Neural Correlates of Consciousness

ISS Summer School

- Neural Correlates of Consciousness
- Disorders of Conscious Perception

Finding the Neuronal Correlate of Consciousness (NCC)

1. Enabling Factors (Prerequisites)

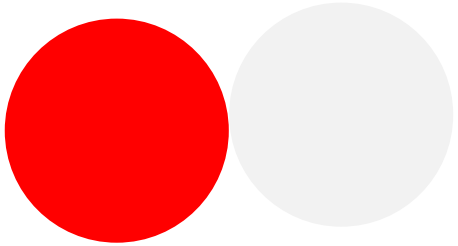
2. Actual Substrates (Content)

3. Consequences (Cognition/Motor Output)

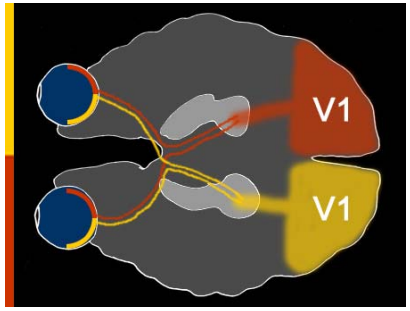
Basic Conditions for Awareness

- General Alterness

- Sensory Input



• Intact transmission of sensory Information to early visual areas



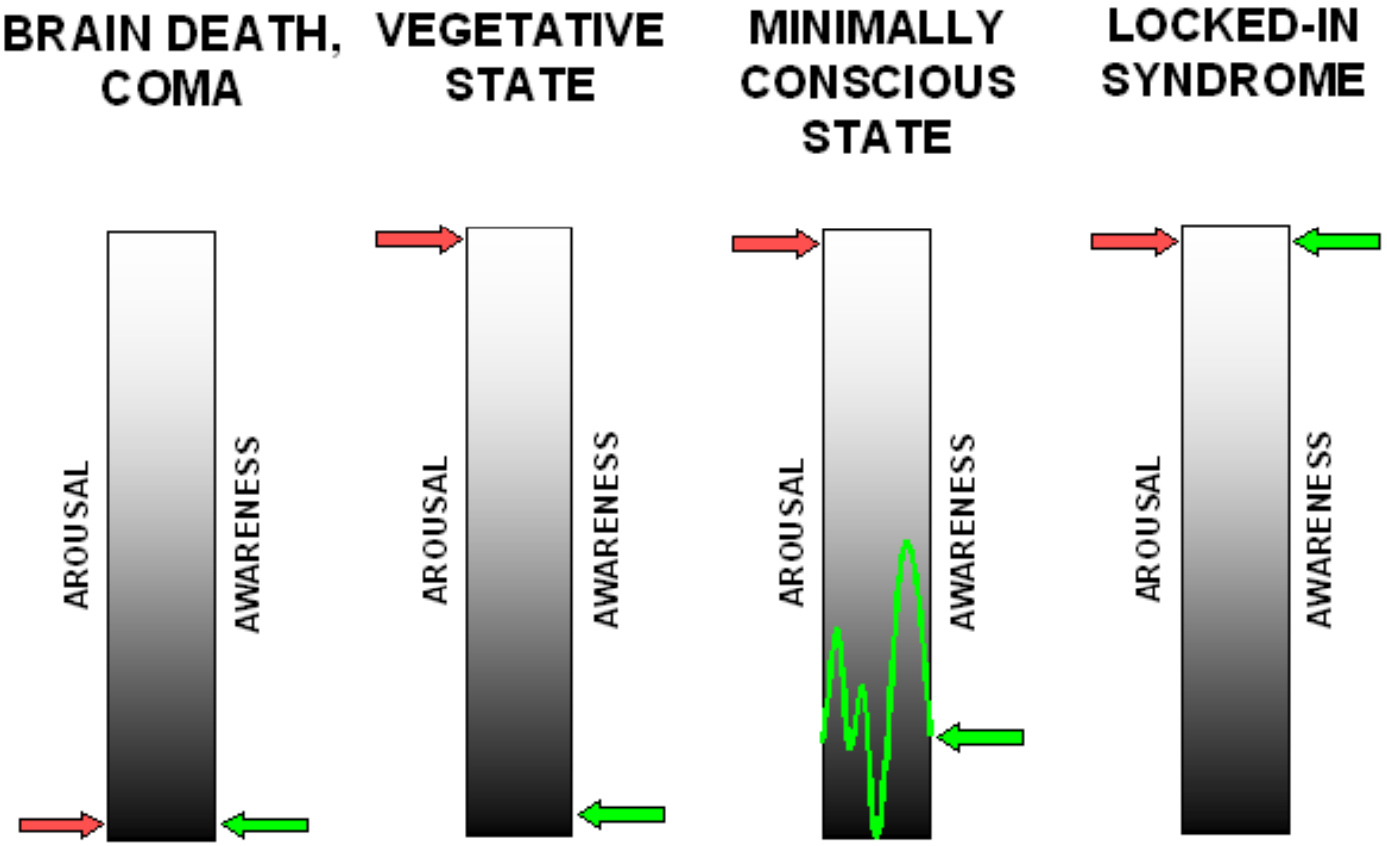
Scoring the level of consciousness: Glasgow coma scale

	1	2	3	4	5	6
Eye	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneously	N/A	N/A
Verbal	Makes no sounds	Incomprehensible sounds	Utters inappropriate words	Confused, disoriented	Oriented, converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli	Abnormal flexion to painful stimuli	Flexion / Withdrawal to painful stimuli	Localizes painful stimuli	Obeys

Generally, brain injury is classified as: Severe, with GCS < 8–9 Moderate, GCS 8-12; Minor, GCS ≥ 13.

