Consciousness & Anesthesia

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Disclosure

- Patent (pending) on the use of directional/effective connectivity for measuring states of consciousness

Outline

- Terminology related to consciousness
- Neurobiology of consciousness and general anesthesia
- Assessing networks during consciousness and general anesthesia

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- **Terminology related to consciousness**
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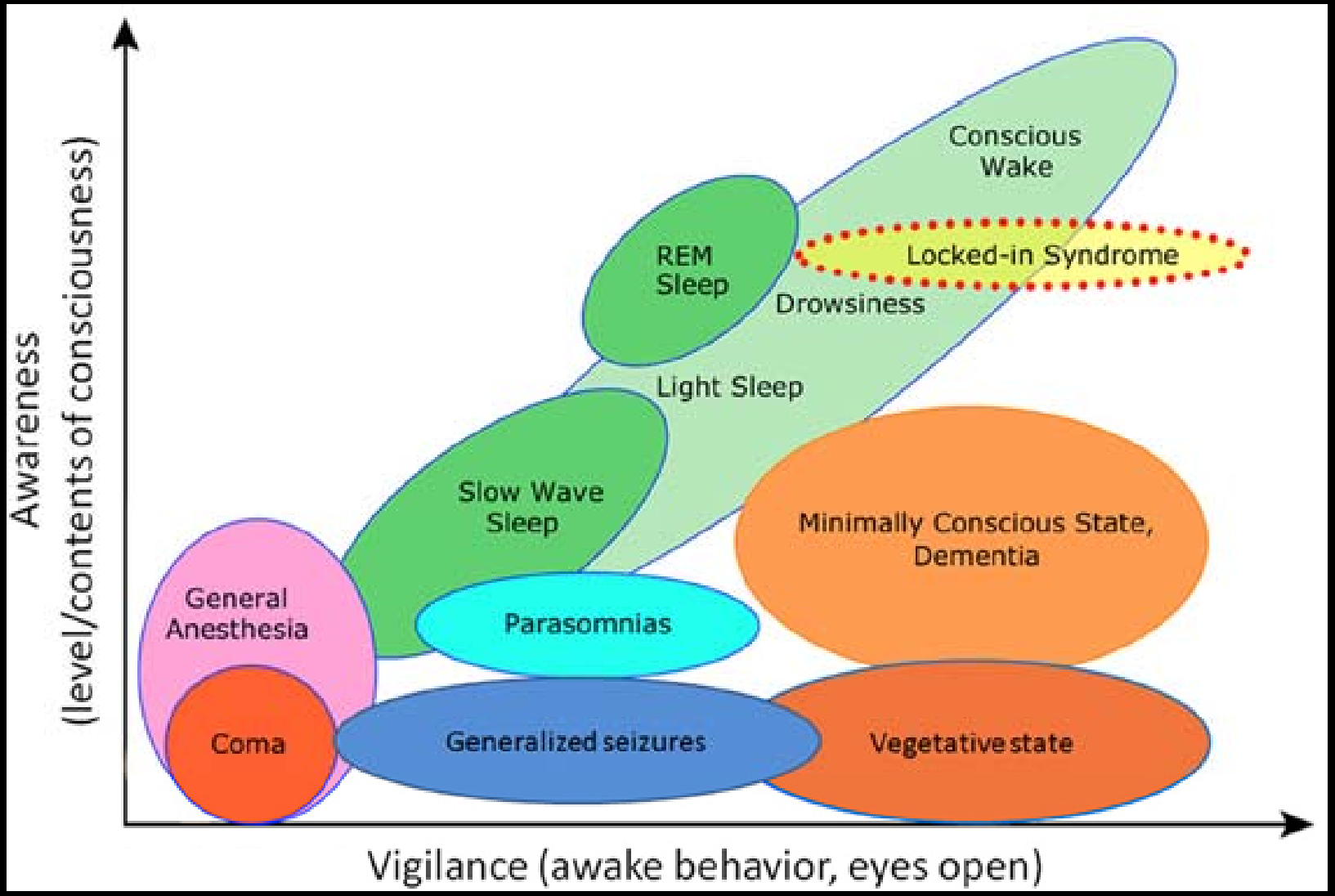
Awake vs. Aware

- ***Wakefulness*** **can be manifest as sleep-wake cycles in the absence of experience**

- ***Awareness*** **refers to the <u>experiential</u> component of consciousness**

Awake vs. Aware



Levels vs. Contents

- ***Levels*** **refer to the overall state of consciousness**

- ***Contents*** **refer to the particular qualities (or "qualia") of consciousness**

Phenomenal vs. Access

- ***Phenomenal consciousness*** **is pure experience**

- ***Access consciousness*** **refers to the availability of that experience**

Connected vs. Disconnected

- ***Connected consciousness*** **relates to environmental stimuli**

- ***Disconnected consciousness*** **relates to endogenous experience**

Easy vs. Hard Problems

- ***Easy problems*** **of consciousness relate to integration, verbal report, etc.**

- ***Hard problem*** **relates to experience itself**

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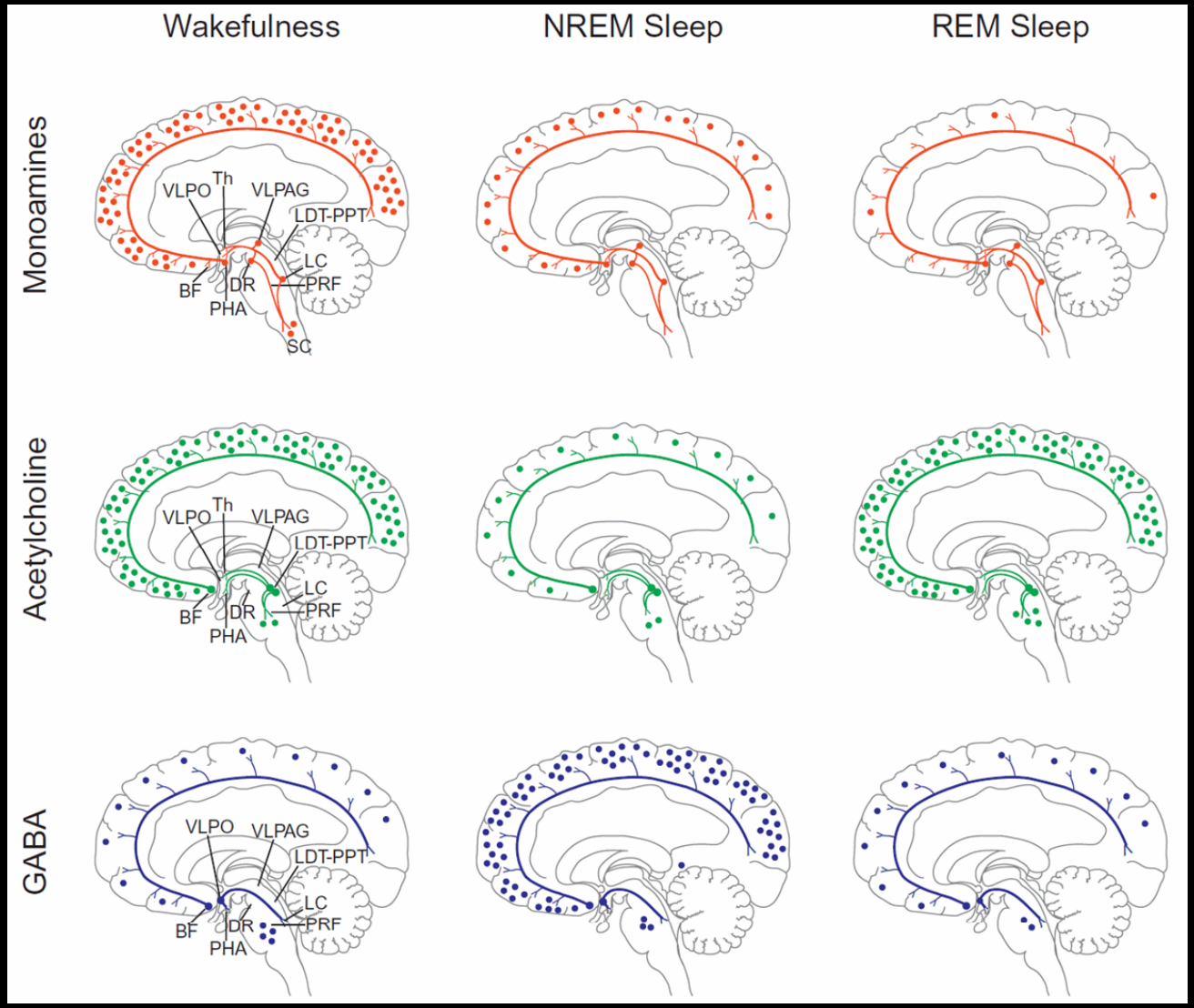
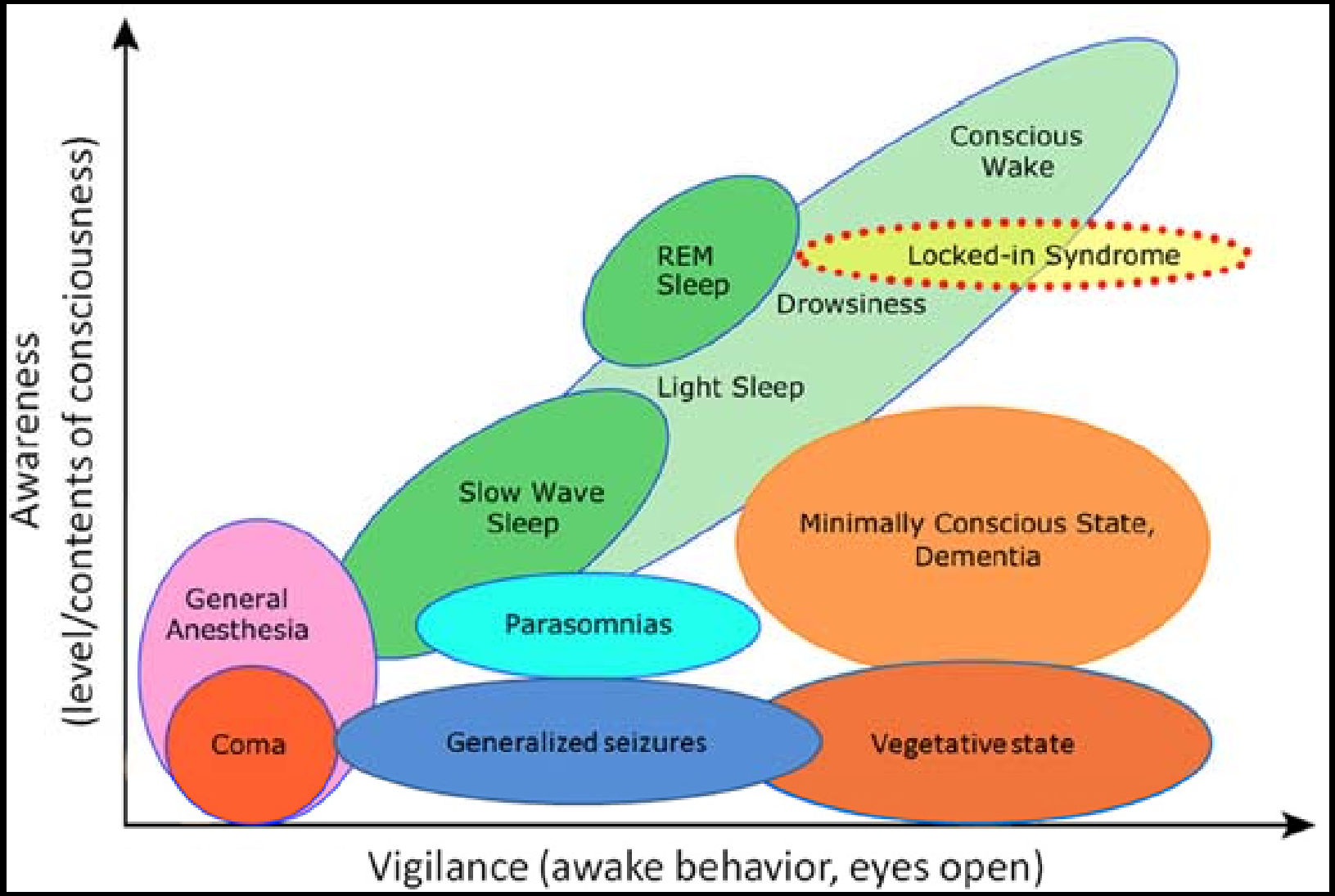
Neurochemistry of wakefulness & sleep

