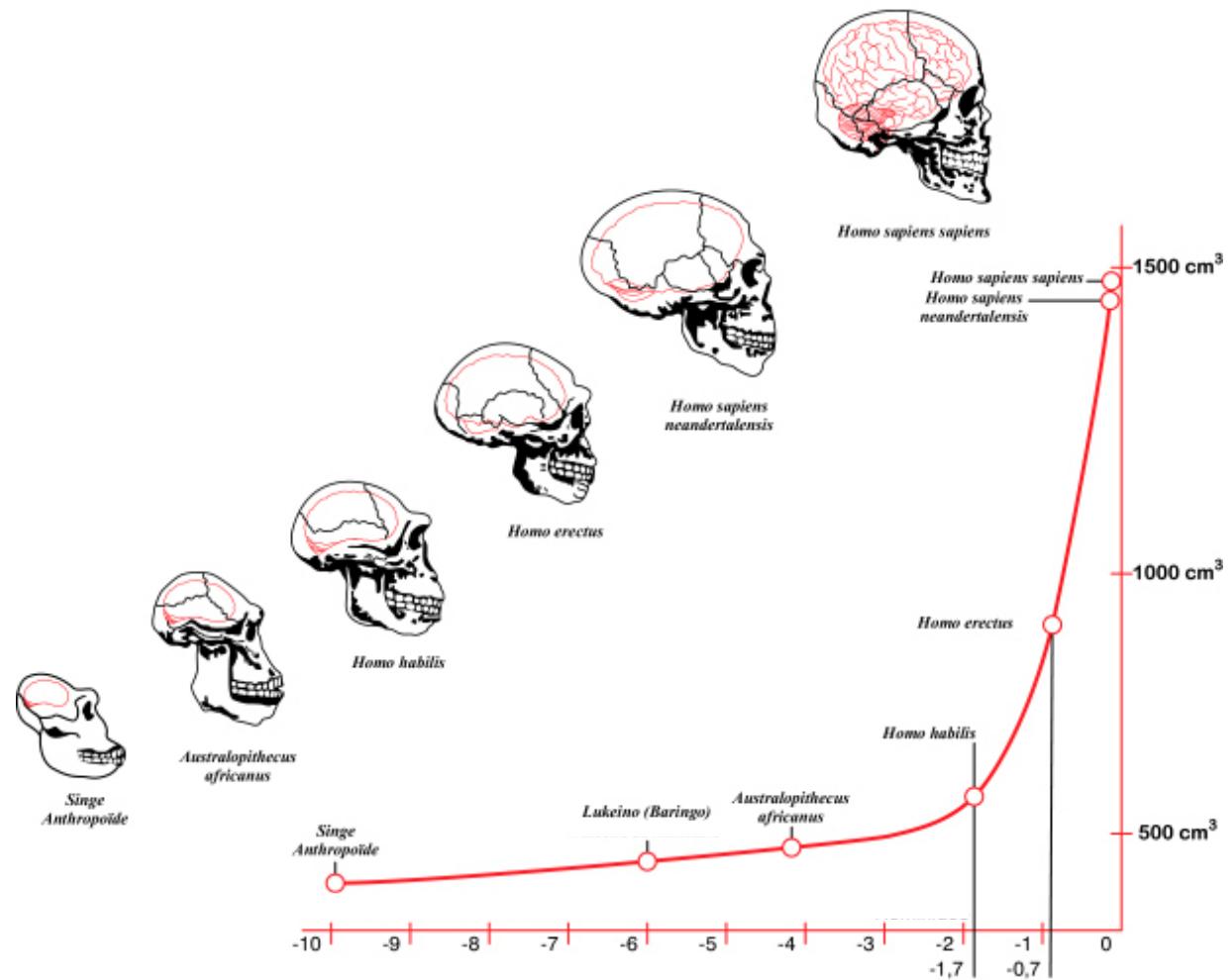
Cerebro-Cerebellar Circuit



Example Validation

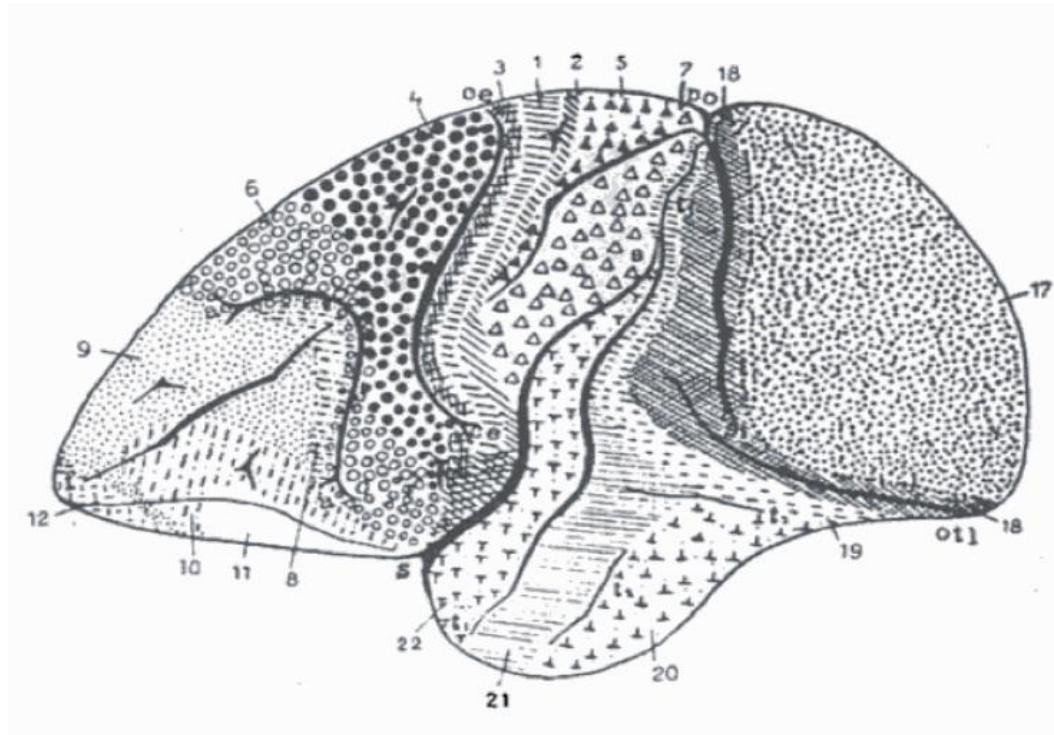
Cerebro-Cerebellar Circuit



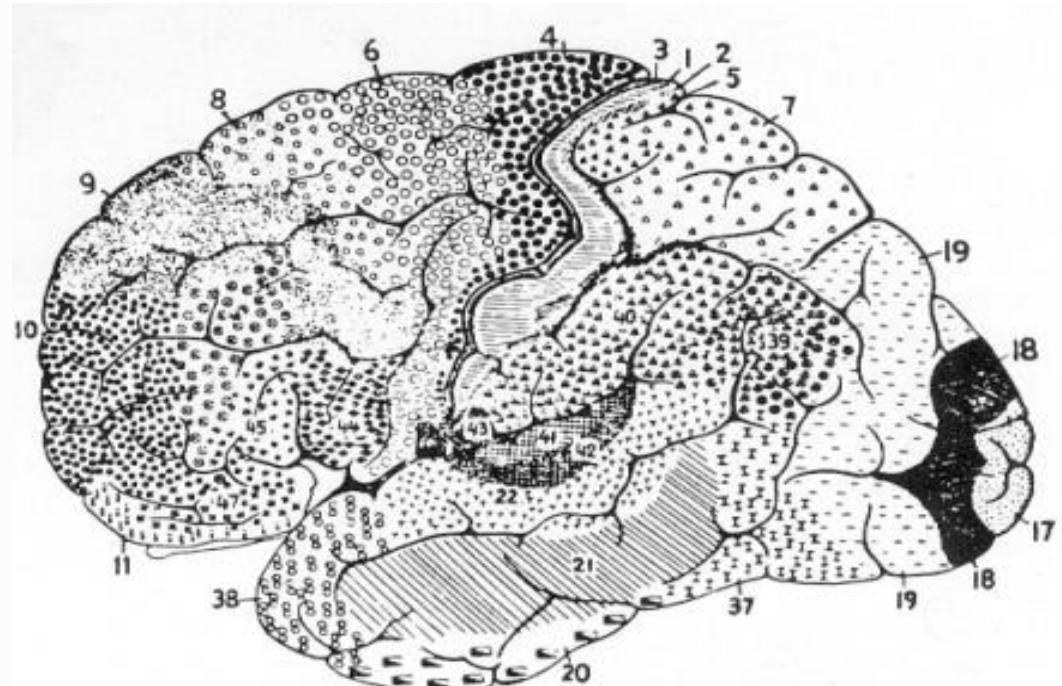


Human Association Cortex is Dramatically Expanded

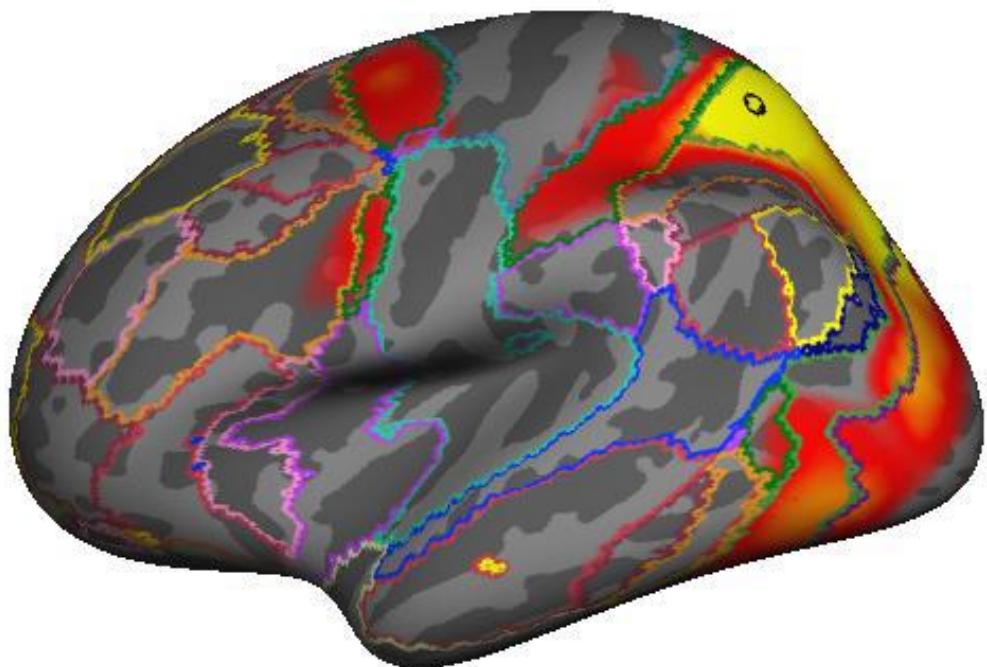
Monkey



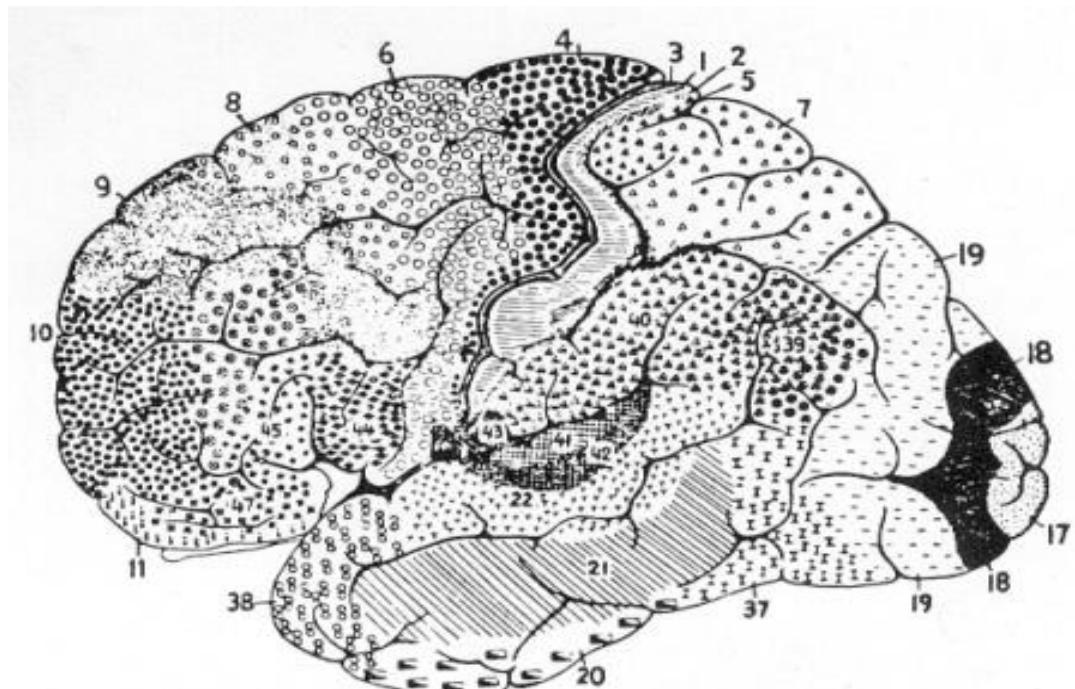
Human



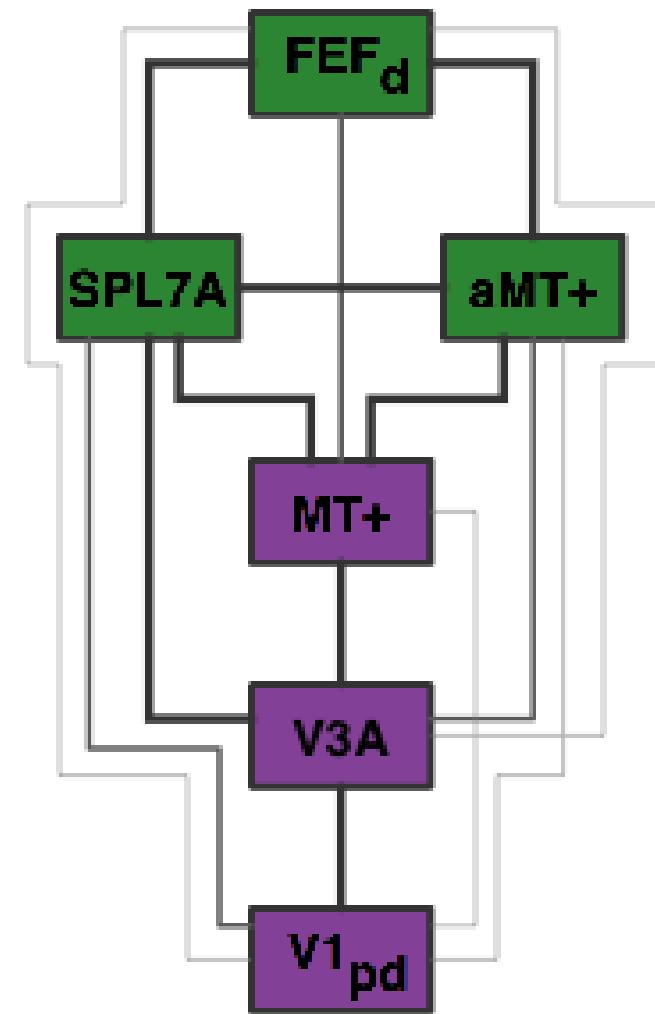
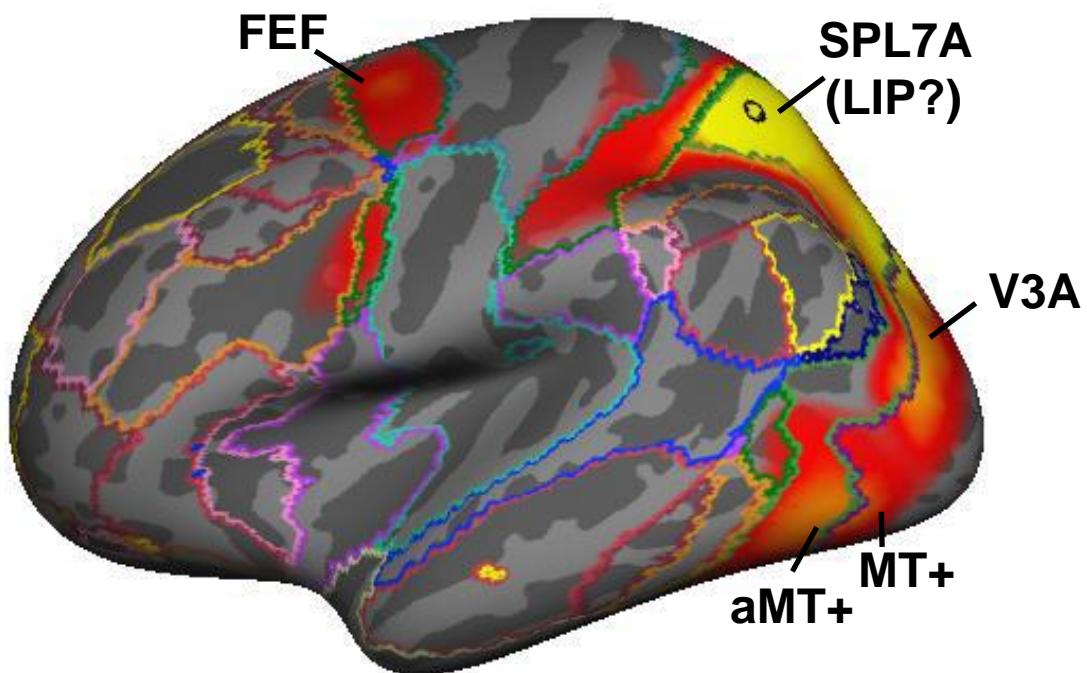
Canonical Hierarchical Sensory-Motor Network