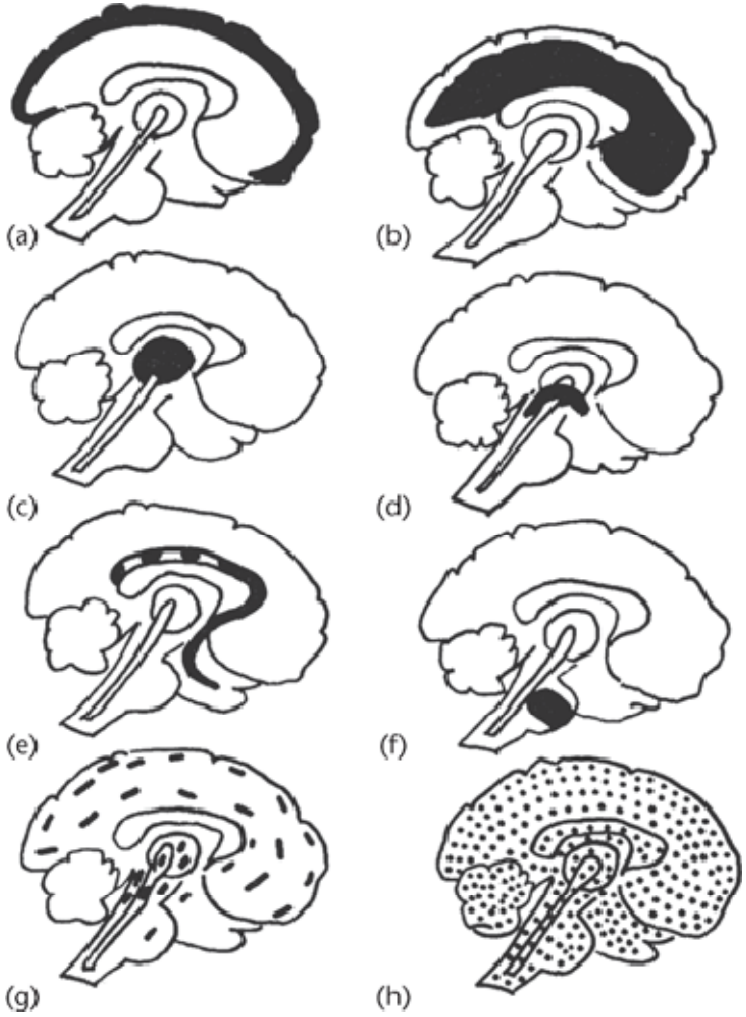
Dimensions of Consciousness:

→ Behavioral observation assesses two dimensions of consciousness: **Arousal and Awareness**



1. Enabling Factors: Arousal/Wakefulness

Lesions interfering with the level of consciousness

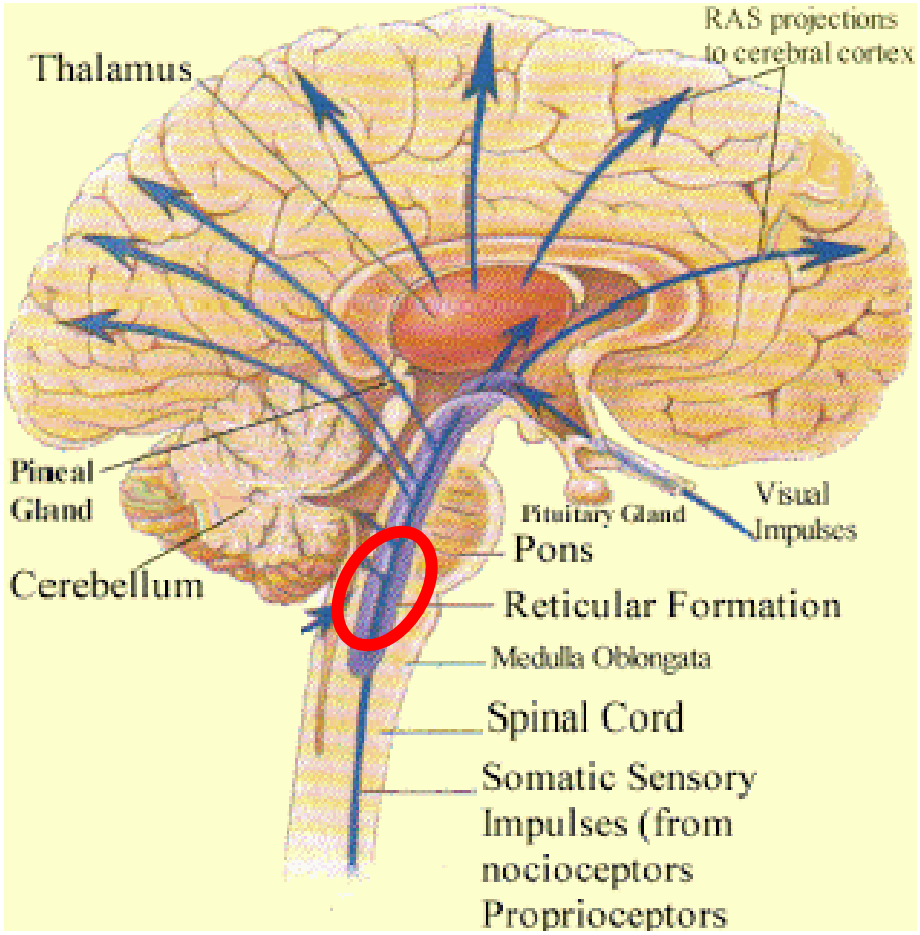


Artifical Ventilator

(a) Diffuse lesion of the cerebral cortex
(b) Diffuse damage to the white matter.
(c) and (d) Lesions of the upper brainstem involving the ascending reticular system.
(e) Lesions of the limbic system.
(f) Lesions of the pontine basis (locked-in-syndrome).
(g) Multiple cerebral lesions
(h) Diffuse anoxic panencephalopathy

1. Enabling Factors: Arousal/Wakefulness

Lesions interfering with the level of consciousness



-Structural brain lesions
-Toxins
-CNS Infections
-Trauma

Coma

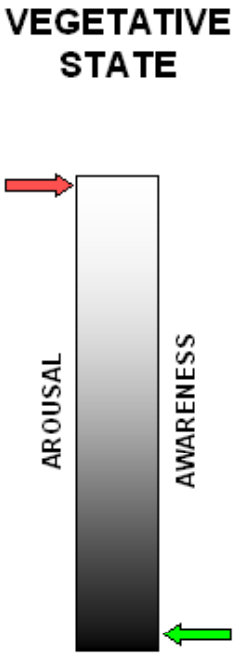
Attributes

- Unarousable, unresponsive
- Eyes closed
- No response to intense/painful stimuli

Recovery

- Full recovery, minimally conscious state, or vegetative states are possible

Vegetative State
(‚unresponsive wakefulness syndrome‘)



Attributes

- Wakefulness without awareness of self and surroundings (‚unresponsive wakefulness‘)
- Sleep-wake cycles
- Only reflexive motor activity

Recovery

- Full recovery rare
- Results in permanent (> 1 year) or minimal conscious state

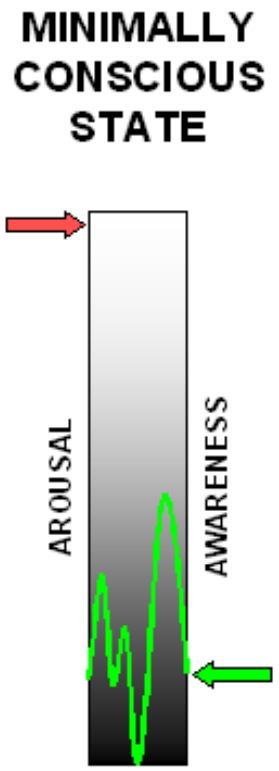
Minimal Conscious State (MSC)

