MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

The Human Connectome Project
Mapping Brain Networks With MRI

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Disclosures

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

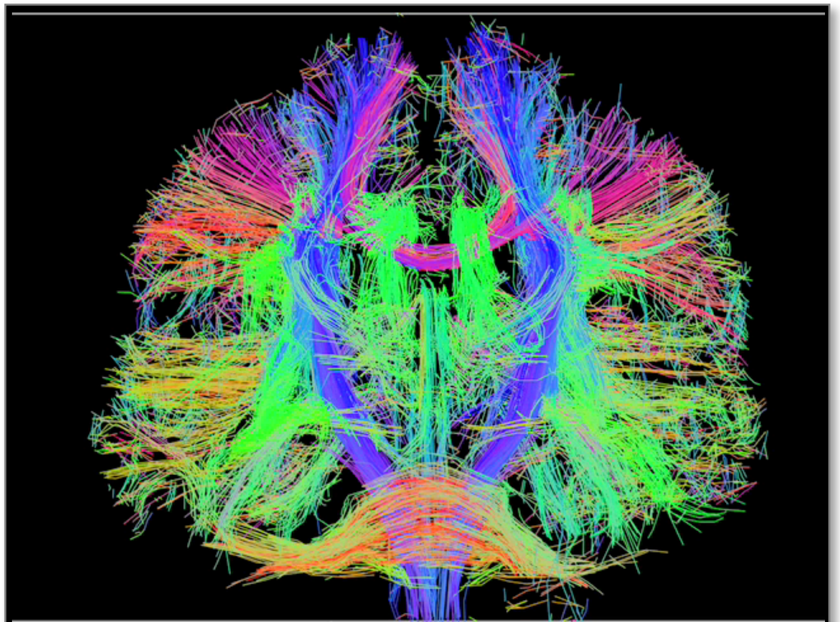
Consultant Pfizer, Roche

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

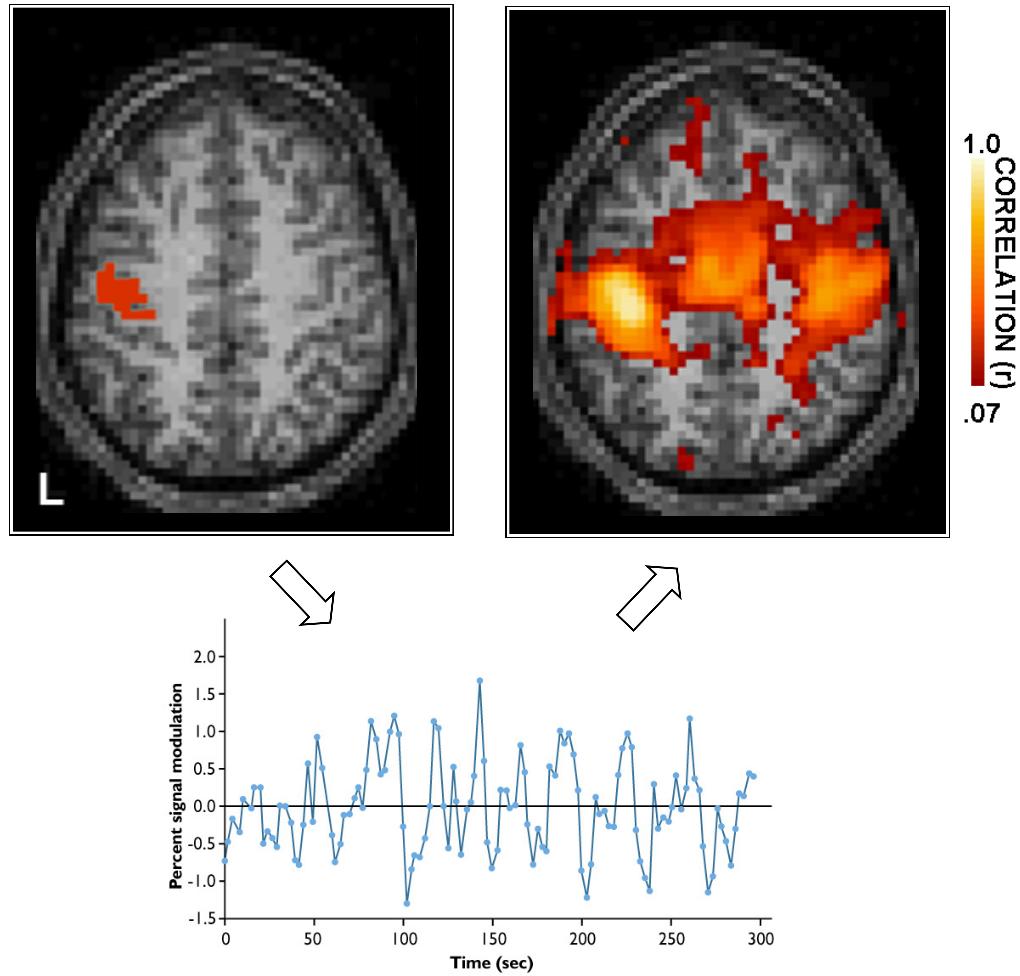
Diffusion



Intrinsic Activity

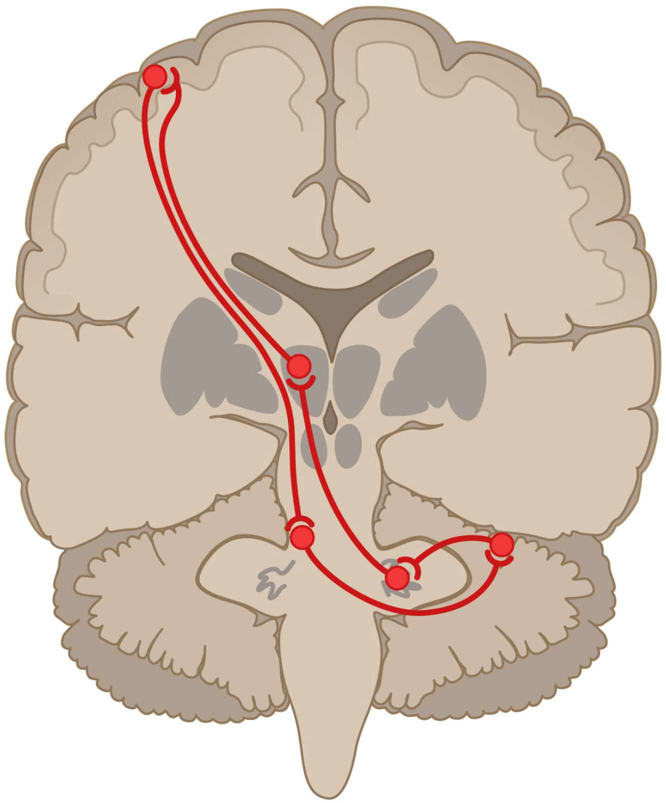
SEED REGION

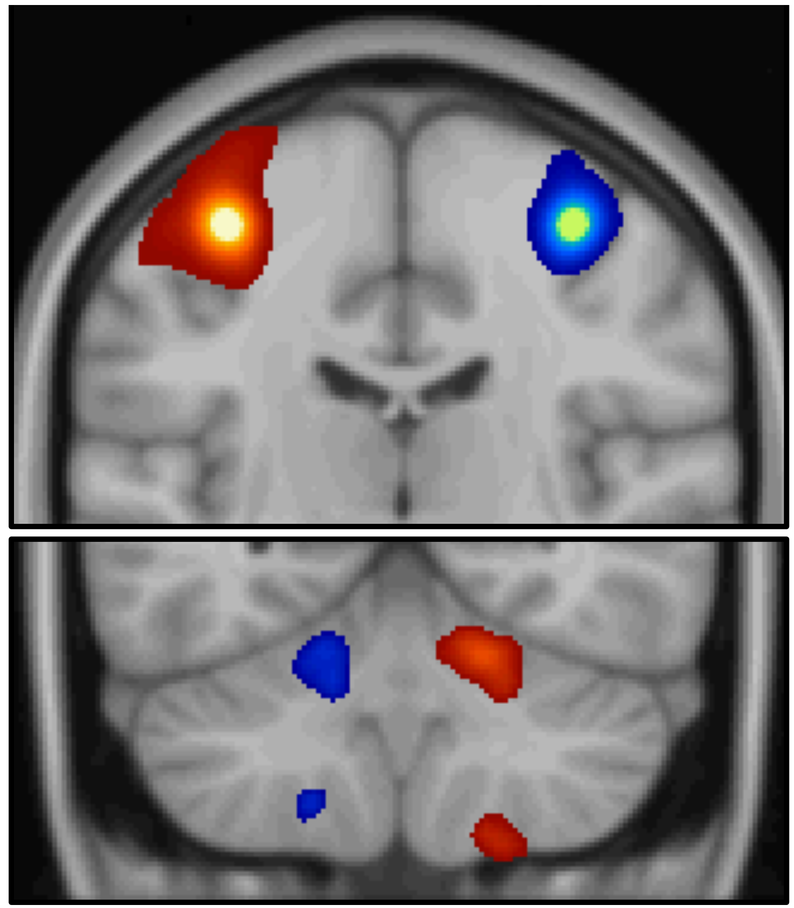
CORRELATED NETWORK



Example Validation

Cerebro-Cerebellar Circuit





Krienen and Buckner, 2009, *Cerebral Cortex*

Example Validation

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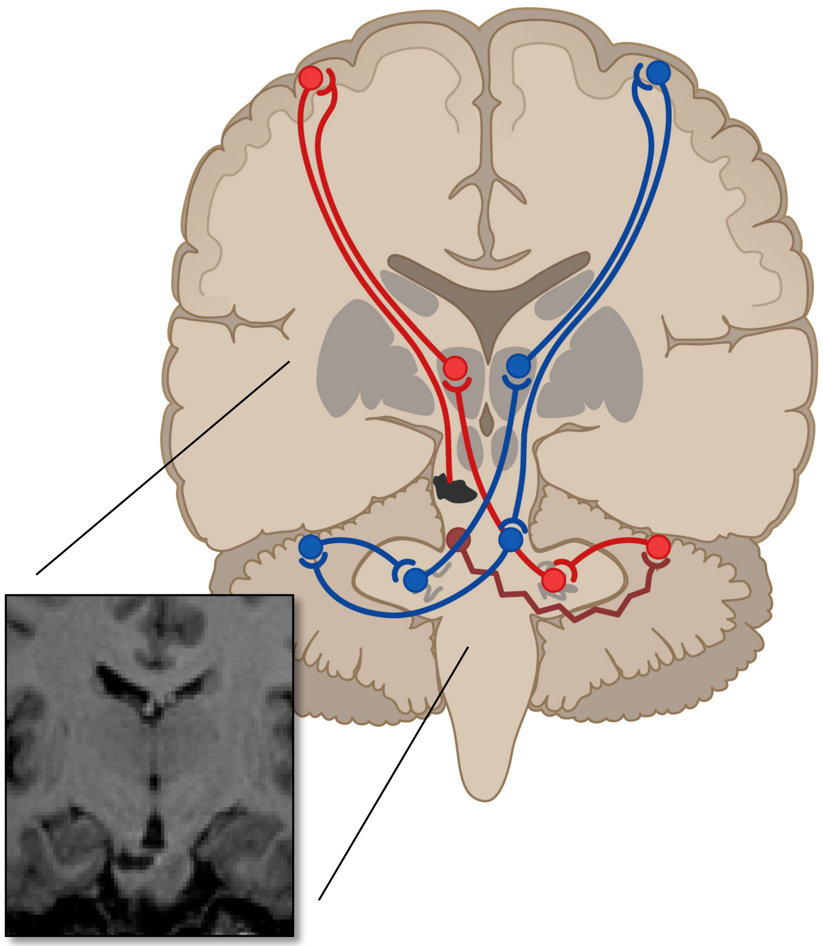
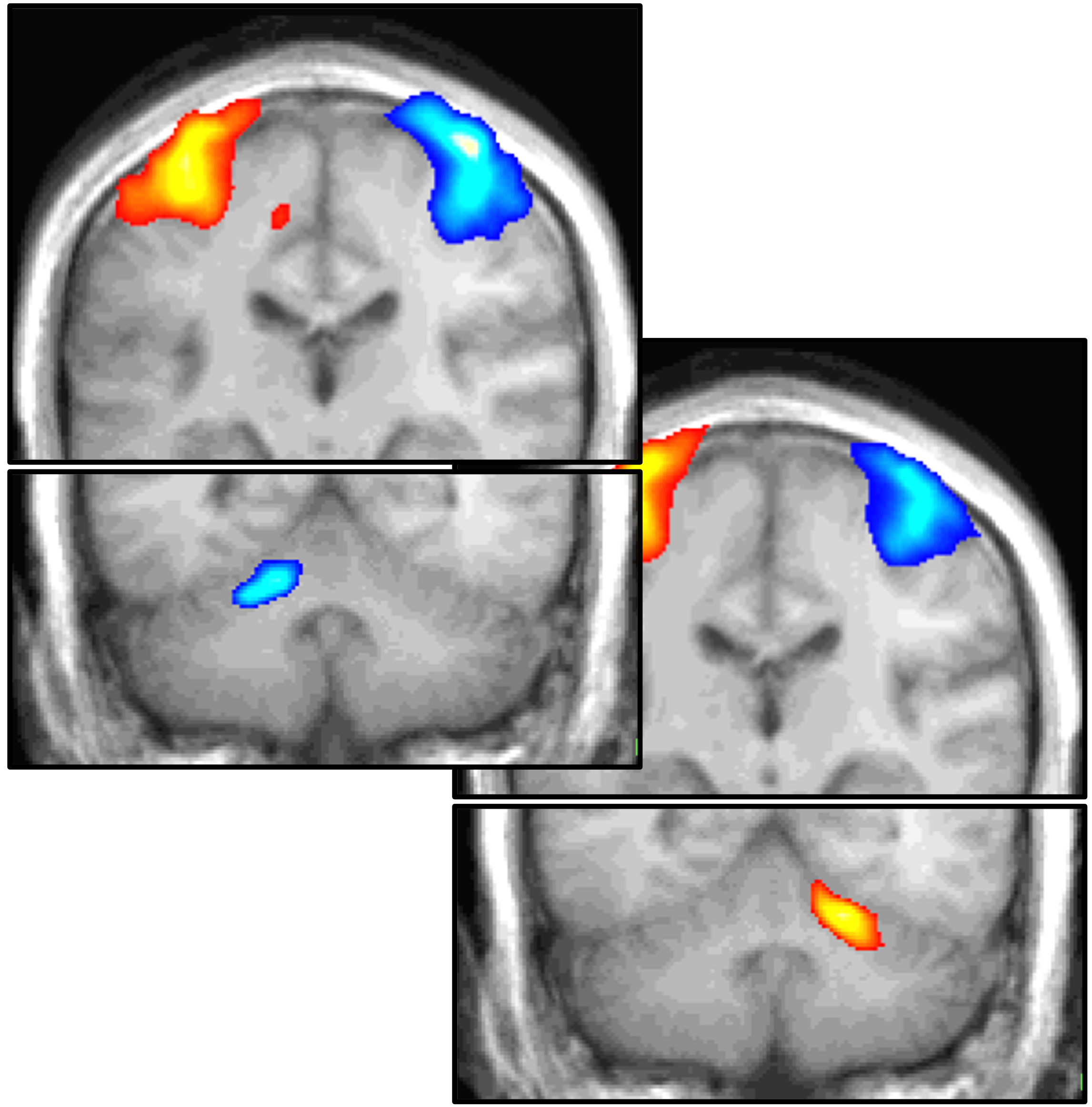
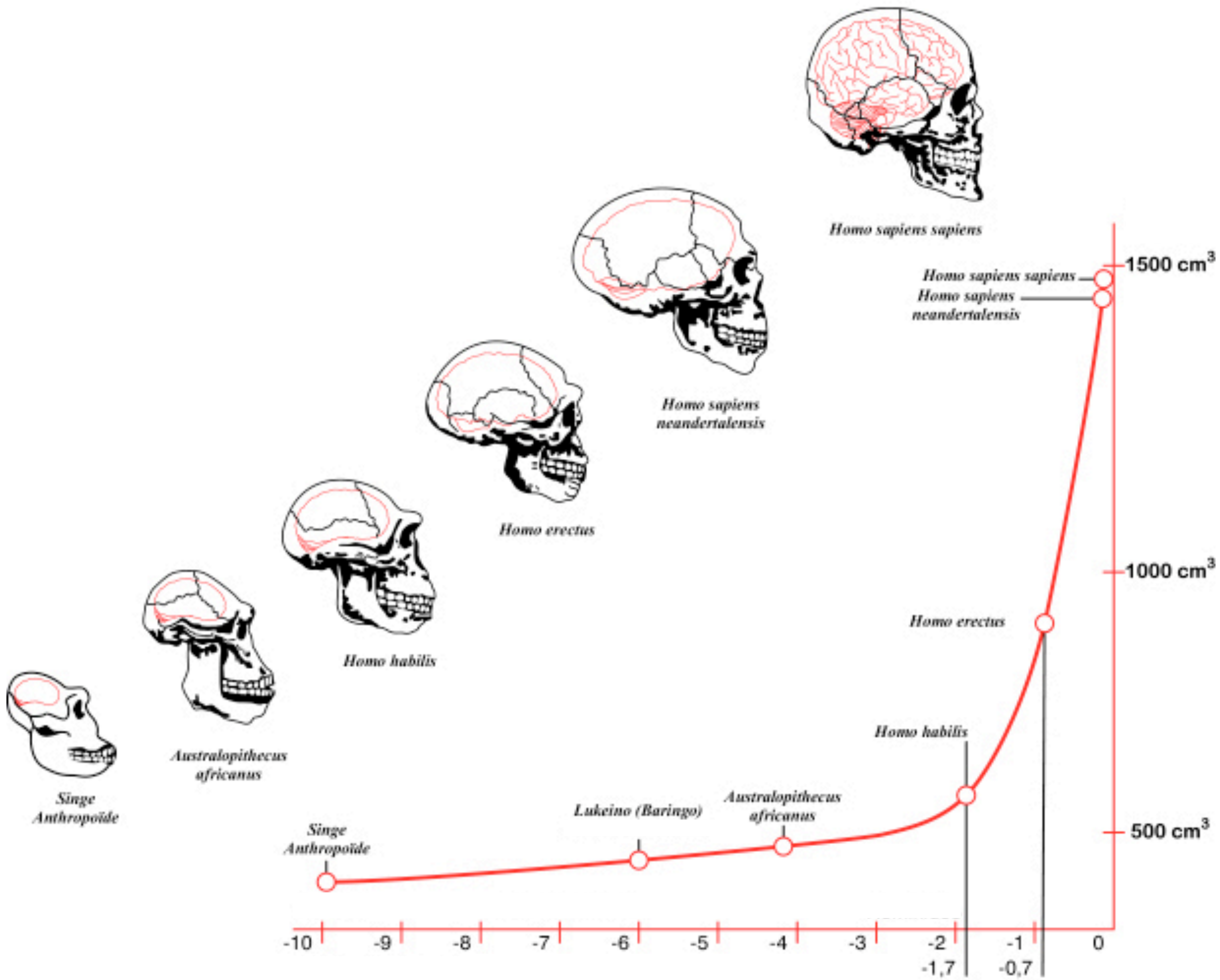
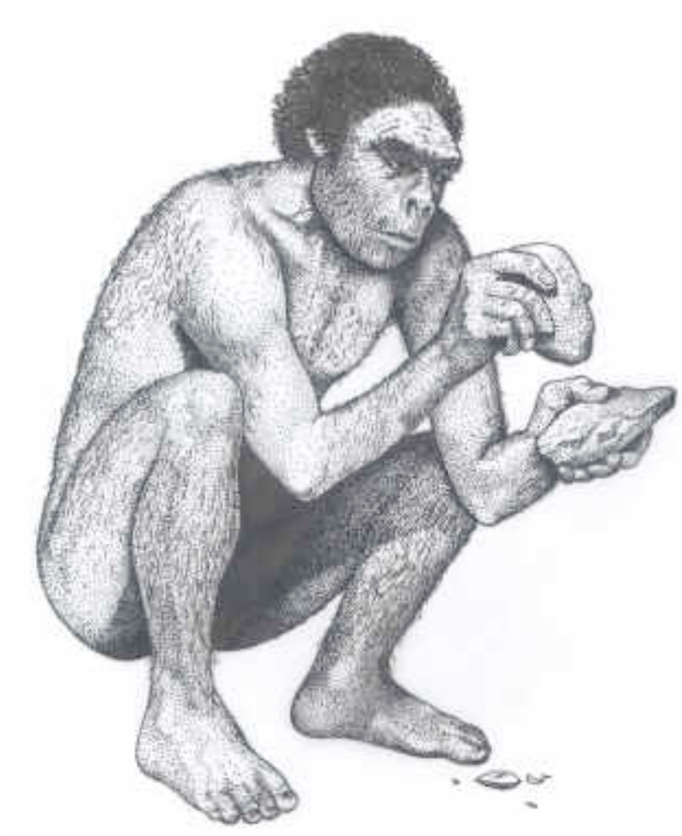