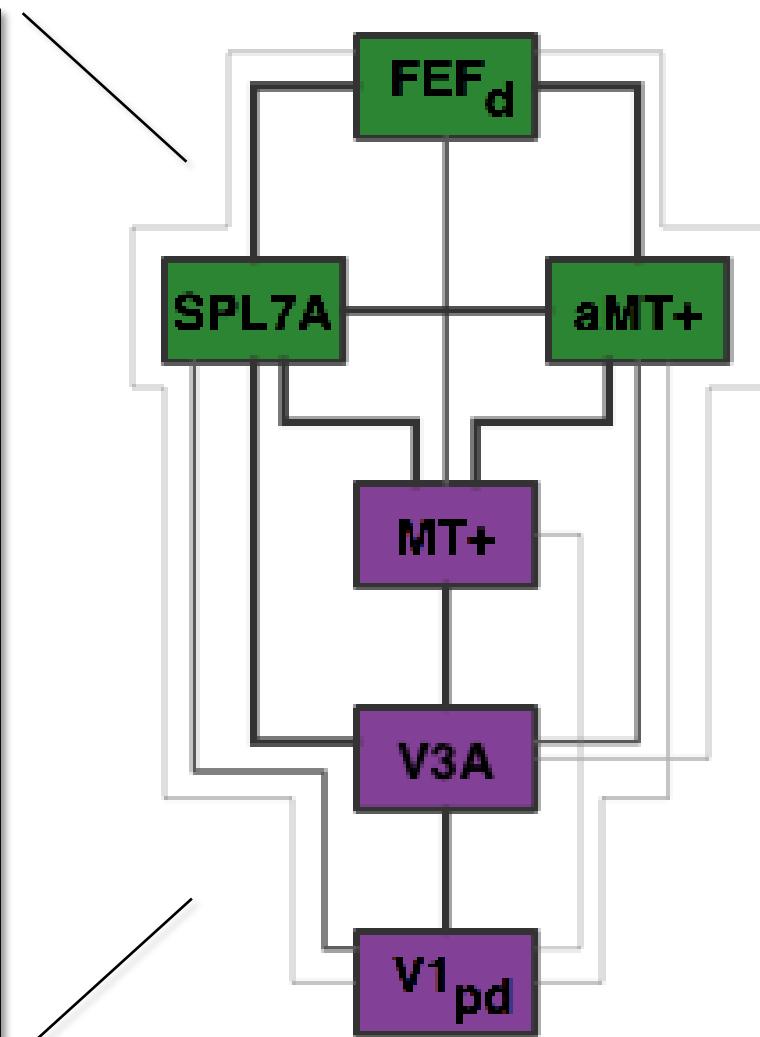
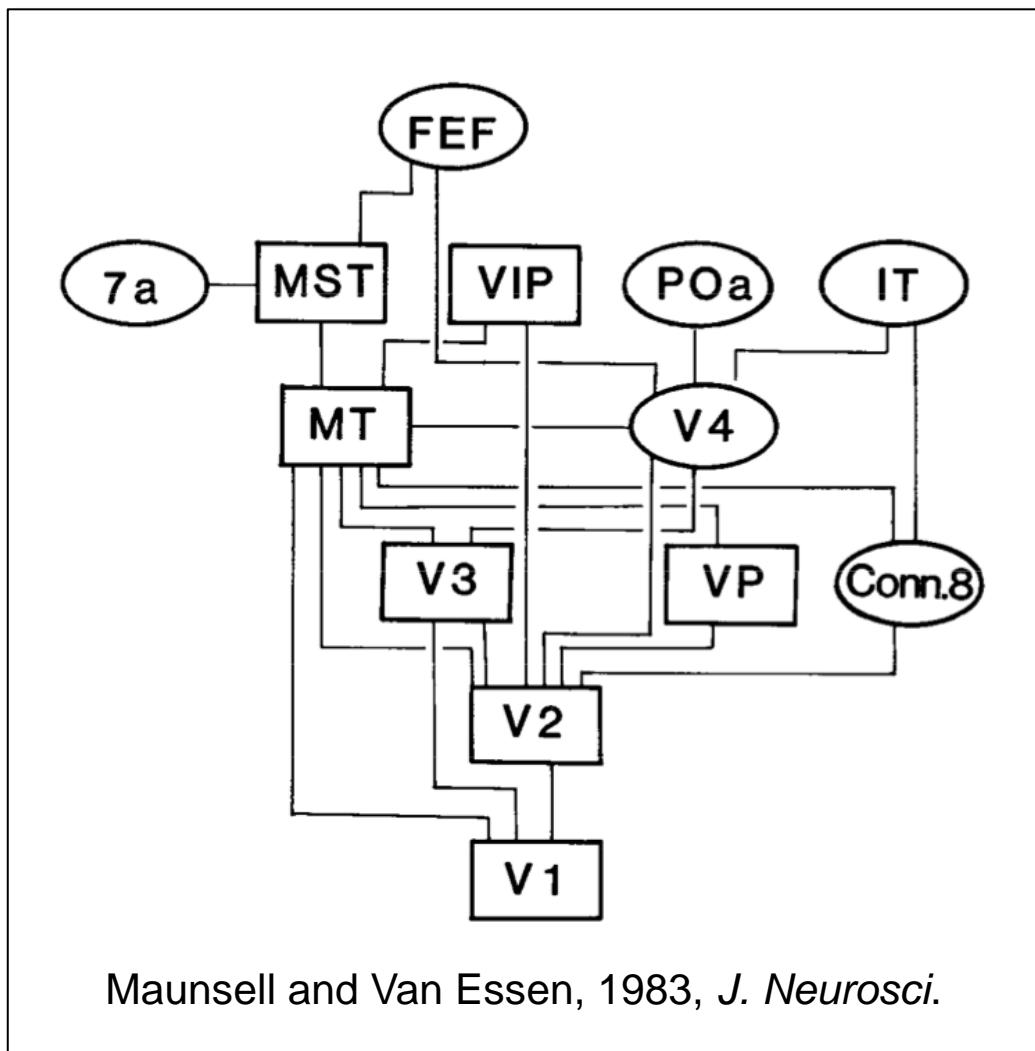
Human



Canonical Hierarchical Sensory-Motor Network

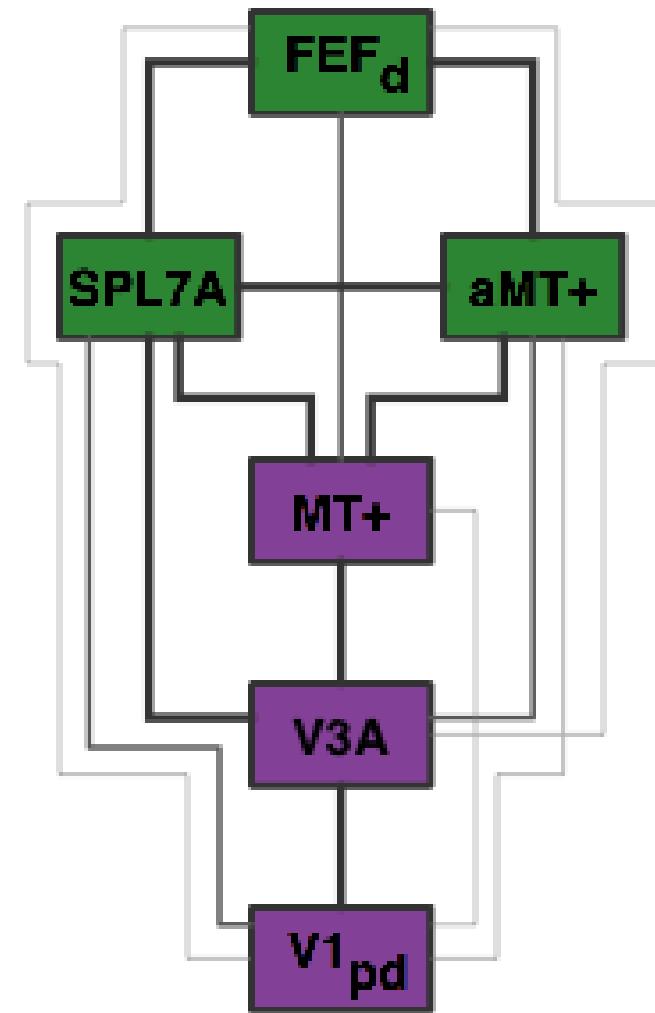
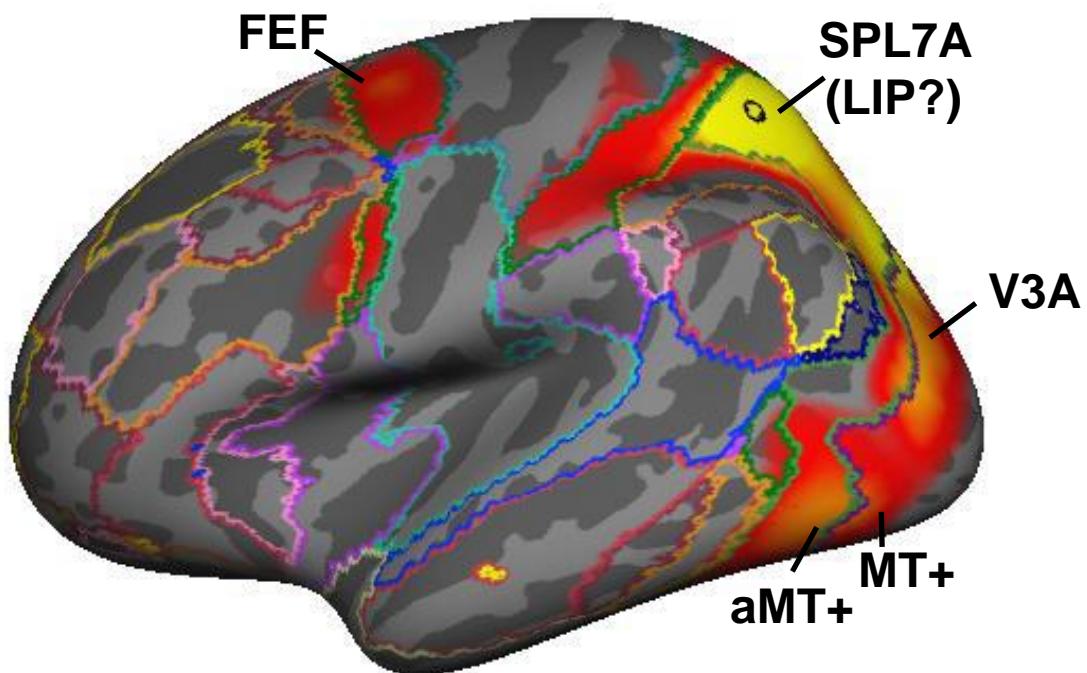


Canonical Hierarchical Sensory-Motor Network

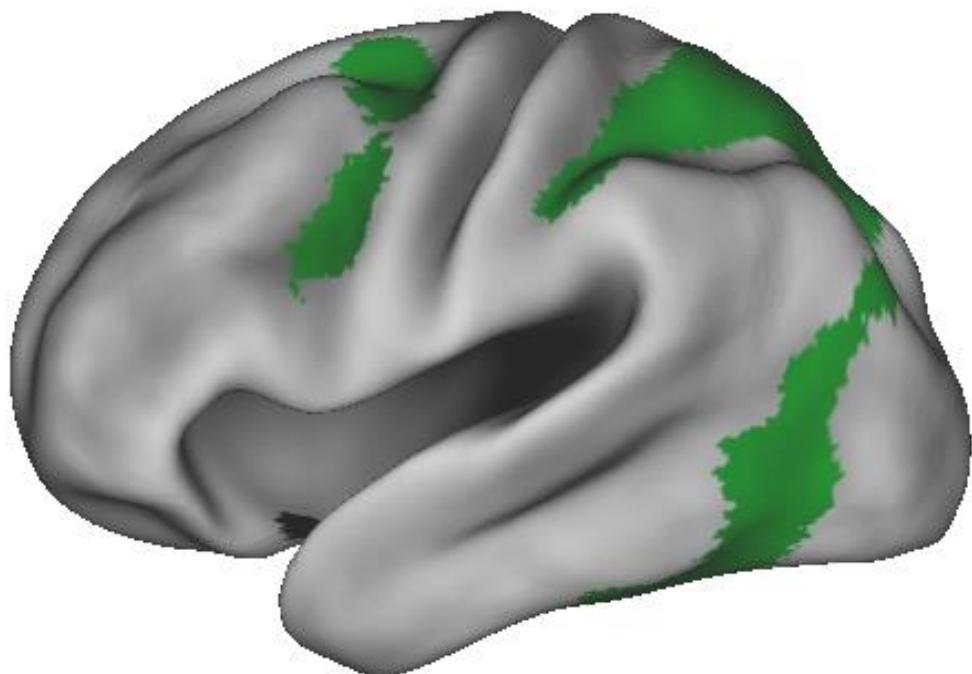
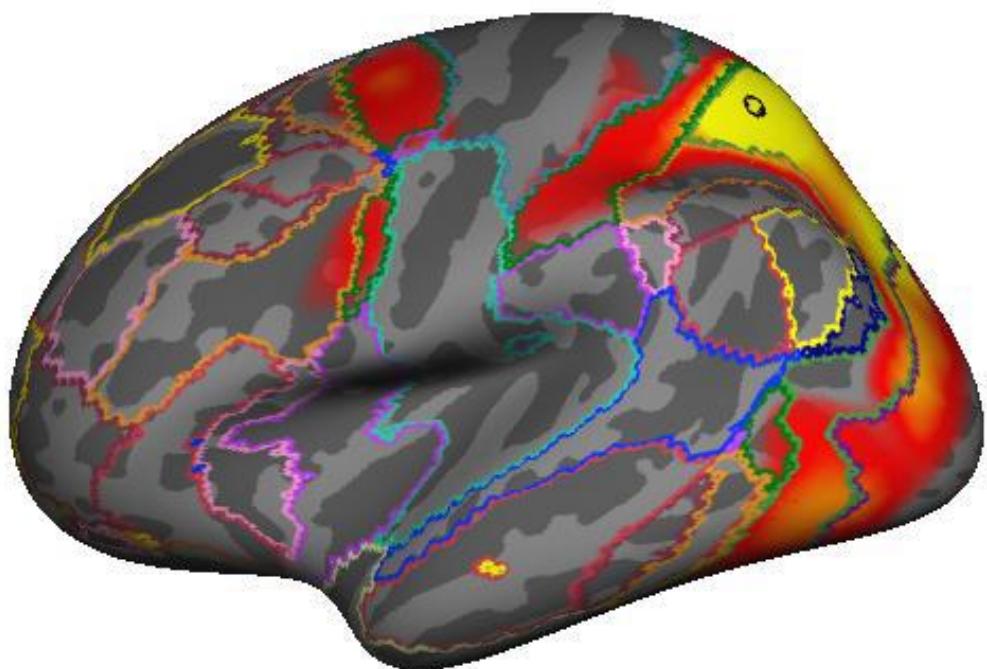


Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Canonical Hierarchical Sensory-Motor Network

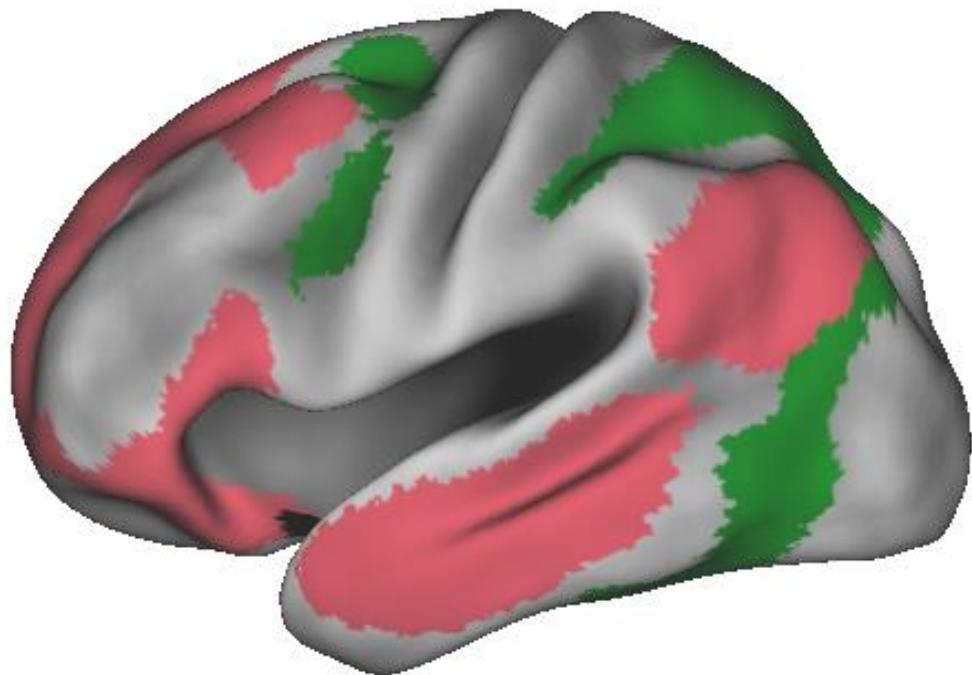
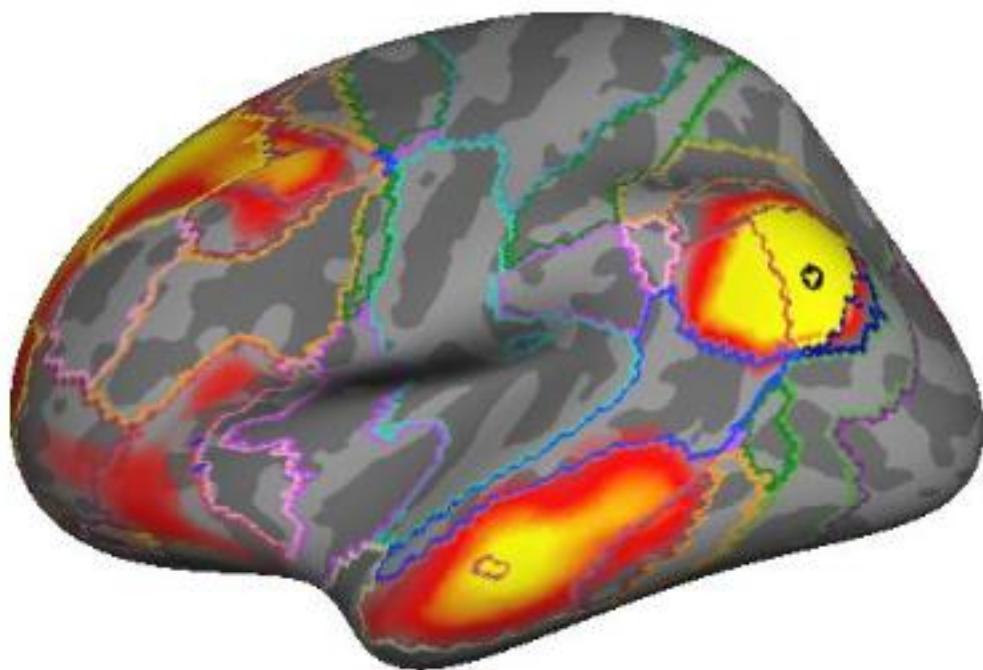