Attributes

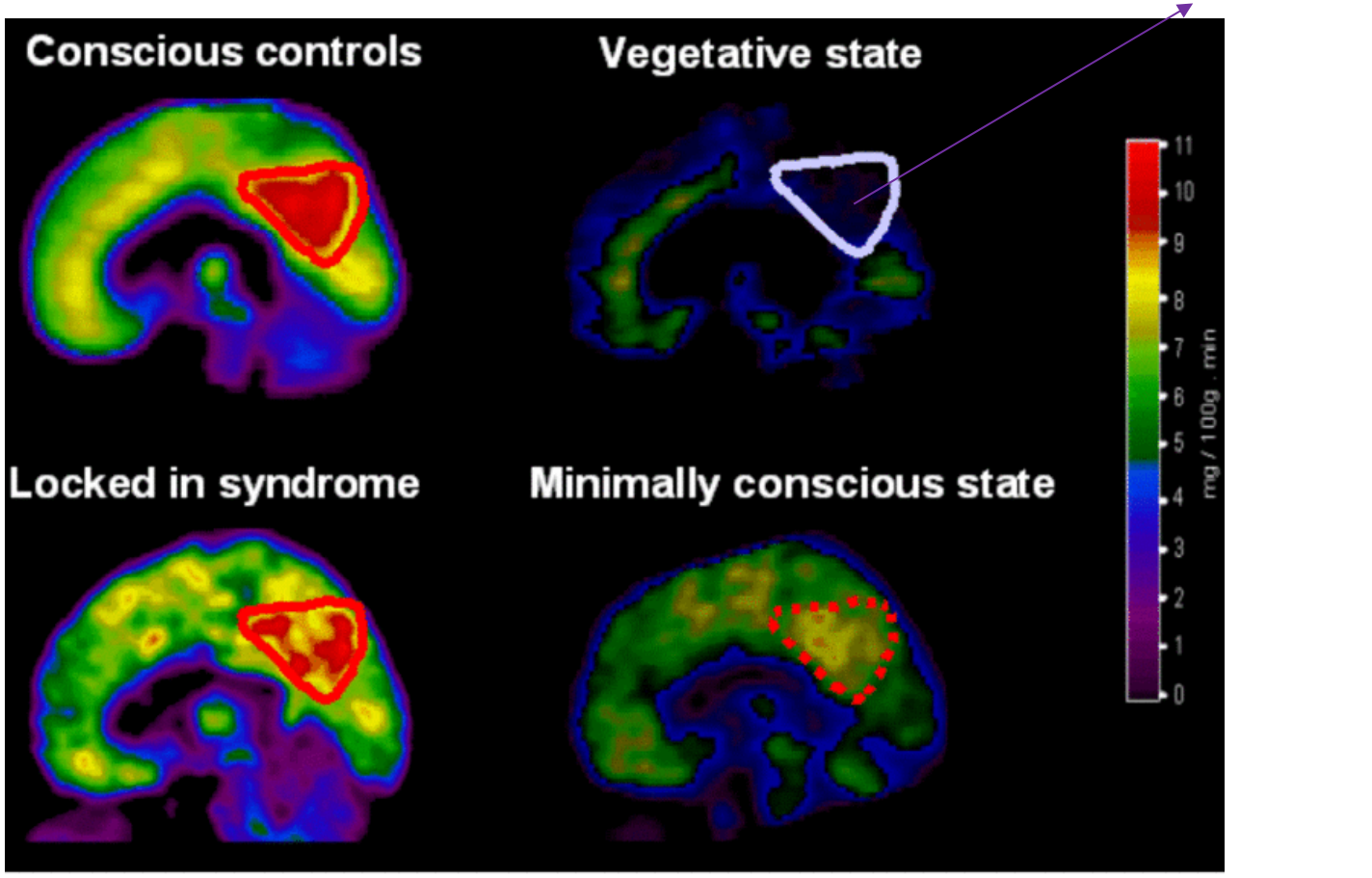
- Following simple commands
- Gestural or verbal yes/no responses (regardless of accuracy)
- Purposeful behavior (e.g. reaching for objects, pursuit eye movements/***appropriate*** smiling)

Recovery

- Continuous improvement and significantly more favorable outcomes post injury when compared with vegetative state



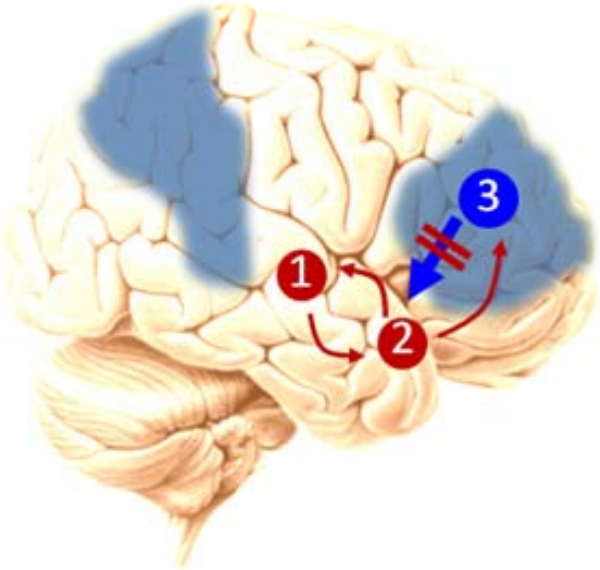
Cortical Metabolism in Disorders of Consciousness

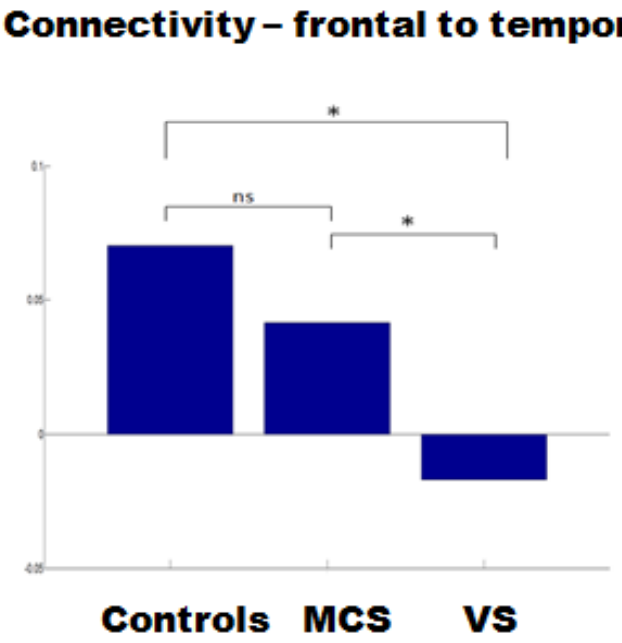


Precuneus and adjacent posterior cingulate cortex (red triangle) is most active in conscious waking, most impaired in vegetative, preserved in locked-in and minimally active in minimally conscious states