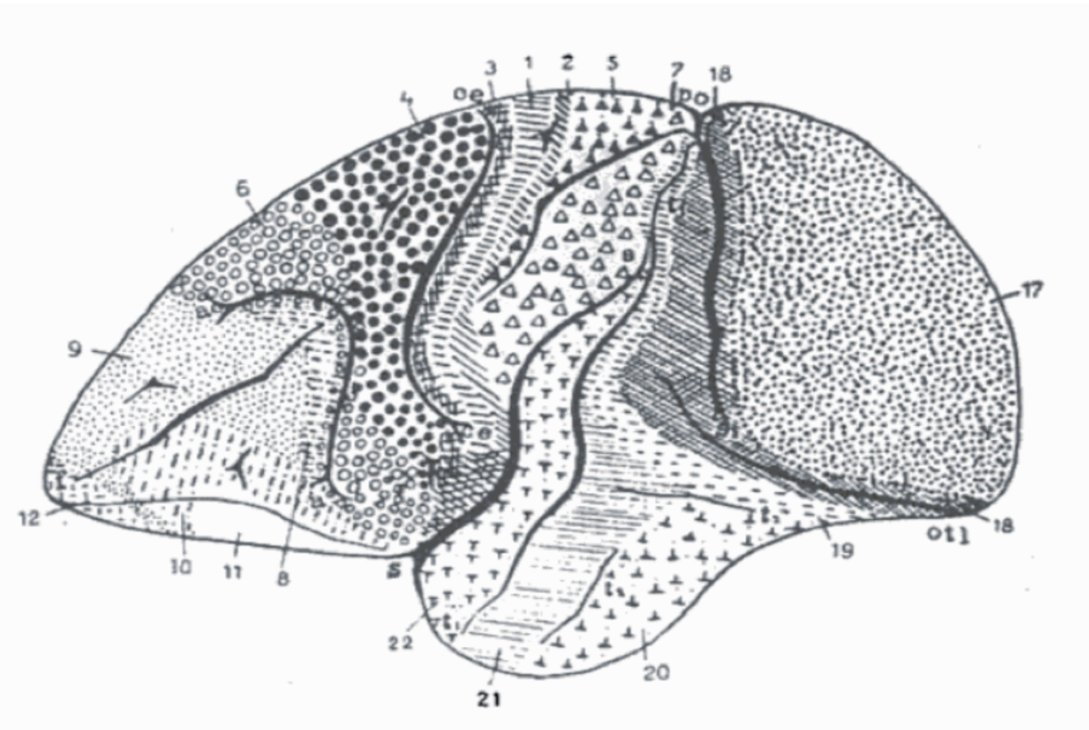
Lu, Liu et al., 2011, *J. Neurosci.*


Singe
Anthropoïde
Australopithecus
africanus
Homo habilis
Homo erectus
Homo sapiens
neandertalensis
Homo sapiens sapiens
Homo sapiens sapiens
Homo sapiens
neandertalensis
1500 cm³
1000 cm³
500 cm³
Homo erectus
Homo habilis
Australopithecus
africanus
Lukeino (Baringo)
Singe
Anthropoïde
-10
-9
-8
-7
-6
-5
-4
-3
-2
-1
0
-1,7
-0,7

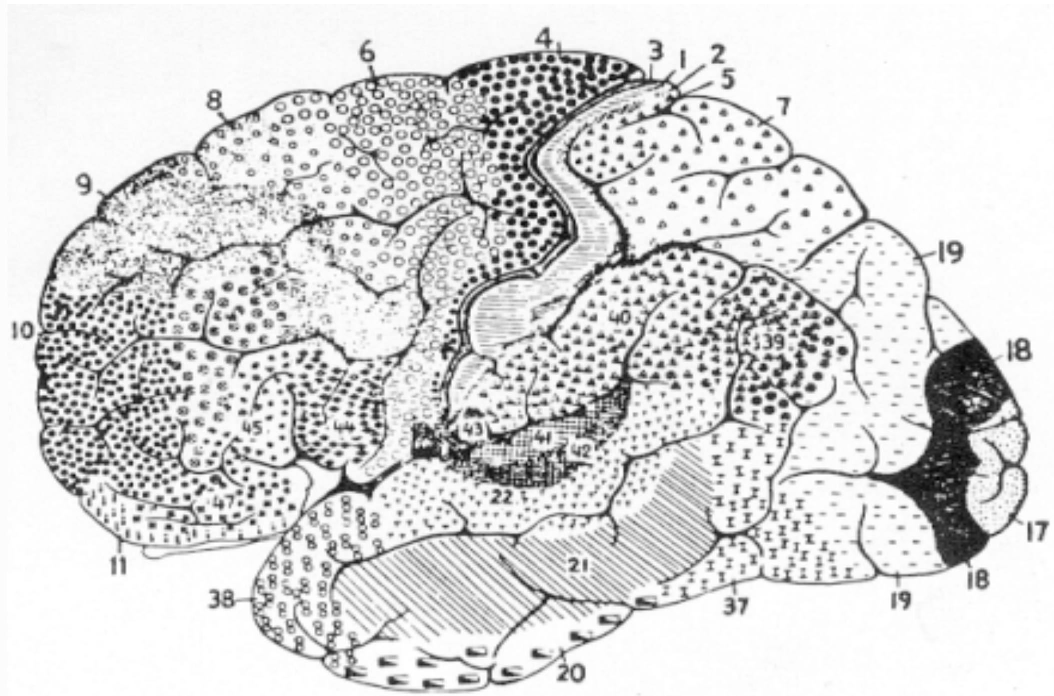


Human Association Cortex is Dramatically Expanded

Monkey

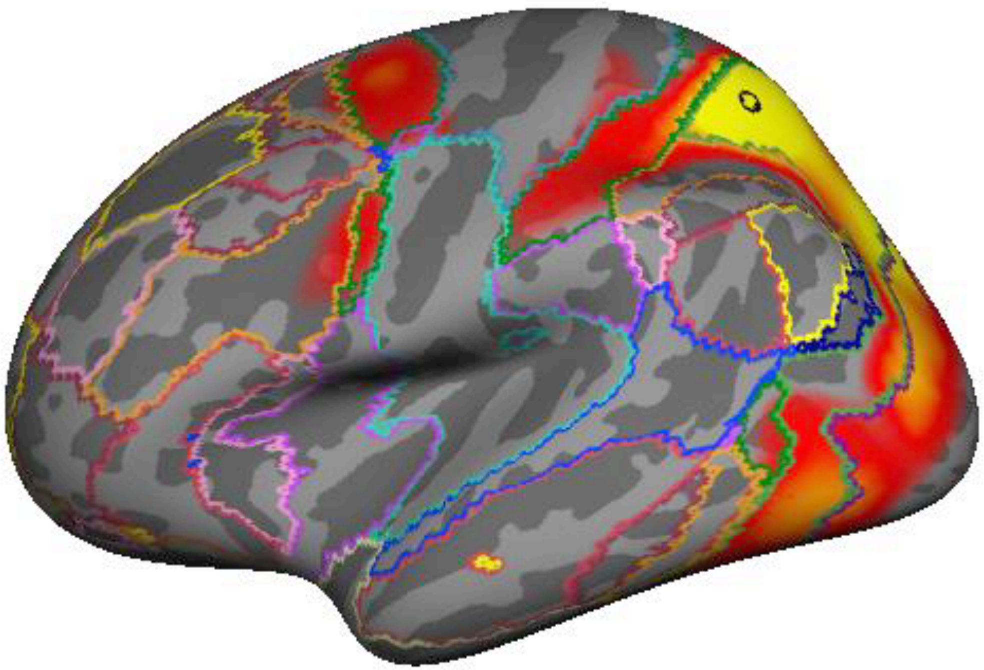


Human

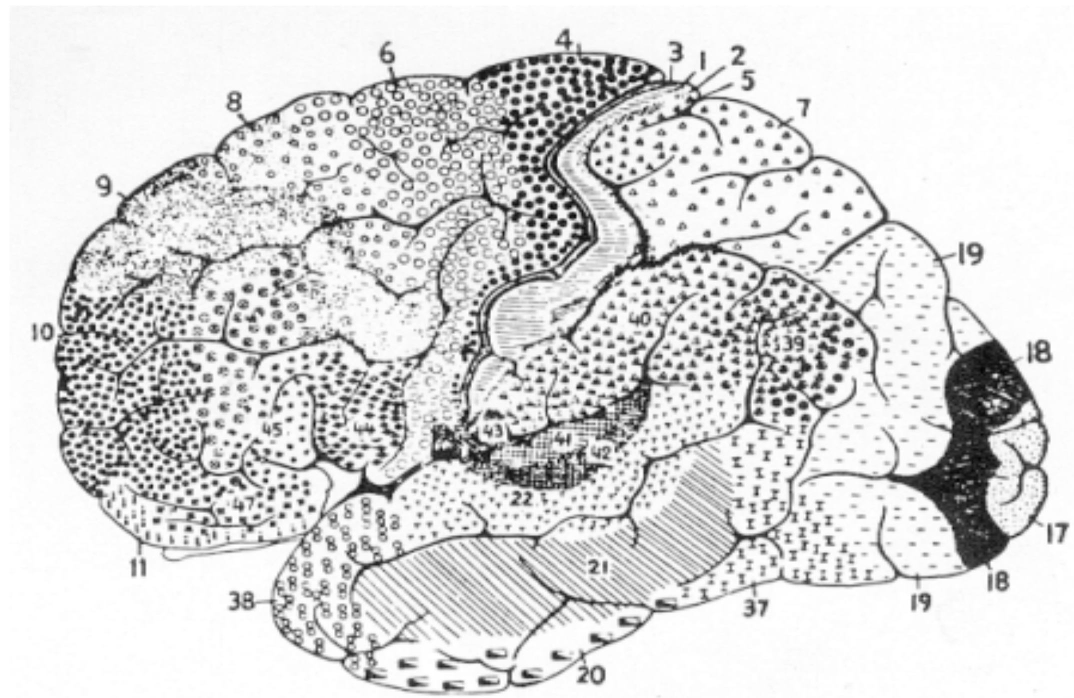


Korbinian Brodmann

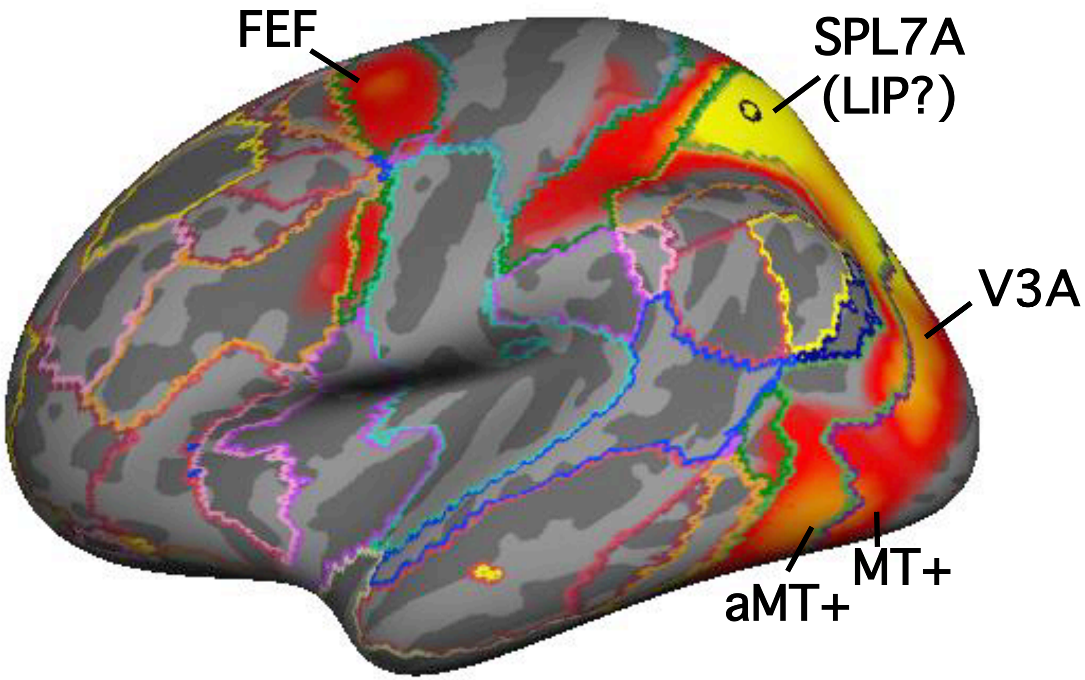
Canonical Hierarchical Sensory-Motor Network

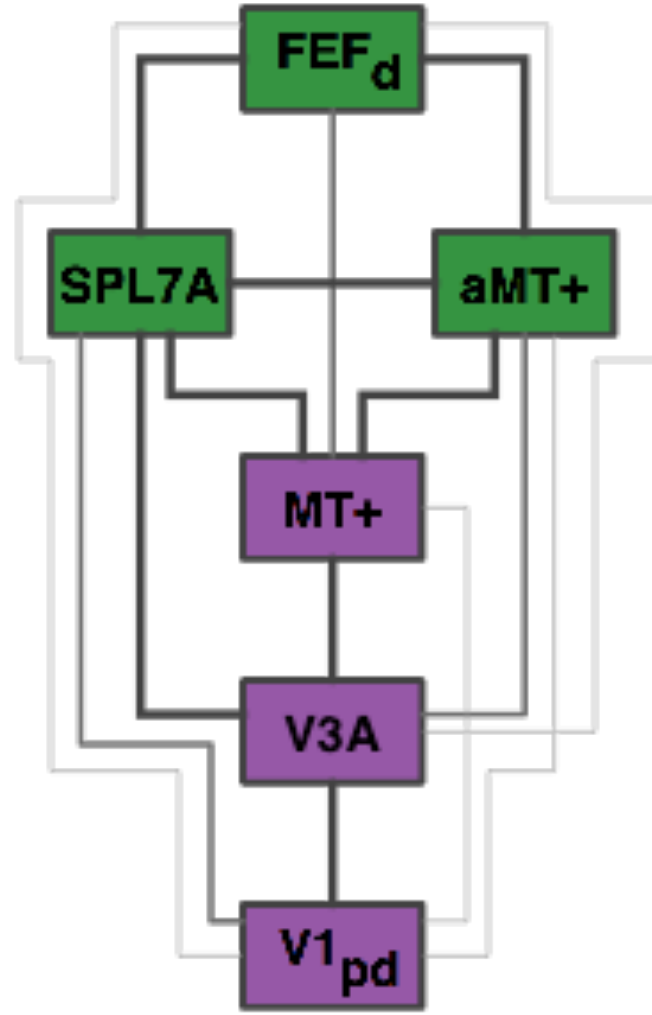


Human



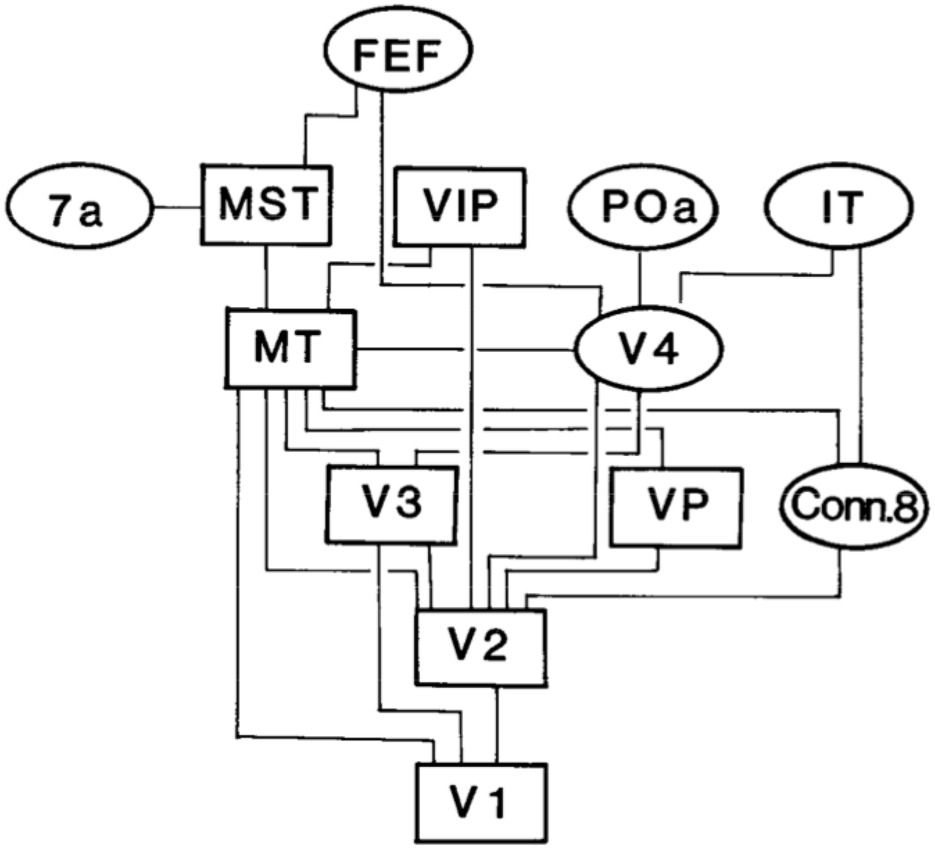
Canonical Hierarchical Sensory-Motor Network