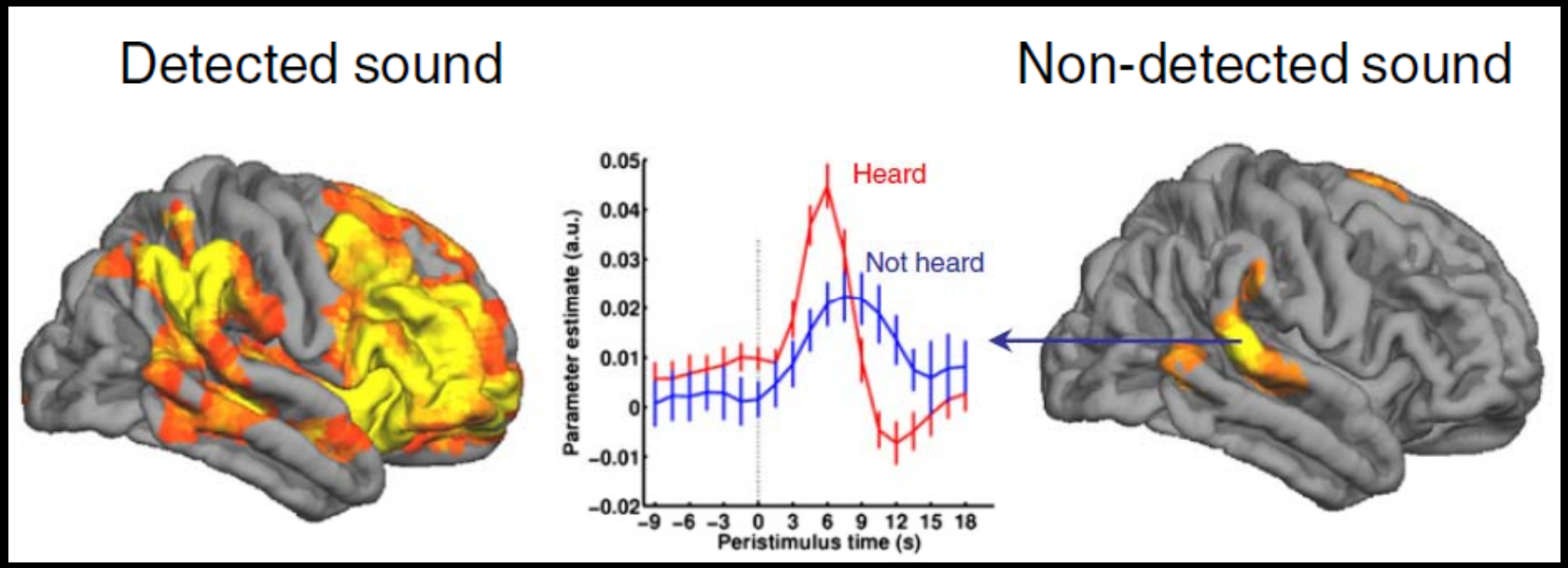


Lydic & Baghdoyan, 2012, Brady (ed.)

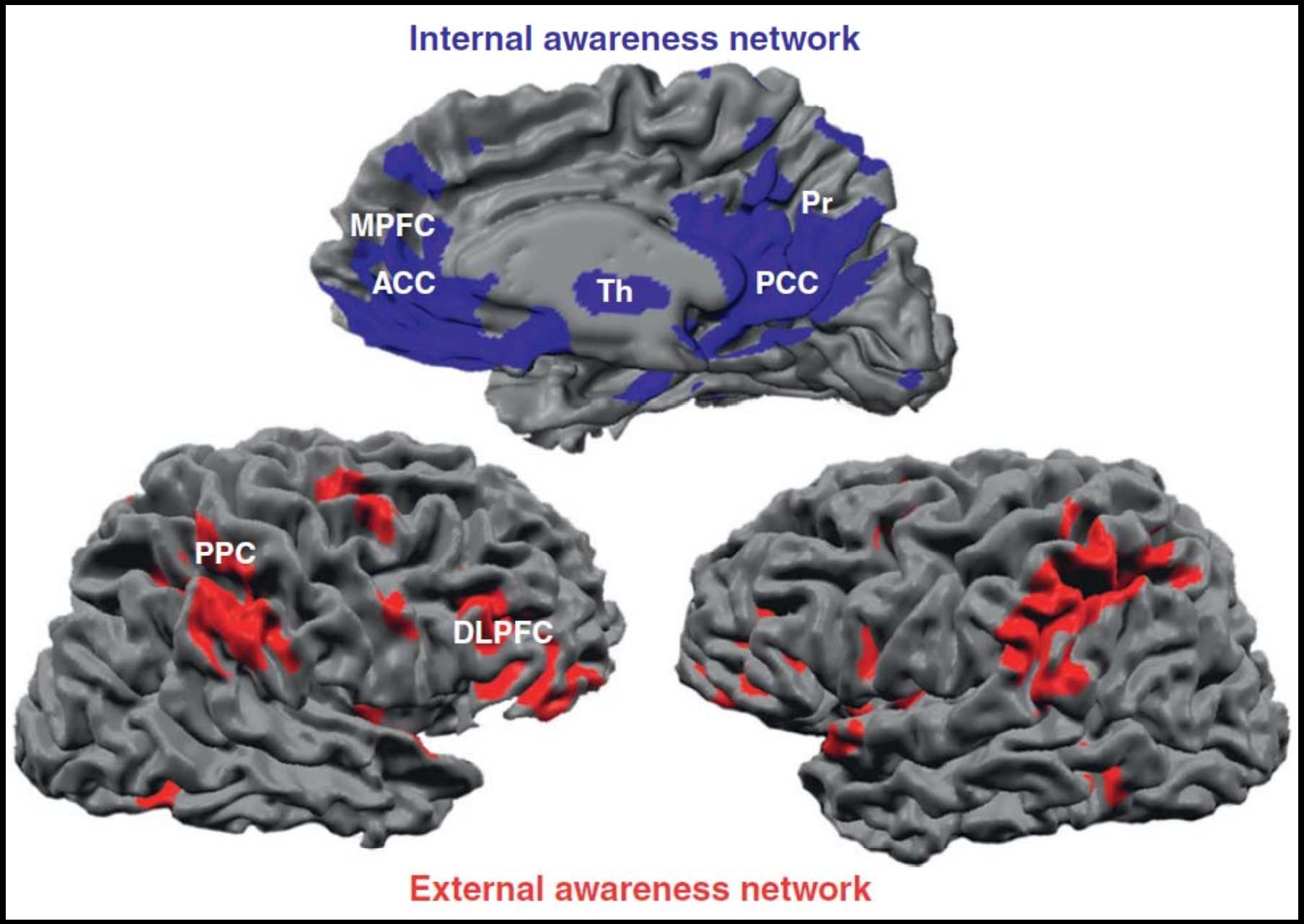
Wakefulness ≠ Awareness



Consciousness is not correlated with primary sensory processing

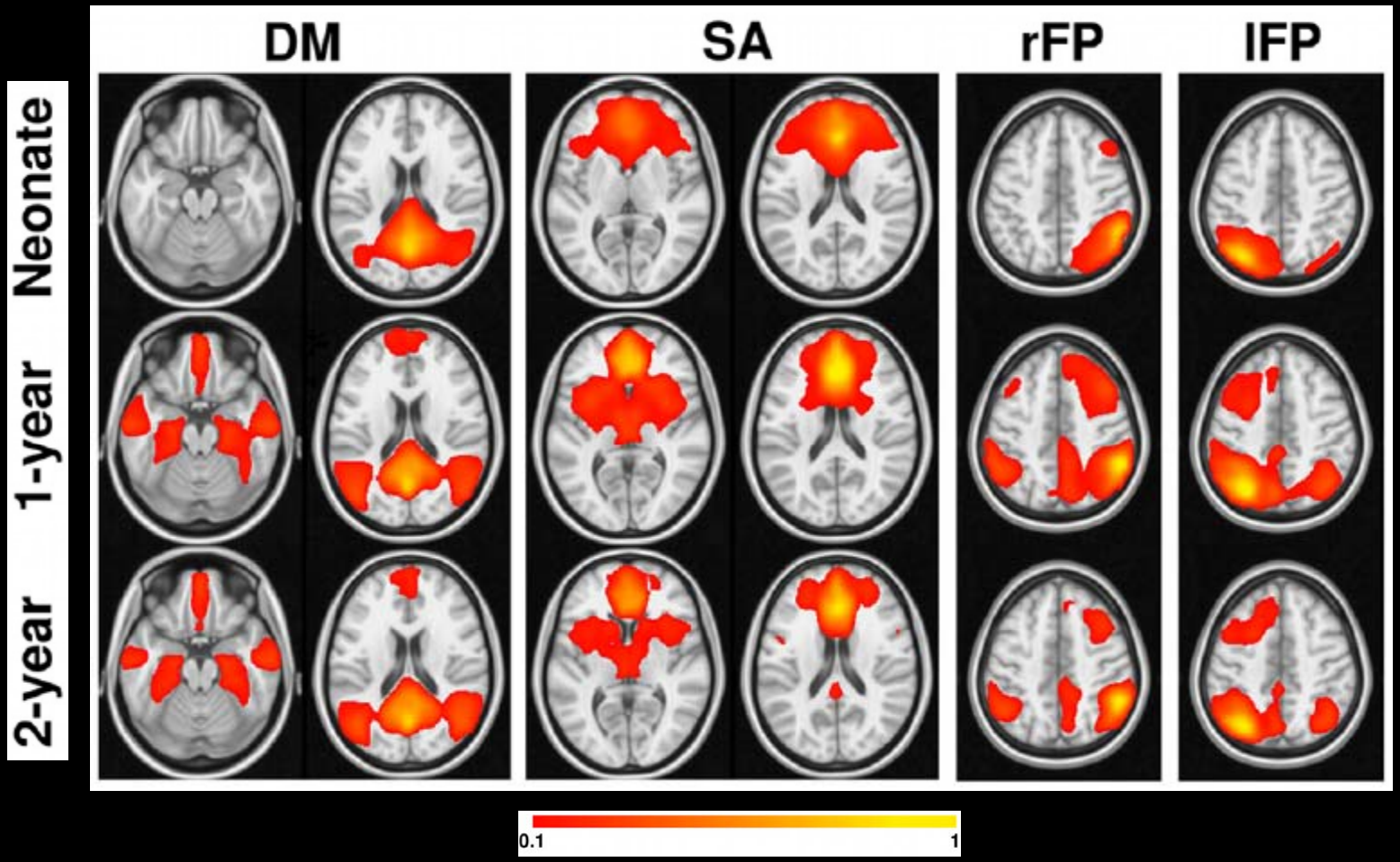


Sadaghiani et al, J Neurosci, 2009;29:13410
Dehaene & Changeux, Neuron, 2011;70:200