Distributed Association Networks



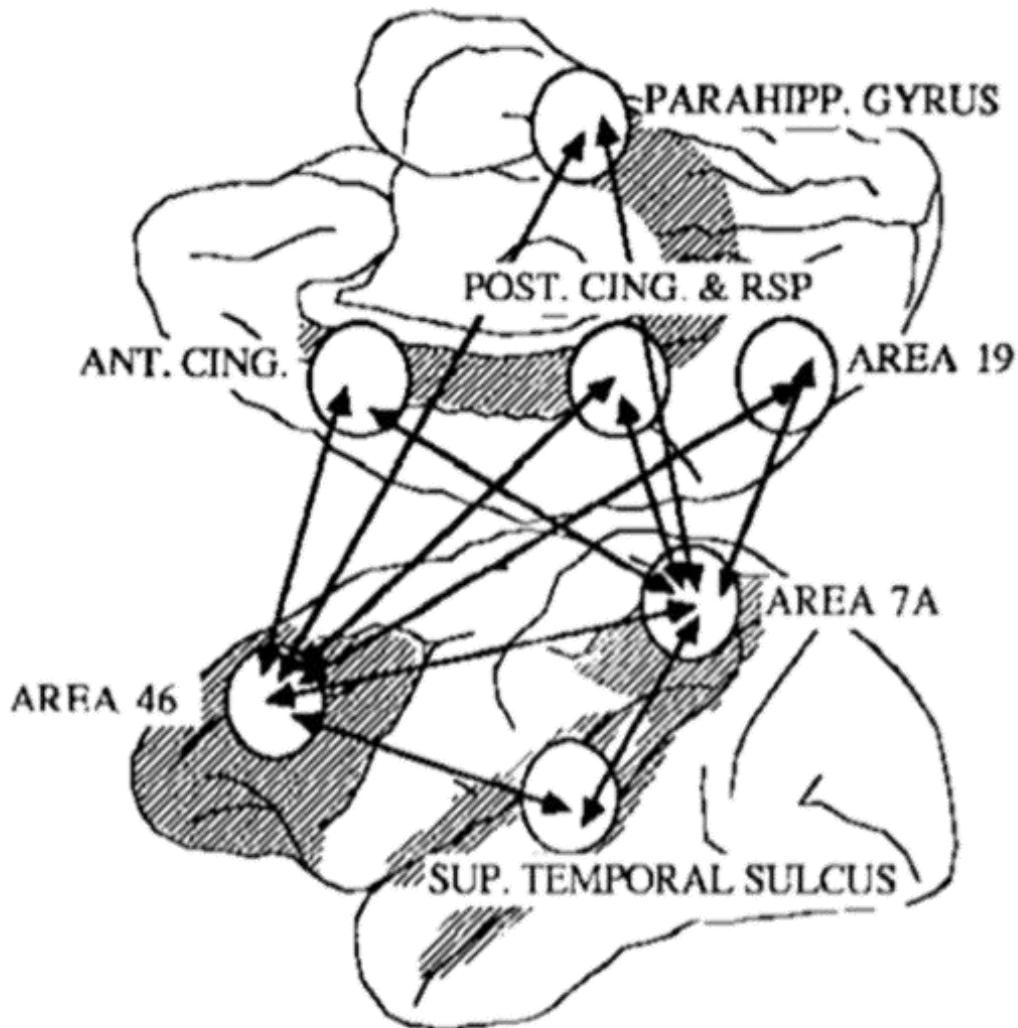
Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks

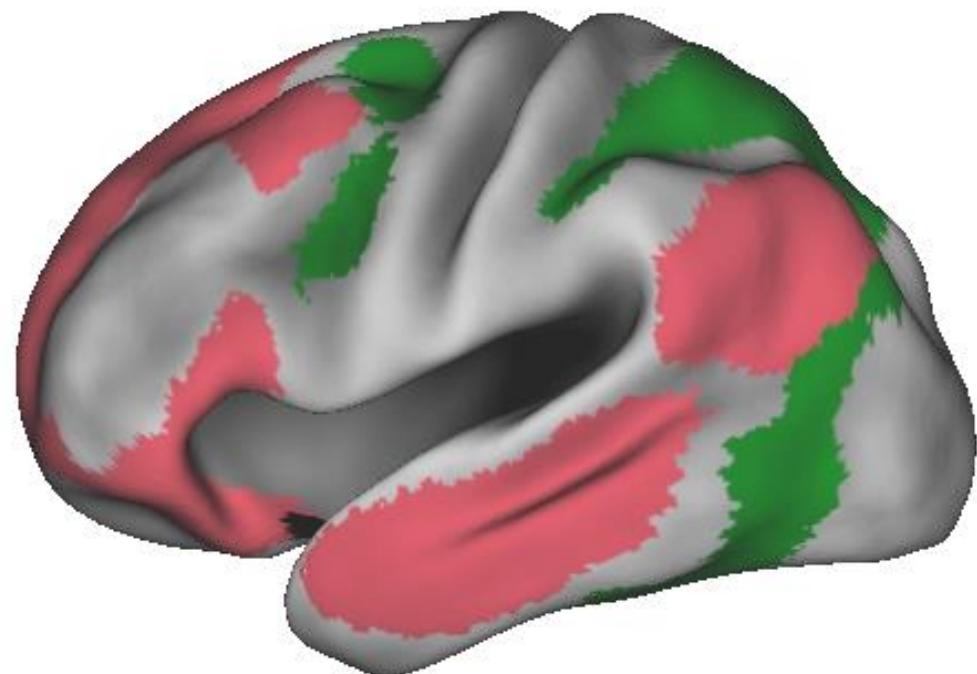


Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks

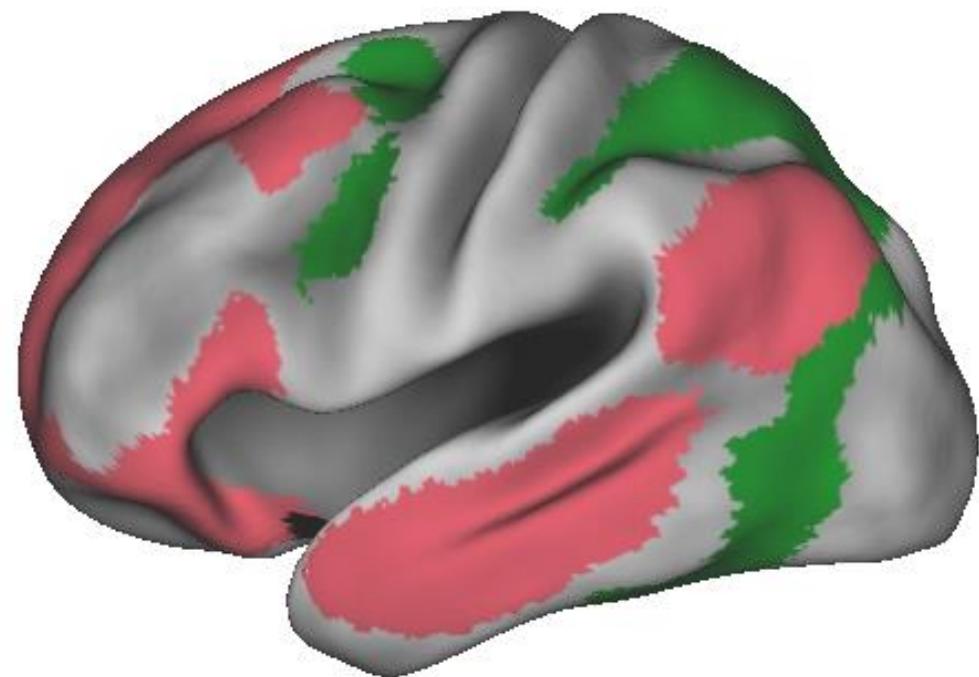
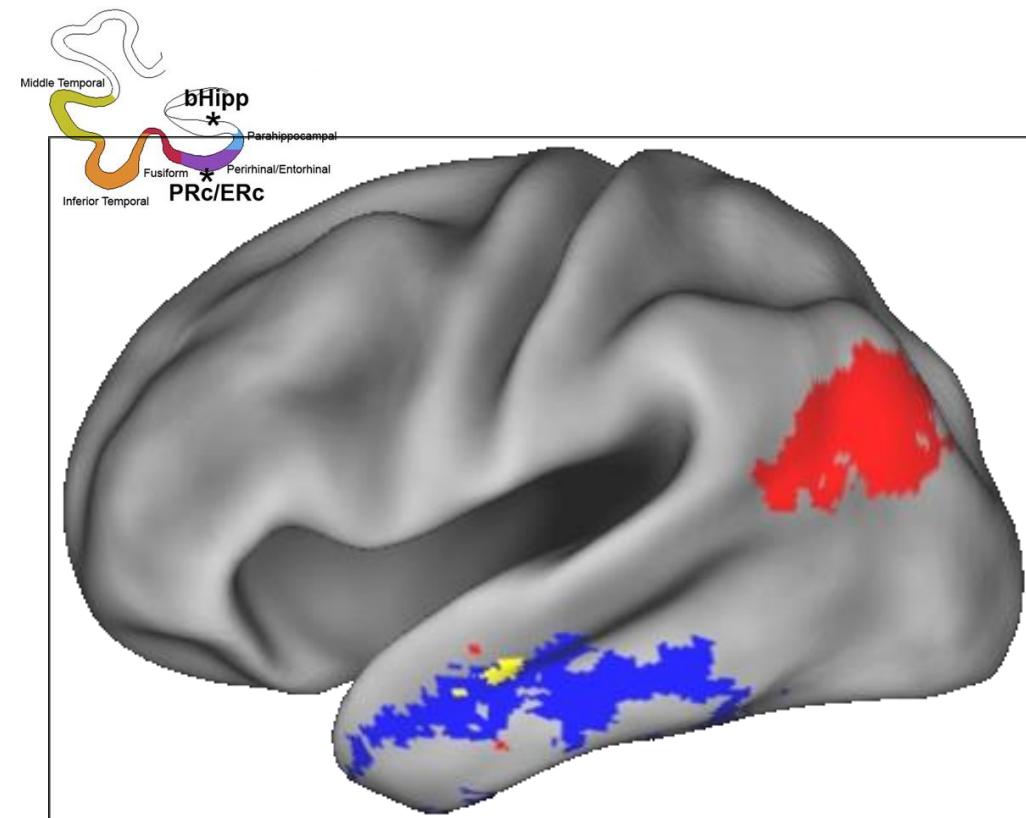


Goldman-Rakic (1988) *Ann. Rev. Neurosci.*



Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks

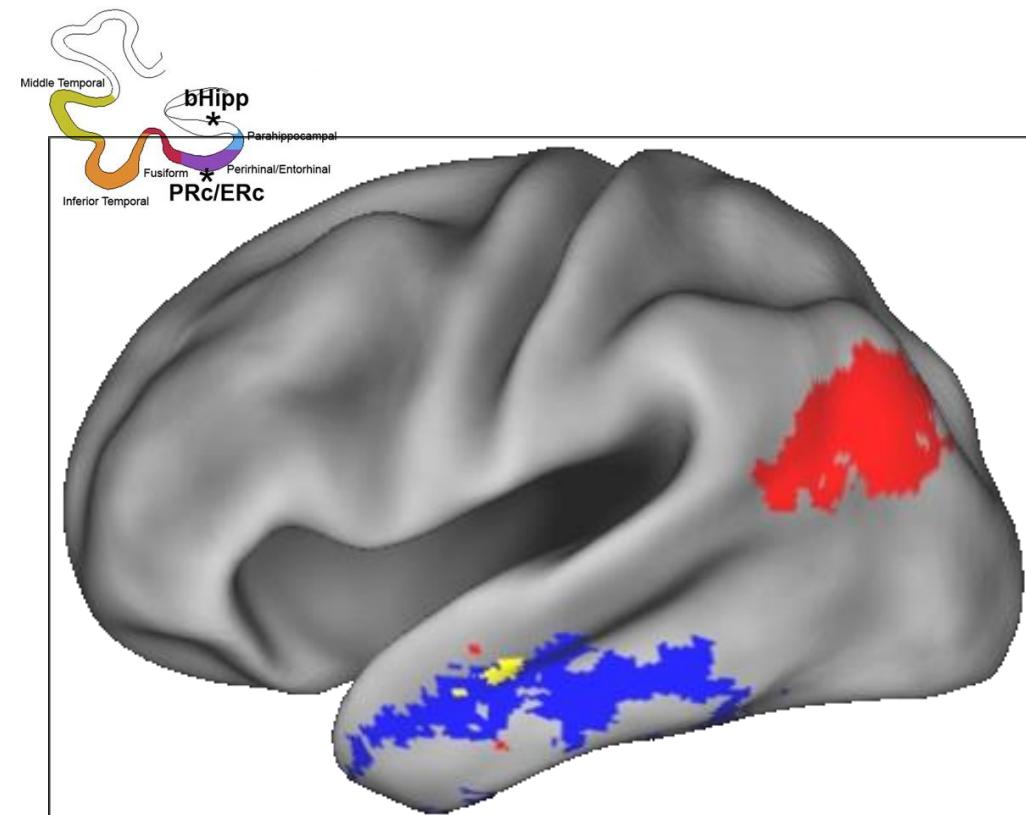


Coupled to Hippocampal
Memory System

Vincent et al., 2007, *J. Neurophysiol.*
Kahn et al., 2008, *J. Neurophysiol.*

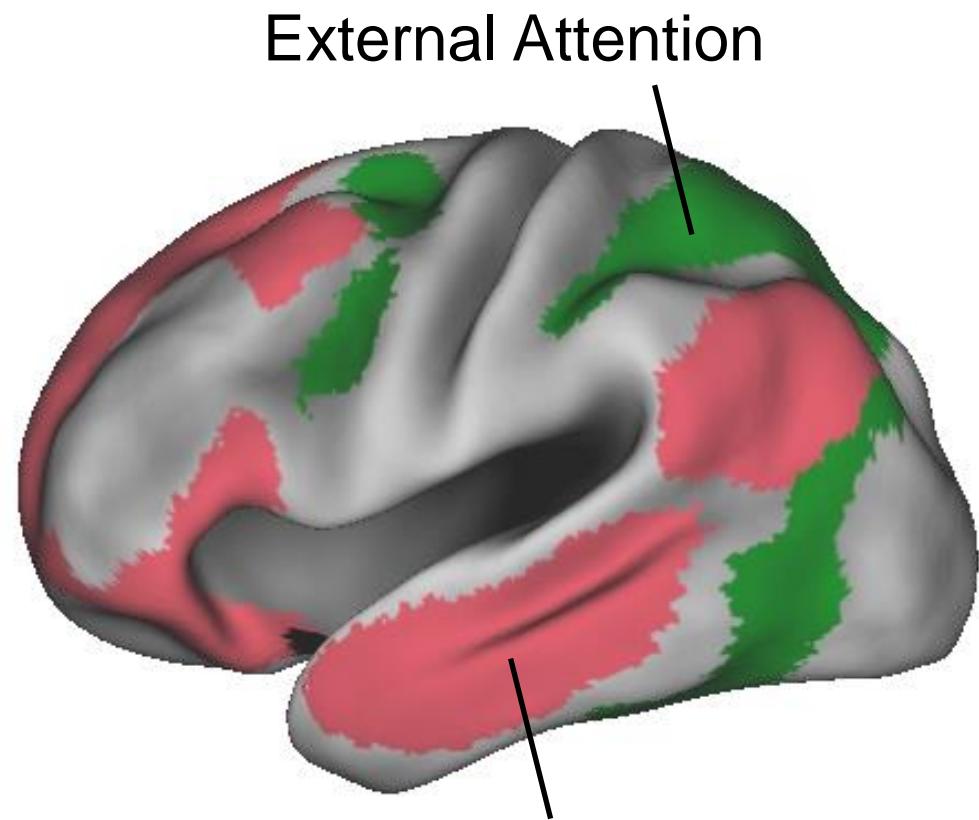
Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks



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Vincent et al., 2007, *J. Neurophysiol.*
Kahn et al., 2008, *J. Neurophysiol.*