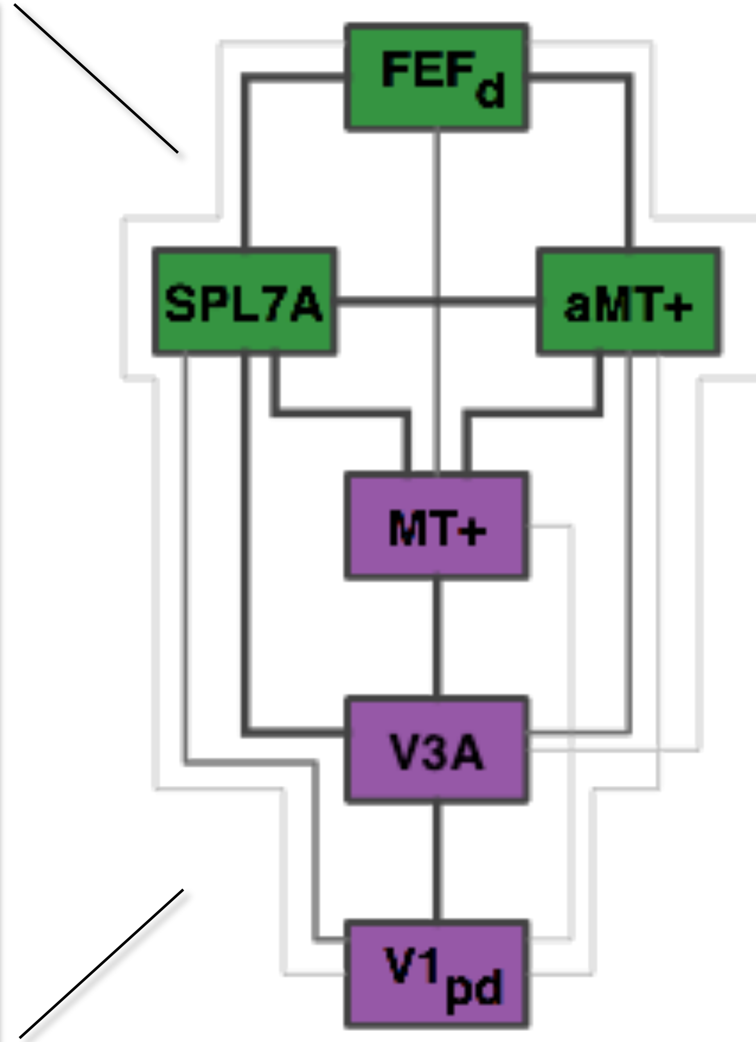


Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Canonical Hierarchical Sensory-Motor Network



Maunsell and Van Essen, 1983, *J. Neurosci.*



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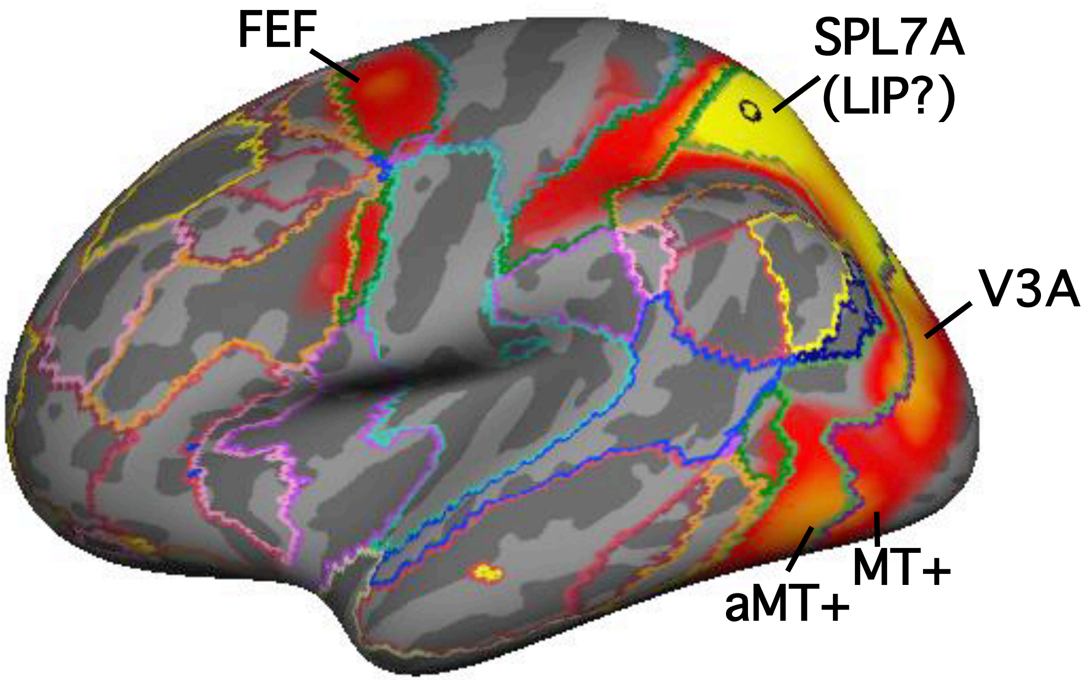
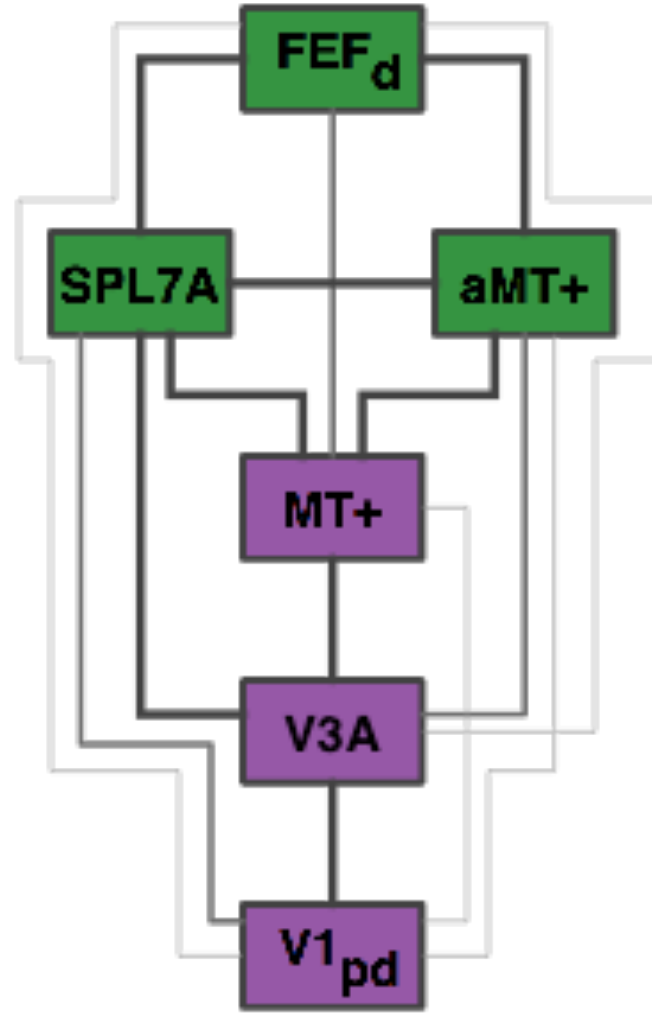
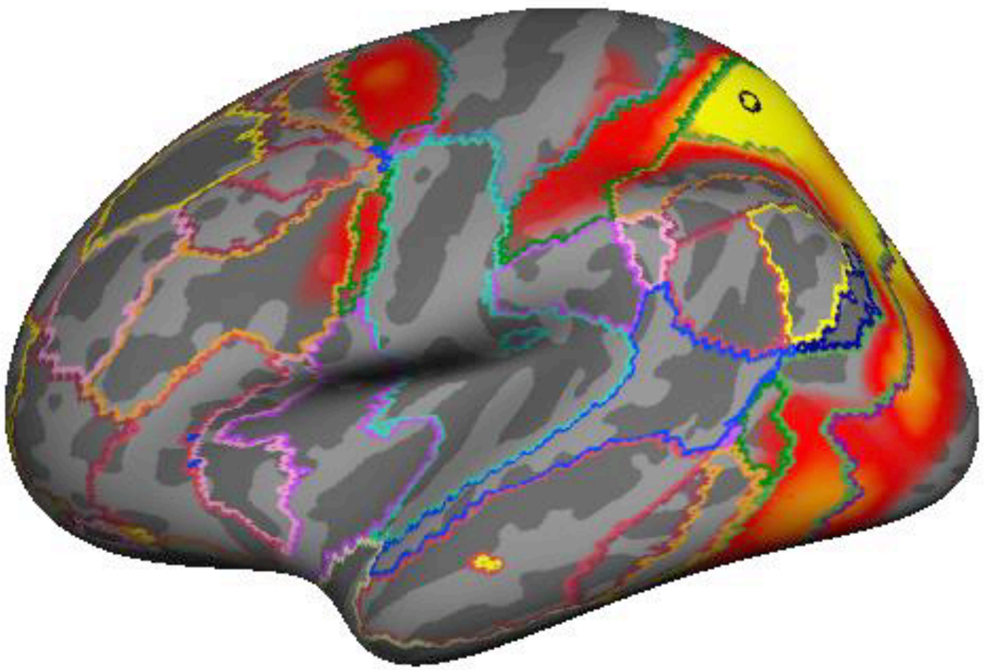
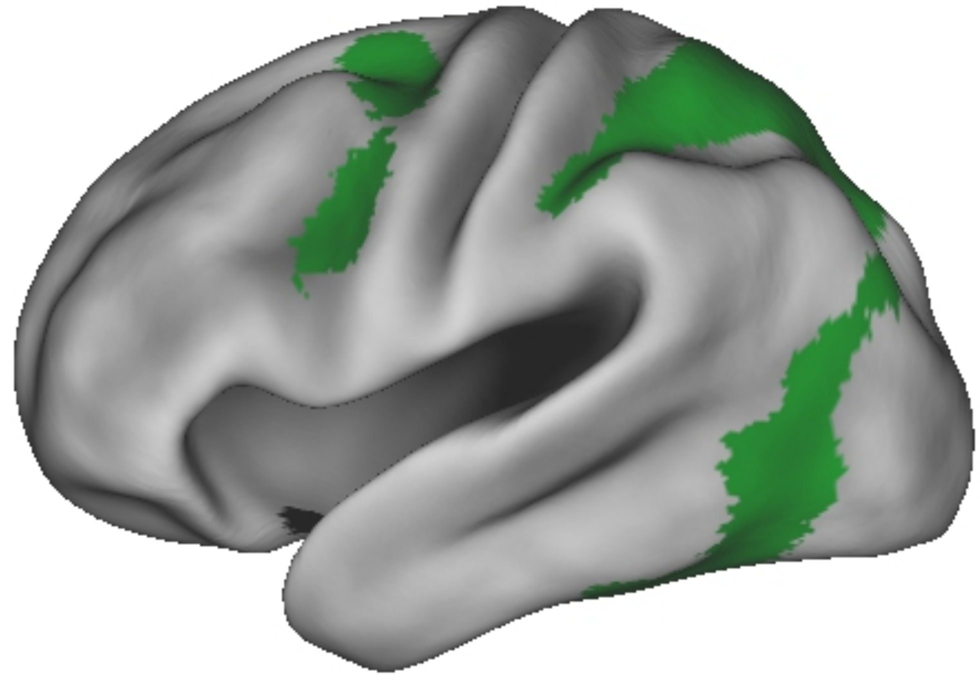




Yeo, Krienen et al., 2011, *J. Neurophysiol.*

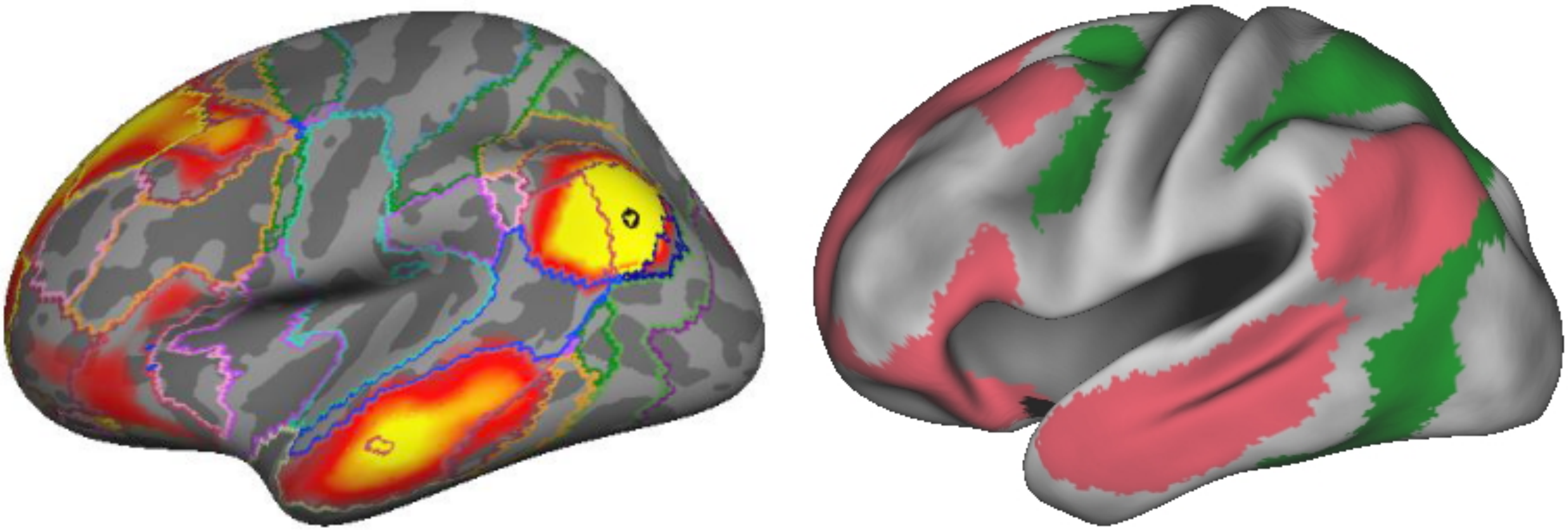
Distributed Association Networks





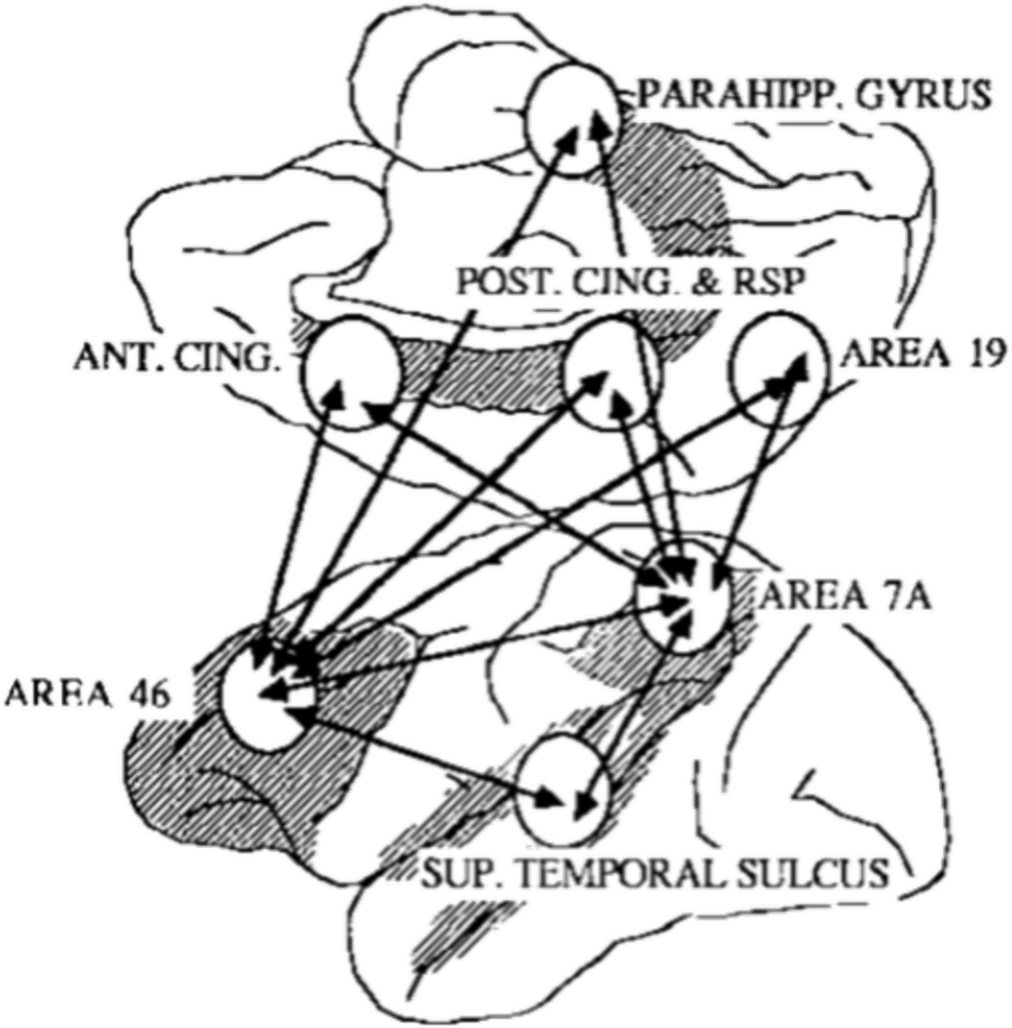
Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks

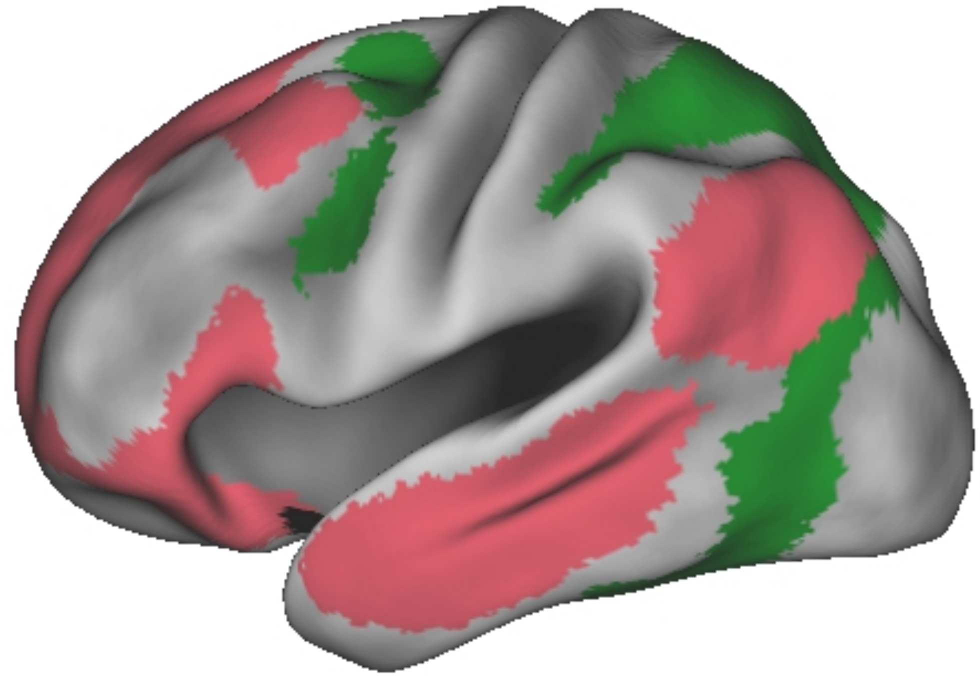


Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks

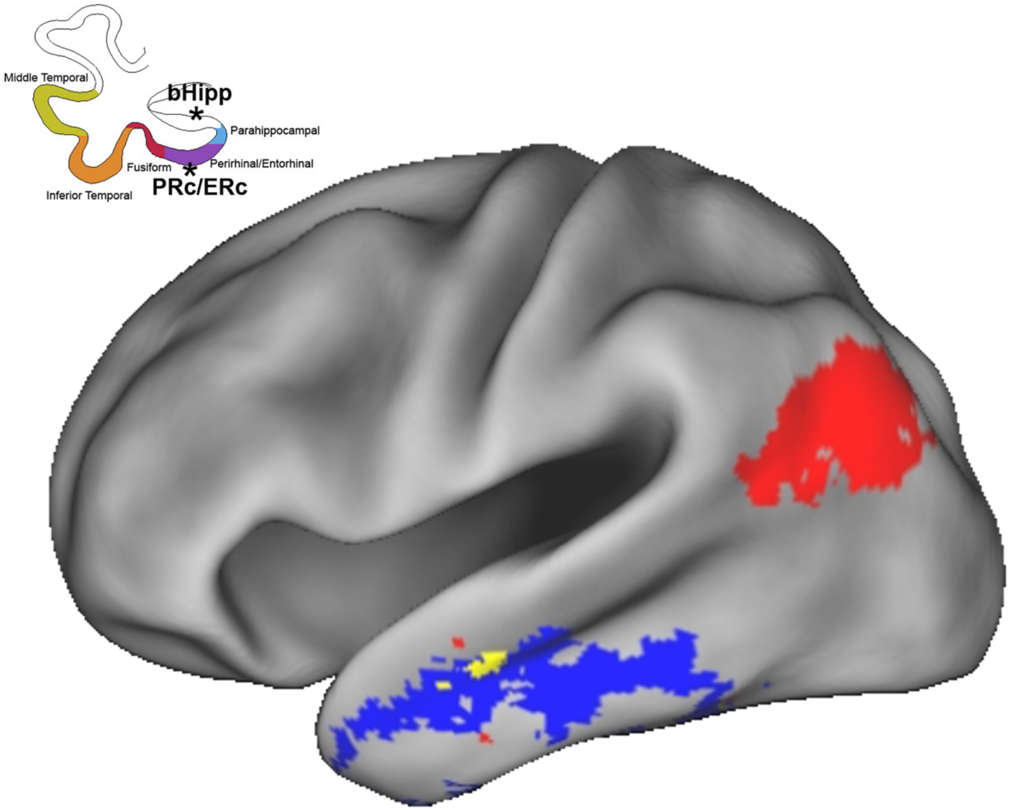


Goldman-Rakic (1988) *Ann. Rev. Neurosci.*



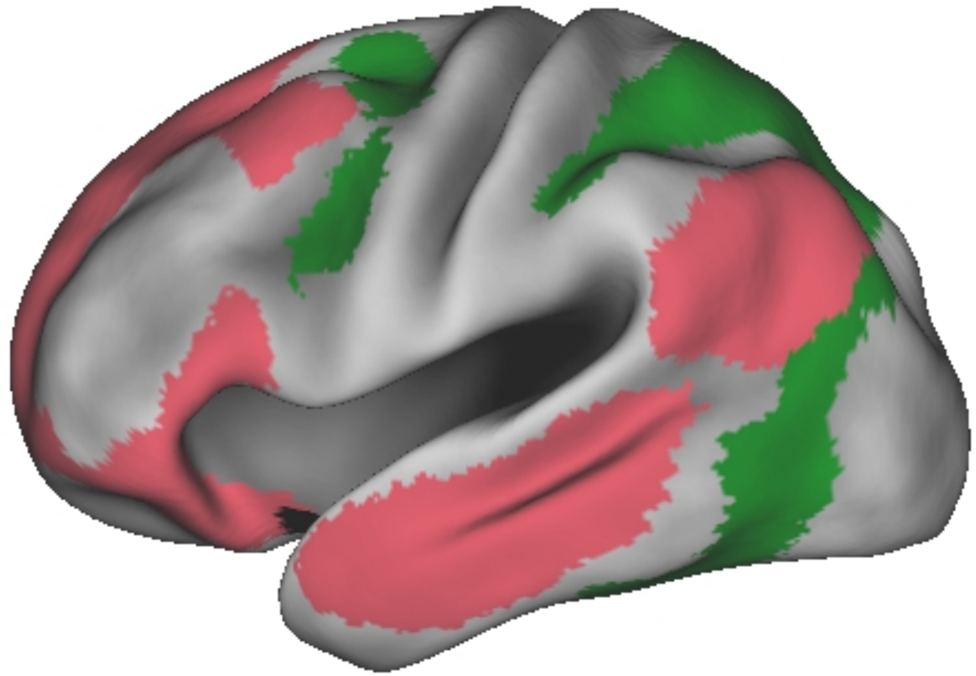
Yeo, Krienen et al., 2011, *J. Neurophysiol.*

Distributed Association Networks



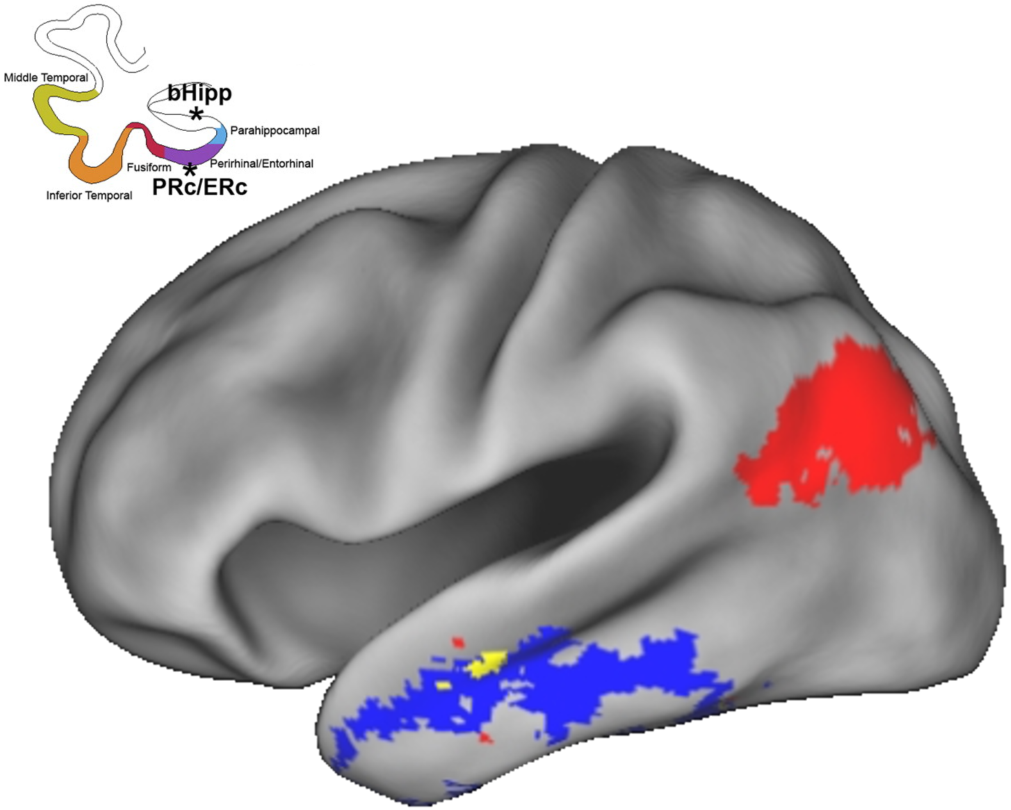
Coupled to Hippocampal Memory System

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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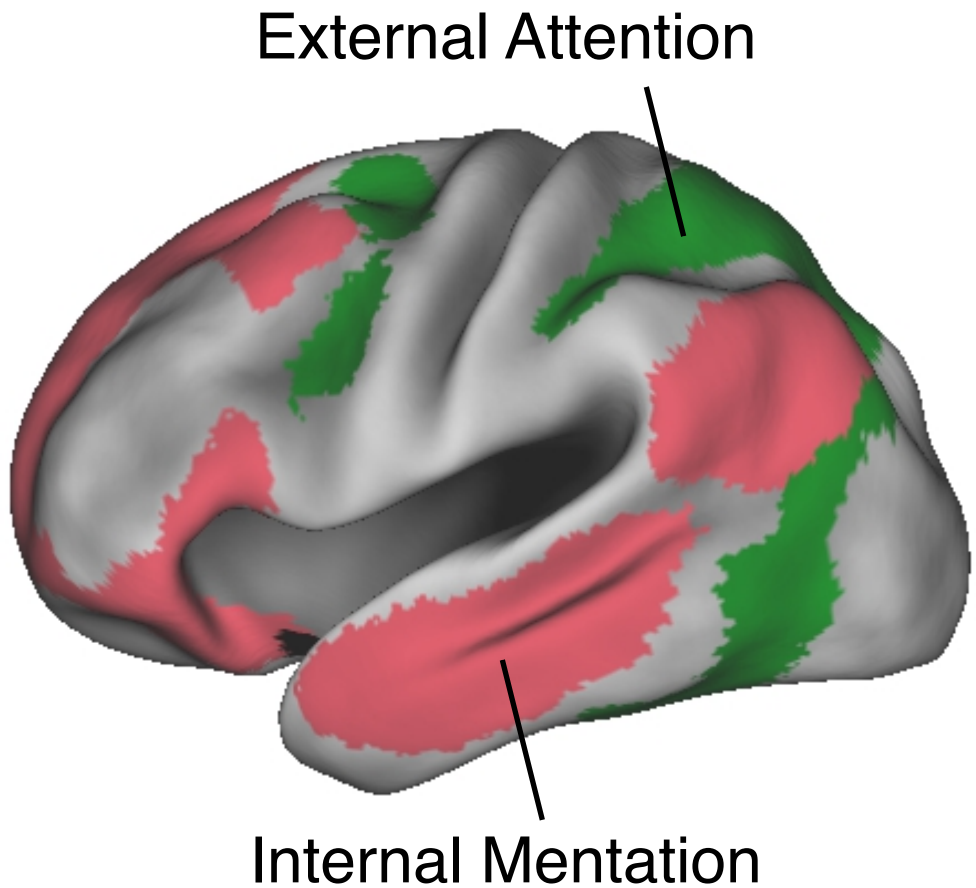
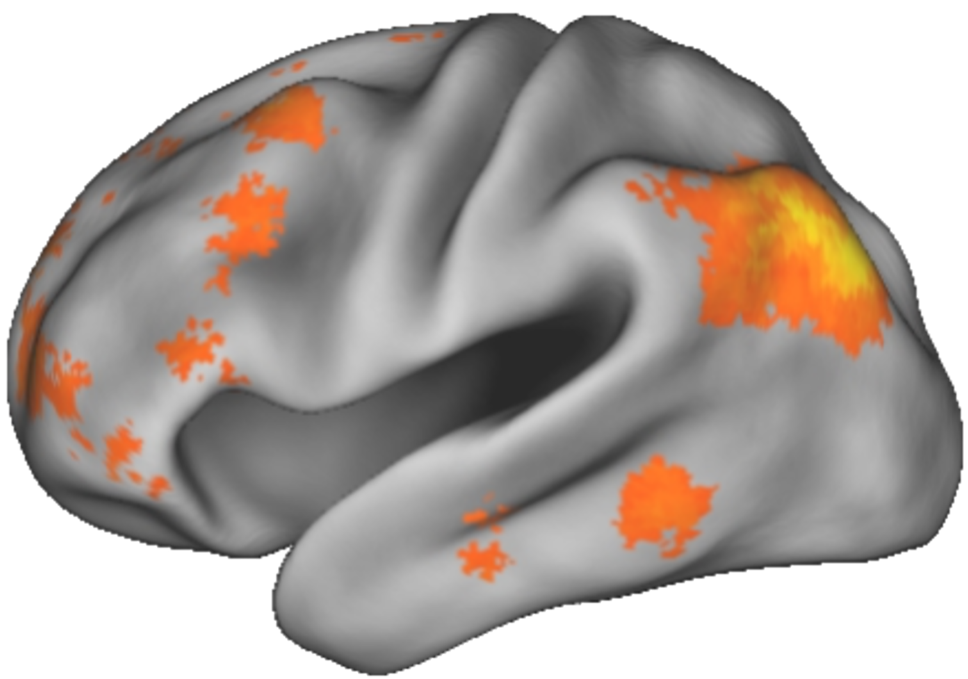
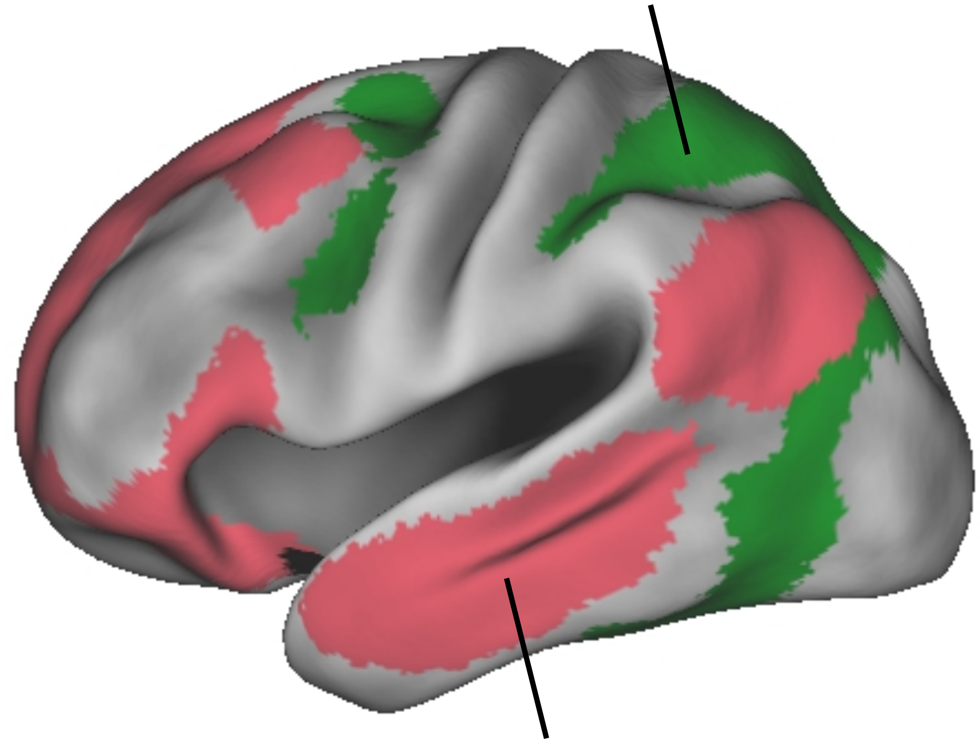


Yeo, Krienen et al., 2011, *J. Neurophysiol.*
(Andreasen et al., 1995, *Am. J. Psychiatry*)

Distributed Association Networks

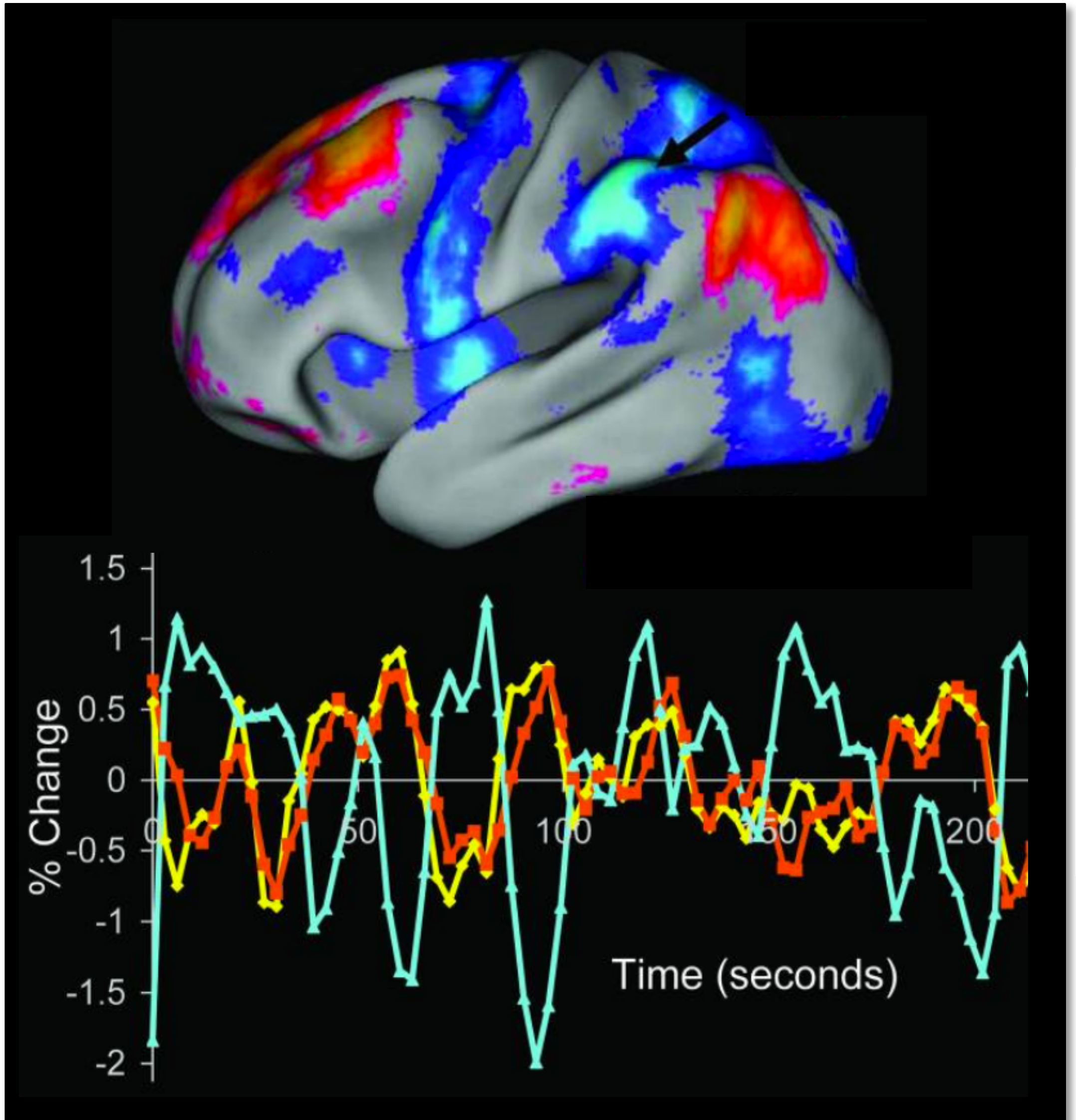




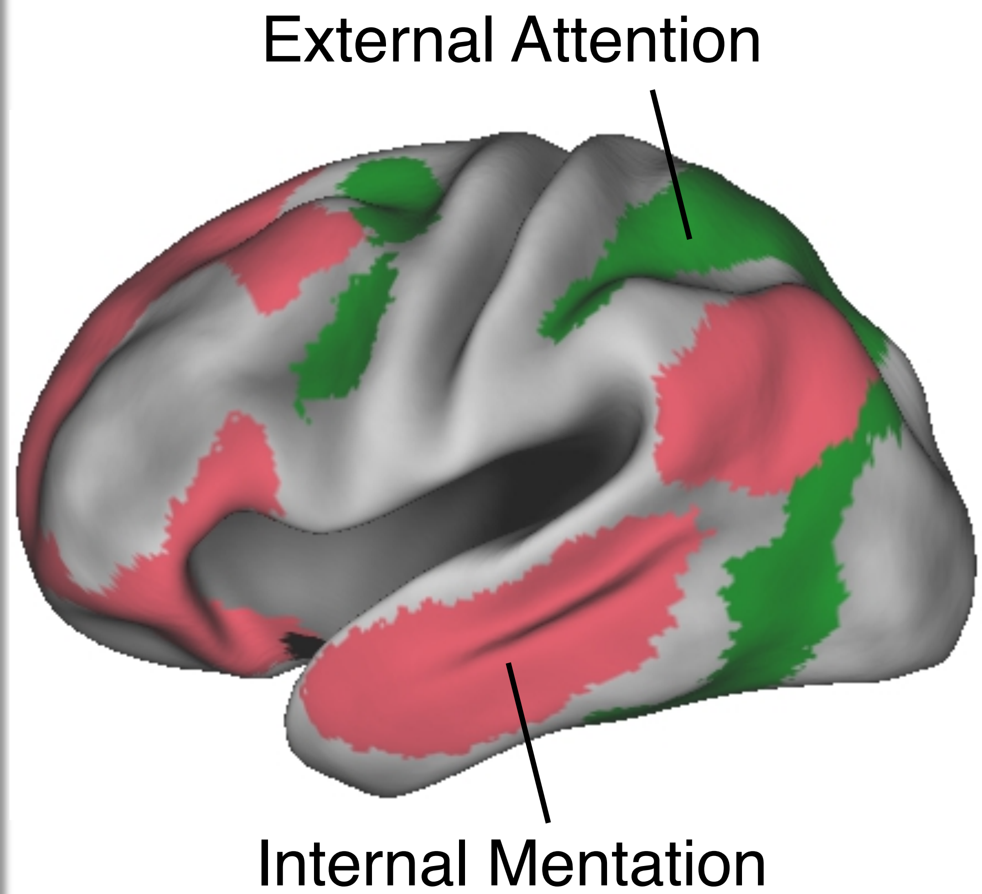
Andrews-Hanna, Saxe, & Yarkoni, 2014, *NeuroImage*