Functional Connectivity in Disorders of Consciousness

Vegetative state

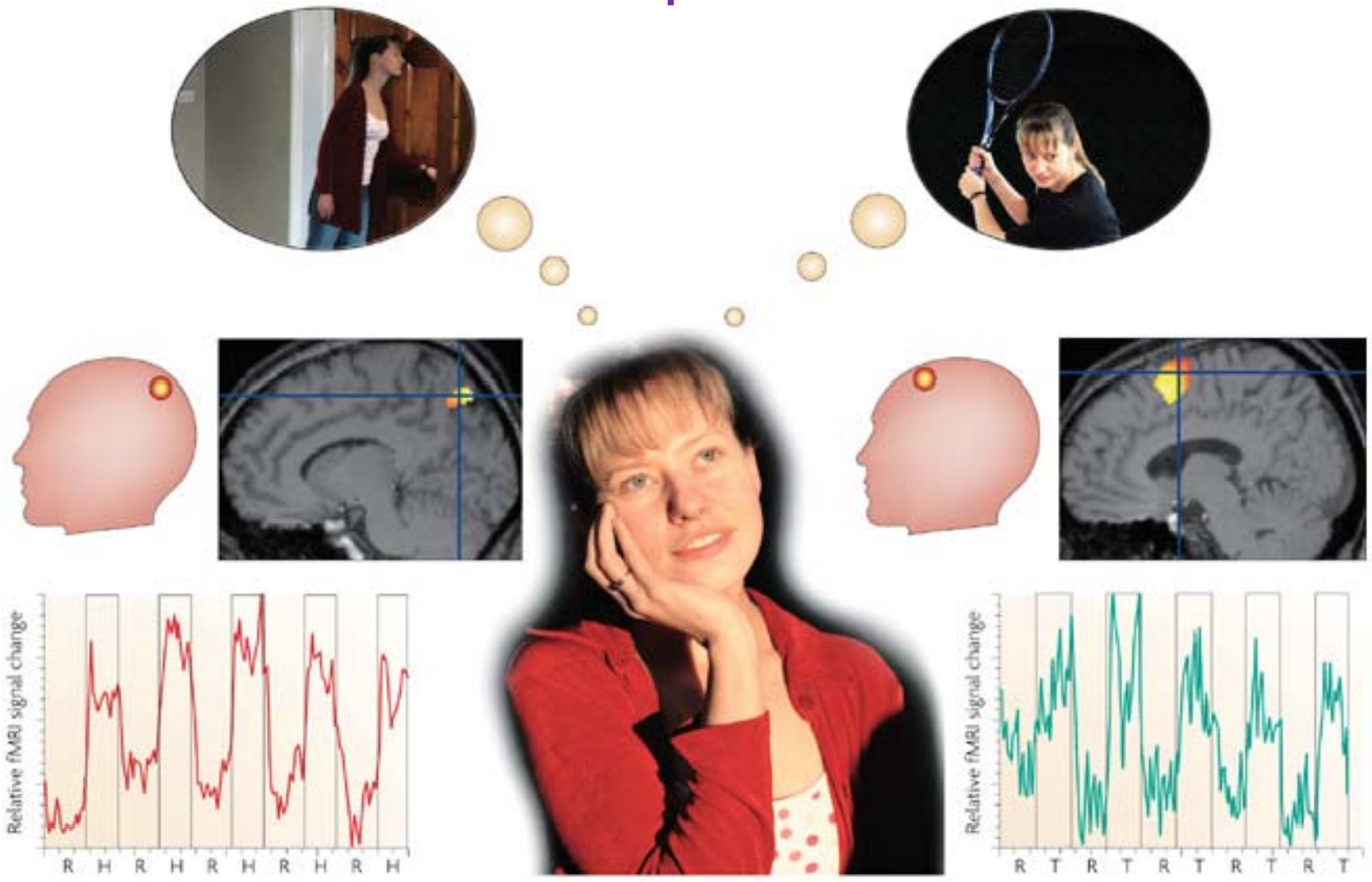




Boly, Garrido et al. 2011

→ **Loss of feedback connectivity in fronto-parieal cortices in the vegetative state**

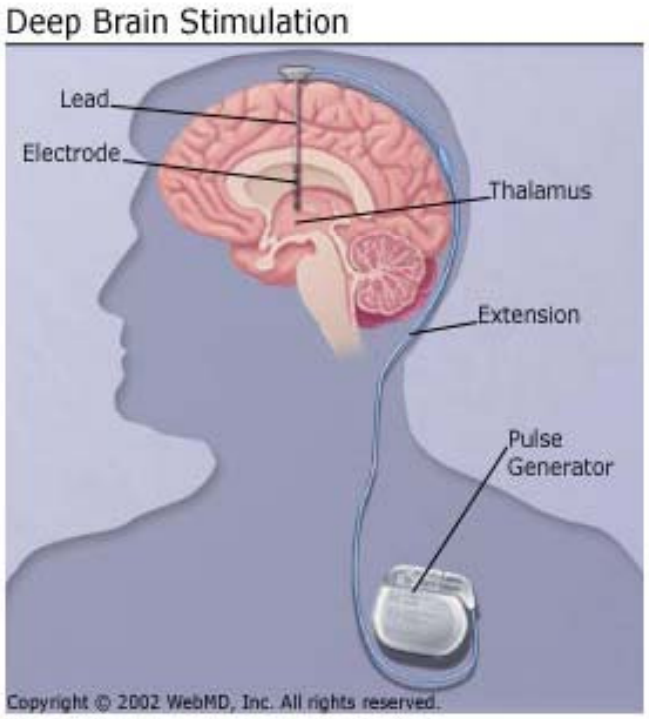
How to figure out whether a patient is conscious if there is no motor output?