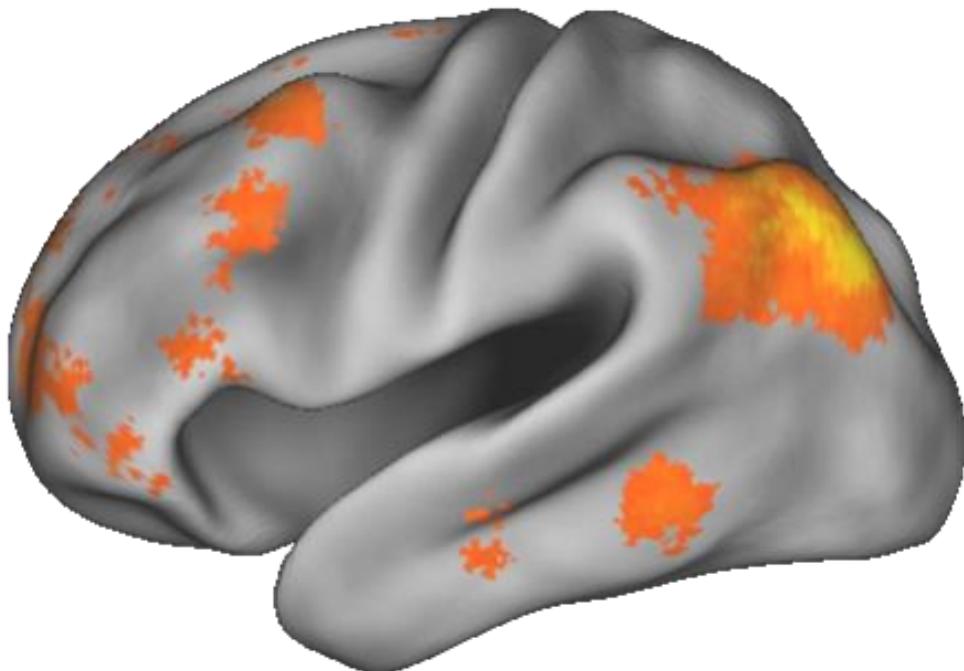
External Attention

Internal Mentation

Yeo, Krienen et al., 2011, *J. Neurophysiol.*
(Andreasen et al., 1995, *Am. J. Psychiatry*)

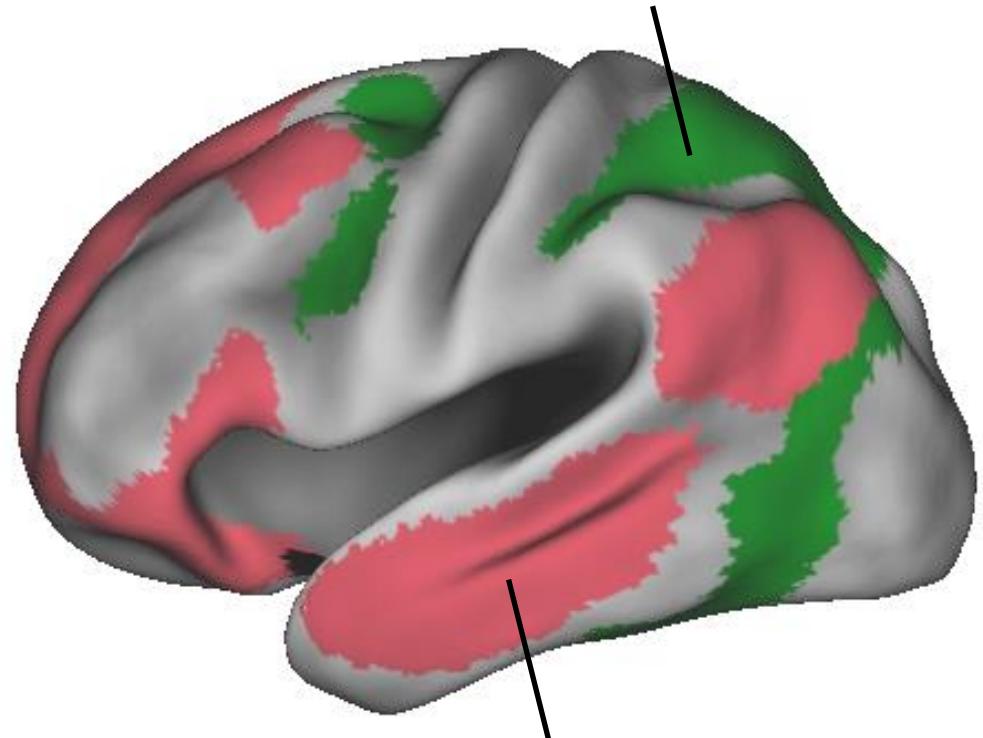
Distributed Association Networks

Remembering



95 Independent Studies

External Attention

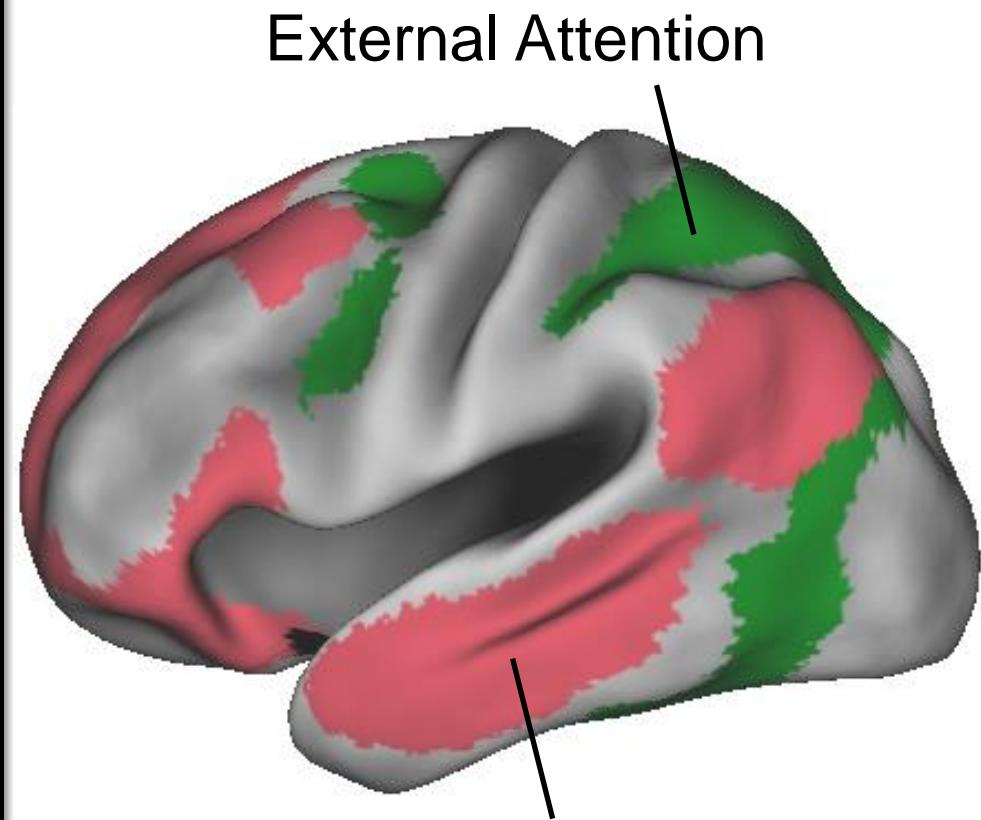
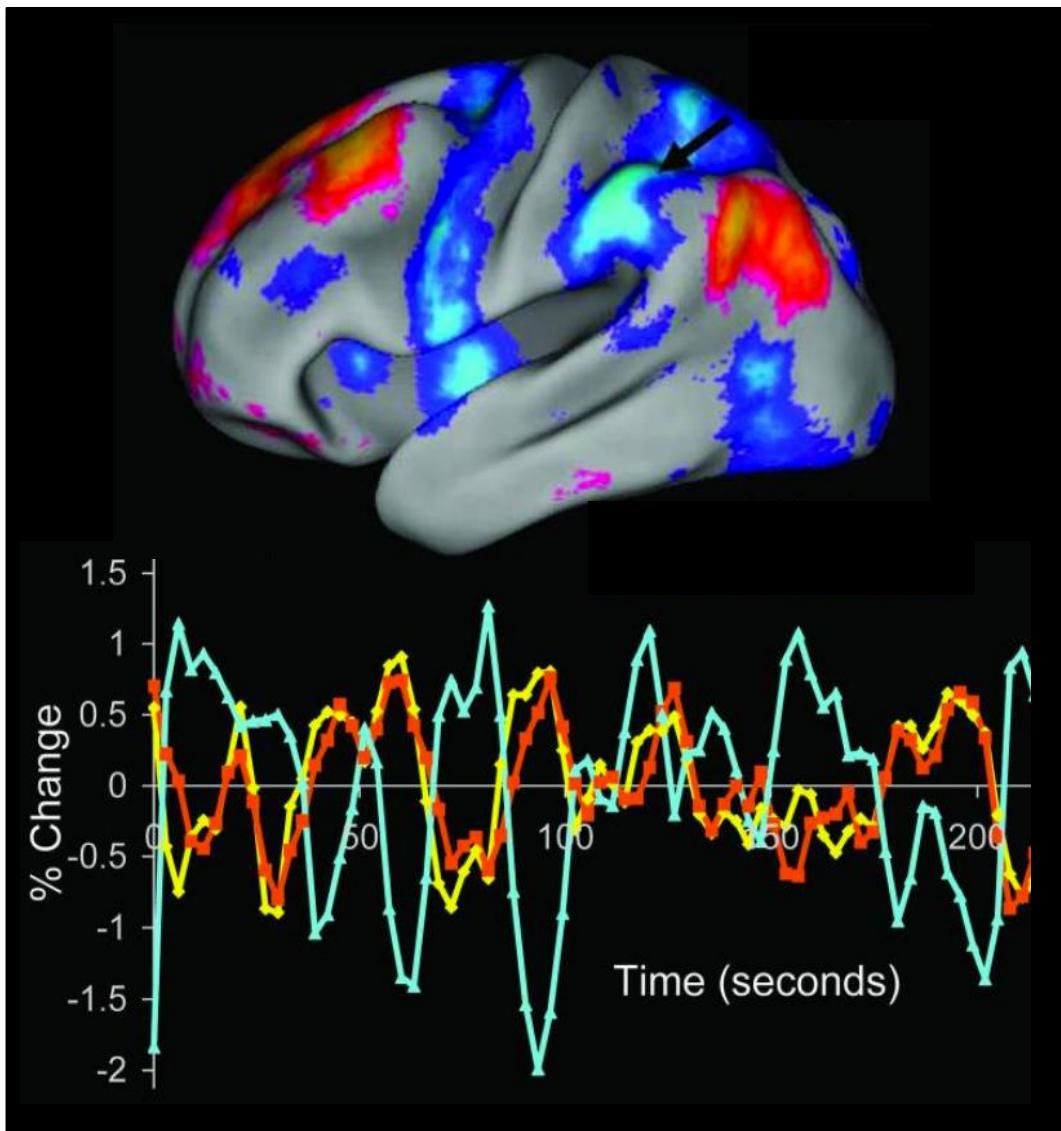


External Attention

Yeo, Krienen et al., 2011, *J. Neurophysiol.*
(Andreasen et al., 1995, *Am. J. Psychiatry*)

Andrews-Hanna, Saxe, & Yarkoni, 2014, *NeuroImage*

Distributed Association Networks

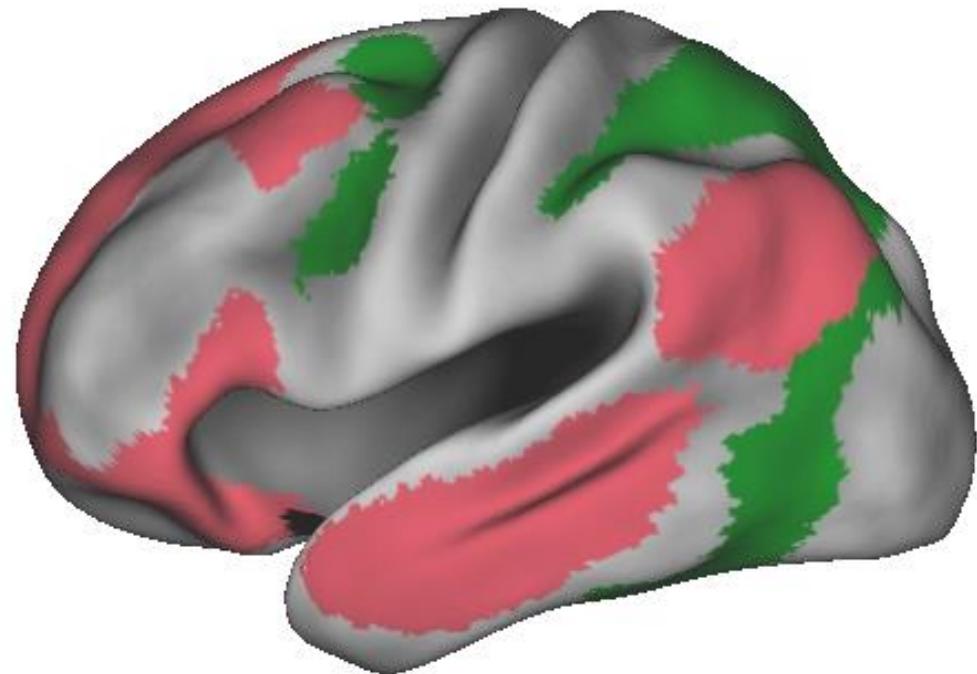


Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Fox et al., 2005, *Proc. Natl. Acad. Sci.*

Distributed Association Networks

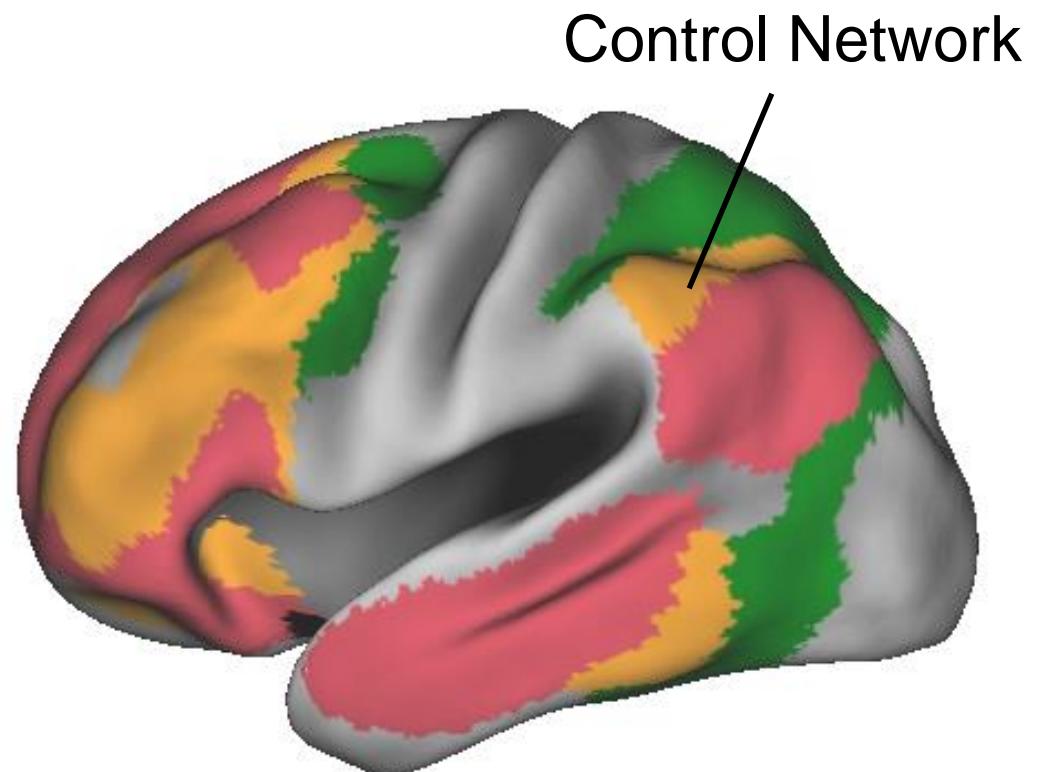
Control Network?



Yeo, Krienen et al., 2011, *J. Neurophysiol.*

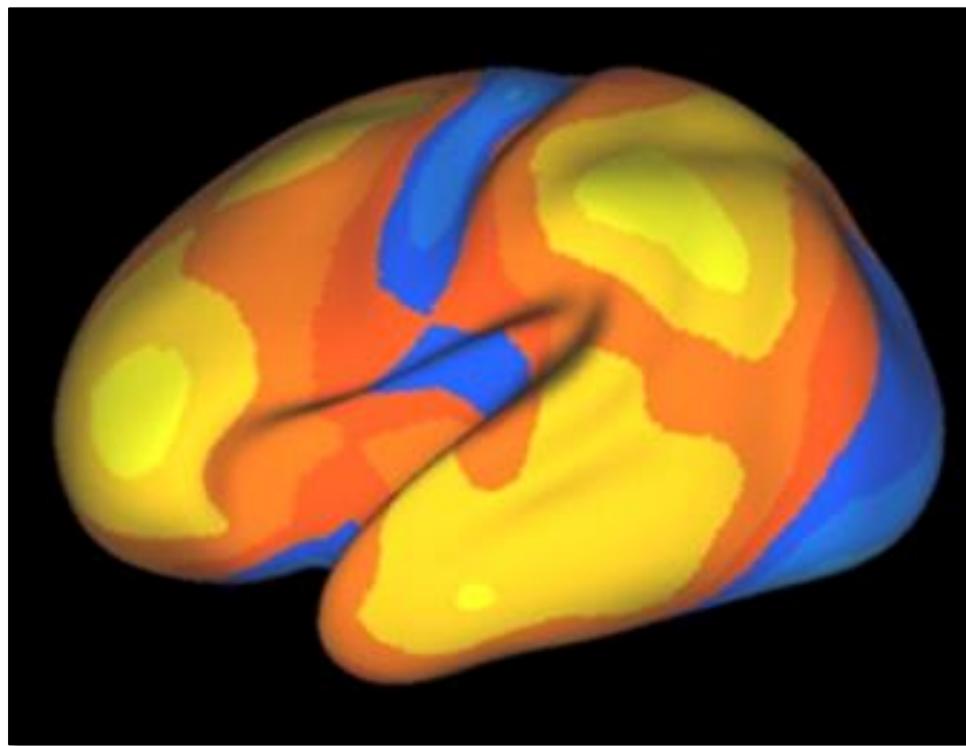
Distributed Association Networks

Control Network?