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

Distributed Association Networks



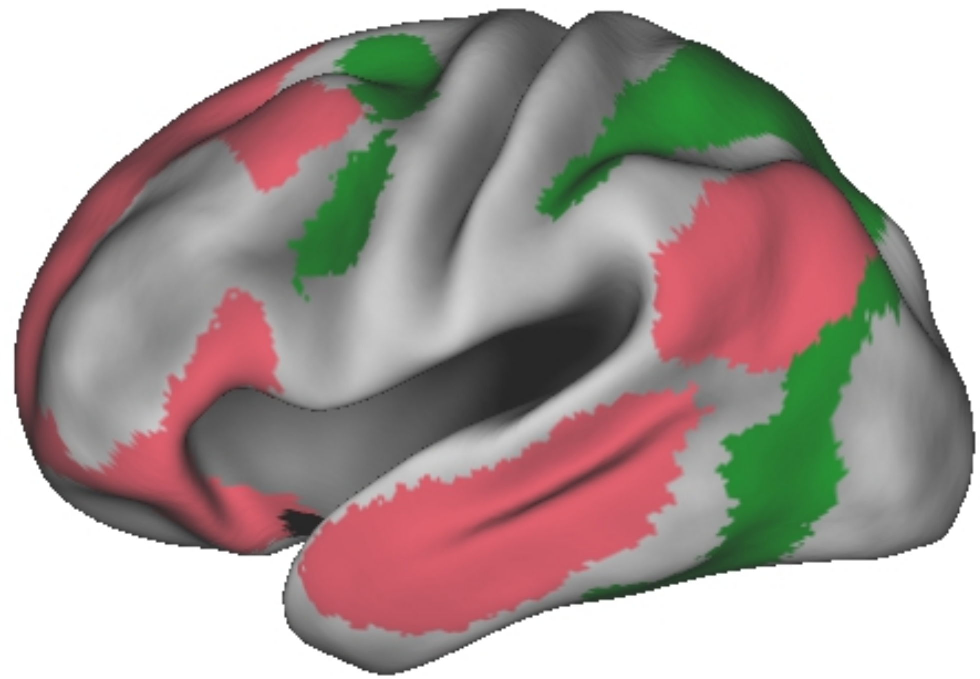
Fox et al., 2005, *Proc. Natl. Acad. Sci.*



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

Distributed Association Networks

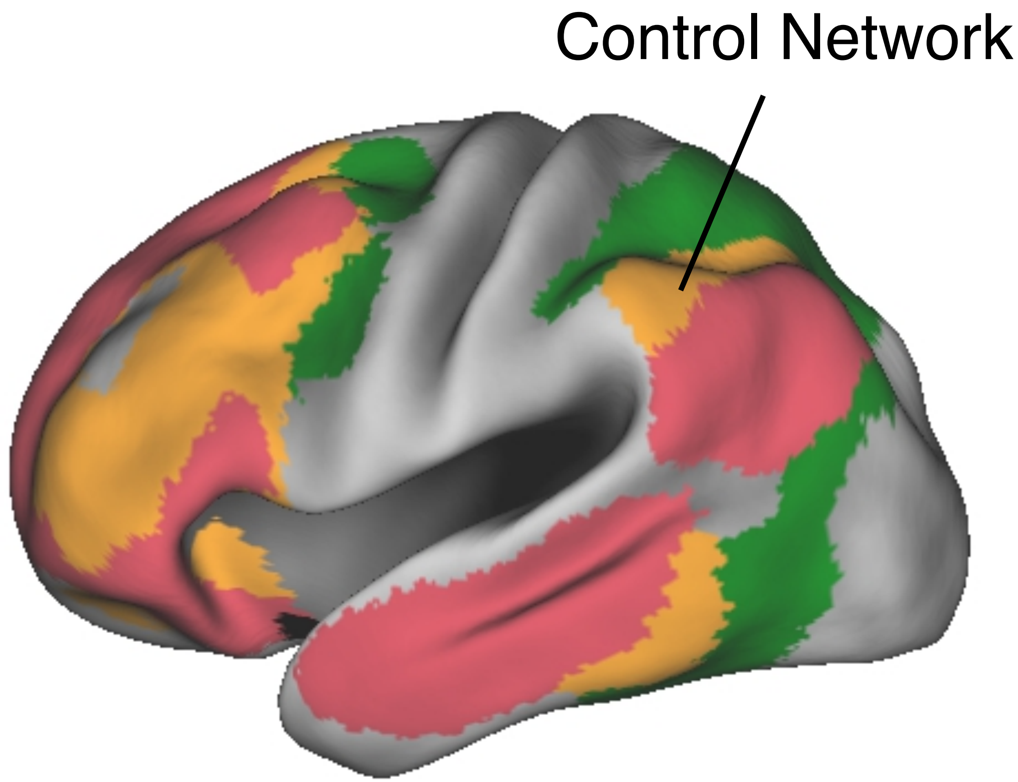
Control Network?



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

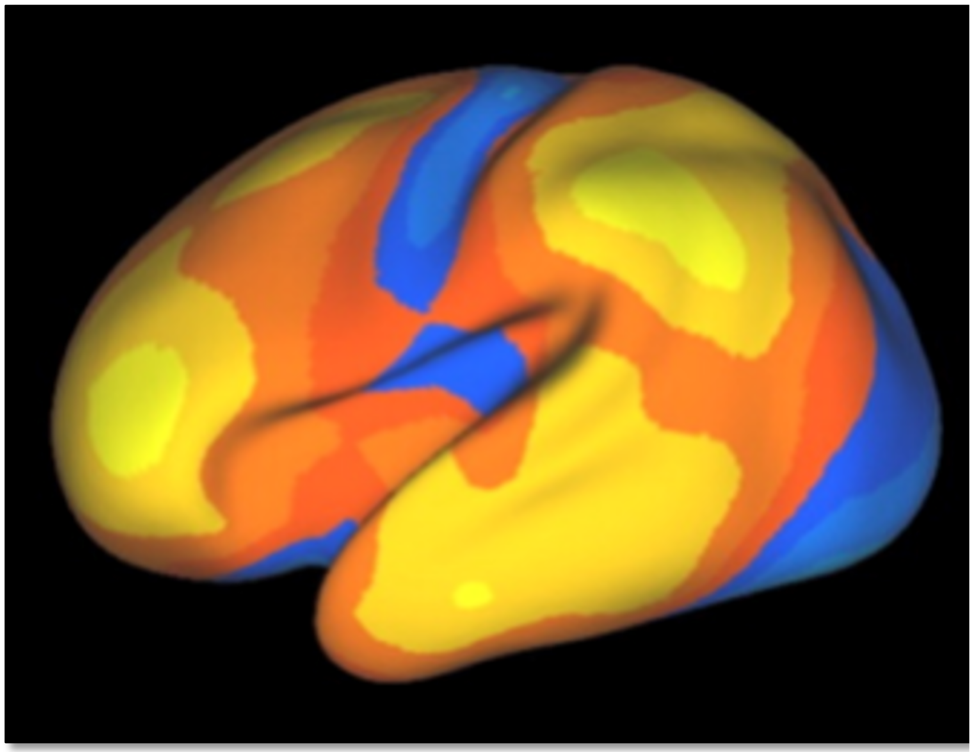
Distributed Association Networks

Control Network?