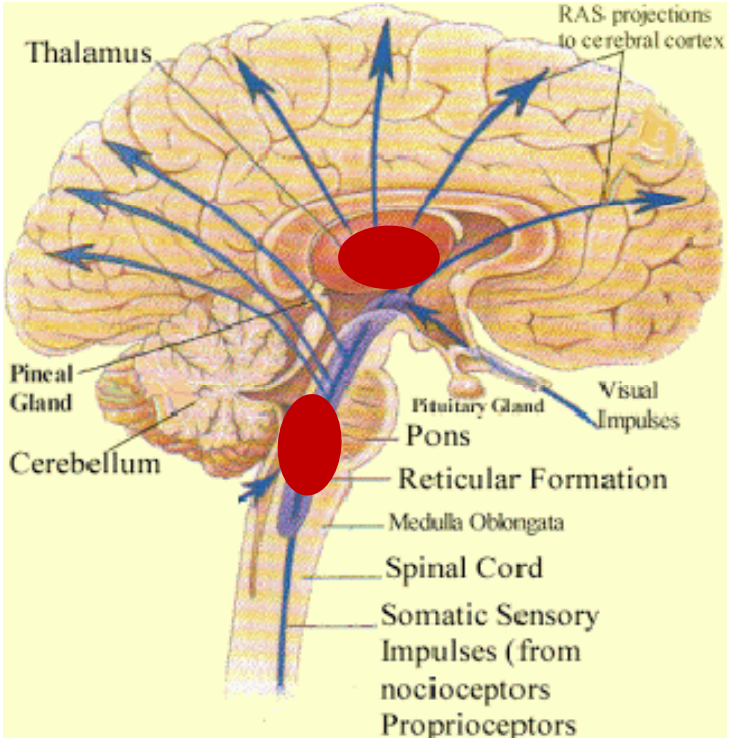


Owen et al., 2008

Owen & Coleman, 2006, Science

„Jump starting“ consciousness with deep brain stimulation





By electrically stimulating a brain region called the central thalamus, Schiff et al. were able to help a MCS-patient name objects on request and make precise hand gestures

Consciousness Restored to Man After Six Years with Deep Brain Stimulation!, Schiff et al., Nature, 2007
See Yamamoto et al., 2005 for earlier reports!!

Enabling Factors for Consciousness

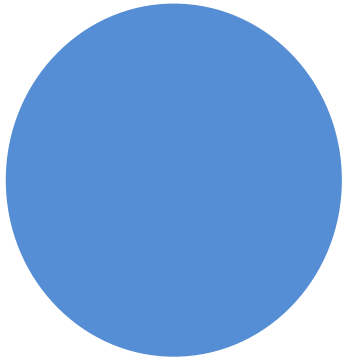
- **Heart must beat** to supply the brain with oxygenated blood
- Nuclei in the **reticular formation and brain stem must be active**
- **Cholinergic release in the cortico-thalamic complex**
- **Fronto-parietal communication** – Volition?

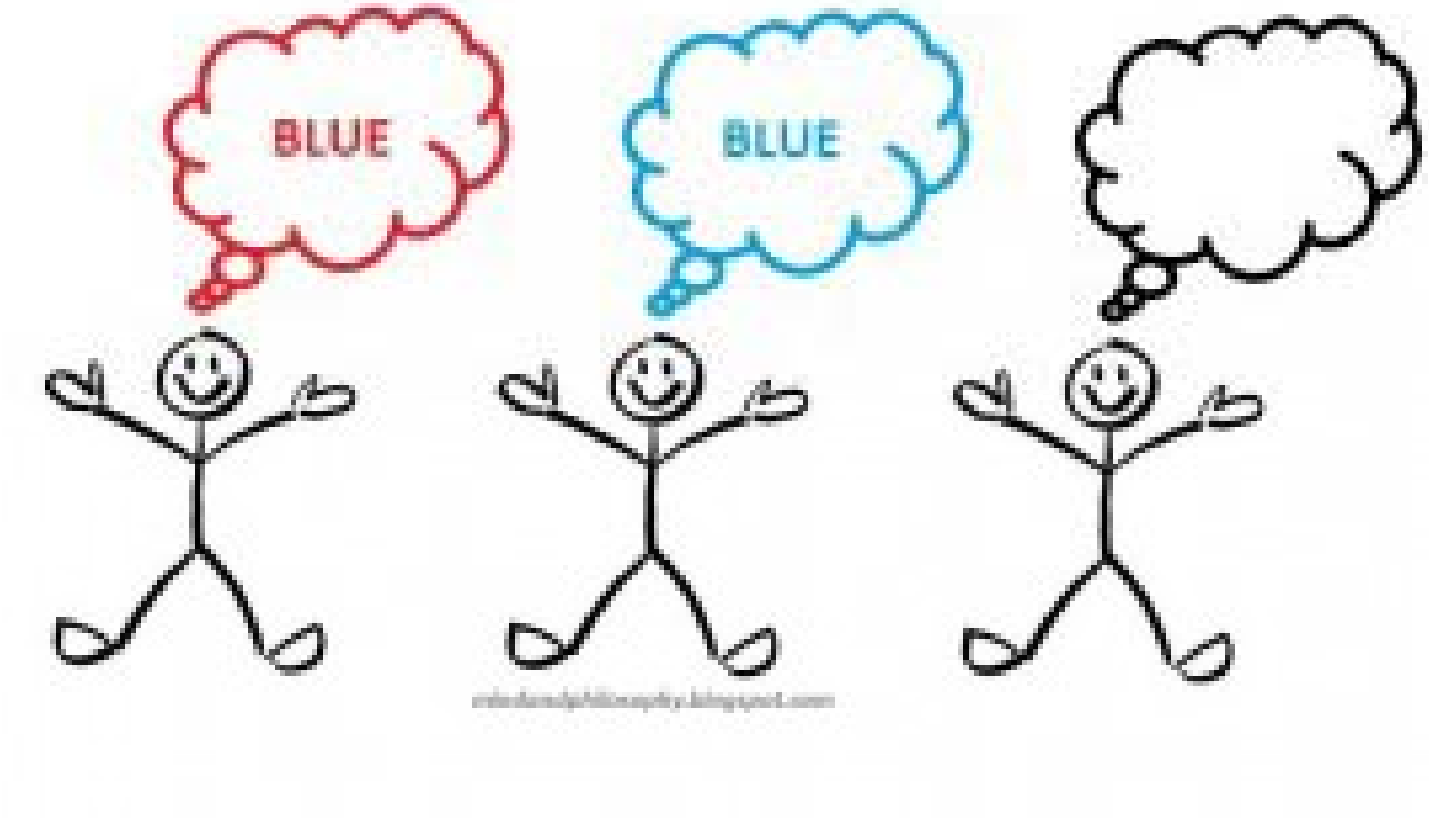
Consciousness

1.2. Conscious contents (‘Qualia’/NCC)

Conscious Contents: Qualia (“awareness”)