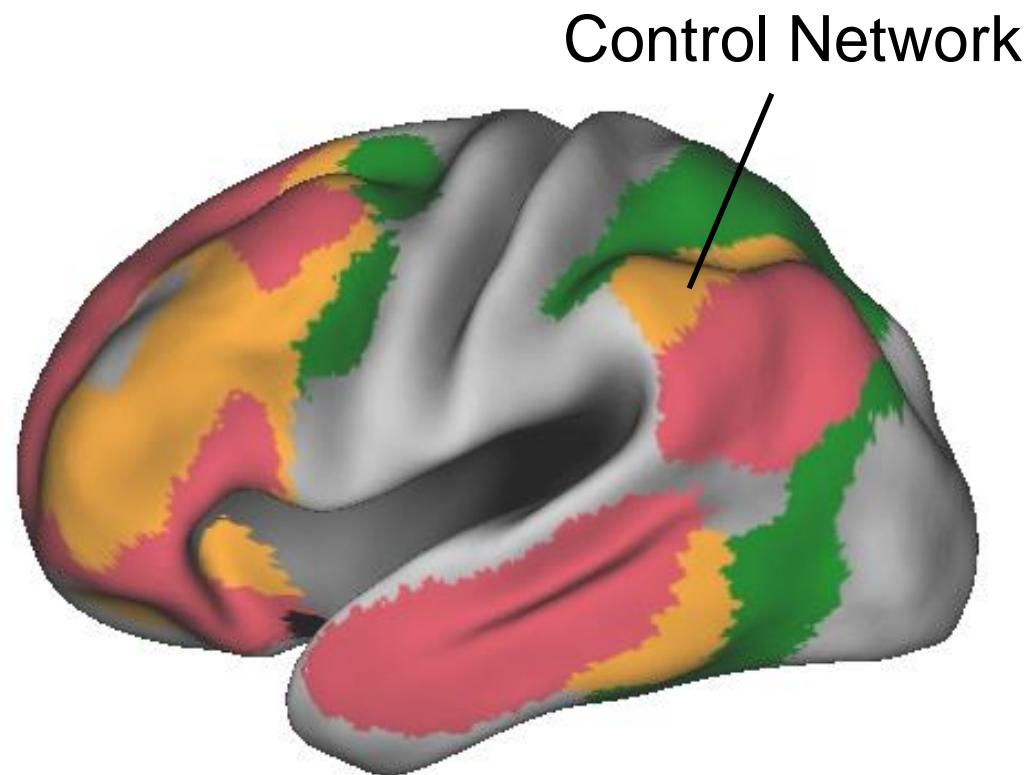


Vincent et al., 2006, *J. Neurophysiol.*

Expansion in Human Evolution



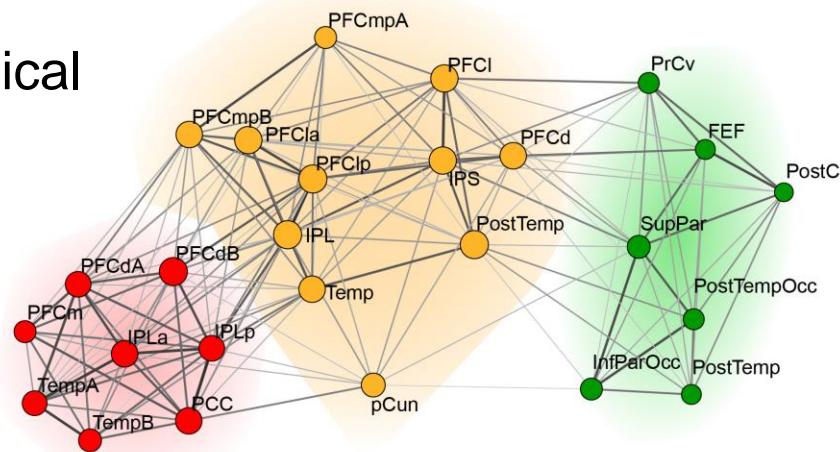
Hill et al., 2010 *Proc Natl Acad Sci*



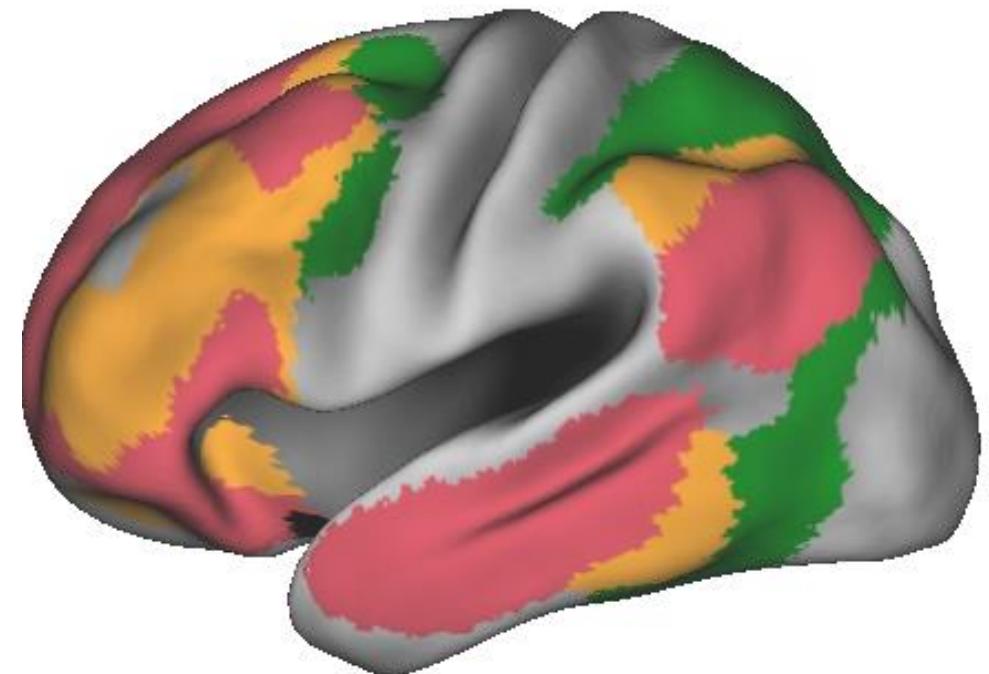
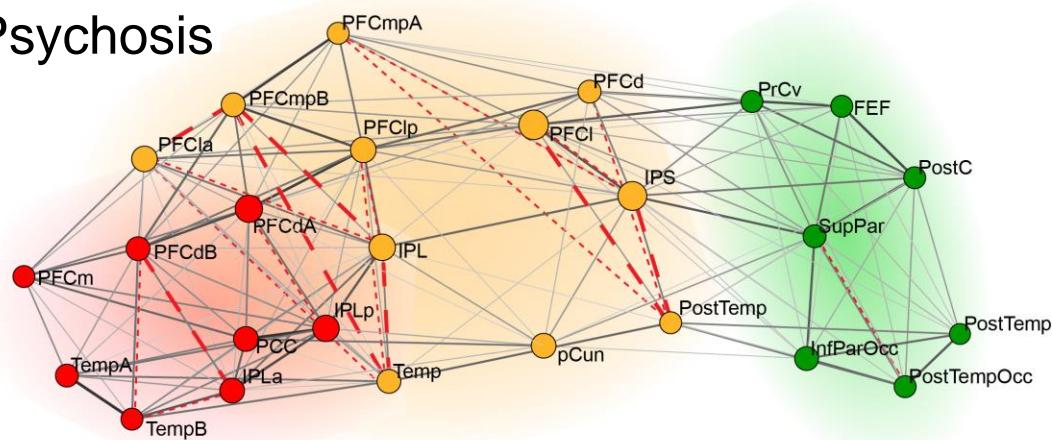
Vincent et al., 2006, *J. Neurophysiol.*

Relevance to Mental Illness

Typical



Psychosis

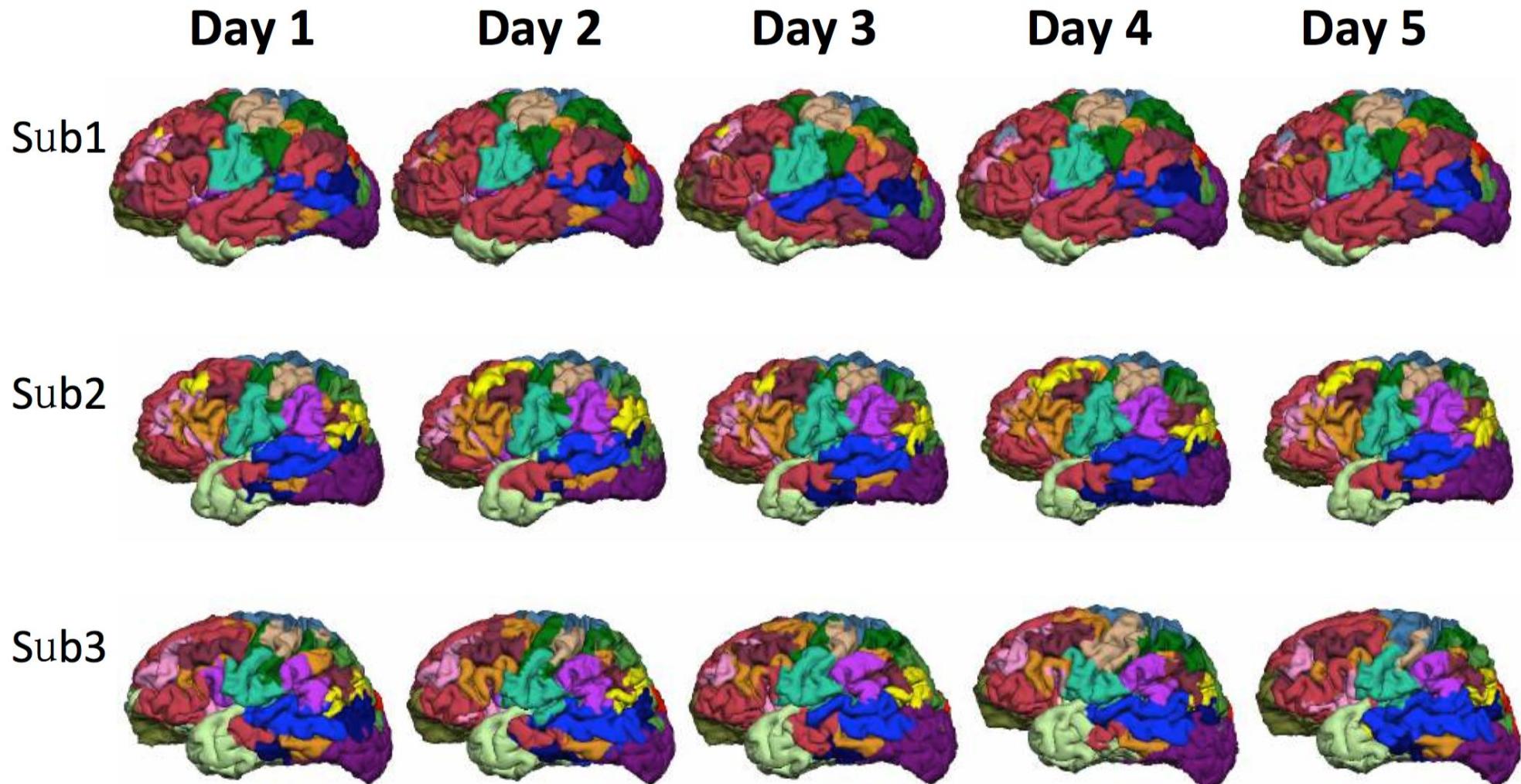


Baker et al., 2013, *JAMA Psychiatry*

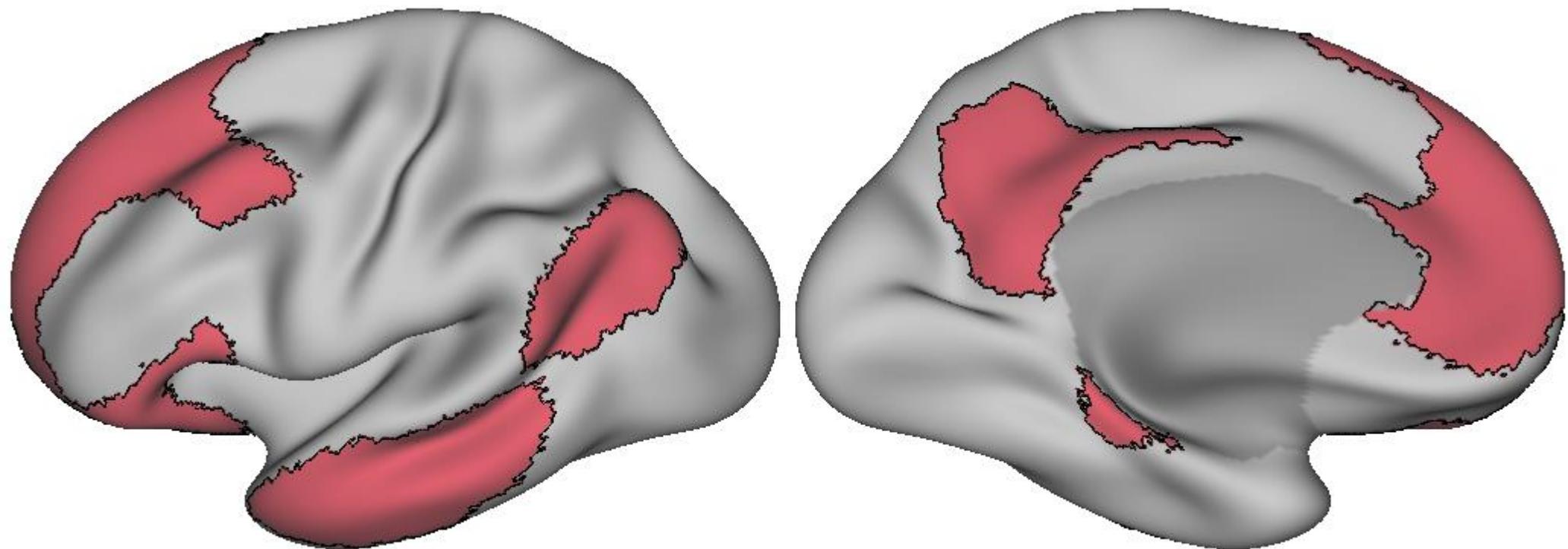
Vincent et al., 2006, *J. Neurophysiol.*

(See also Whitfield-Gabrieli et al., 2009, *PNAS*; Anticivic et al., 2013 *Cereb Ctx*; Yang et al., 2016 *PNAS*)

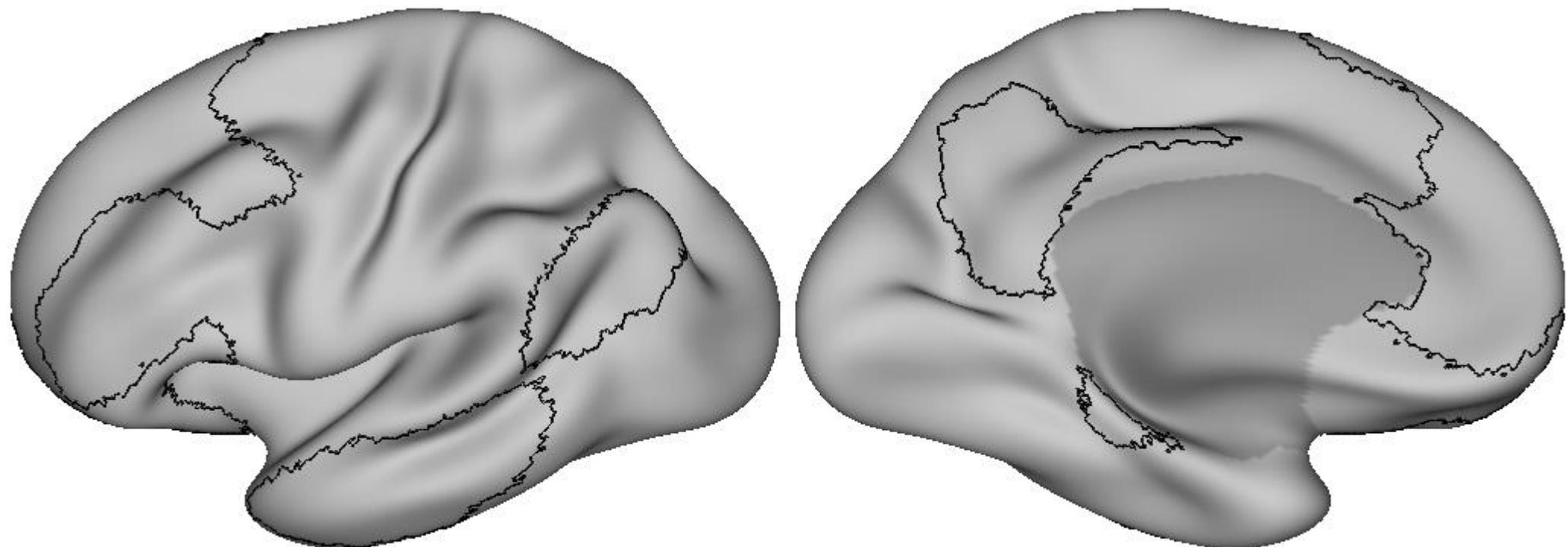
Variability Across Individuals



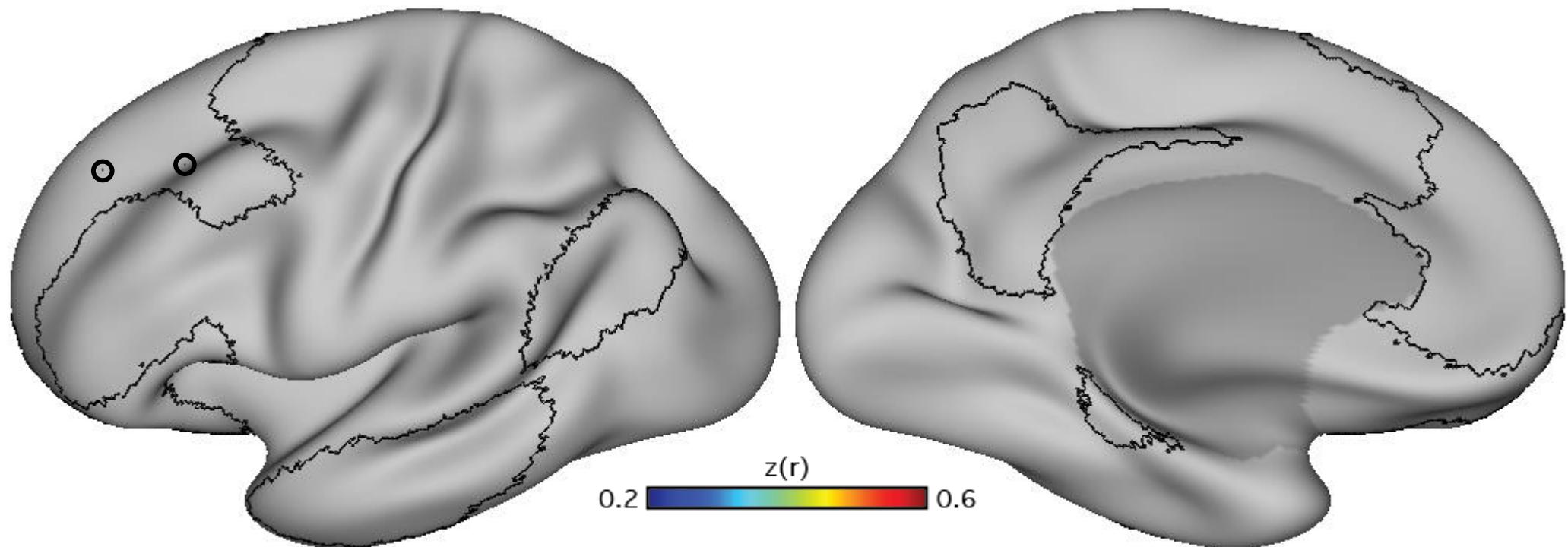
Group Association Network (n=1000)