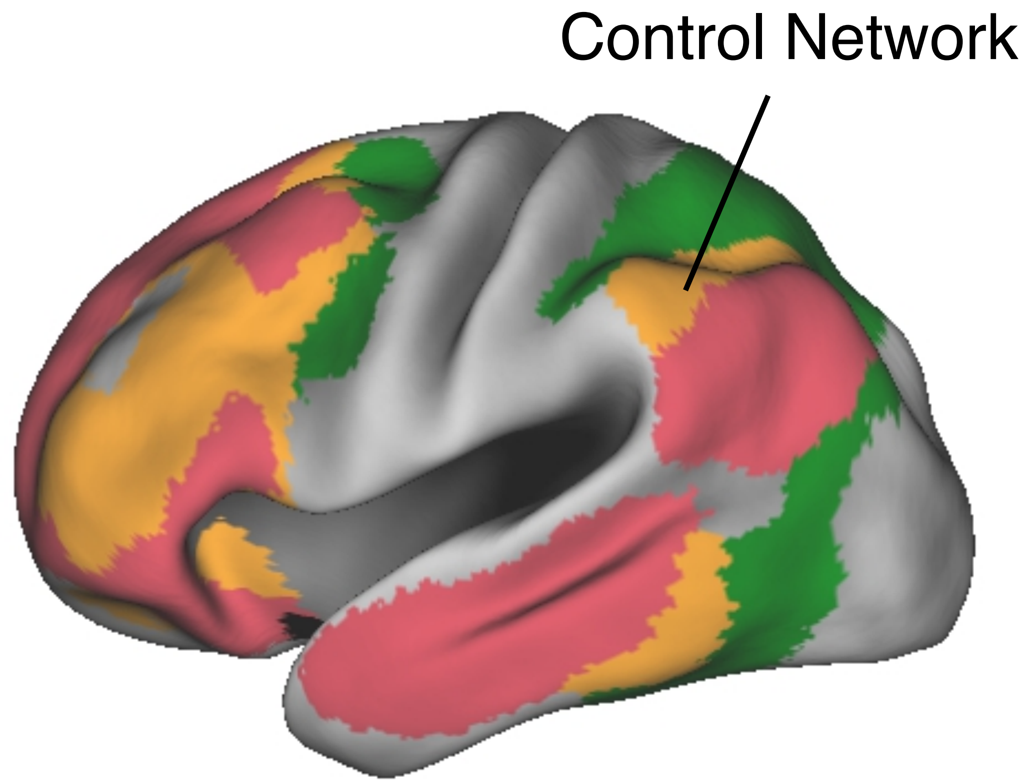


Vincent et al., 2006, *J. Neurophysiol.*

Expansion in Human Evolution

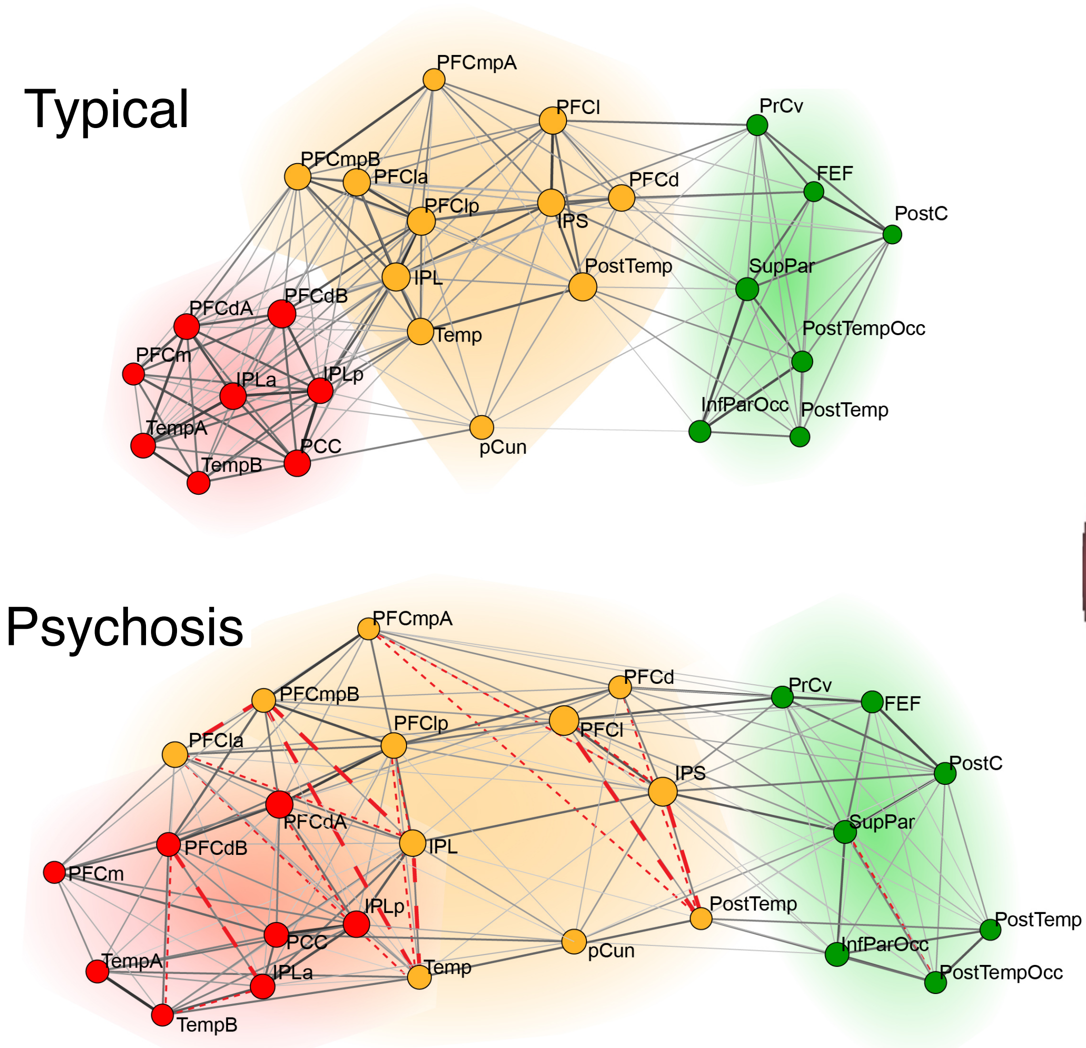


Hill et al., 2010 *Proc Natl Acad Sci*

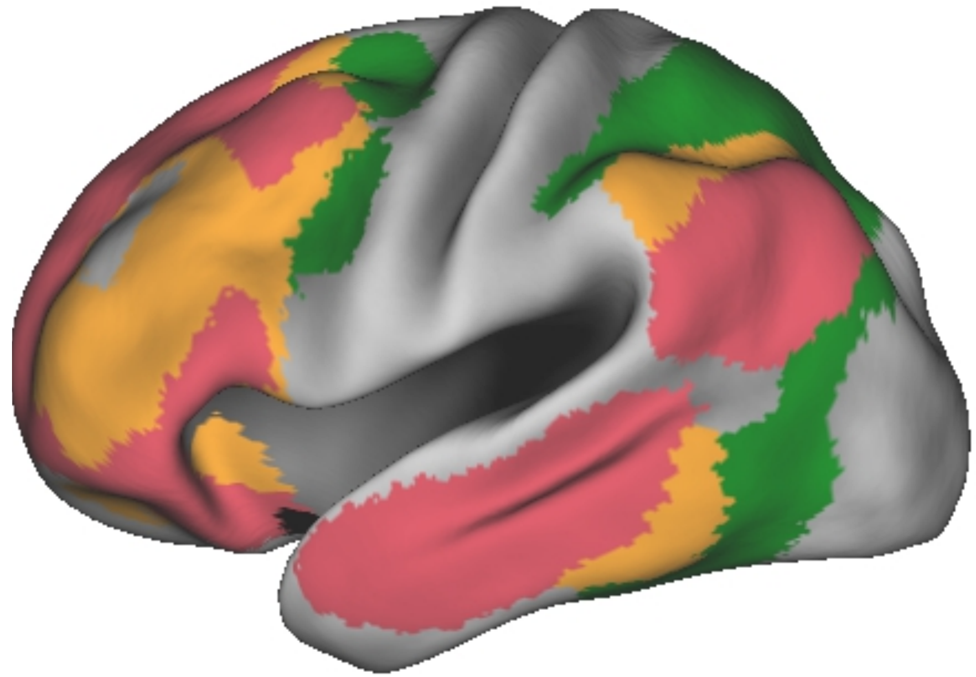


Vincent et al., 2006, *J. Neurophysiol.*

Relevance to Mental Illness

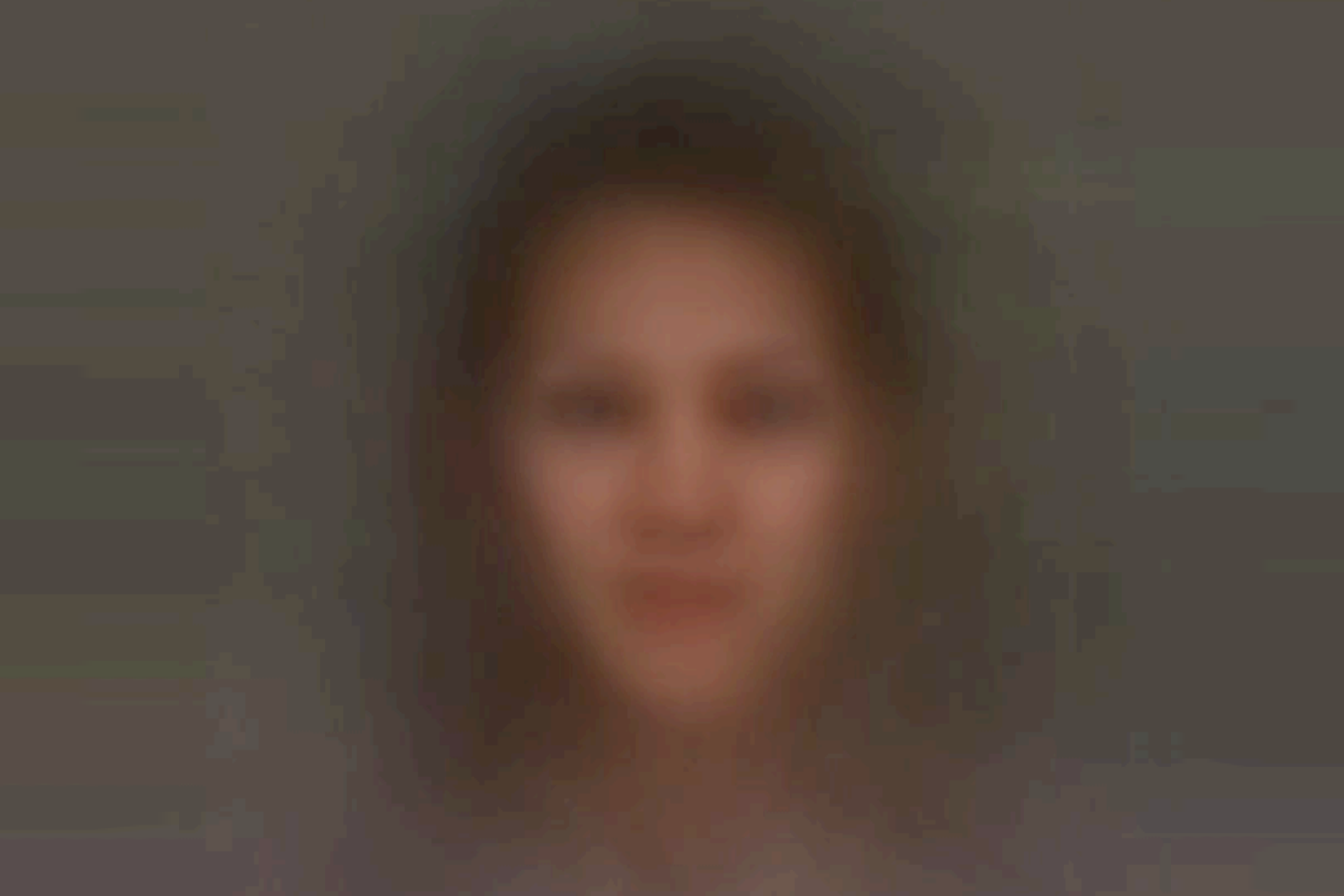


Baker et al., 2013, *JAMA Psychiatry*

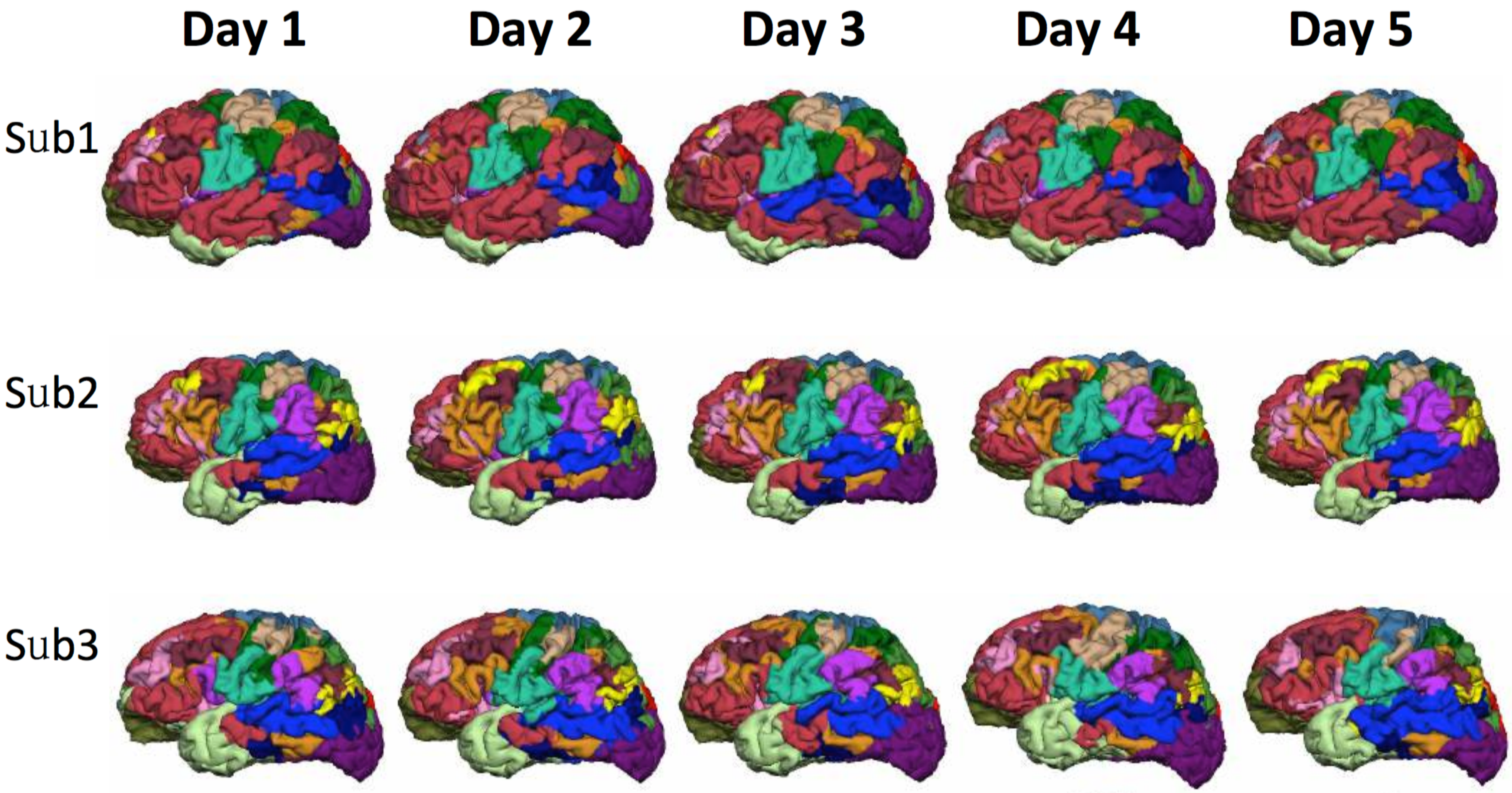


Vincent et al., 2006, *J. Neurophysiol.*

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

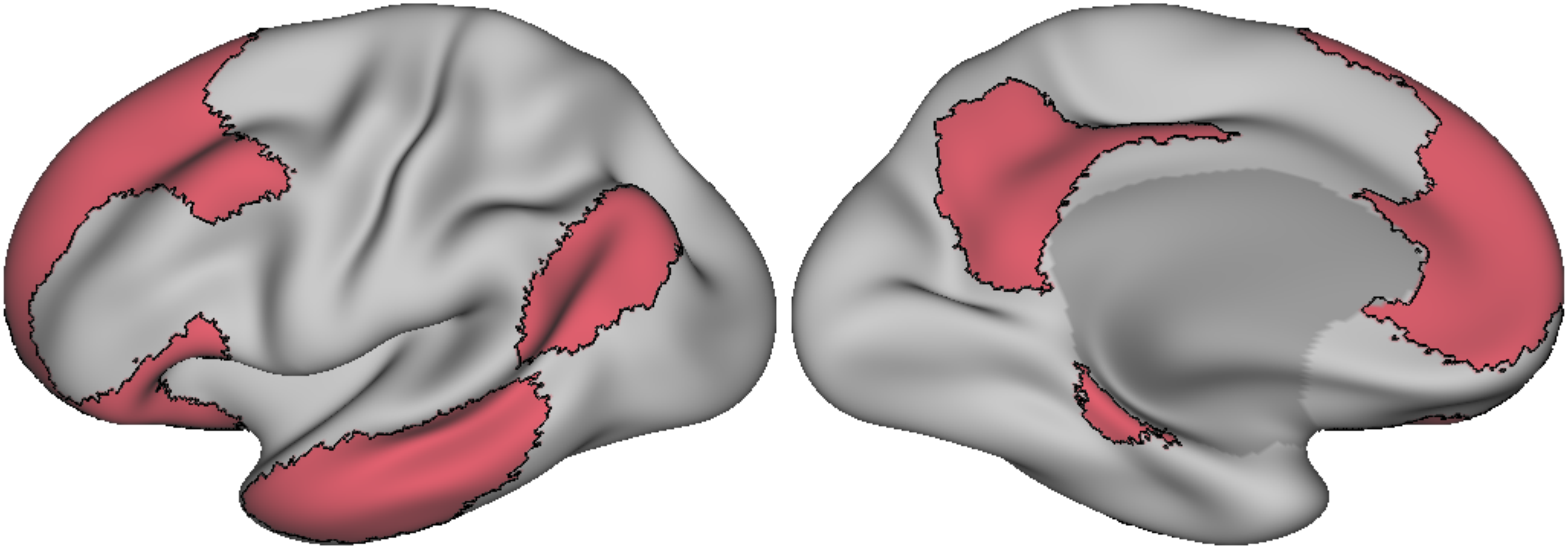


Variability Across Individuals



Mueller…Liu, 2013 *Neuron*; Wang…Liu, 2015, *Nat Neurosci;*

Group Association Network (n=1000)



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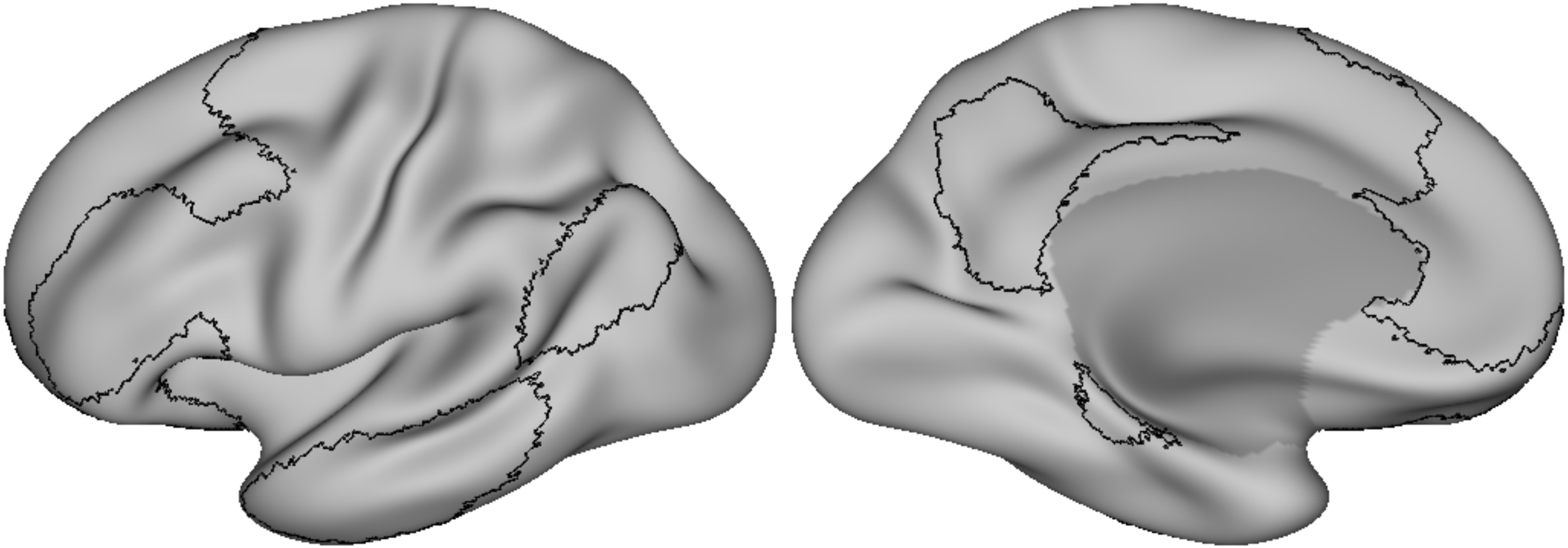
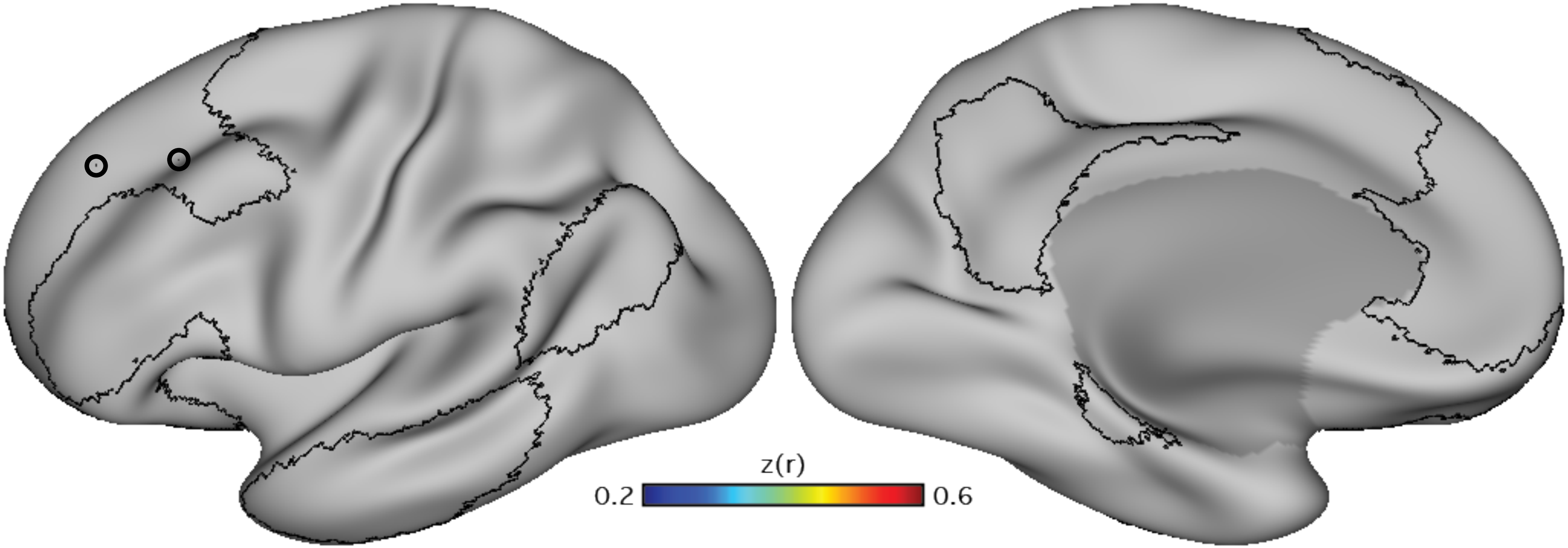
Group Association Network (n=1000)



Braga and Buckner, 2017, *Neuron*

Single Subject (24 MRI Sessions)



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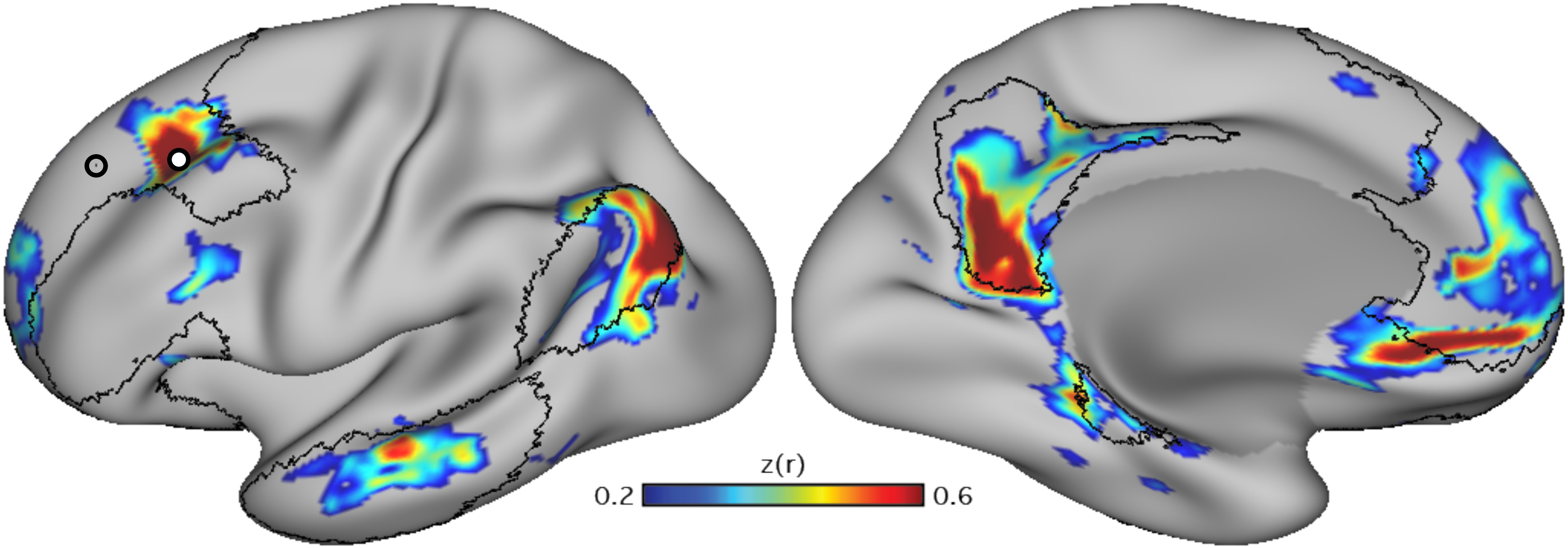

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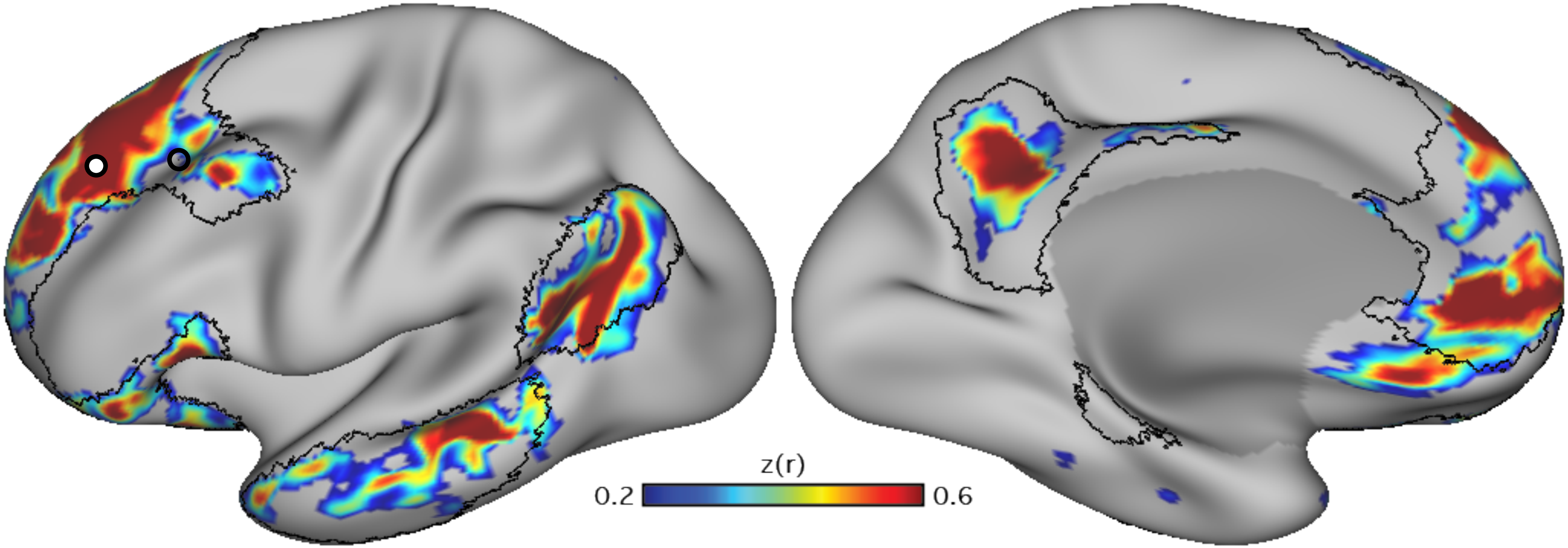