Demertzi et al, Curr Opin Neurobiol, 2013;23:239

The developing neuroanatomy of consciousness



Alcauter et al, J Neurosci, 2014;34:9067

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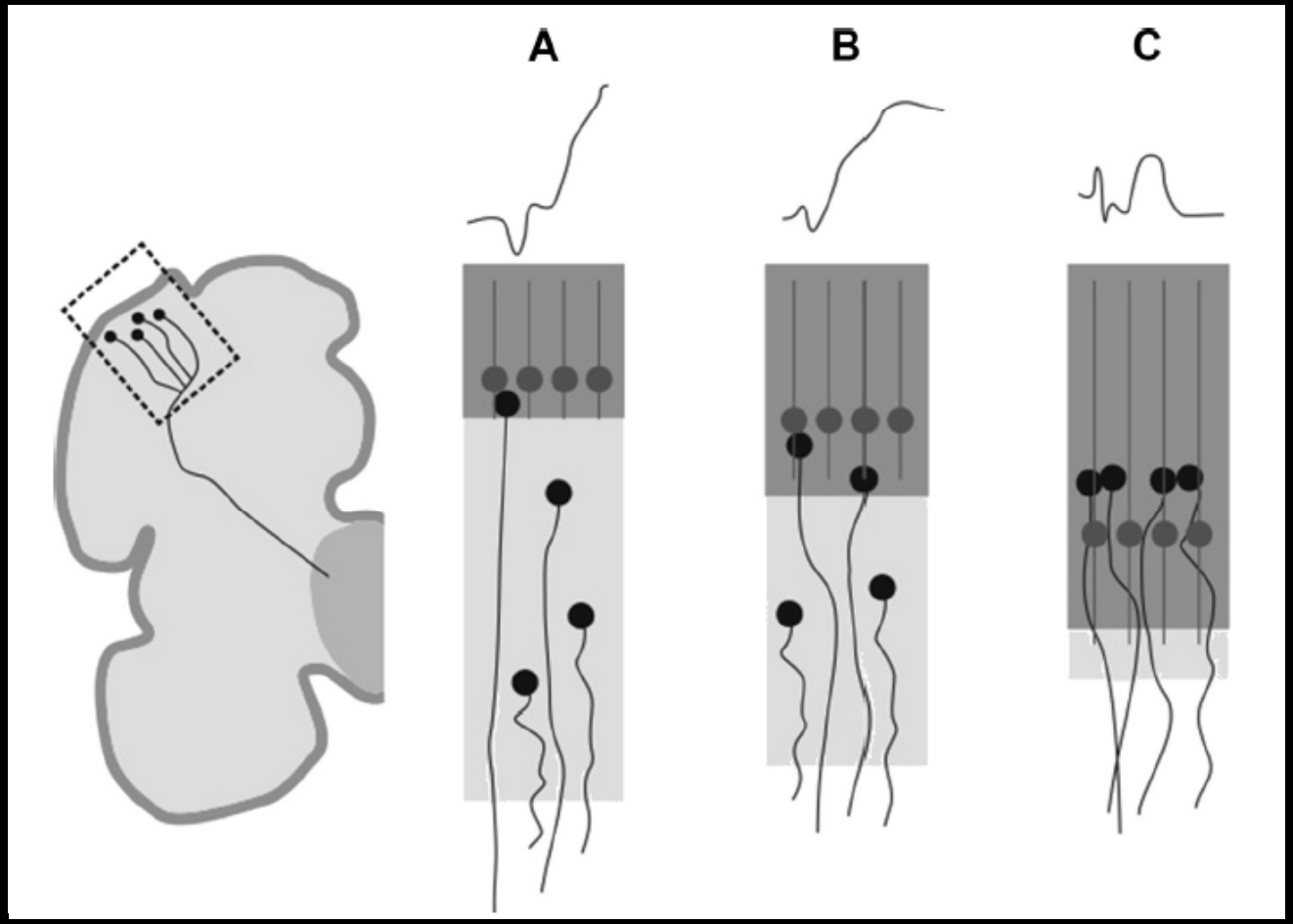
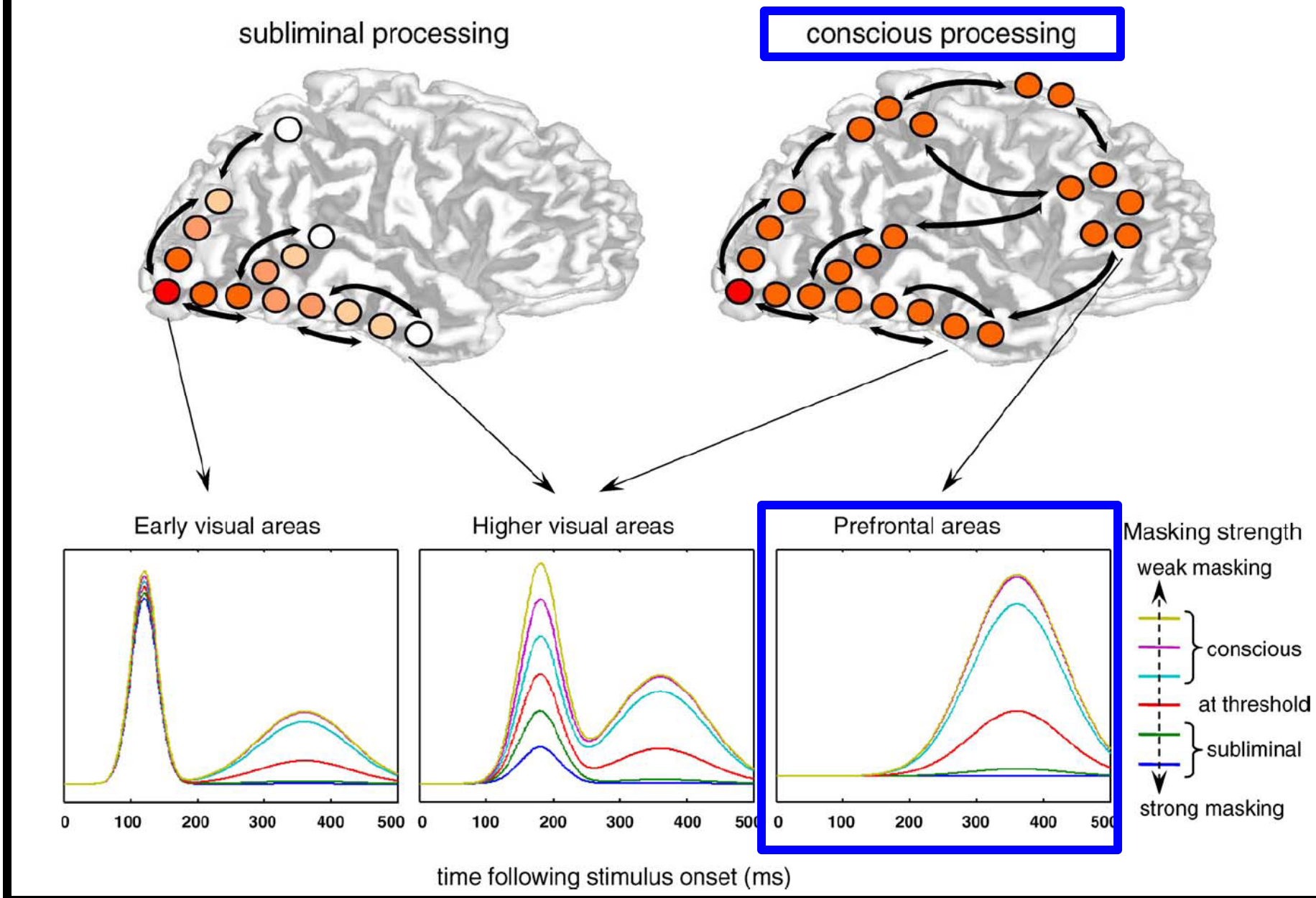
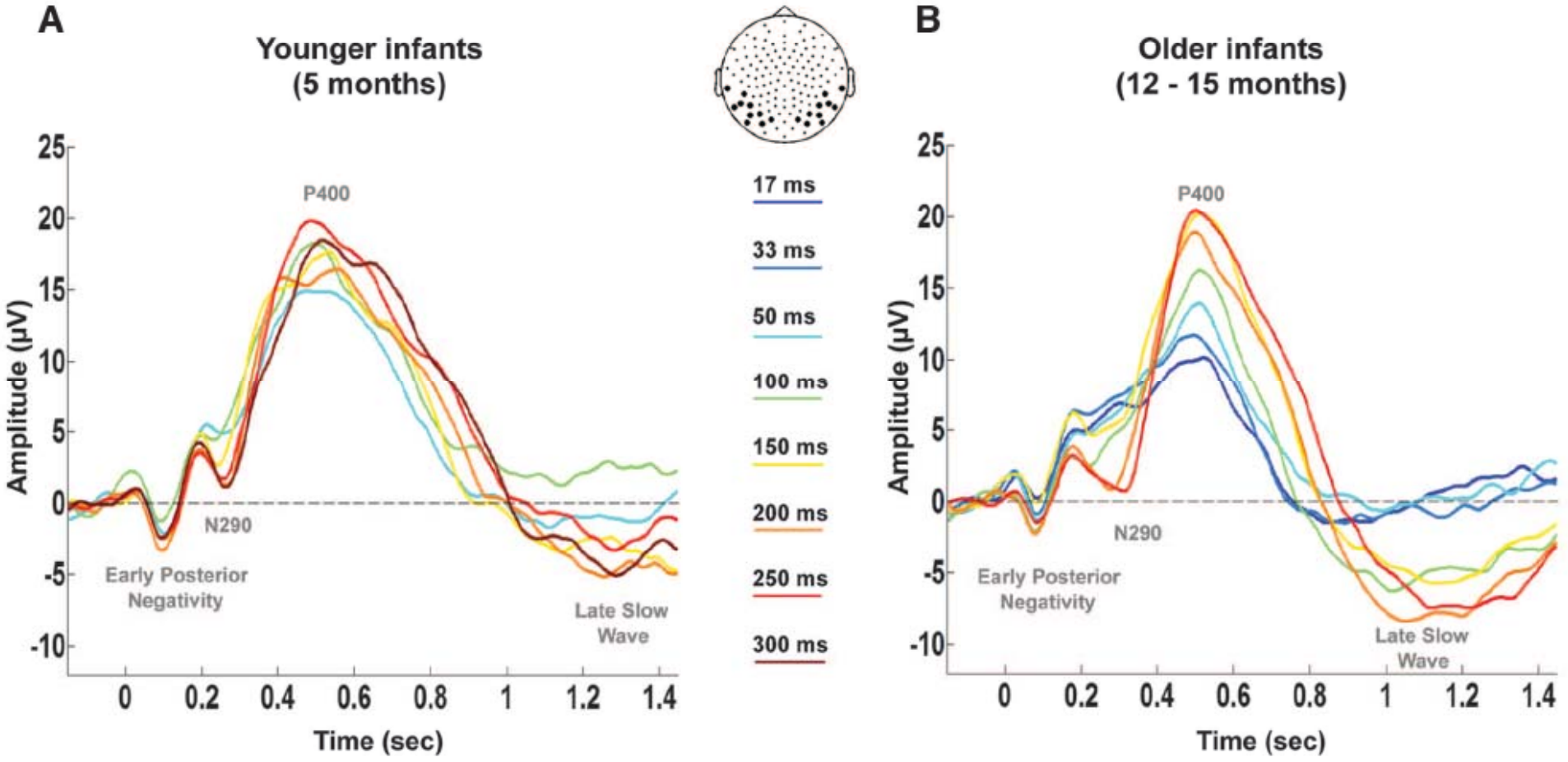