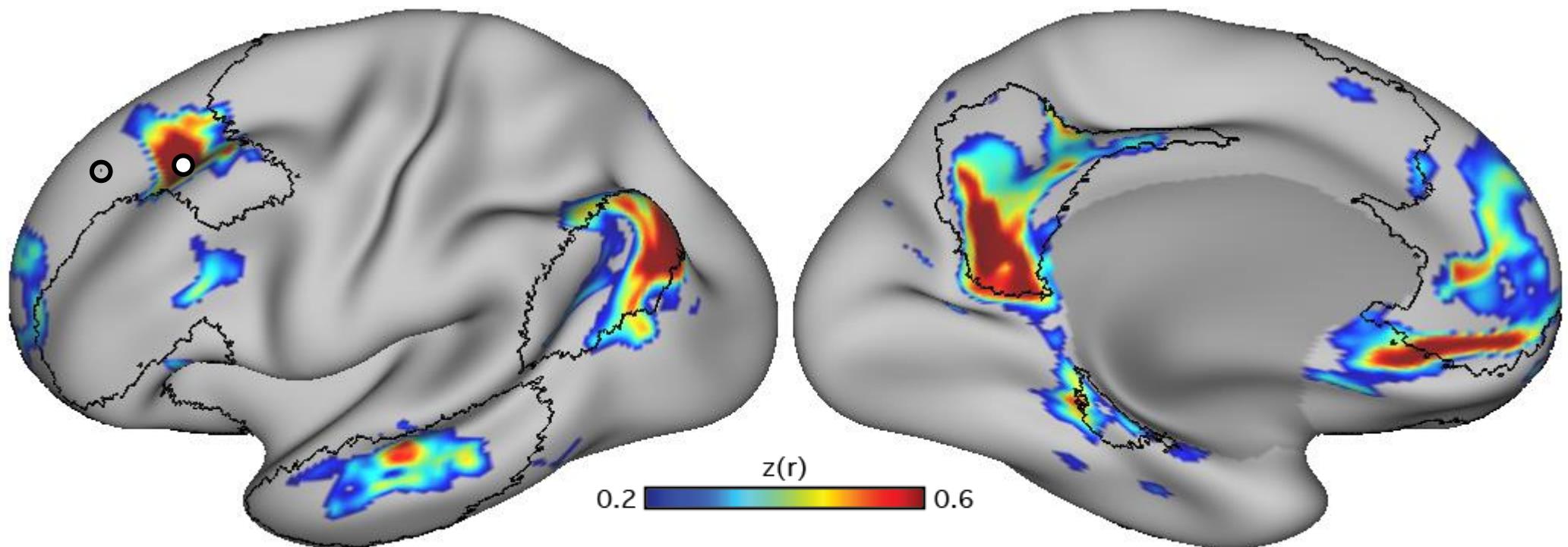
Group Association Network (n=1000)



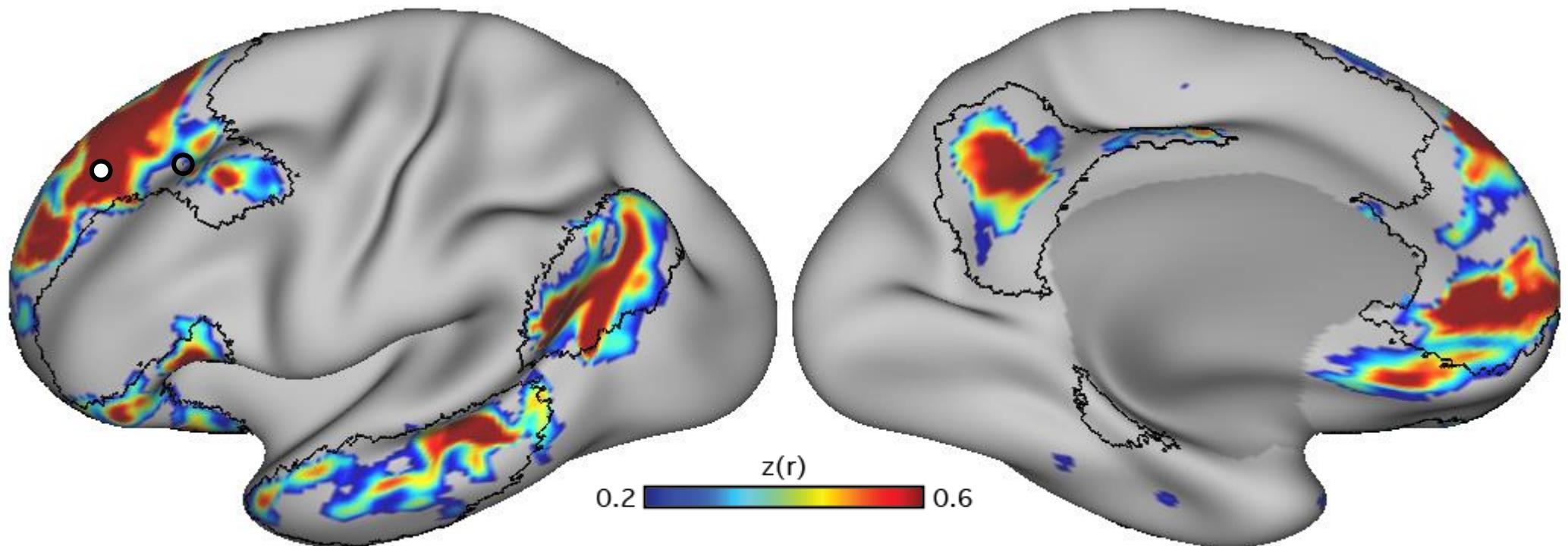
Single Subject (24 MRI Sessions)



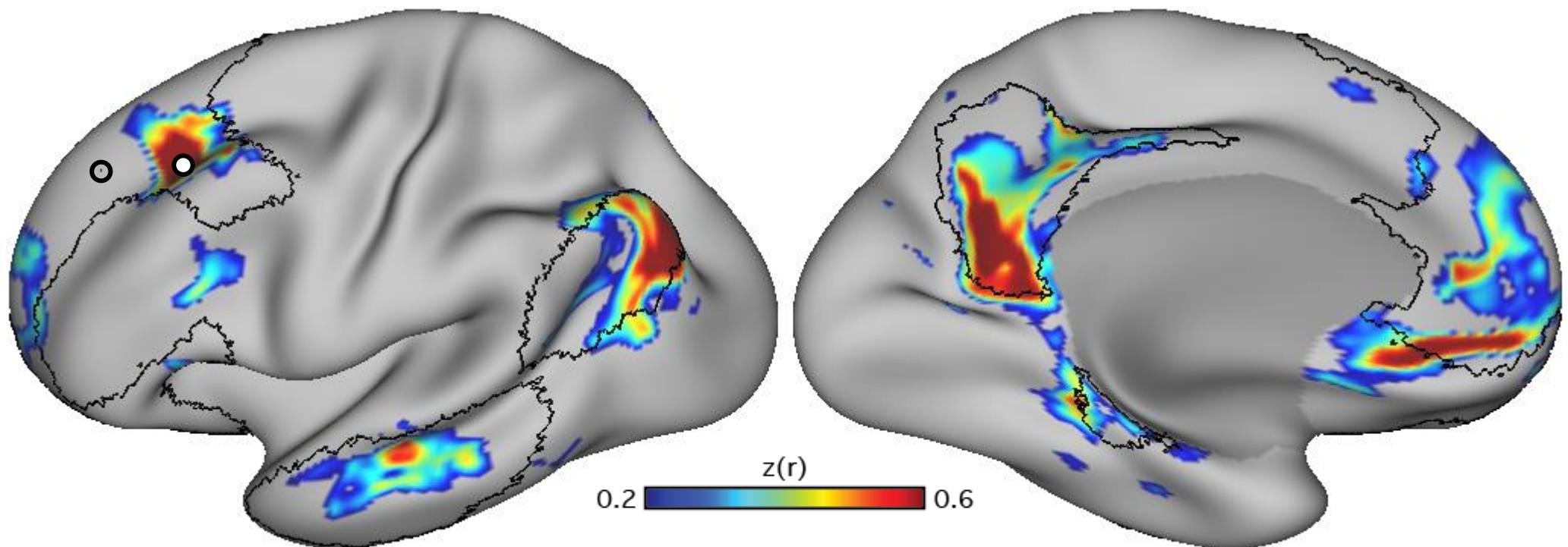
Single Subject (24 MRI Sessions)



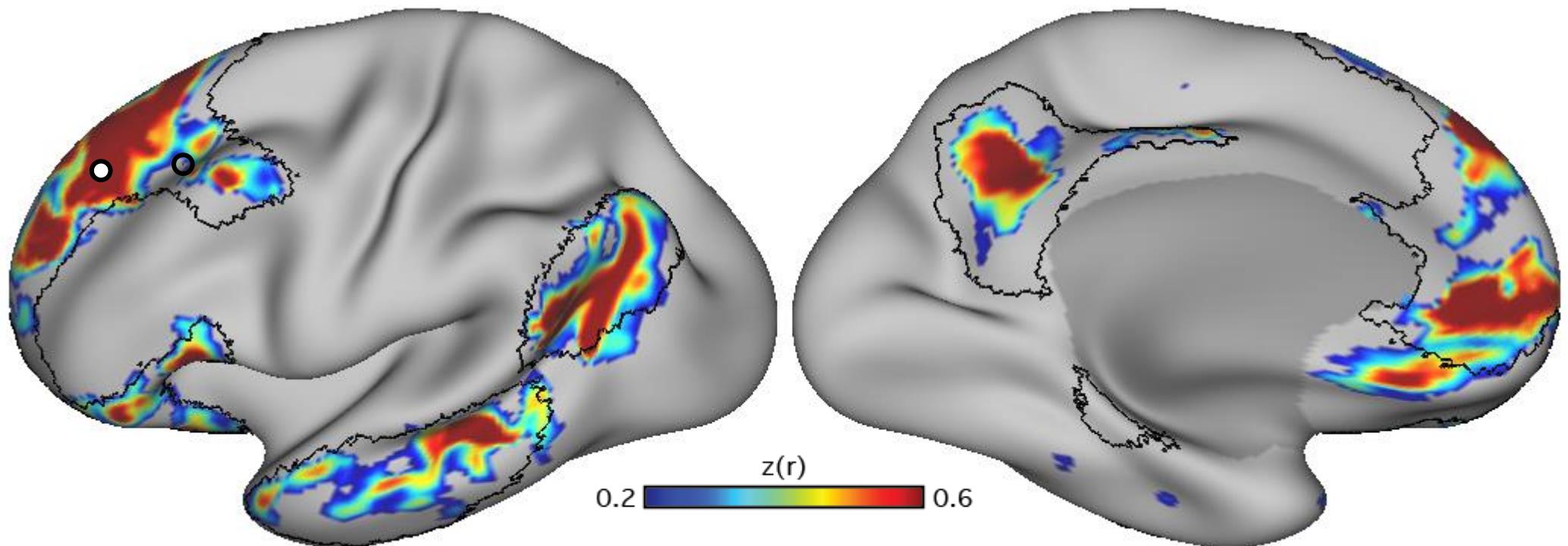
Single Subject (24 MRI Sessions)



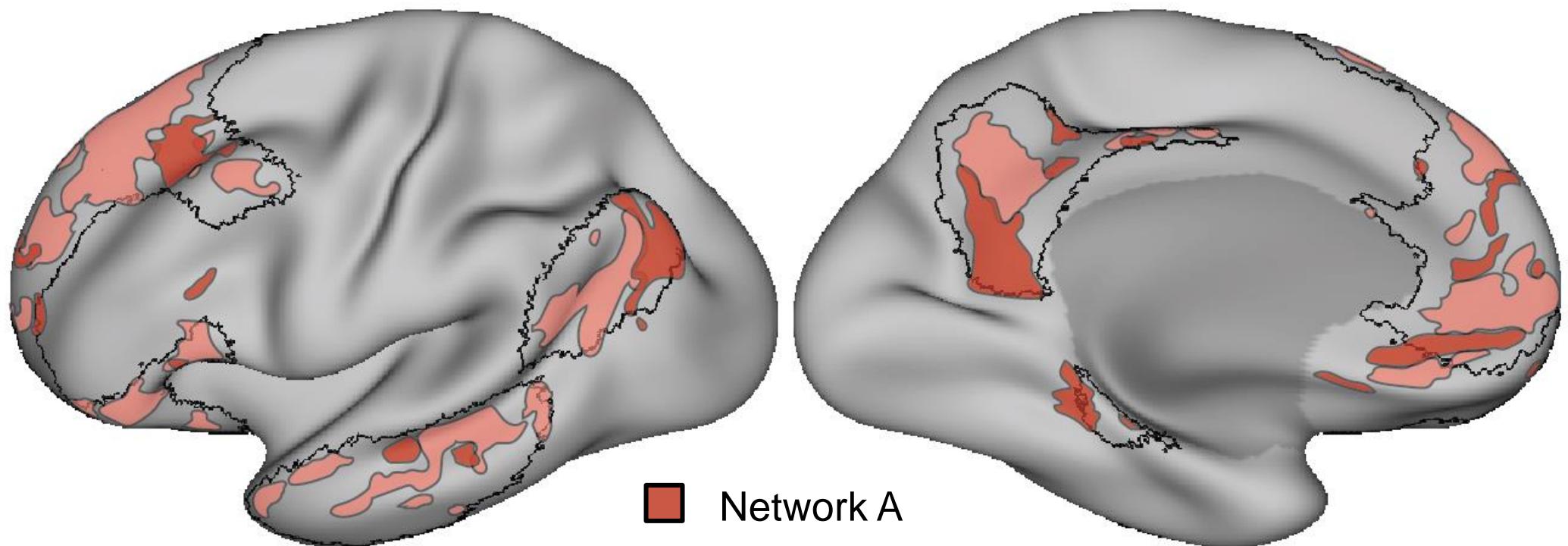
Single Subject (24 MRI Sessions)



Single Subject (24 MRI Sessions)



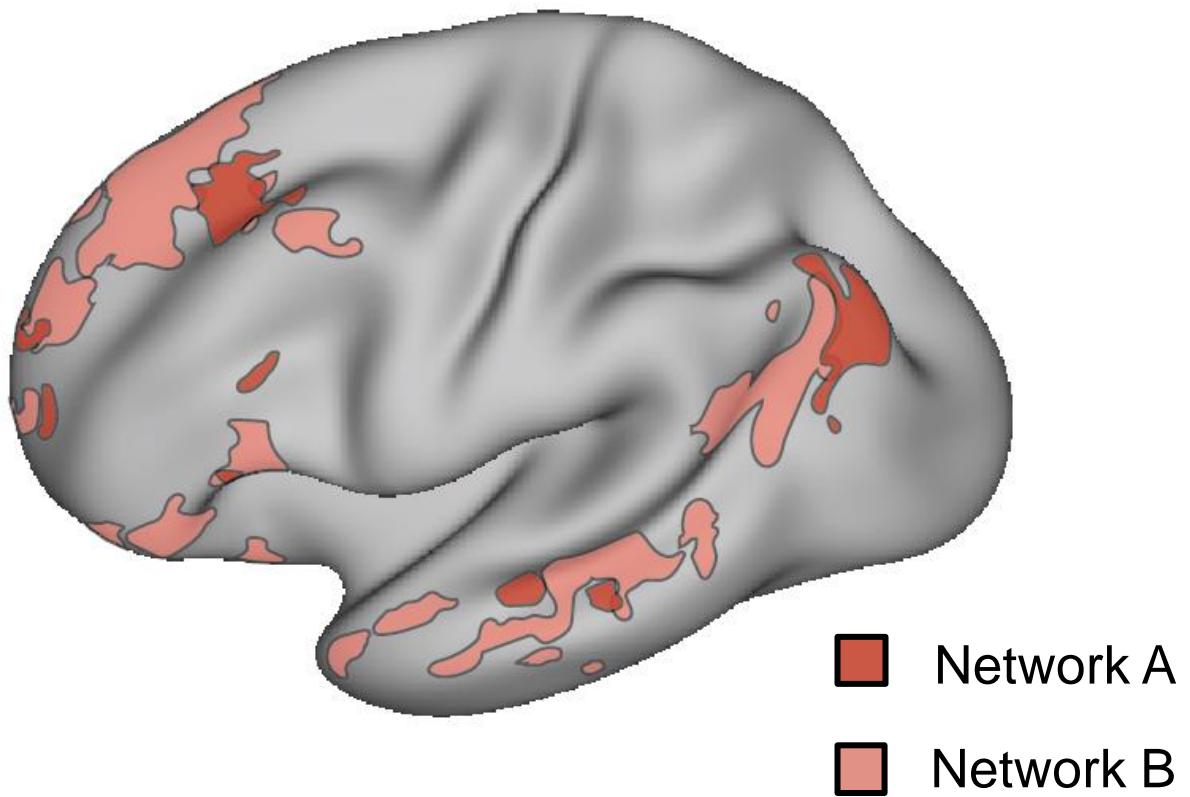
Single Subject (24 MRI Sessions)