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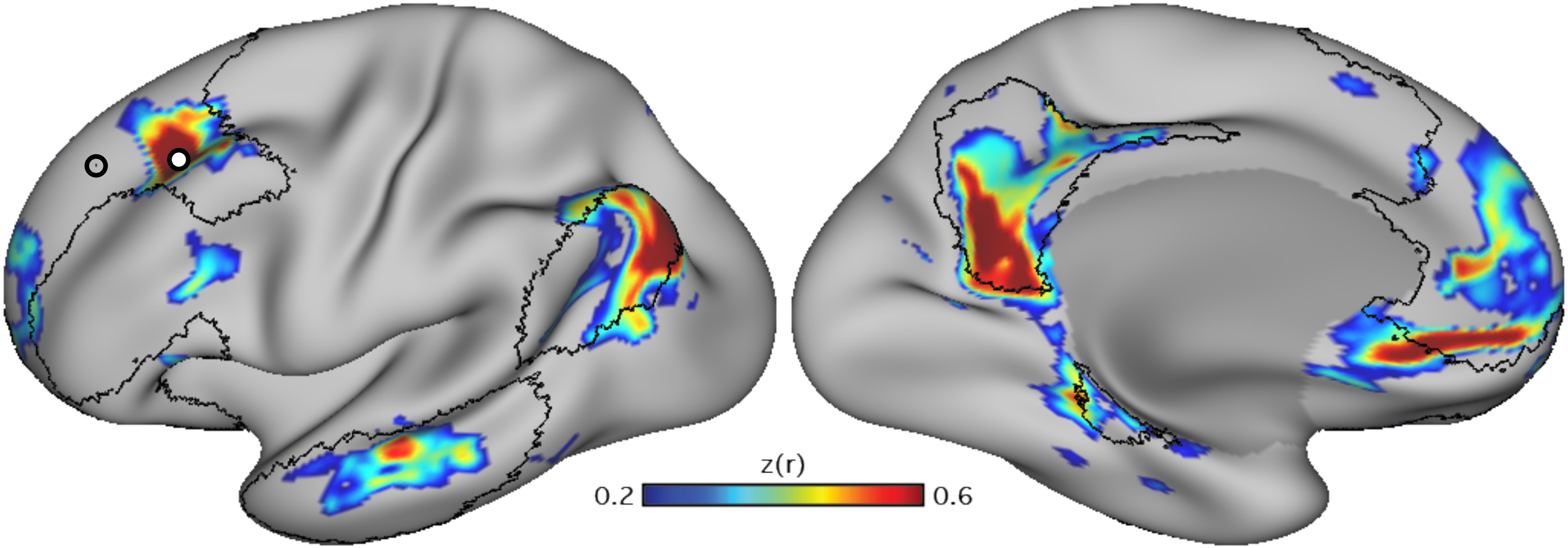

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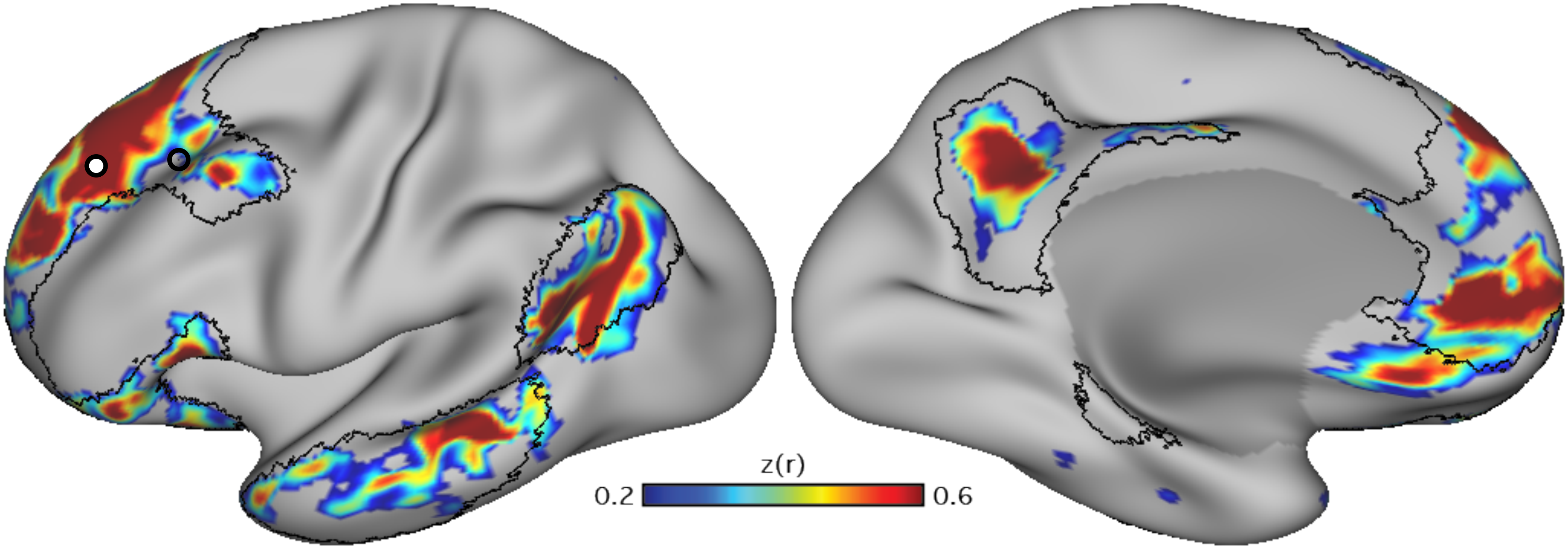

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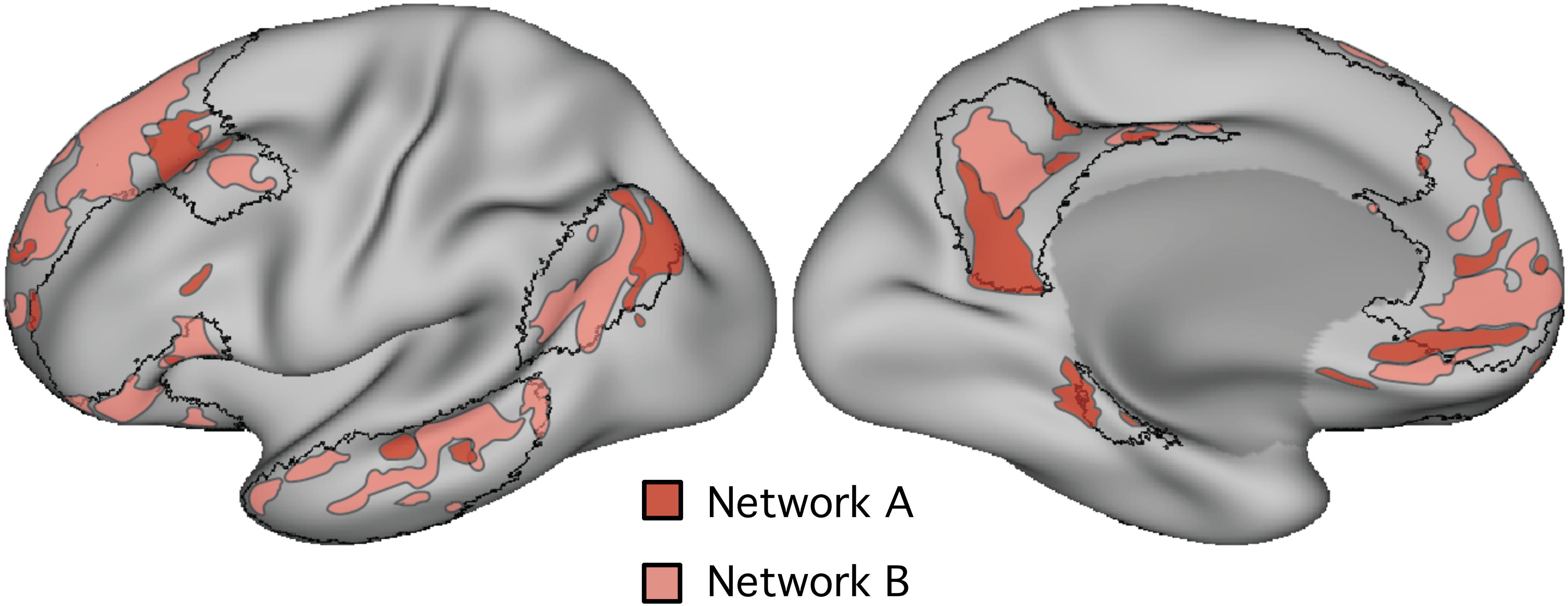

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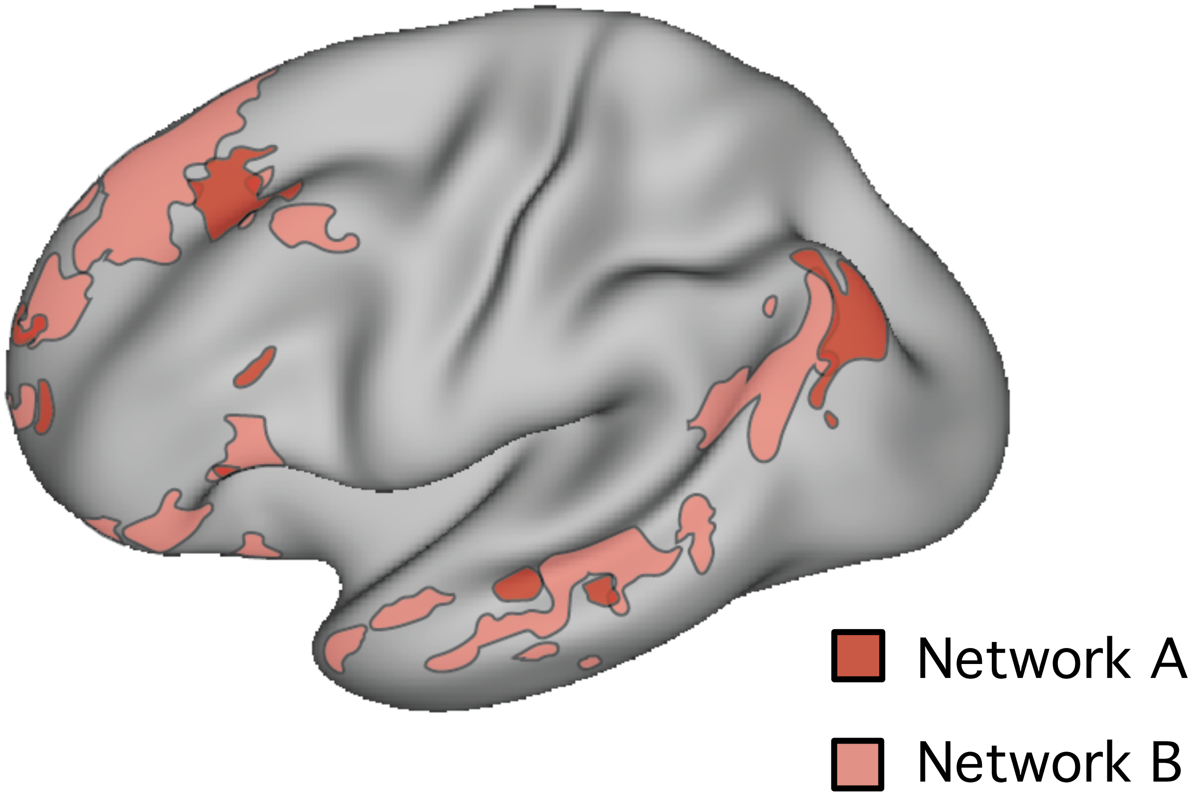
Human Specialization for Higher Brain Function?



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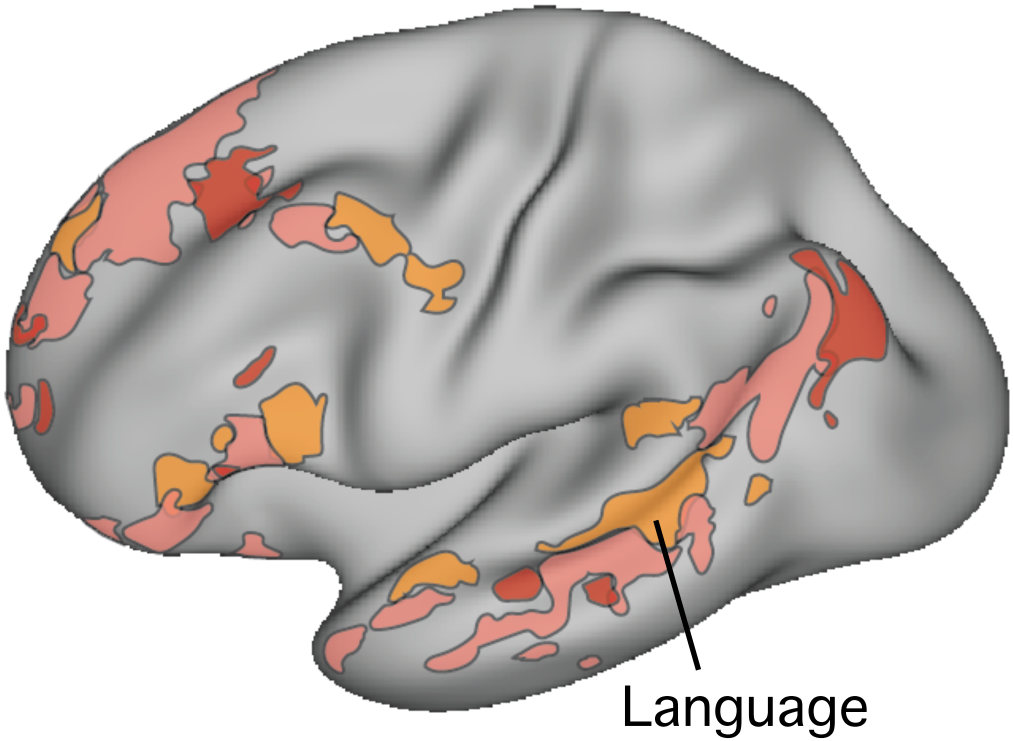
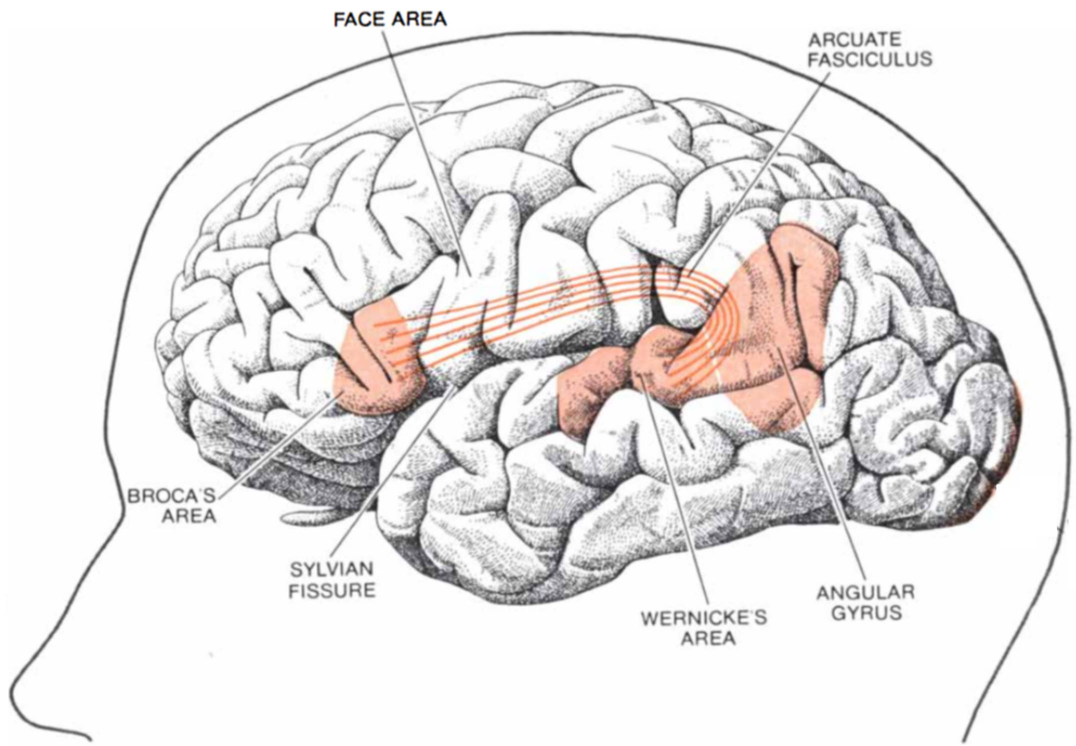
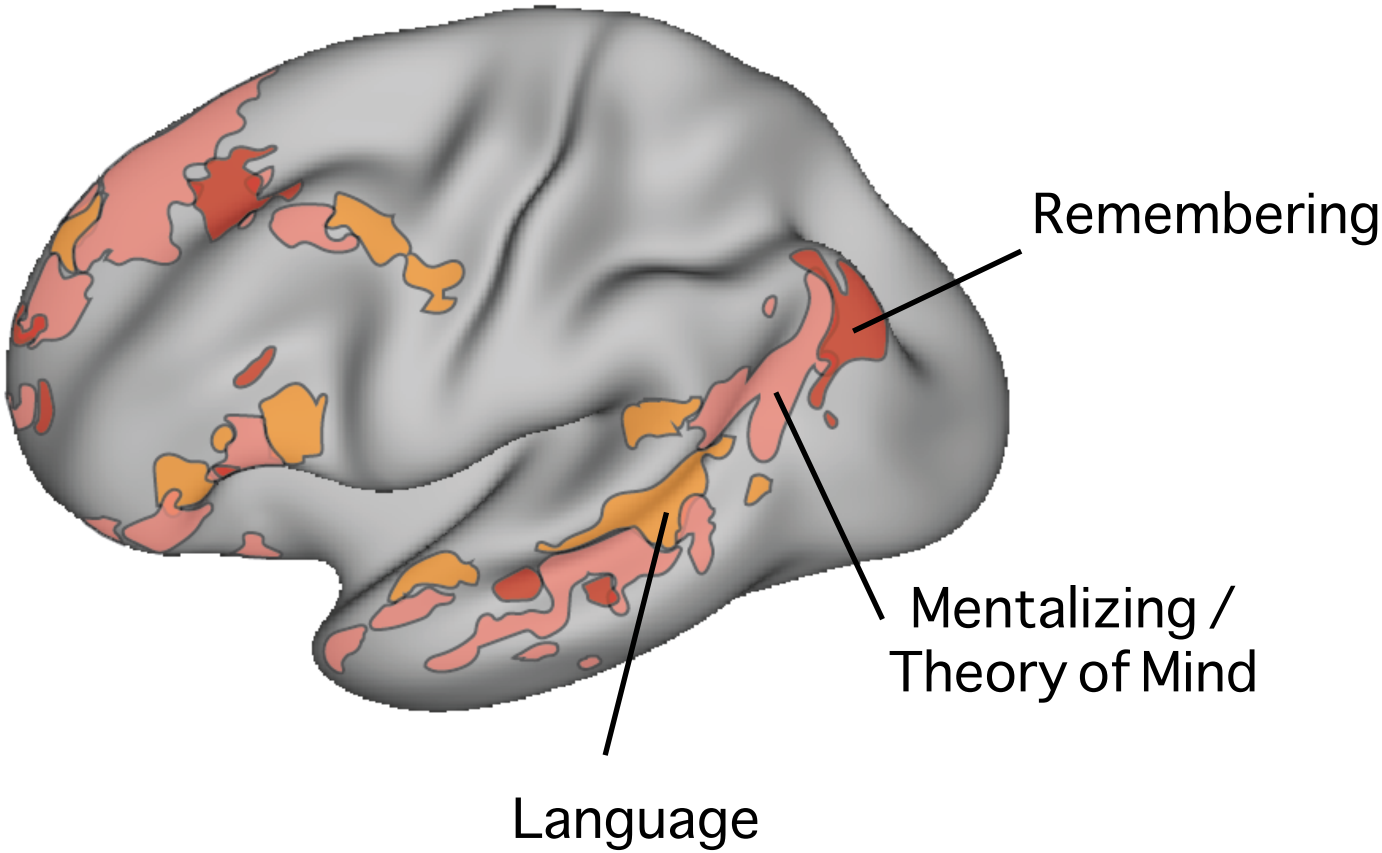