Lagercrantz, Semin Fetal & Neonat Med, 2014;in press



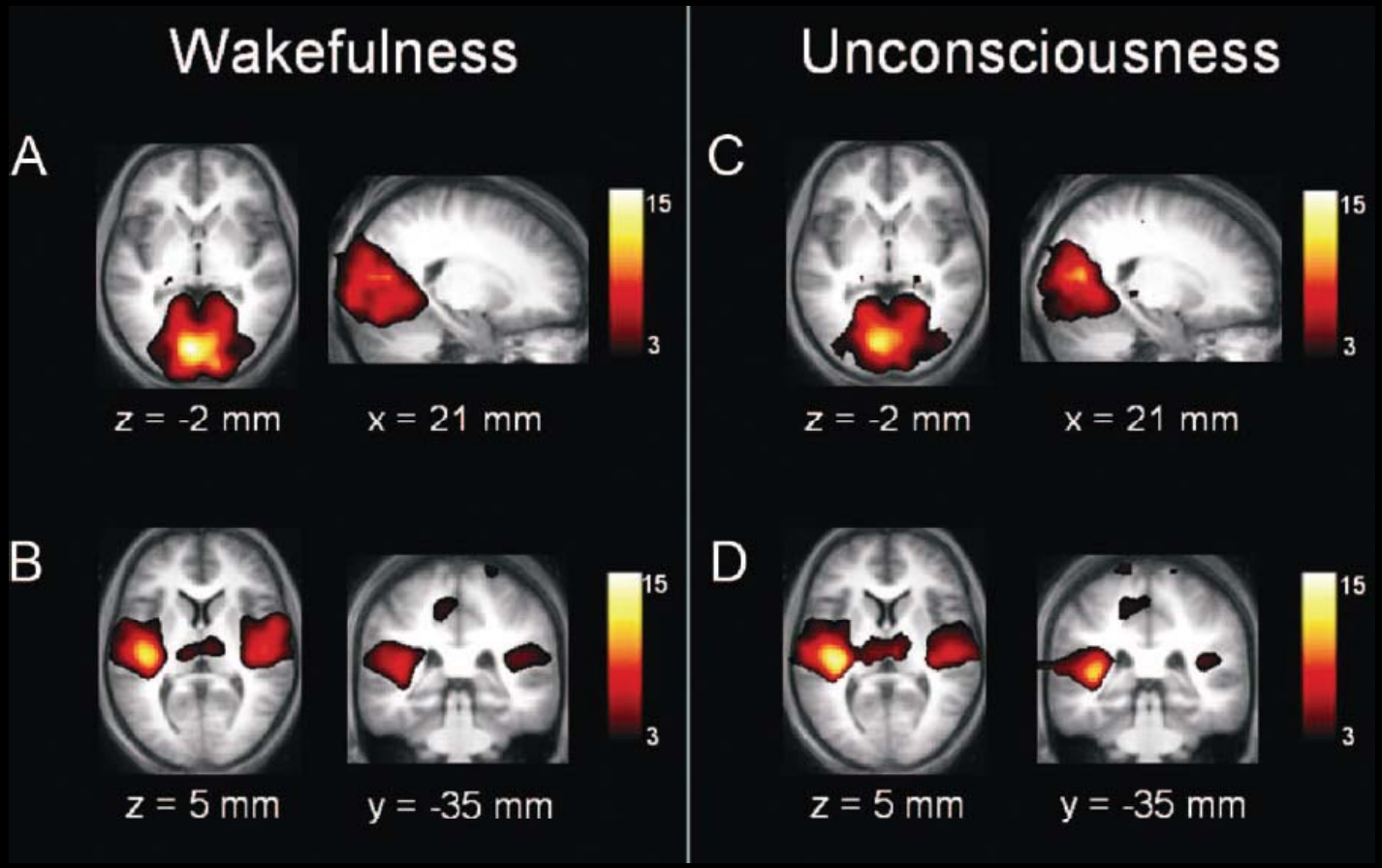
Del Cul et al, PLoS Biol, 2007;5:e260

The developing neurophysiology of consciousness



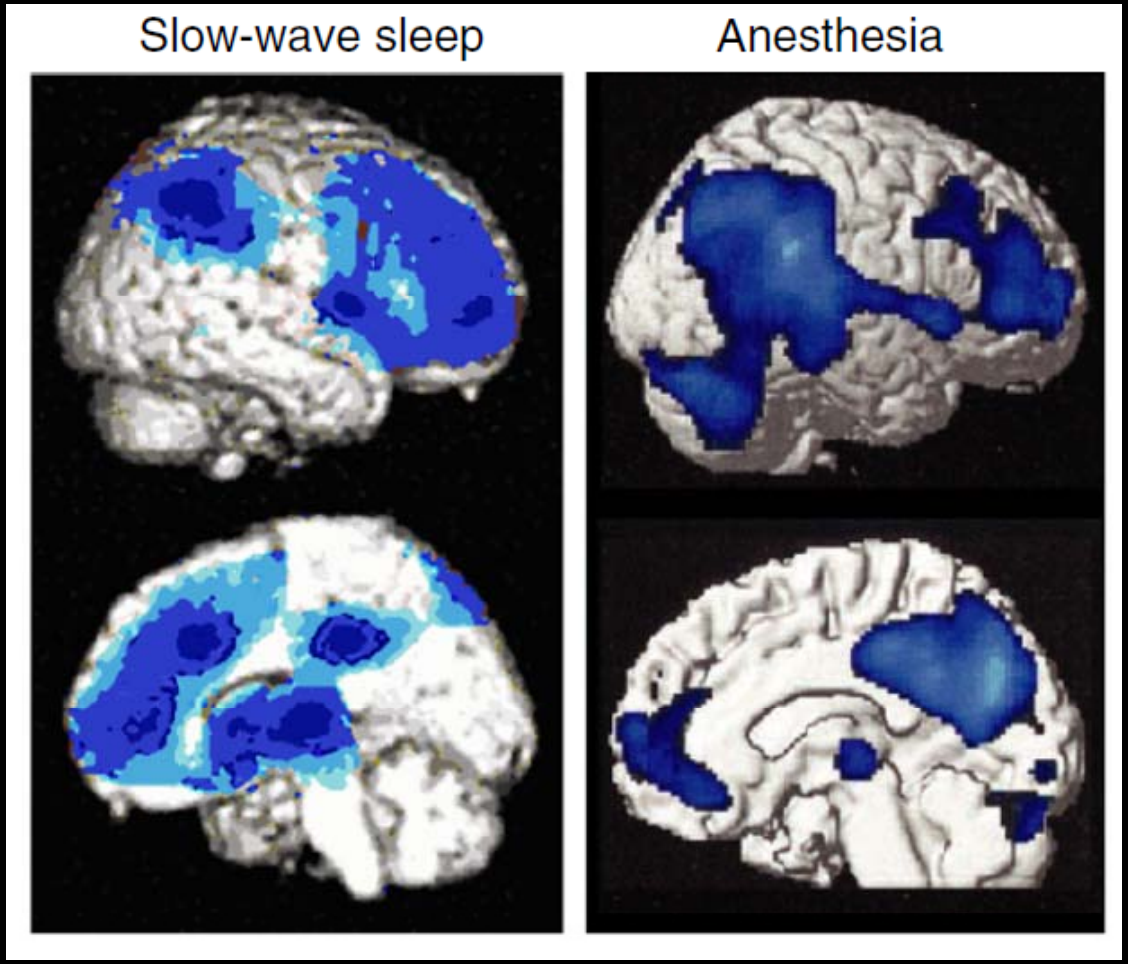
Koudier et al, Science, 2013;340:376

Anesthetic-induced unconsciousness is not correlated with primary processing



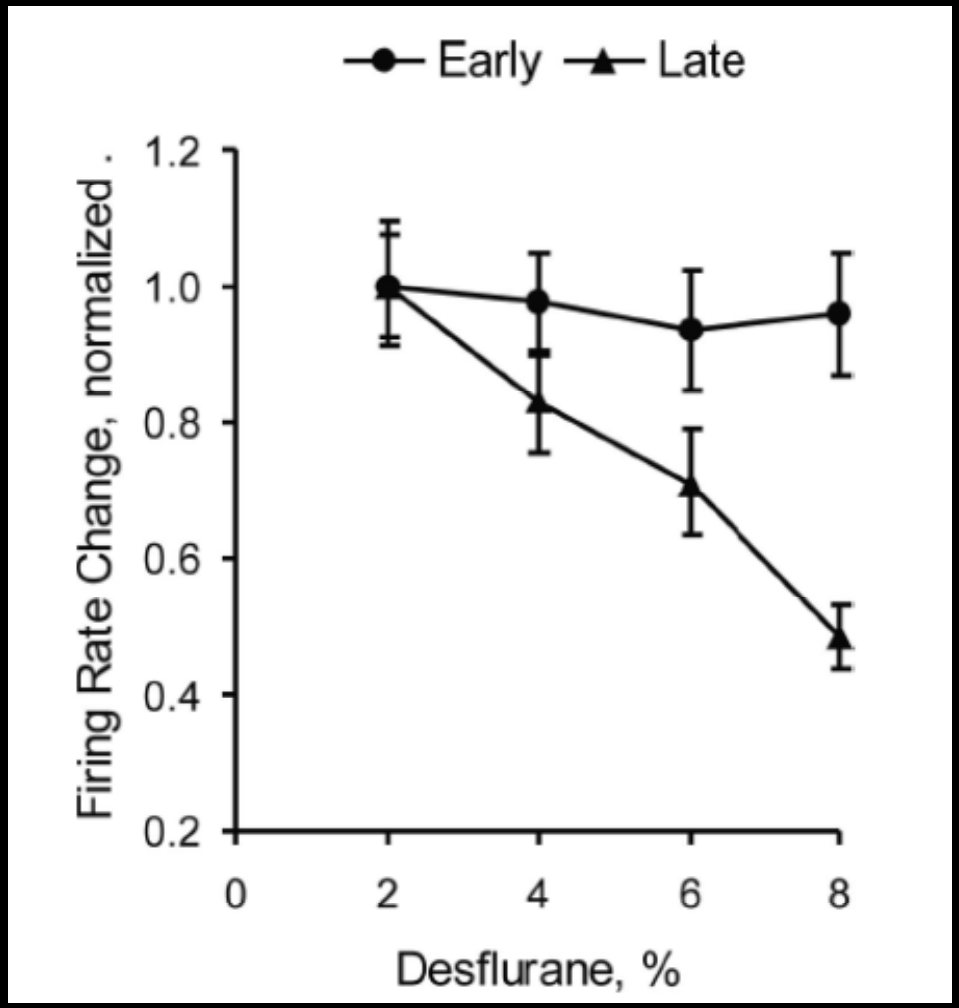
Boveroux et al, Anesthesiology, 2010;113:1038

Deactivation of frontoparietal networks during anesthesia and sleep



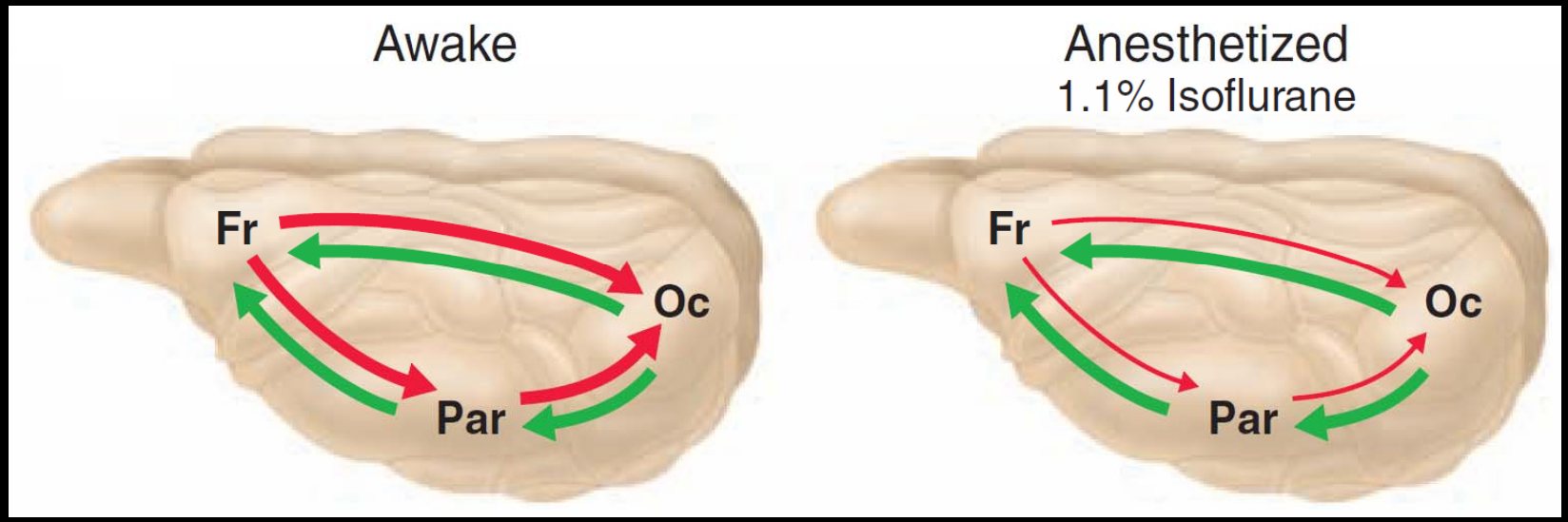
Maquet et al, J Neurosci,1997;17:2807
Kaisti et al, Anesthesiology, 2002;96:1358

General anesthetics suppress long-latency potentials



Hudetz et al, Anesthesiology, 2009;11:231

Feedback connectivity is selectively inhibited during anesthesia in rats



Imas et al, Neurosci Lett, 2005;387:145
Alkire et al, Science, 2008;322:876

Summary

- Neither consciousness nor anesthetic-induced unconsciousness is correlated with primary sensory processing
- Both relate to long-latency activity in extended frontal-parietal networks
- Experiments in animals suggest inhibition of anterior-posterior connectivity by GABAergic anesthetics