■ Network A

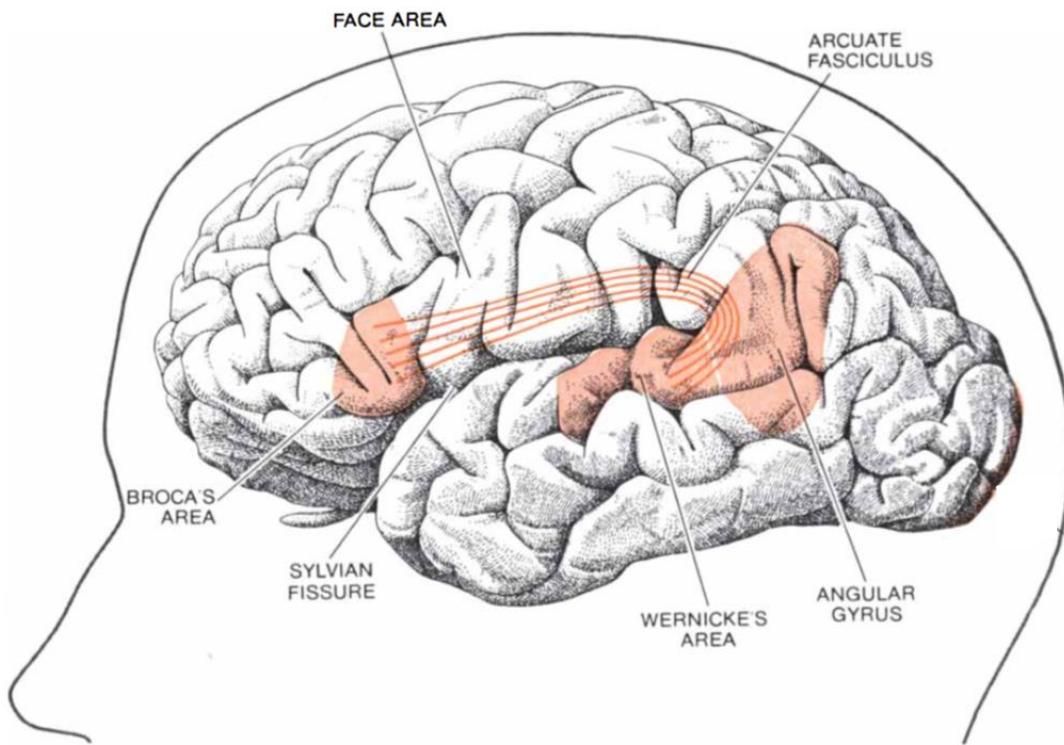
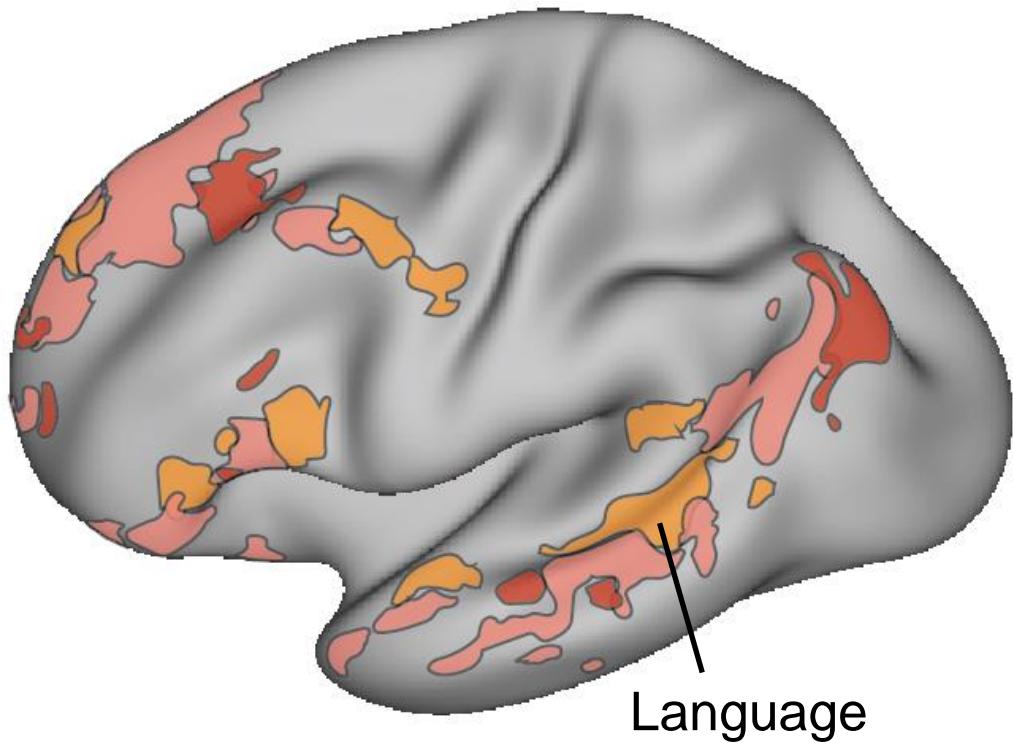
■ Network B

Human Specialization for Higher Brain Function?

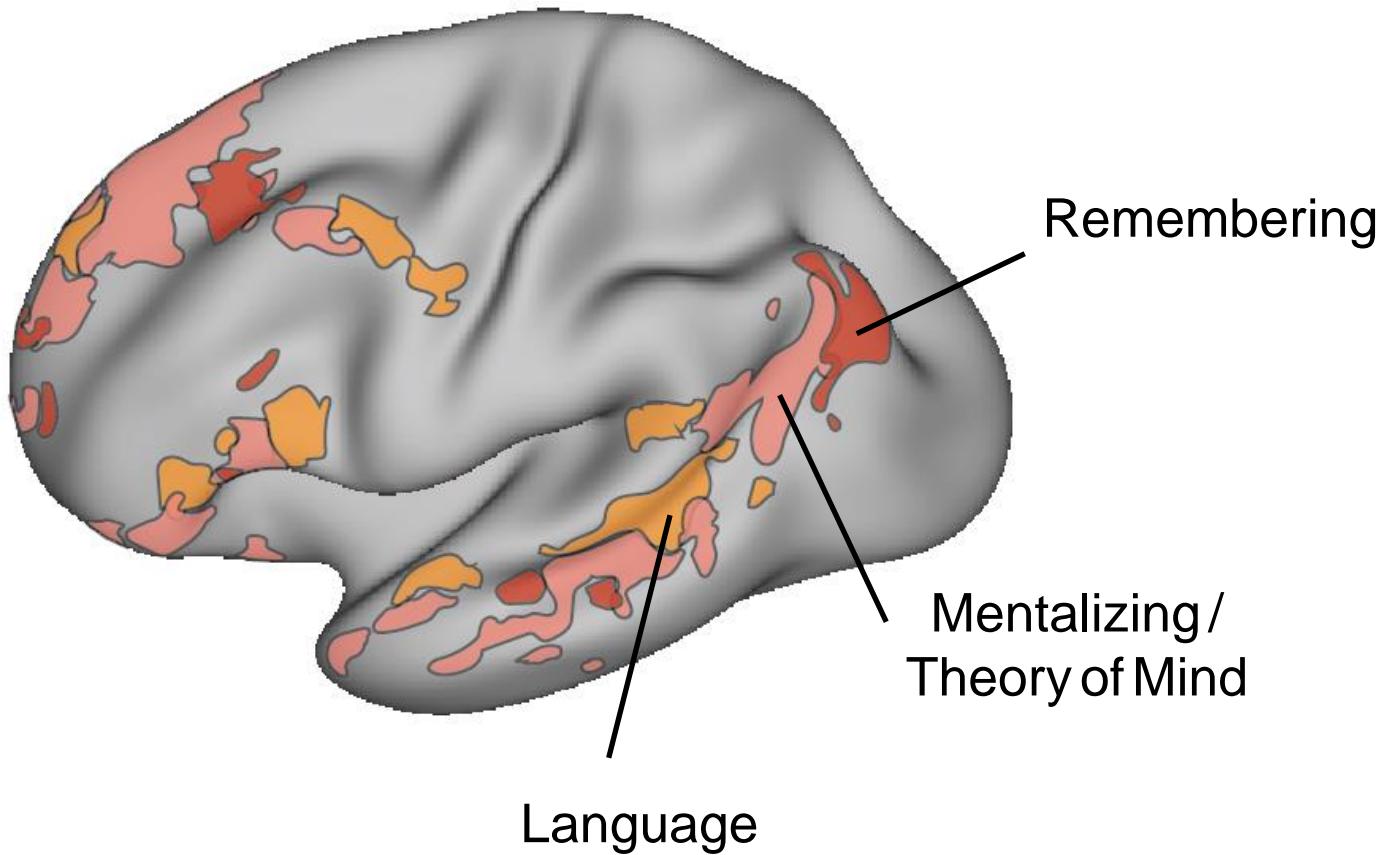


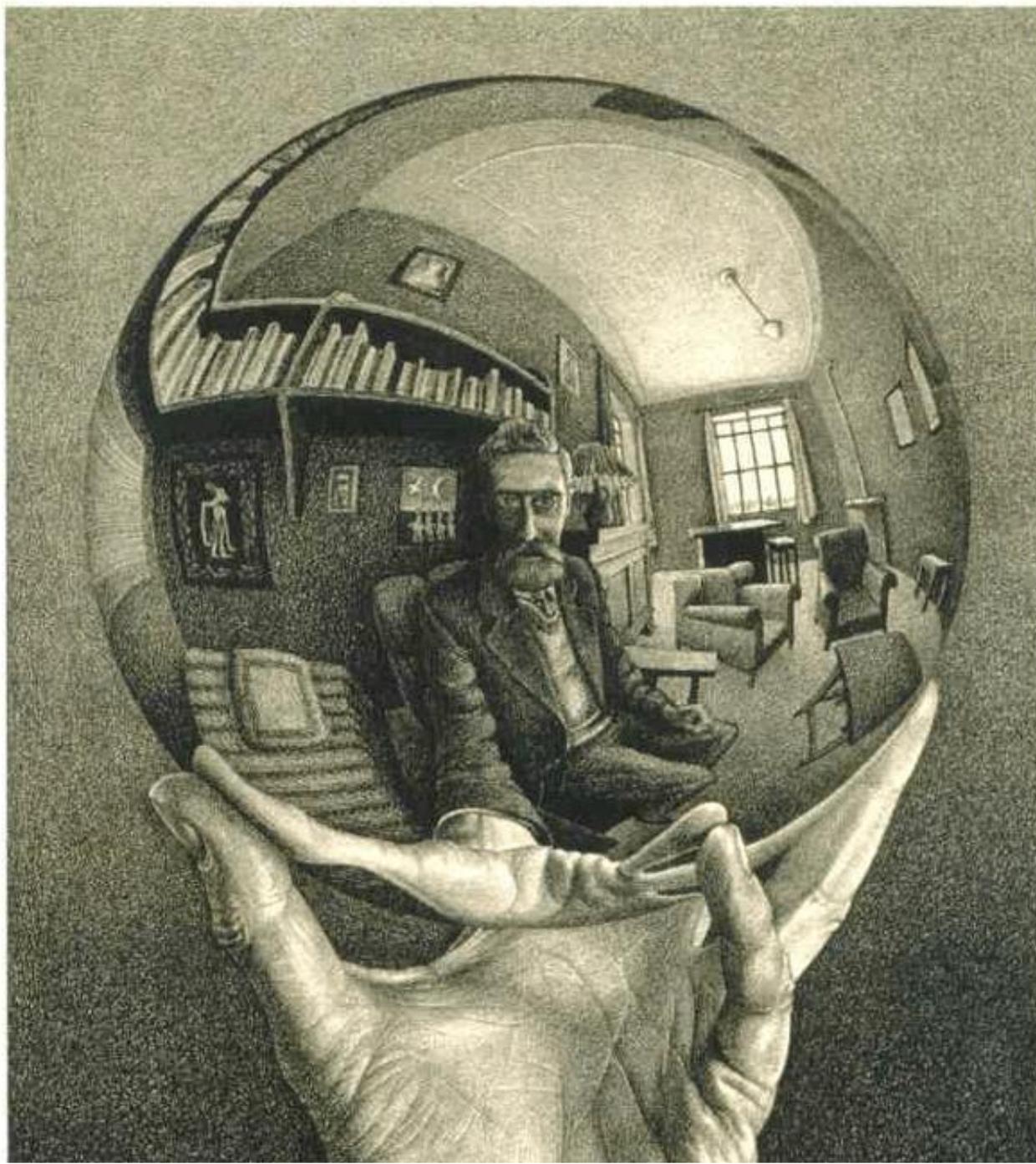
Human Specialization for Higher Brain Function?

Geschwind's Language Network



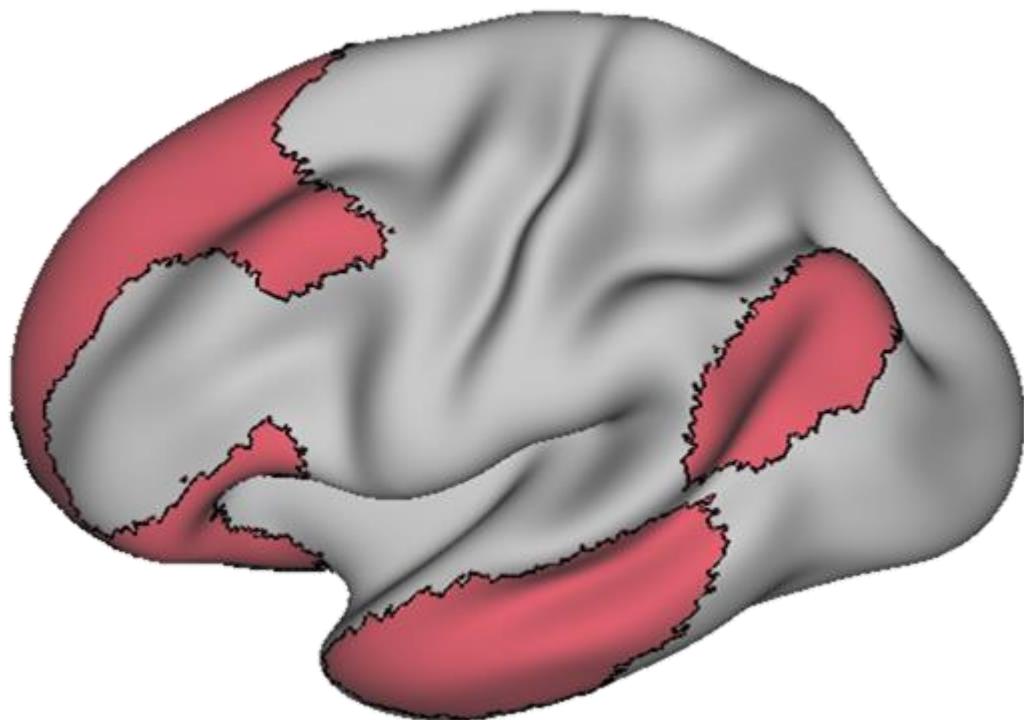
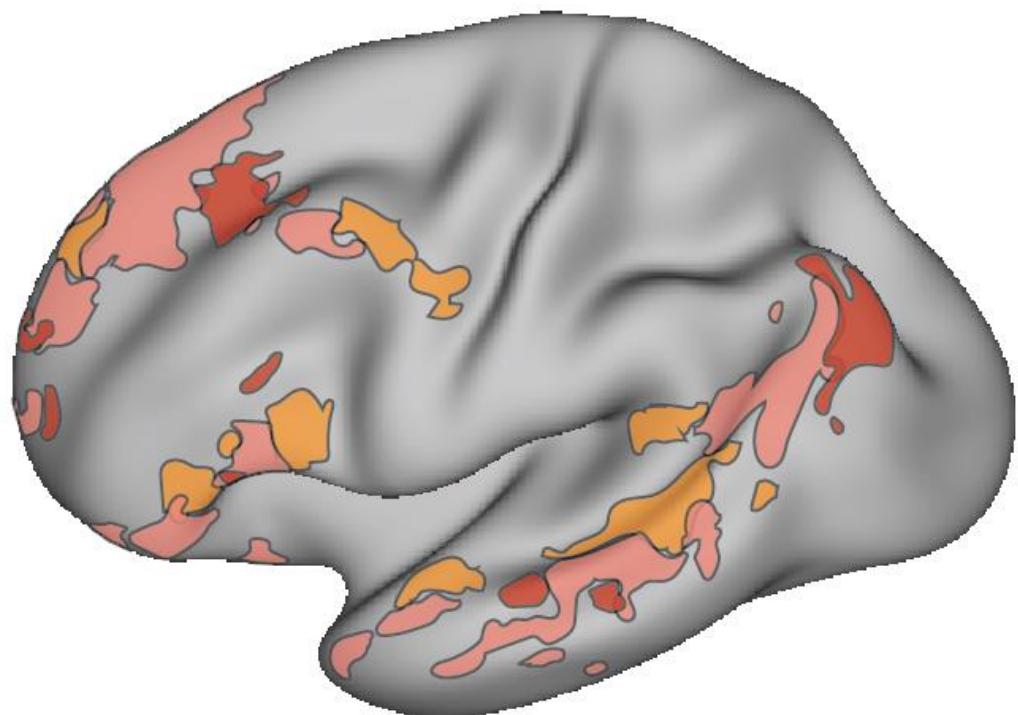
Human Specialization for Higher Brain Function?