Geschwind's Language Network

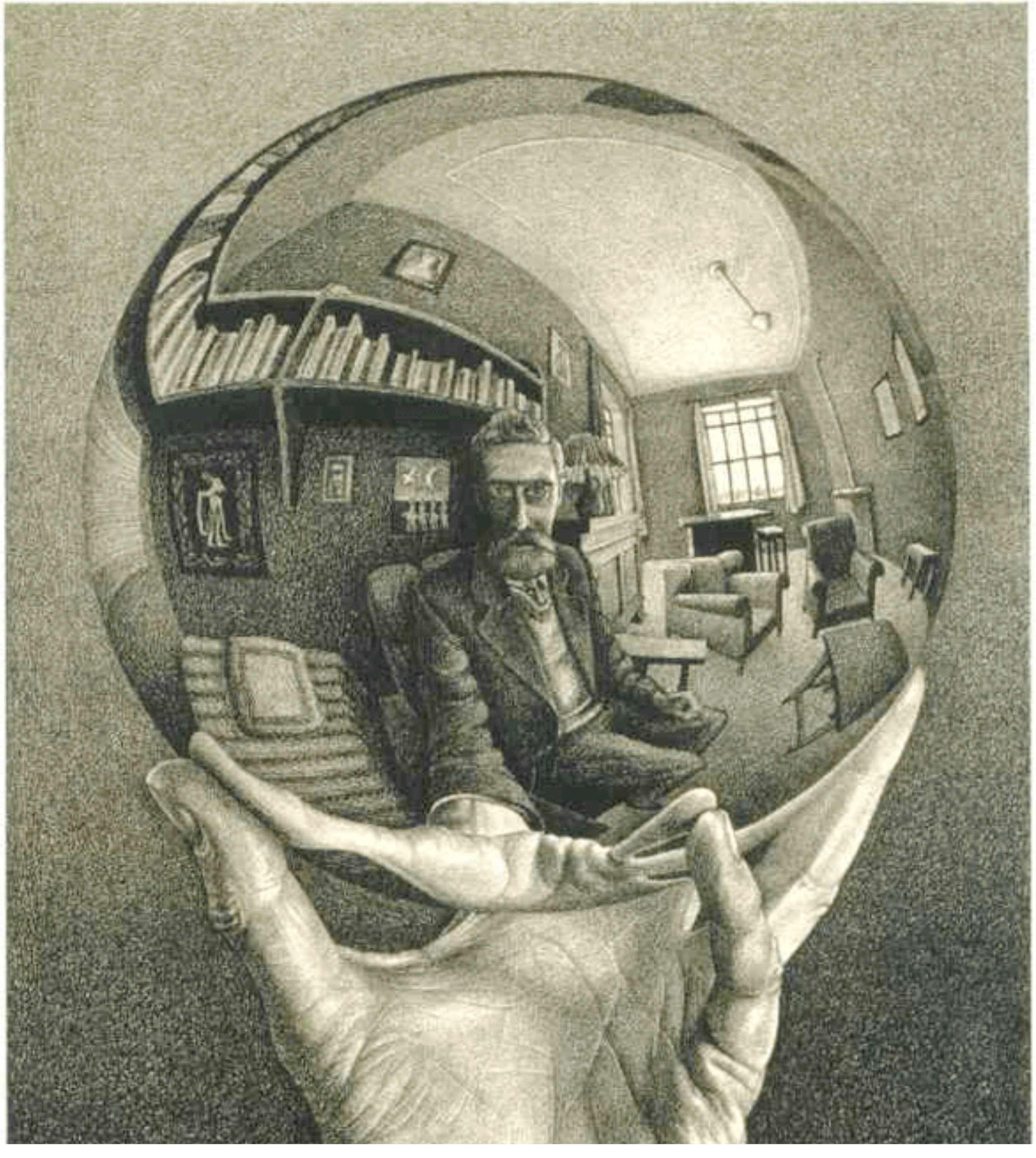


Courtesy of Rodrigo Braga

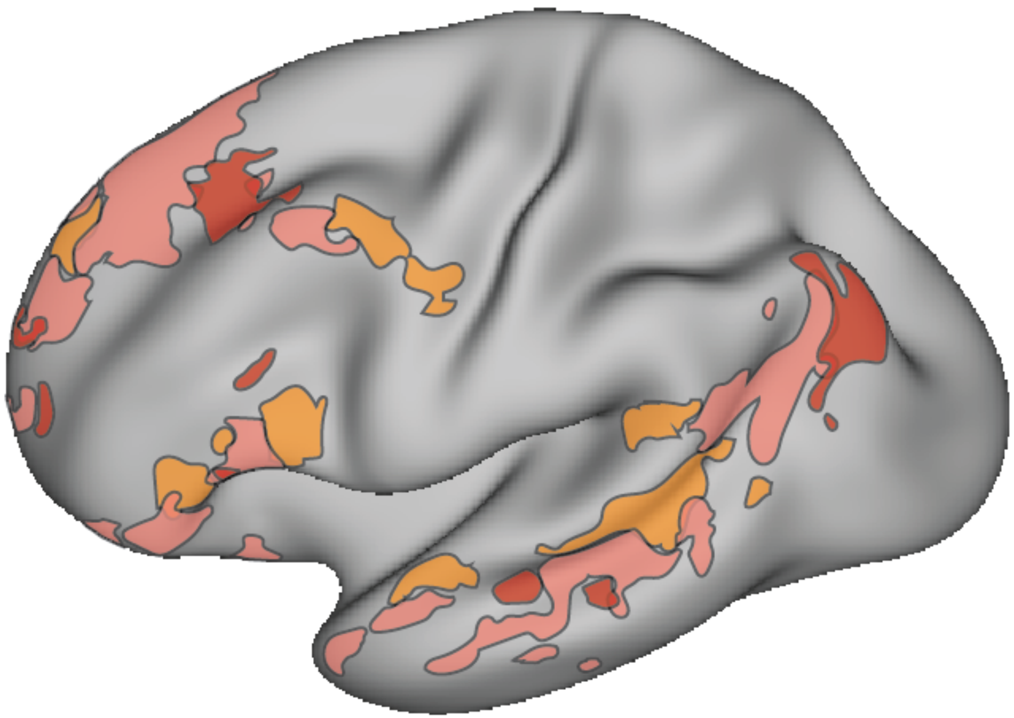
Human Specialization for Higher Brain Function?

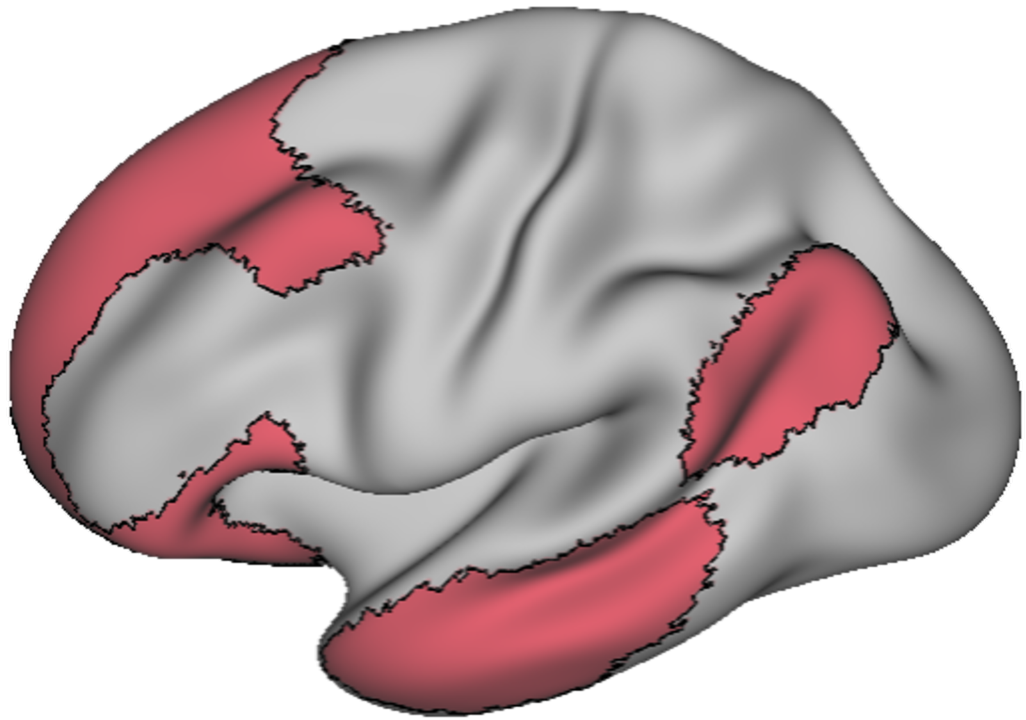


Courtesy of Rodrigo Braga



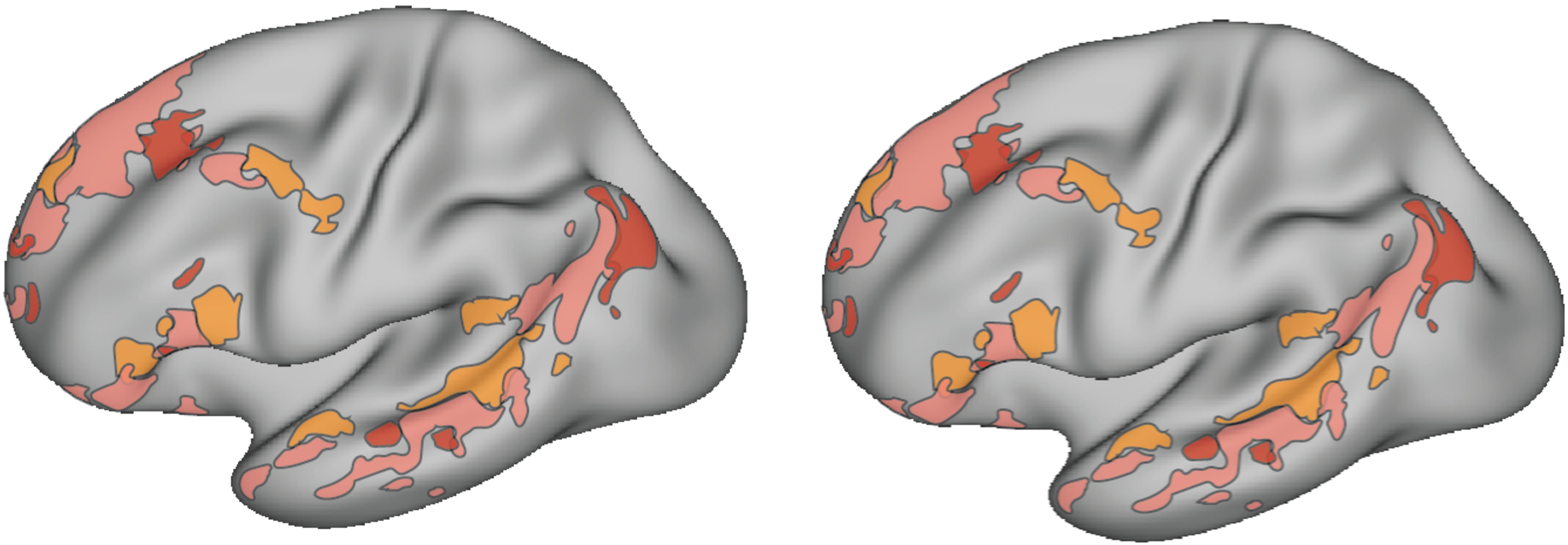
Developmental Specialization





Courtesy of Rodrigo Braga

Developmental Specialization



Courtesy of Rodrigo Braga

Human Neuromodulation

PNAS

CrossMark

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]

[a]Berenson-Allen Center for Noninvasive Brain Stimulation, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215; [b]Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114; [c]Athinoula A. Martinos Center for
Biomedical Imaging, Harvard Medical S
[e]Department of Psychology, Center for
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Neurosurgery, Department of Surgery,
Toronto, ON, Canada M5T 2S8

Edited by Michael S. Gazzaniga, Univers

Brain stimulation, a therapy increas
psychiatric disease, traditionally is d
such as deep brain stimulation (DB
such as transcranial magnetic stimul
these approaches is unknown, th
unclear, and the ideal stimulation si
ambiguous, limiting optimization o
tion in further disorders. In this arti
with both types of stimulation, list
be most effective in each disease, a
sites are different nodes within the
by resting-state functional-connect
effective were functionally connec
brain stimulation was effective ac
sion, Parkinson's disease, obsessive
tremor, addiction, pain, minimally c
disease. A lack of functional connect
ulation was ineffective, and the si
whether excitatory or inhibitory no
clinically effective. These results s
tional connectivity may be useful f
stimulation modalities, optimizing
stimulation targets. More broadly,
perspective toward understanding
disease, highlighting the therapeu
network modulation.

human connectome project | neurosurg
clinical application

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 (± 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*

A promising treatment appro
neurological diseases is foc
ally divided into invasive approach
noninvasive approaches that stimu
skull. The dominant invasive treat
(DBS) in which an electrode is su
brain and used to deliver electr
(generally 120–160 Hz) (1, 2). In s
effects of DBS resemble those of st
but in other cases DBS appears 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-

serves on the scientific advisory boards for Nexstim, Neuronix, Starlab Neuroscience, Allied Mind, Neosync, 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/gsp.

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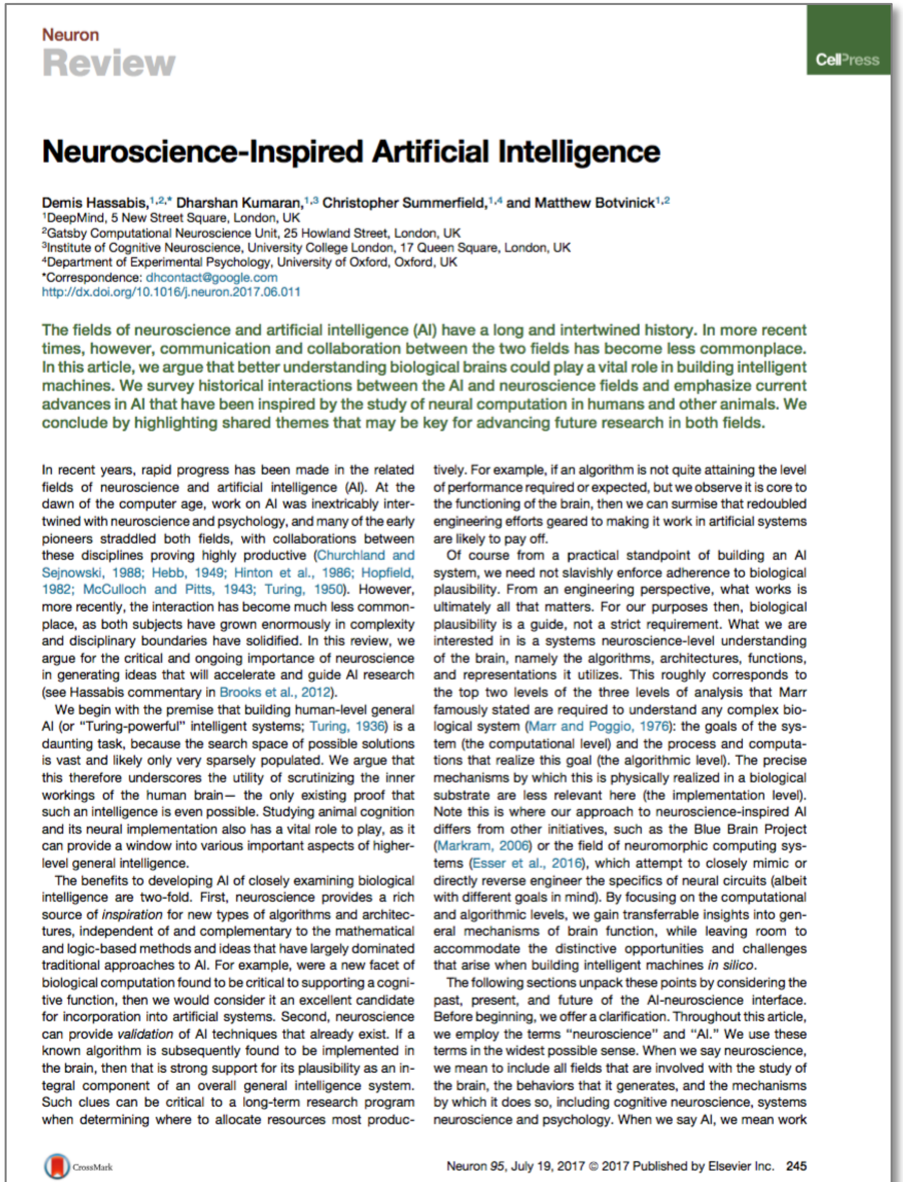
This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1405003111/-/DCSupplemental.

Artificial Intelligence



Neuron
Review

CellPress

Neuroscience-Inspired Artificial Intelligence

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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.

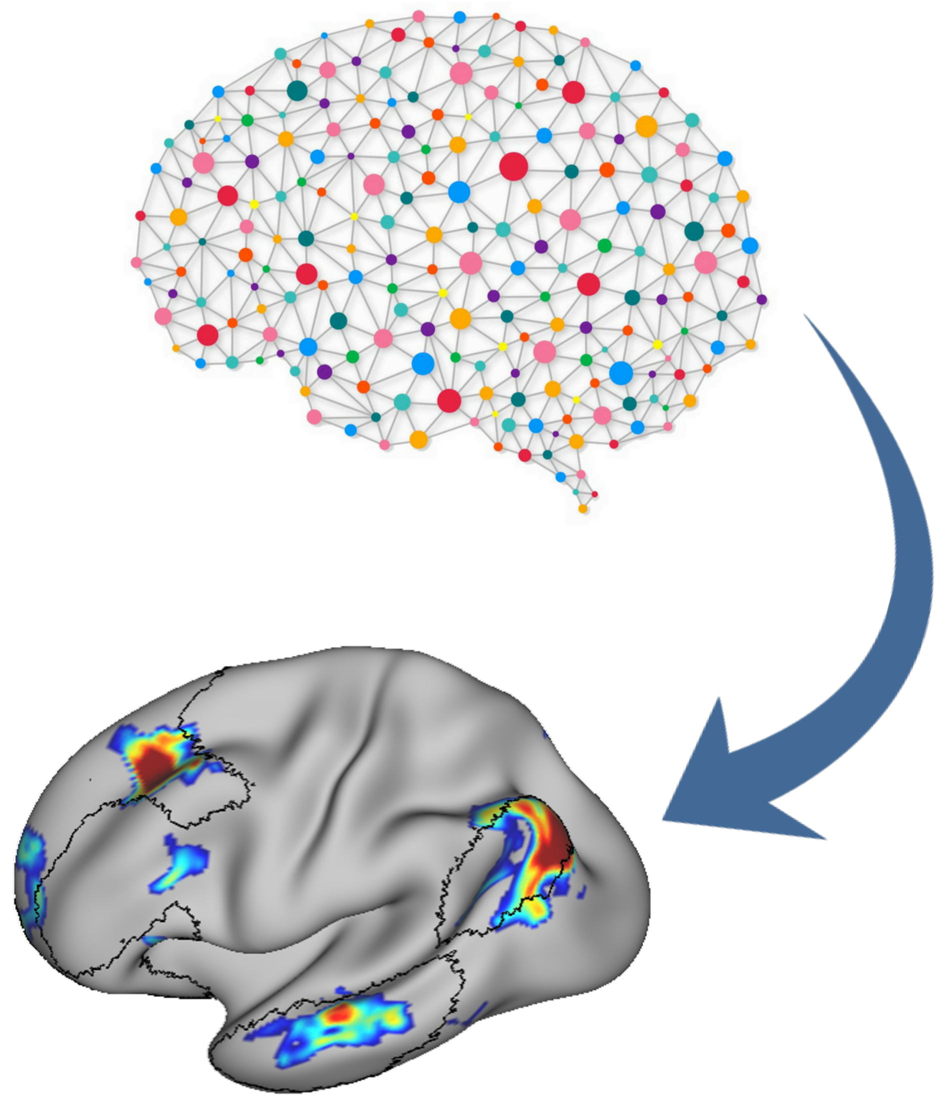
In recent years, rapid progress has been made in the related fields of neuroscience and artificial intelligence (AI). At the dawn of the computer age, work on AI was inextricably intertwined with neuroscience and psychology, and many of the early pioneers straddled both fields, with collaborations between 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 core 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 transferrable 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



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.