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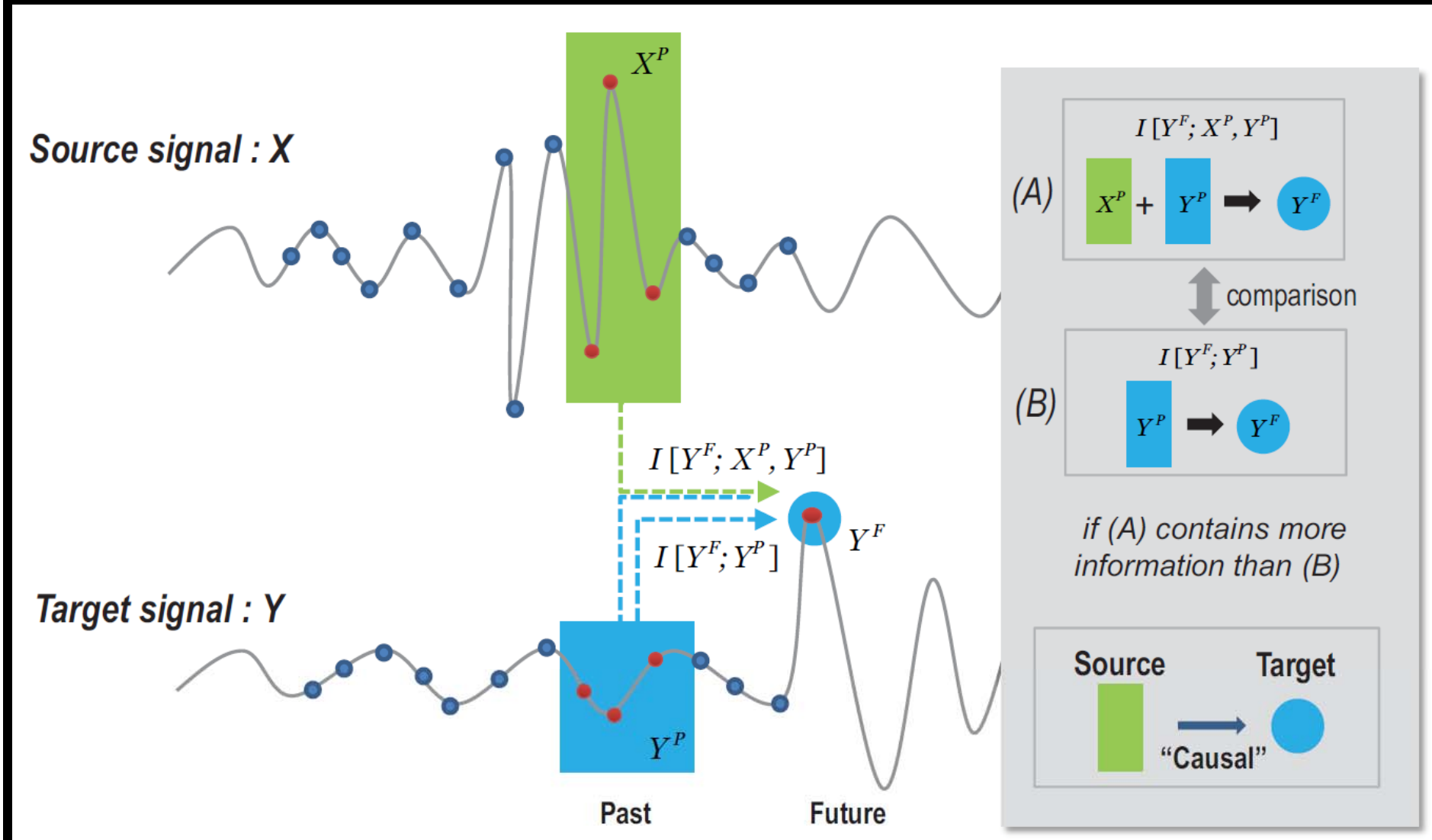
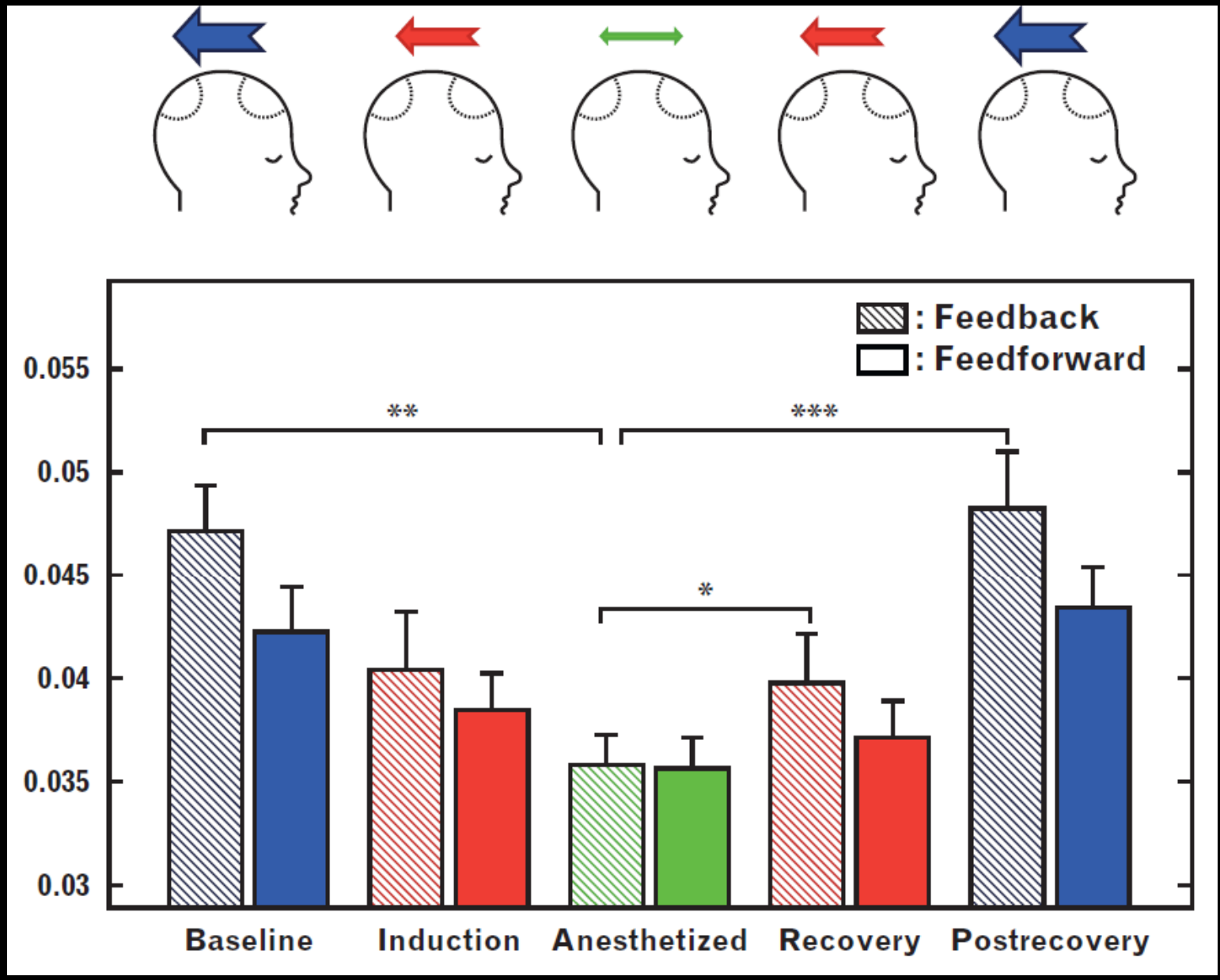
Transfer entropy



Vicente et al, J Comp Neurosci, 2011;30:45
Lee et al, Anesthesiology, 2013;118:1264



Ku et al, PLoS ONE, 2011;6:e25155

Frontoparietal disruption confirmed with high-density EEG and fMRI

Directional Connectivity

Functional Connectivity

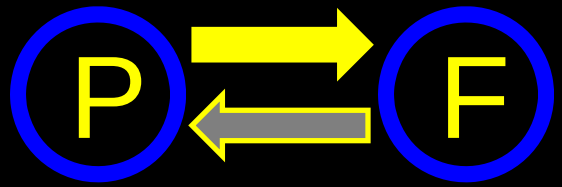
Permutation Entropy

Conscious

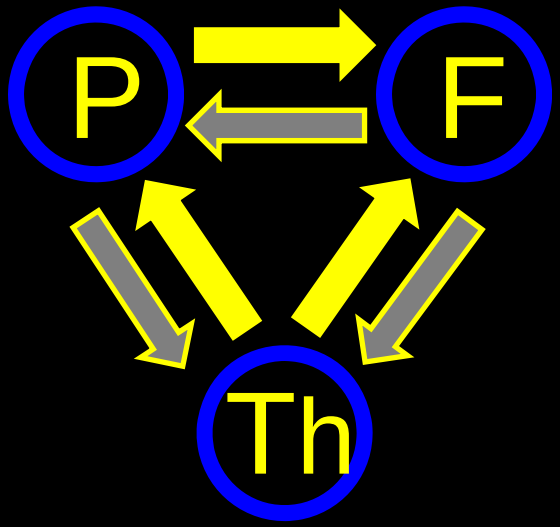
Propofol

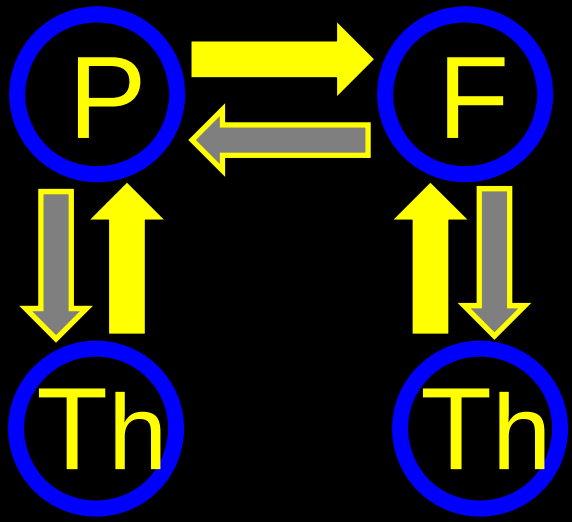
Jordan et al, Anesthesiology, 2013;119:1031
Mashour, Anesthesiology, 2013;119:1003