Developmental Specialization

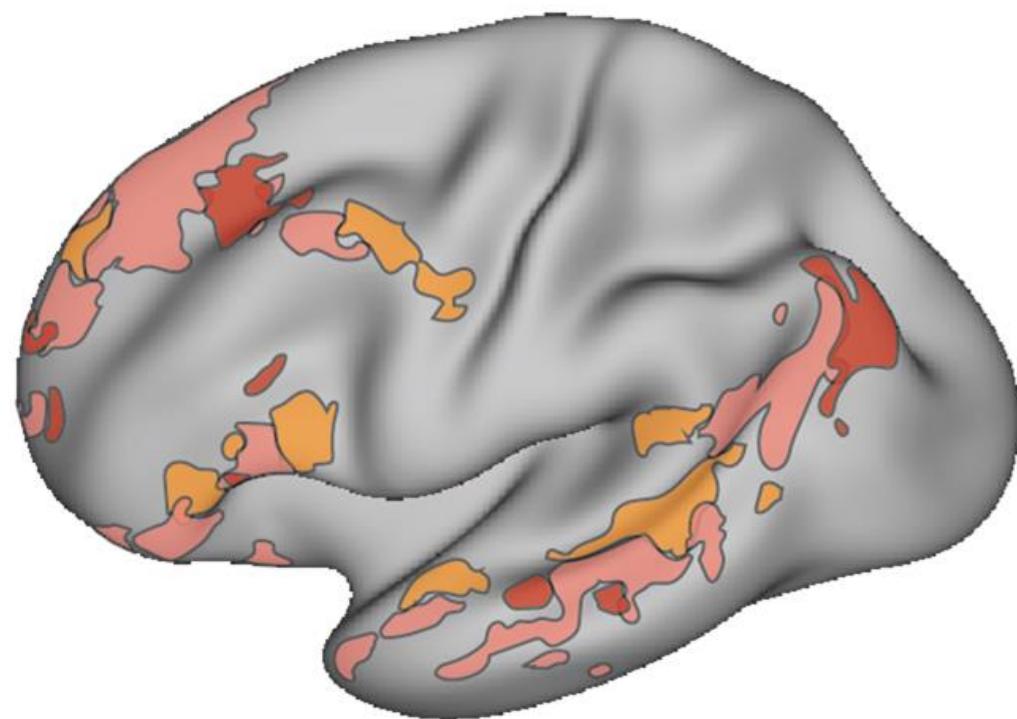
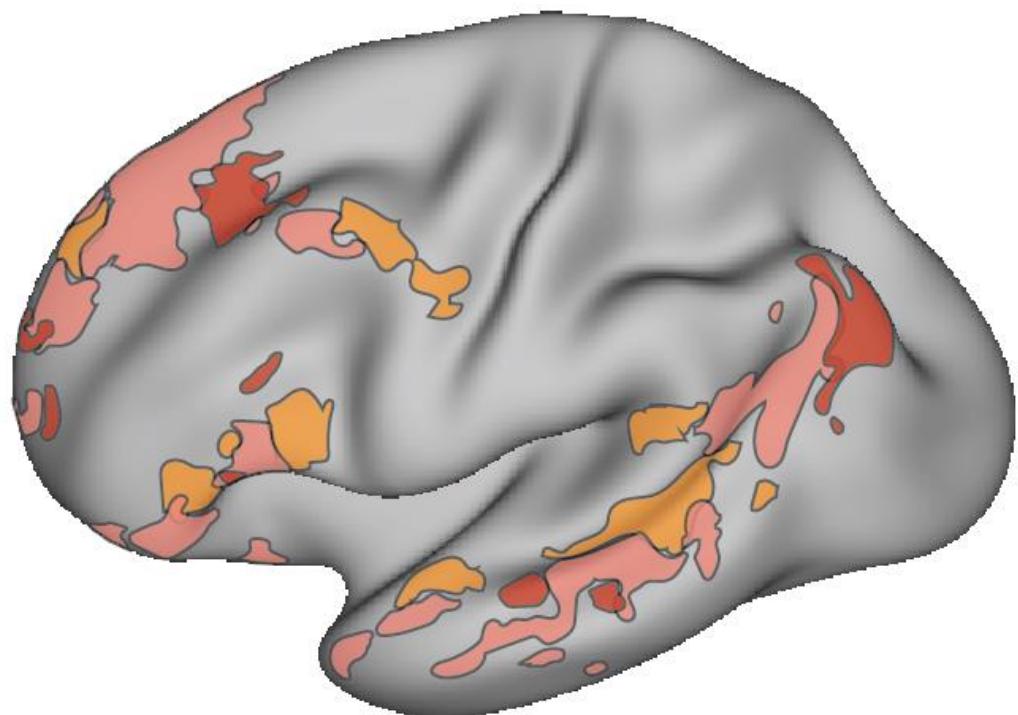
Mature
Proto-Organization ➡ Specialization



Early Development

Developmental Specialization

Mature
Proto-Organization ➡ Specialization



Late Development

Human Neuromodulation



PNAS PLUS

Resting-state networks link invasive and noninvasive brain stimulation across diverse psychiatric and neurological diseases

Michael D. Fox^{a,b,c,1}, Randy L. Buckner^{c,d,e}, Hesheng Liu^c, M. Mallar Chakravarty^{f,g}, Andres M. Lozano^{h,i}, and Alvaro Pascual-Leone^a

^aBerenson-Allen Center for Noninvasive Brain Stimulation, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215; ^bDepartment of Neurology, Center for Biomedical Imaging, Harvard Medical School, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114; ^cAthinoula A. Martinos Center for Biomedical Imaging, Harvard Medical School, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114; ^dDepartment of Psychology, Center for Verdun, QC, Canada H4H 1R3; ^eDepartment of Neurosurgery, Department of Surgery, University of Toronto, ON, Canada M5T 2S8

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Brain stimulation, a therapy increasing psychiatric disease, traditionally is done such as deep brain stimulation (DBS) such as transcranial magnetic stimulation; these approaches is unknown, the unclear, and the ideal stimulation is ambiguous, limiting optimization of stimulation in further disorders. In this article with both types of stimulation, list the most effective in each disease, and sites are different nodes within the by resting-state functional-connectivity were functionally connected brain stimulation was effective action, Parkinson's disease, obsessive-compulsive disorder, tremor, addition, pain, minimally effective. A lack of functional connectivity was ineffective, and the side whether excitatory or inhibitory not clinically effective. These results suggest connectivity may be useful for stimulation modalities, optimizing stimulation targets. More broadly, a perspective toward understanding disease, highlighting the therapeutic network modulation.

human connectome project | neurosurgery clinical application

A promising treatment approach for neurological diseases is currently divided into invasive approaches and noninvasive approaches that stimulate the skull. The dominant invasive treatment (DBS) in which an electrode is surgically implanted into the brain and used to deliver electrical stimulation (generally 120–160 Hz) (1, 2). In some cases, DBS resembles those of stimulators, but in other cases DBS appears to be delivered to adjacent white matter fibers (1, 2). DBS systems are approved by the US Food and Drug Administration (FDA) for treatment of essential tremor and Parkinson's disease, have humanitarian device exemptions for dystonia and obsessive-compulsive disorder, and are being explored as a therapy for many other diseases including depression, Alzheimer's disease, and even minimally conscious states (1, 3–6).

Although DBS can result in dramatic therapeutic benefit, the risk inherent in neurosurgery has motivated research into non-

Table 1. Diseases with evidence of efficacy for both invasive and noninvasive brain stimulation

Disease	Target for invasive stimulation (DBS)	Target for noninvasive stimulation (TMS, tDCS)
Addiction	NA	DLPFC (laterality unclear)
Alzheimer's disease	Fornix	Bilateral DLPFC (\pm parietal, temporal)
Anorexia	NA, subgenual	Left DLPFC
Depression	Subgenual, VC/VS, NA, MFB, habenula	Left DLPFC, right DLPFC
Dystonia	GPi	SMA/ACC, premotor
Epilepsy	Thalamus (AN, CM), MTL	Active EEG focus, cerebellum
Essential tremor	VIM	Midline cerebellum, lateral cerebellum, M1
Gait dysfunction	PPN	M1 (leg area)
Huntington's disease	GPi	SMA
Minimally conscious	Thalamus (intralaminar/CL, CM/Pf)	Right DLPFC, M1
Obsessive compulsive disorder	VC/VS, NA, ALIC, STN	Left orbitofrontal, pre-SMA
Pain	PAG, thalamus (VPL/VPM)	M1
Parkinson's disease	STN, GPi	M1, SMA
Tourette's syndrome	Thalamus (CM/Pf), GPi, NA, ALIC	SMA

serves on the scientific advisory boards for Nextstim, Neuronix, Starlab Neuroscience, Allied Mind, NeuroSync, Magstim, Axilum Robotics, and Novavision and is listed as inventor in issued patents and patent applications on the real-time integration of transcranial magnetic stimulation with electroencephalography and MRI.

This article is a PNAS Direct Submission.
Data deposition: MRI data is available for download from <http://neuroinformatics.harvard.edu/>.

¹To whom correspondence should be addressed. Email: foxmdph@gmail.com.
This article contains supporting information online at www.pnas.org/lookup/suppl/doi/10.1073/pnas.1405003111/DCSupplemental.

Artificial Intelligence

Neuron
Review

CellPress

Neuroscience-Inspired Artificial Intelligence

Demis Hassabis,^{1,2,*} Dharshan Kumaran,^{1,3} Christopher Summerfield,^{1,4} and Matthew Botvinick^{1,2}

¹DeepMind, 5 New Street Square, London, UK
²Gatsby Computational Neuroscience Unit, 25 Howland Street, London, UK
³Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London, UK
⁴Department of Experimental Psychology, University of Oxford, Oxford, UK

*Correspondence: dhcontact@google.com
<http://dx.doi.org/10.1016/j.neuron.2017.06.011>

The fields of neuroscience and artificial intelligence (AI) have a long and intertwined history. In more recent times, however, communication and collaboration between the two fields has become less commonplace. In this article, we argue that better understanding biological brains could play a vital role in building intelligent machines. We survey historical interactions between the AI and neuroscience fields and emphasize current advances in AI that have been inspired by the study of neural computation in humans and other animals. We conclude by highlighting shared themes that may be key for advancing future research in both fields.

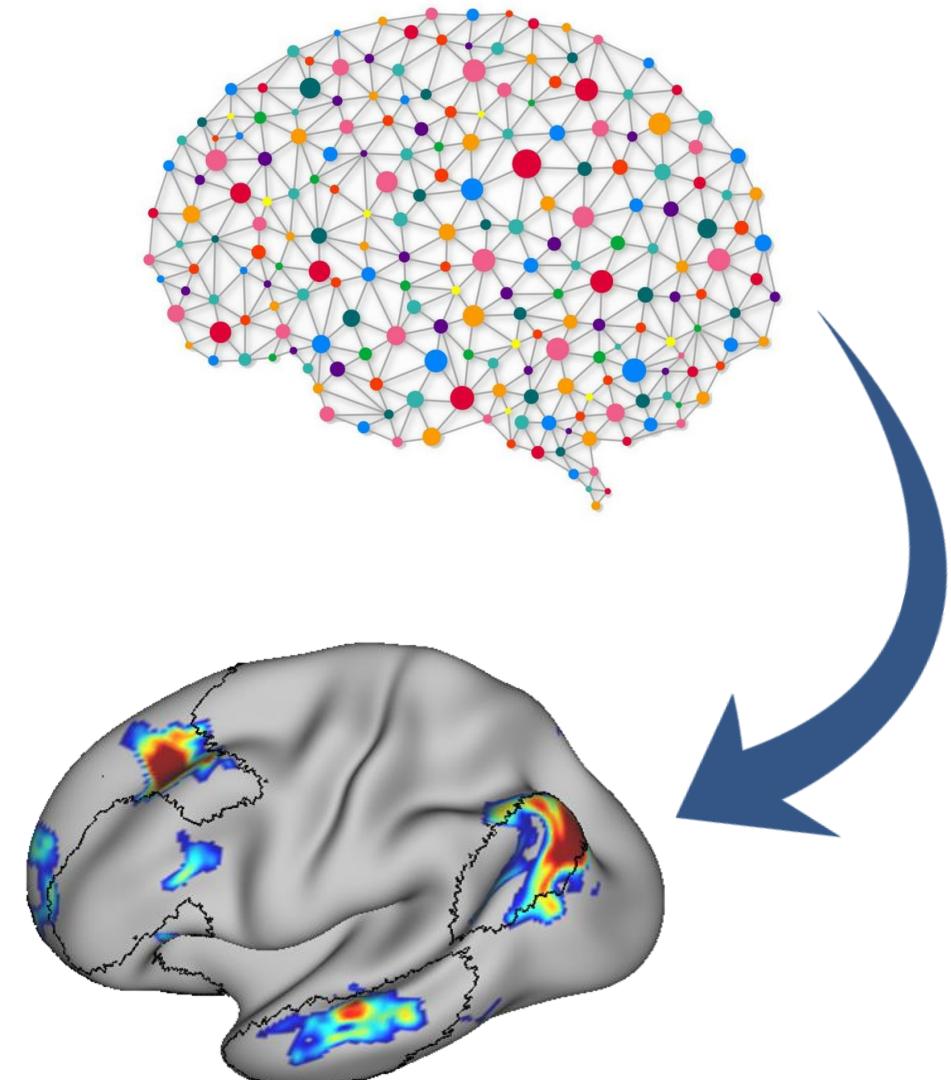
In recent years, rapid progress has been made in the related fields of neuroscience and artificial intelligence (AI). At the dawn of the computer age, work on AI was inextricably intertwined with neuroscience and psychology, and many of the early pioneers straddled both fields, with collaborations between these disciplines proving highly productive (Churchland and Sejnowski, 1988; Hebb, 1949; Hinton et al., 1986; Hopfield, 1982; McCulloch and Pitts, 1943; Turing, 1950). However, more recently, the interaction has become much less commonplace, as both subjects have grown enormously in complexity and disciplinary boundaries have solidified. In this review, we argue for the critical and ongoing importance of neuroscience in generating ideas that will accelerate and guide AI research (see Hassabis commentary in Brooks et al., 2012).

We begin with the premise that building human-level general AI (or “Turing-powerful” intelligent systems; Turing, 1936) is a daunting task, because the search space of possible solutions is vast and likely only very sparsely populated. We argue that this therefore underscores the utility of scrutinizing the inner workings of the human brain—the only existing proof that such an intelligence is even possible. Studying animal cognition and its neural implementation also has a vital role to play, as it can provide a window into various important aspects of higher-level general intelligence.

The benefits to developing AI of closely examining biological intelligence are two-fold. First, neuroscience provides a rich source of *inspiration* for new types of algorithms and architectures, independent of and complementary to the mathematical and logic-based methods and ideas that have largely dominated traditional approaches to AI. For example, were a new facet of biological computation found to be critical to supporting a cognitive function, then we would consider it an excellent candidate for incorporation into artificial systems. Second, neuroscience can provide *validation* of AI techniques that already exist. If a known algorithm is subsequently found to be implemented in the brain, then that is strong support for its plausibility as an integral component of an overall general intelligence system. Such clues can be critical to a long-term research program when determining where to allocate resources most productively. For example, if an algorithm is not quite attaining the level of performance required or expected, but we observe it is close to the functioning of the brain, then we can surmise that redoubled engineering efforts geared to making it work in artificial systems are likely to pay off.

Of course from a practical standpoint of building an AI system, we need not slavishly enforce adherence to biological plausibility. From an engineering perspective, what works is ultimately all that matters. For our purposes then, biological plausibility is a guide, not a strict requirement. What we are interested in is a systems neuroscience-level understanding of the brain, namely the algorithms, architectures, functions, and representations it utilizes. This roughly corresponds to the top two levels of the three levels of analysis that Marr famously stated are required to understand any complex biological system (Marr and Poggio, 1976): the goals of the system (the computational level) and the process and computations that realize this goal (the algorithmic level). The precise mechanisms by which this is physically realized in a biological substrate are less relevant here (the implementation level). Note this is where our approach to neuroscience-inspired AI differs from other initiatives, such as the Blue Brain Project (Markram, 2006) or the field of neuromorphic computing systems (Esser et al., 2016), which attempt to closely mimic or directly reverse engineer the specifics of neural circuits (albeit with different goals in mind). By focusing on the computational and algorithmic levels, we gain transferable insights into general mechanisms of brain function, while leaving room to accommodate the distinctive opportunities and challenges that arise when building intelligent machines *in silico*.

The following sections unpack these points by considering the past, present, and future of the AI-neuroscience interface. Before beginning, we offer a clarification. Throughout this article, we employ the terms “neuroscience” and “AI.” We use these terms in the widest possible sense. When we say neuroscience, we mean to include all fields that are involved with the study of the brain, the behaviors that it generates, and the mechanisms by which it does so, including cognitive neuroscience, systems neuroscience and psychology. When we say AI, we mean work



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Conclusions

- 1) Human brain imaging methods are able to detect network organization in individual people.
- 2) Distinct networks that are distributed across the brain are specialized for language, social, and mnemonic functions.
- 3) The identification of the networks provide targets for neuromodulation but have not yet provided translatable clinical tests or interventions.