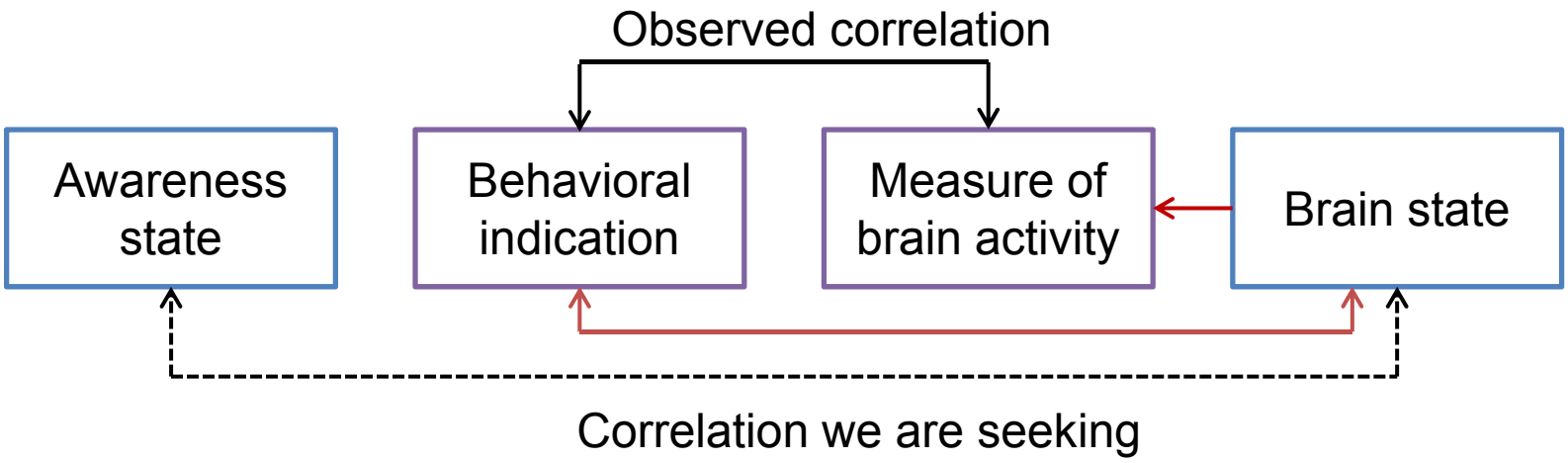
→ Phenomenal experience at one moment (including vision, audition, olfaction etc.)





C. Hallquist, 2013

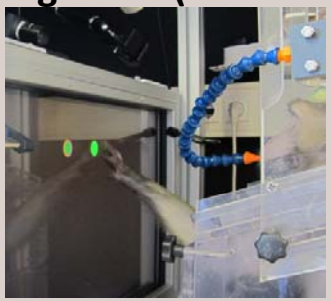
Inherent difficulty in studying neural correlates of awareness



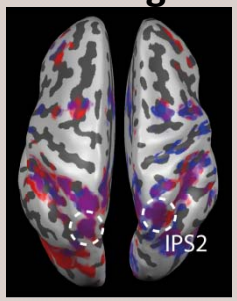
Research approaches

Scales

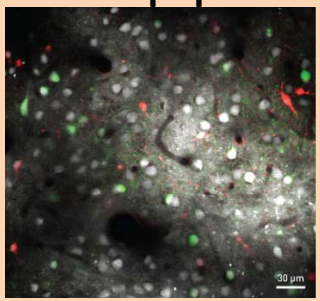
Organism (behavior)