Model 1: Corticocortical



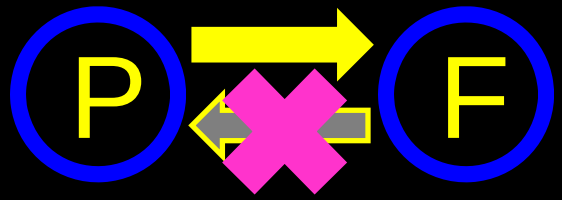
Models 2 & 3: Thalamocortical



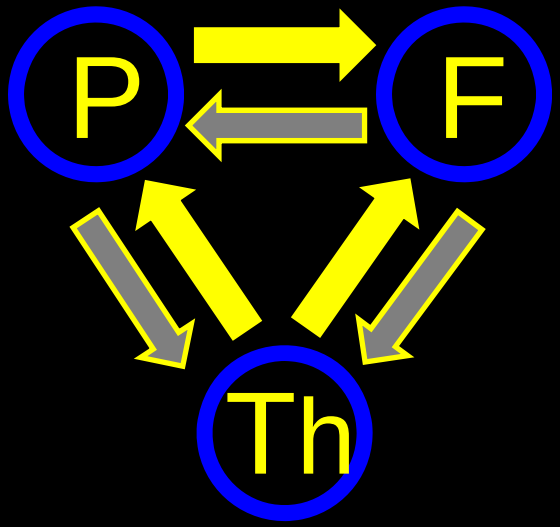


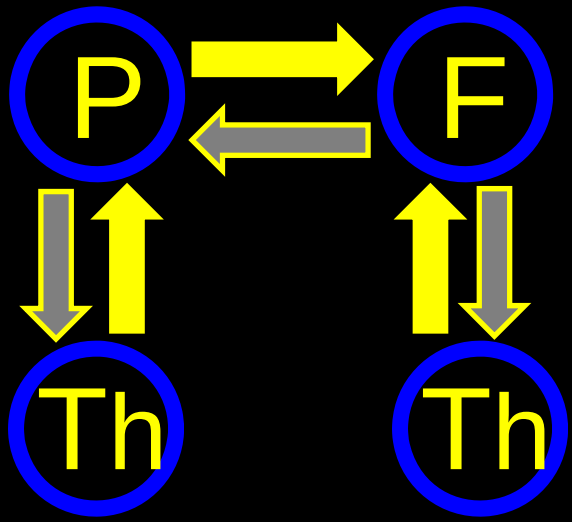
Boly et al, J Neurosci, 2012;32:7082

Model 1: Corticocortical



Models 2 & 3: Thalamocortical

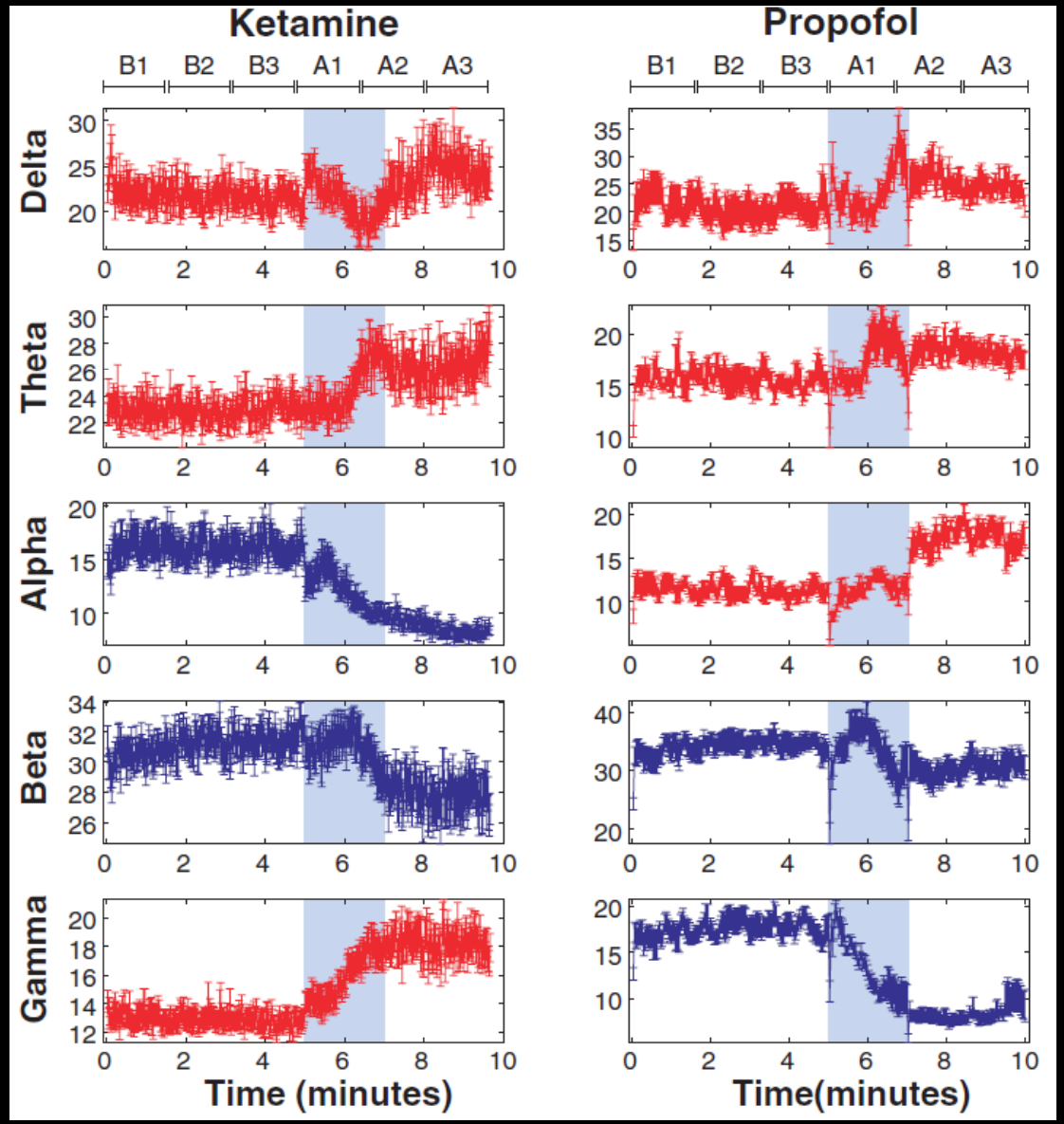




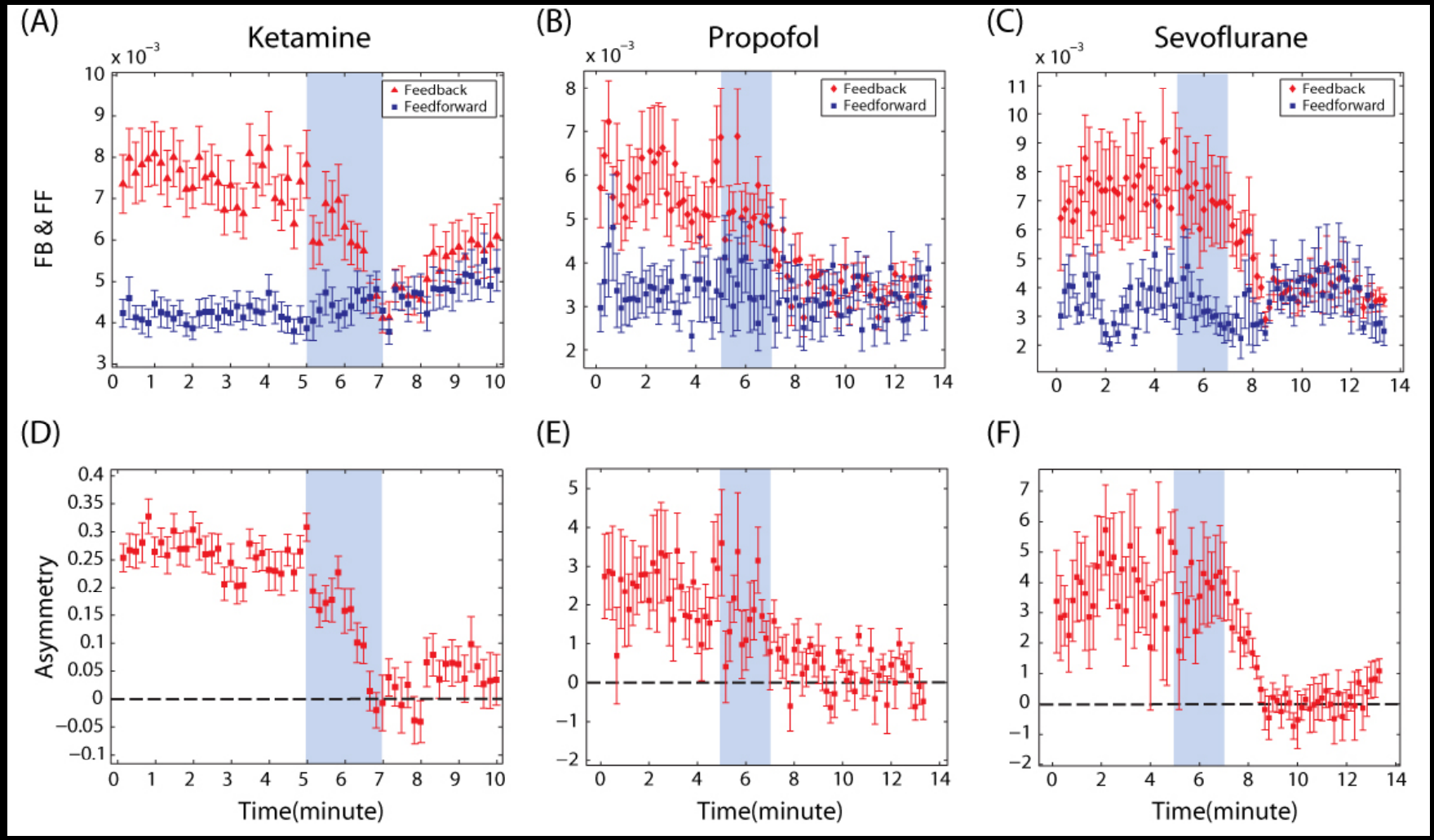
Boly et al, J Neurosci, 2012;32:7082

What about ketamine?

Distinct neurophysiology of anesthetic induction

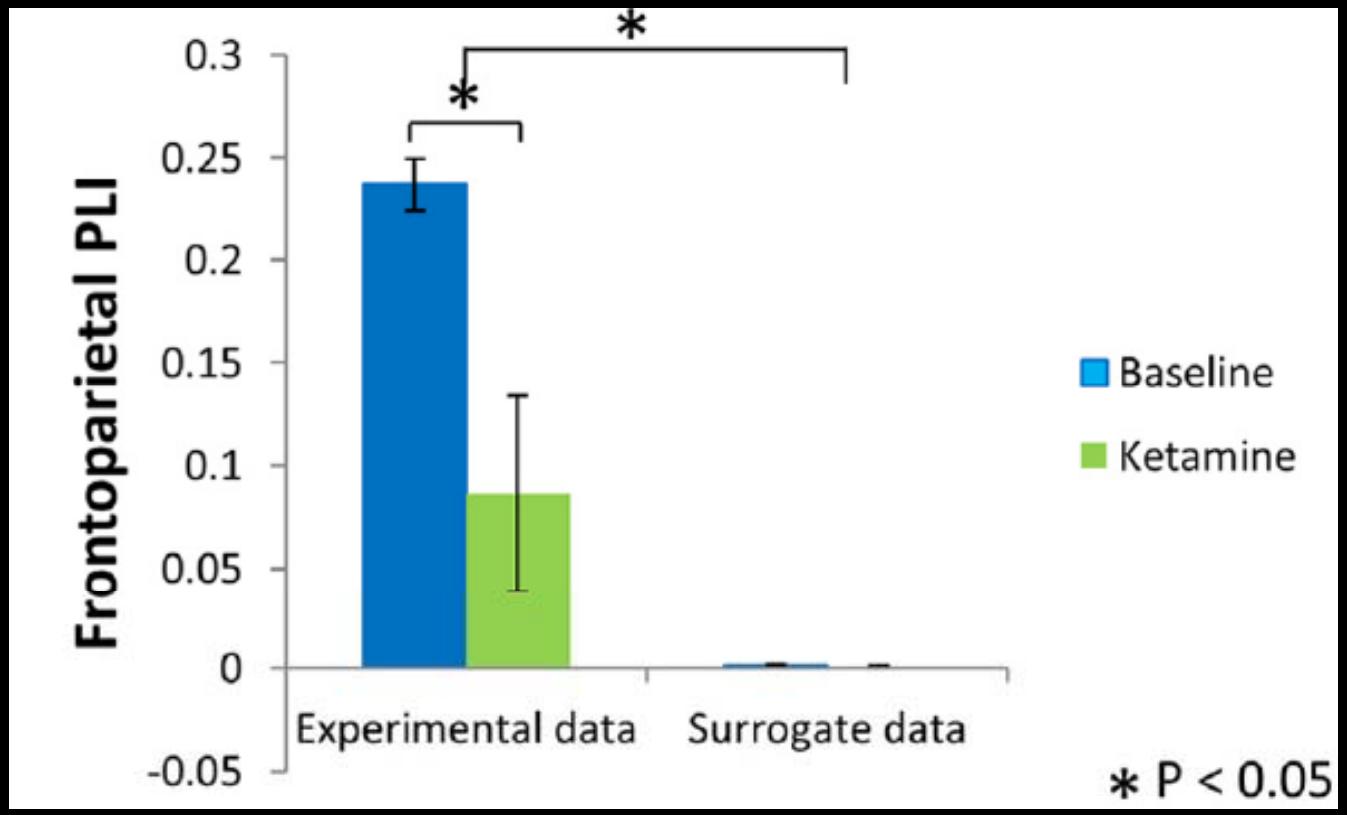


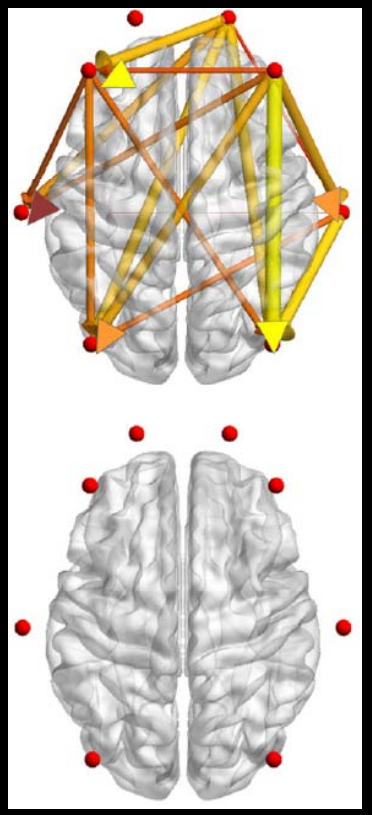
Inhibition of frontoparietal connectivity by ketamine, propofol, & sevoflurane



Lee et al, Anesthesiology, 2013;118:1264

Ketamine disrupts frontoparietal phase relationships





Blain-Moraes et al, Front Syst Neurosci, 2014

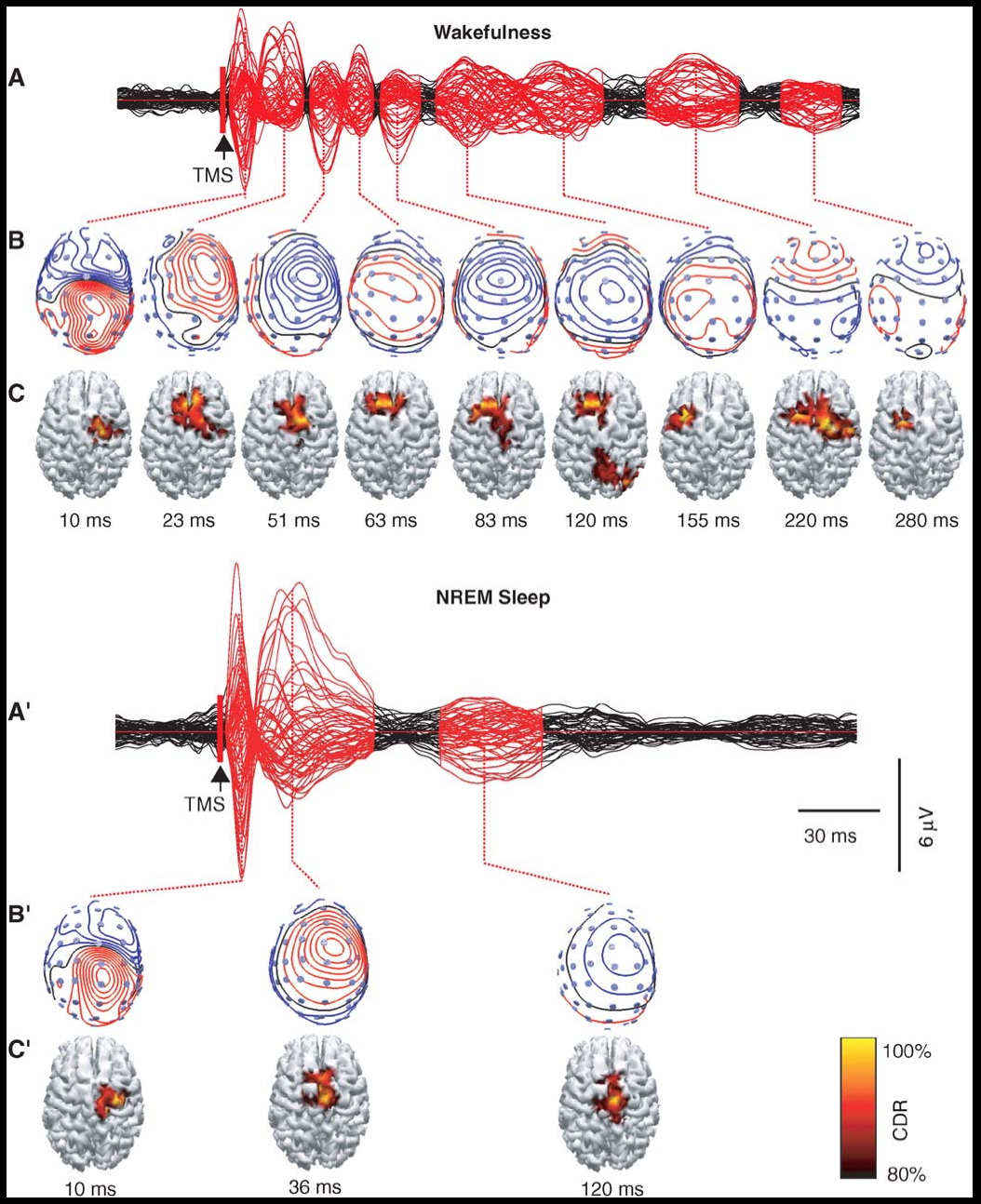
Summary

- Experiments in humans demonstrate consistent patterns of network disruption across multiple anesthetic drug classes
- Findings supported by multiple analytic techniques and imaging modalities