Brain regions

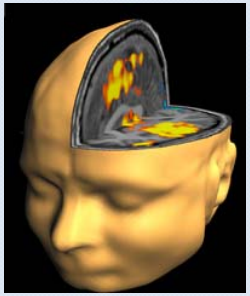


Neuronal populations

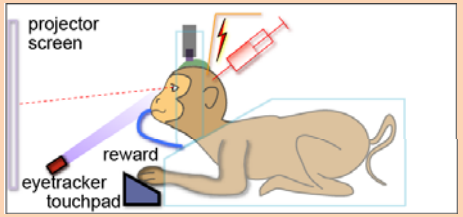


Single cells

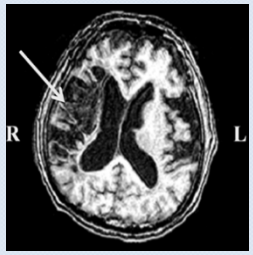
Humans



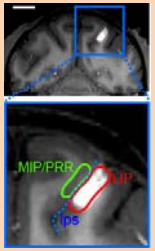
fMRI ⟷ fMRI

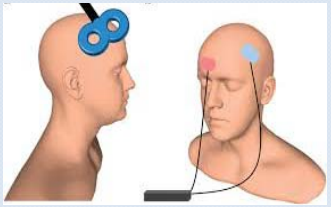


Monkeys



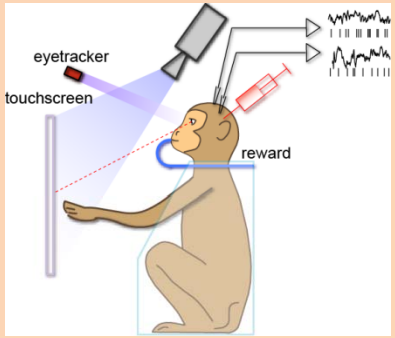
Lesion studies ⟷ Reversible lesions





Noninvasive EM stimulation

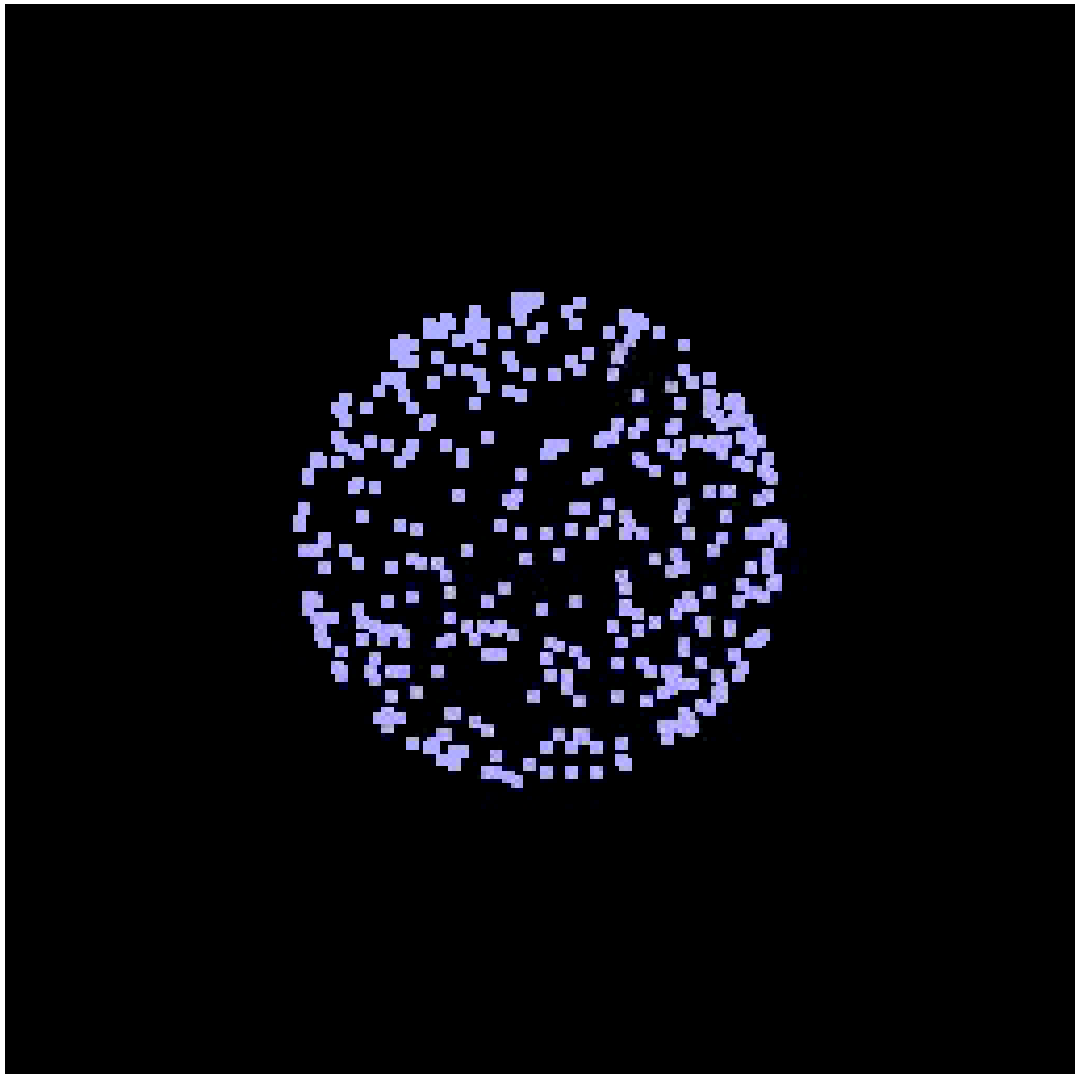
Electrophysiology/ Microstimulation



Study question

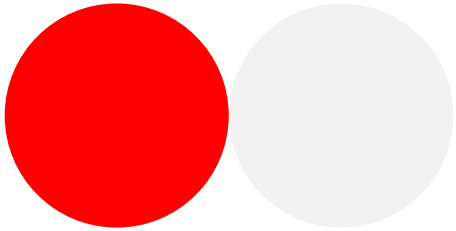
1. What is the correct spatial/temporal scale to look for the Neural Correlates of Consciousness?