Perturbational approach to assessing unconsciousness

Conscious

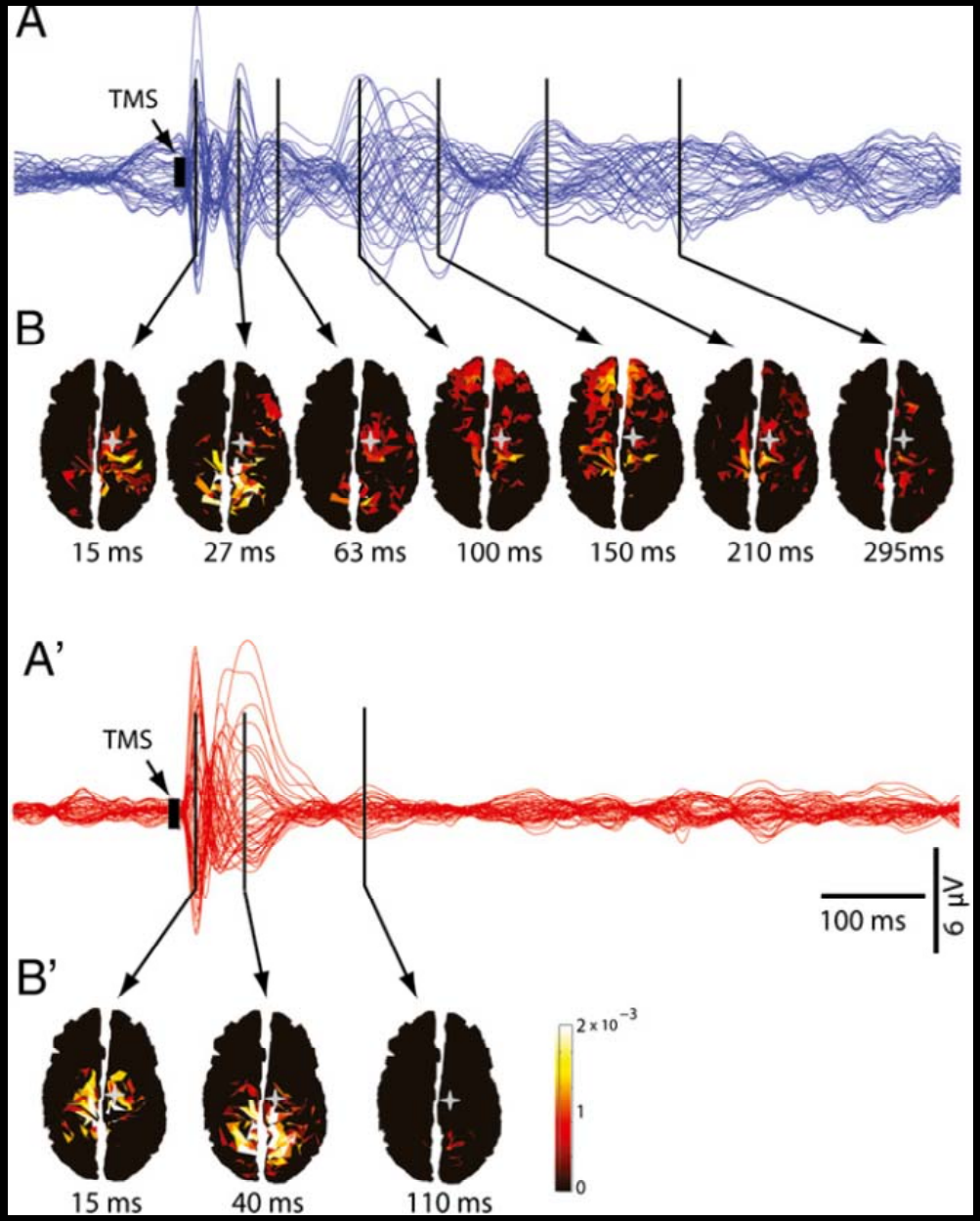
NREM sleep



Massimini et al, Science, 2005;309:2228

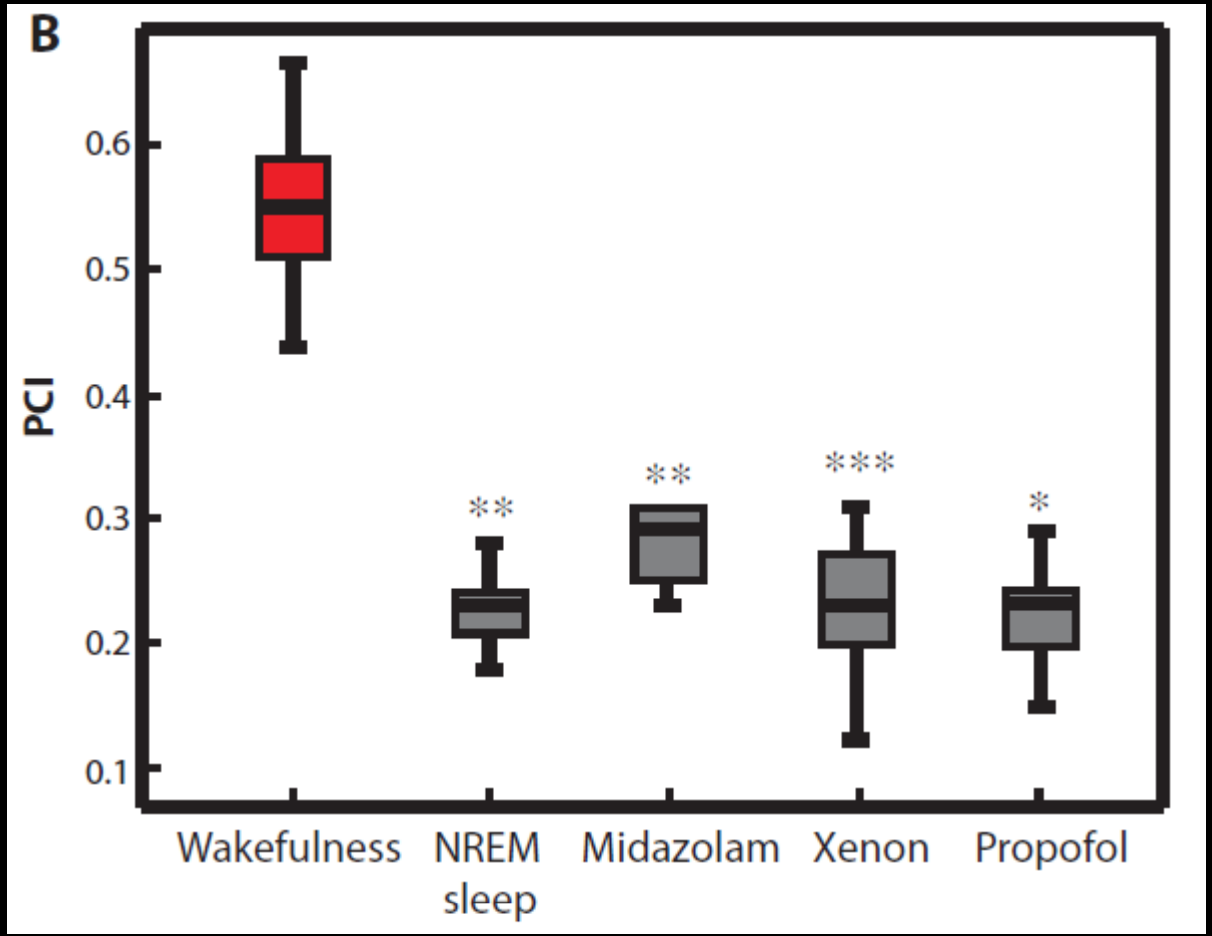
Conscious

Midazolam



Ferrarelli et al, PNAS, 2010;107:2681

Perturbational Complexity Index



Casali et al, Sci Transl Med, 2013;198ra105

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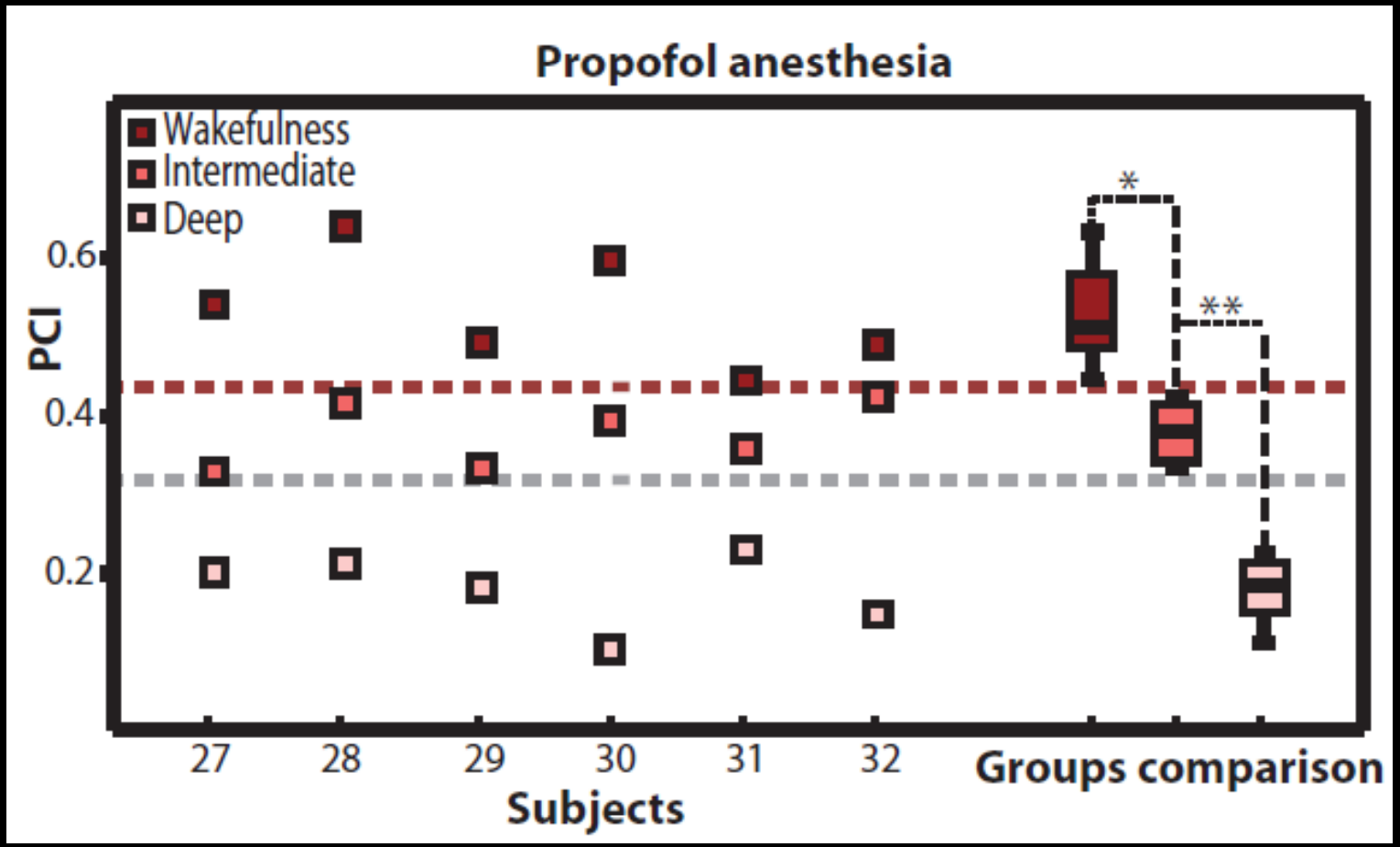

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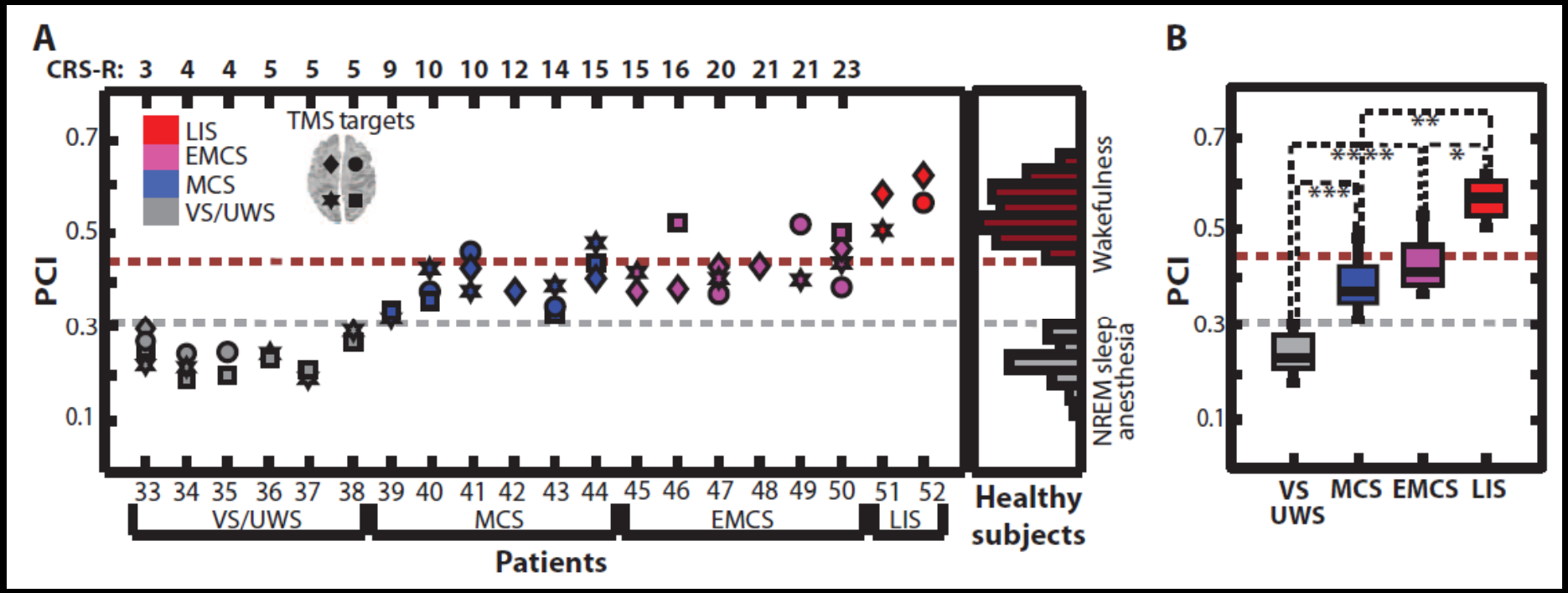


Casali et al, Sci Transl Med, 2013;198ra105

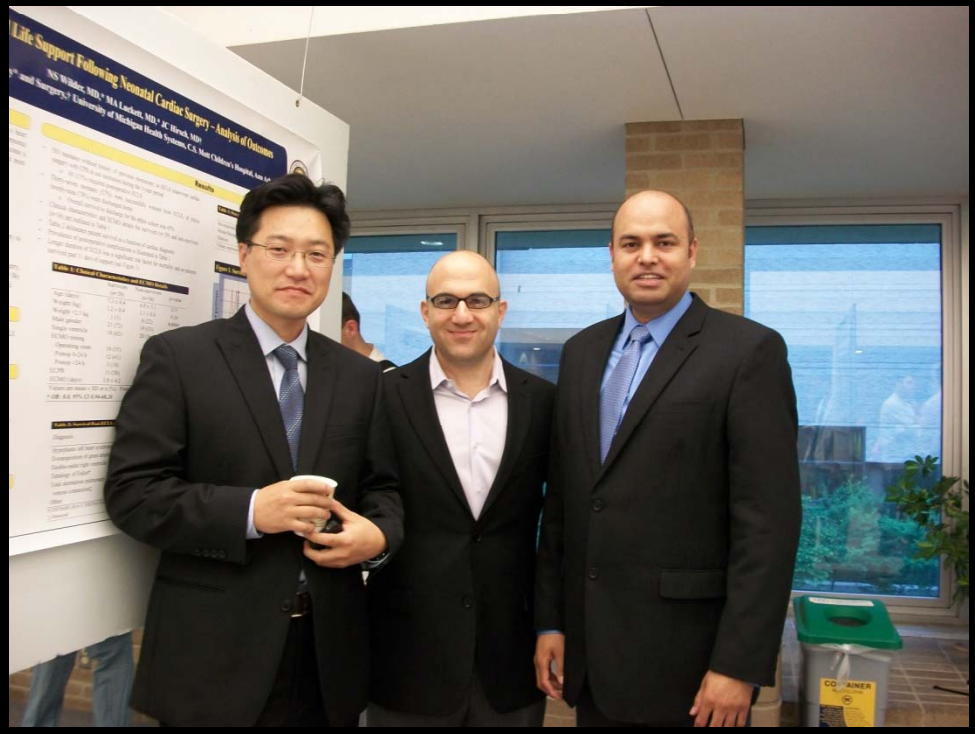
Summary

- TMS/EEG is a perturbational approach to assess levels of consciousness
- Cortical communication in response to perturbation is reduced across sleep, anesthesia, and pathological states

Future directions

- More robust measures of connectivity
- Real-time assessment in a routine clinical setting
- Better understanding of network stability

Acknowledgments—Laboratory



Dr. UnCheol Lee Dr. Dinesh Pal

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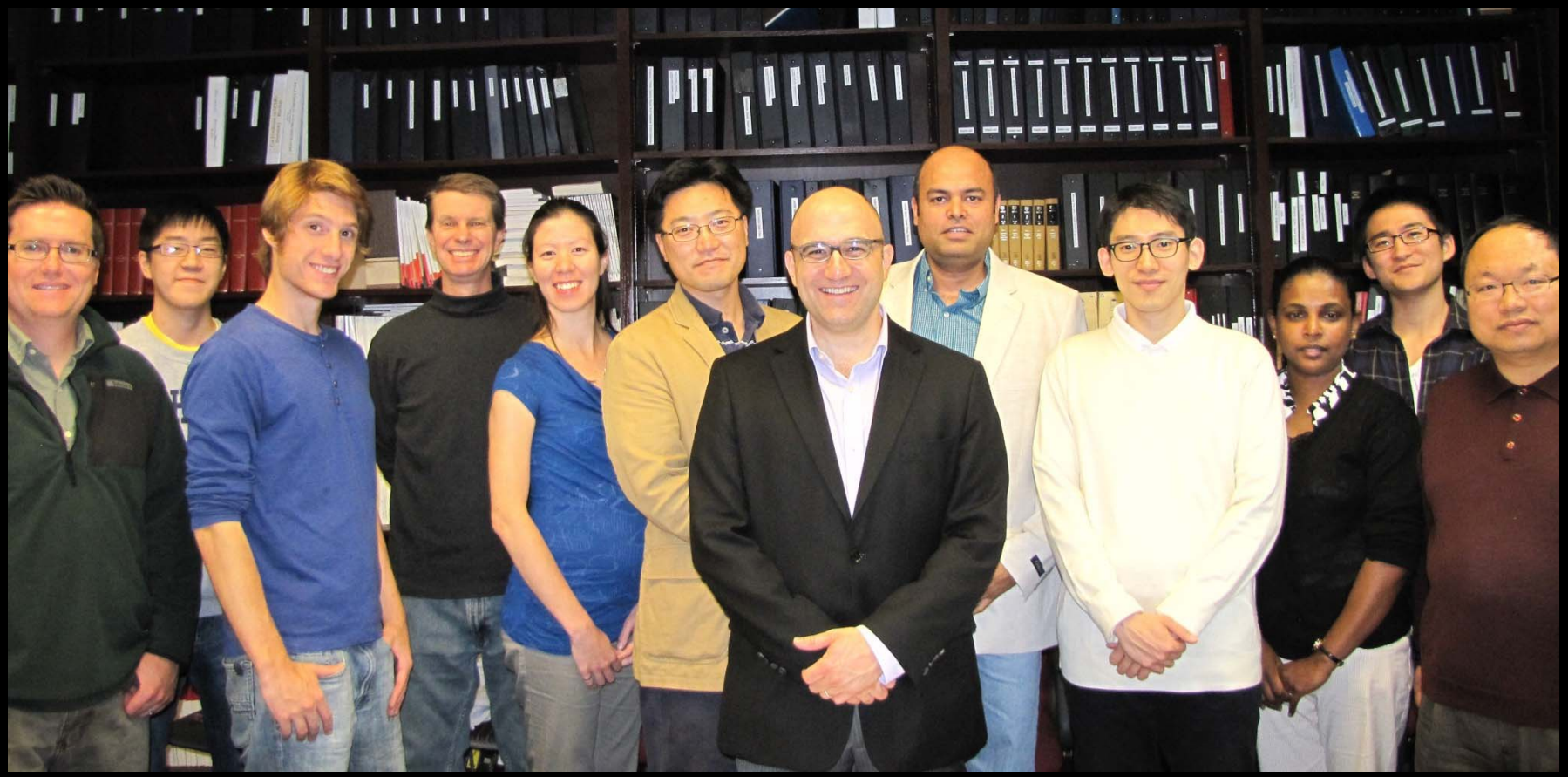

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Current

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- Canadian Institutes of Health Research
- Cerephex Corporation

Past

- National Institutes of Health (KL2)
- Foundation for Anesthesia Education & Research
- American Society of Anesthesiologists