Ambiguous Paradigms for studying visual perception

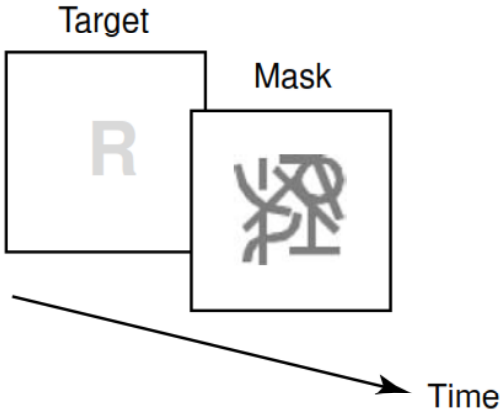


Paradigms for manipulating conscious visibility

Low/Noisy sensory input

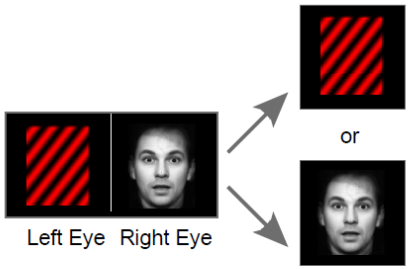


Visual Masking

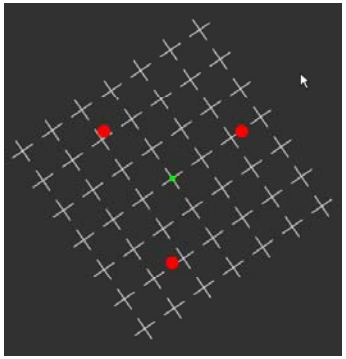


Perceptual Suppression

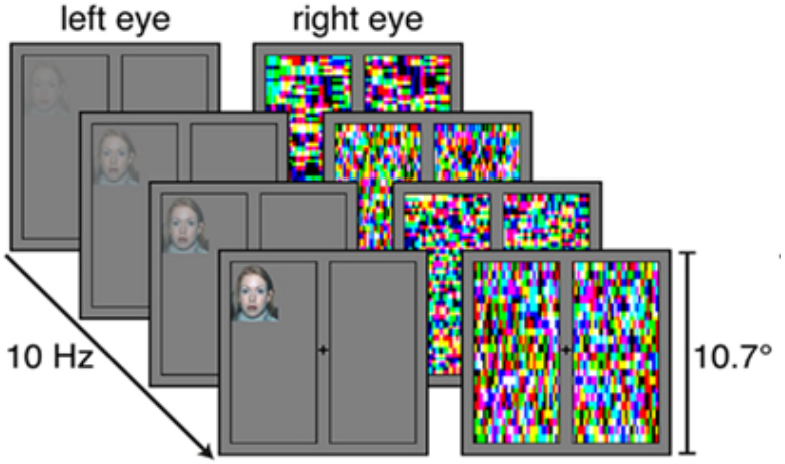
Binocular Rivalry



Motion induced Blindness



Continuous Flash Suppression



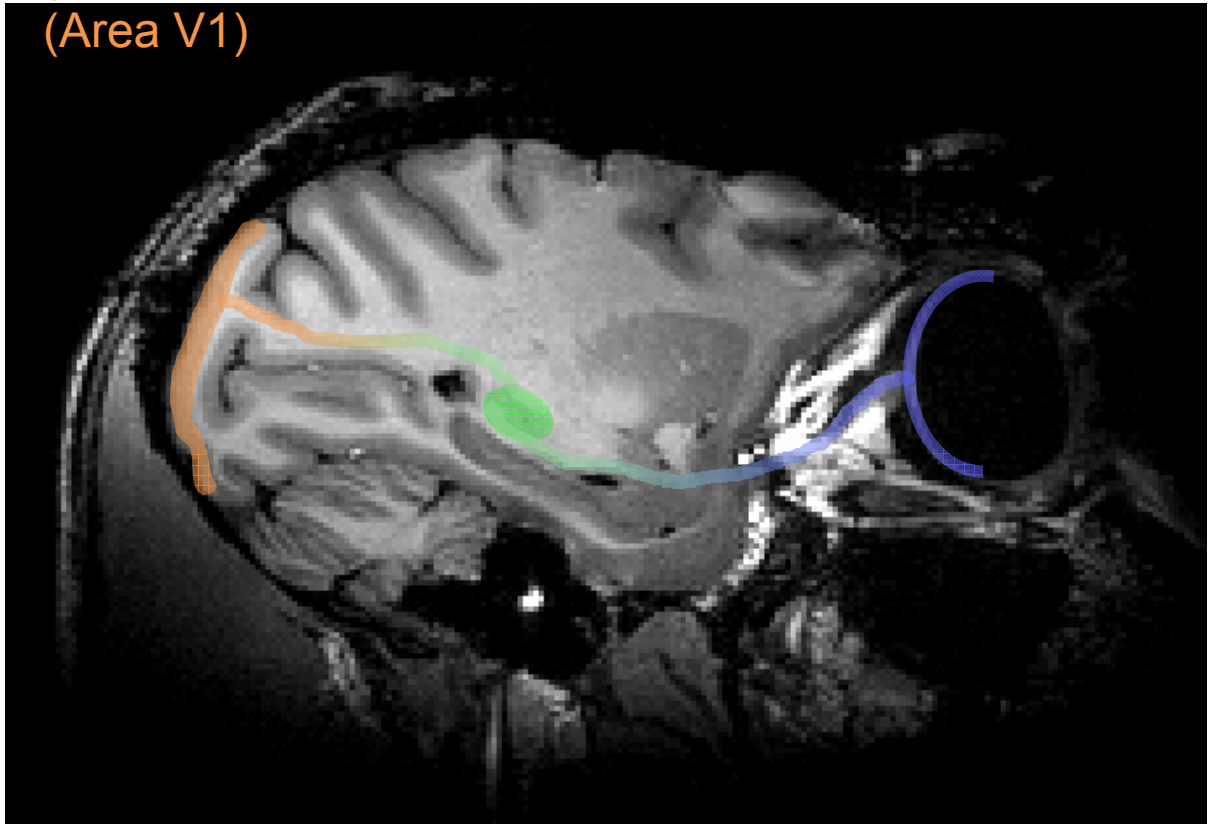
Bonneh et al., 2001; Tsuchiya et al., 2005


How does our vision work?

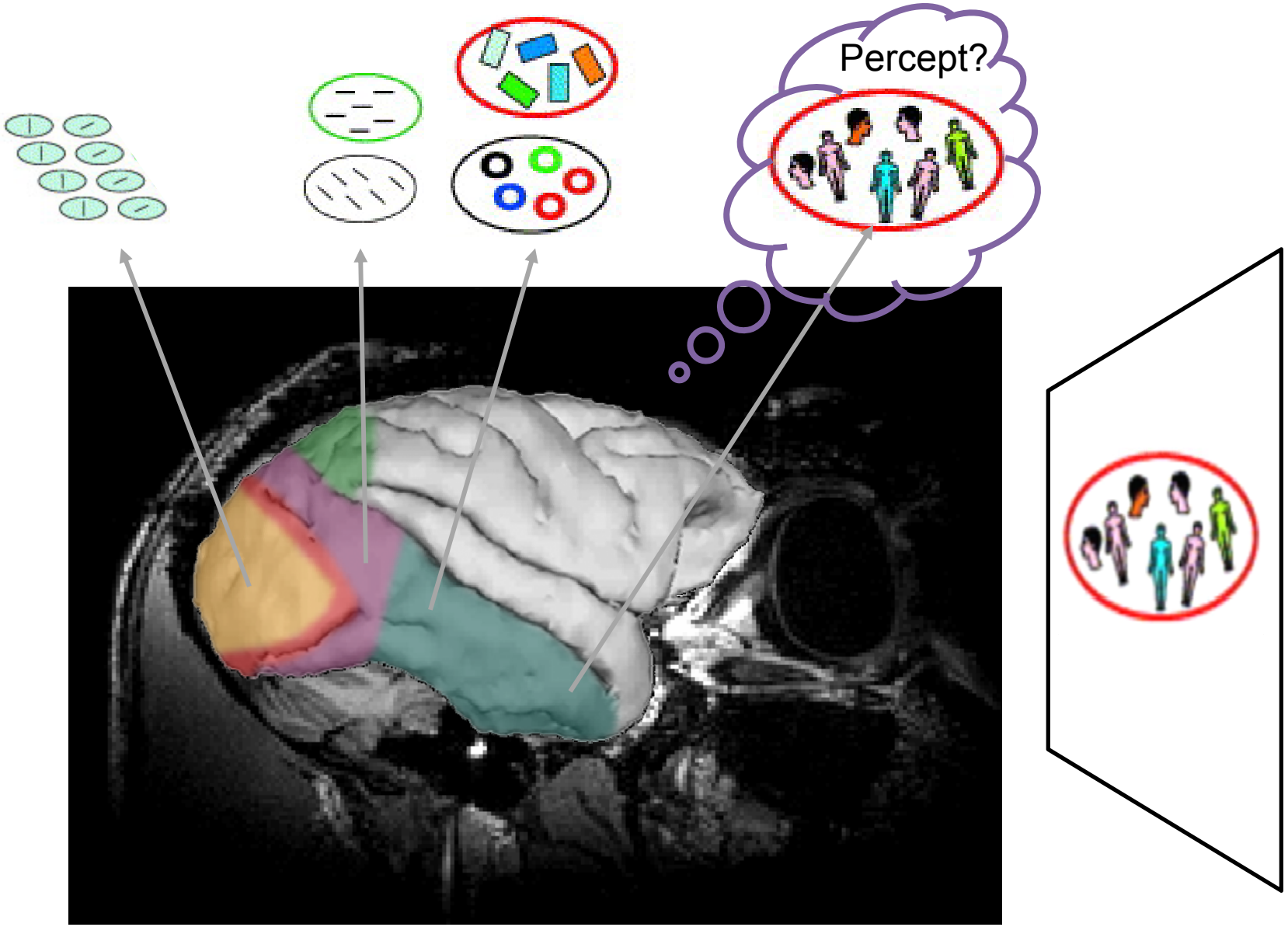
Primary Visual Cortex (Area V1)

LGN

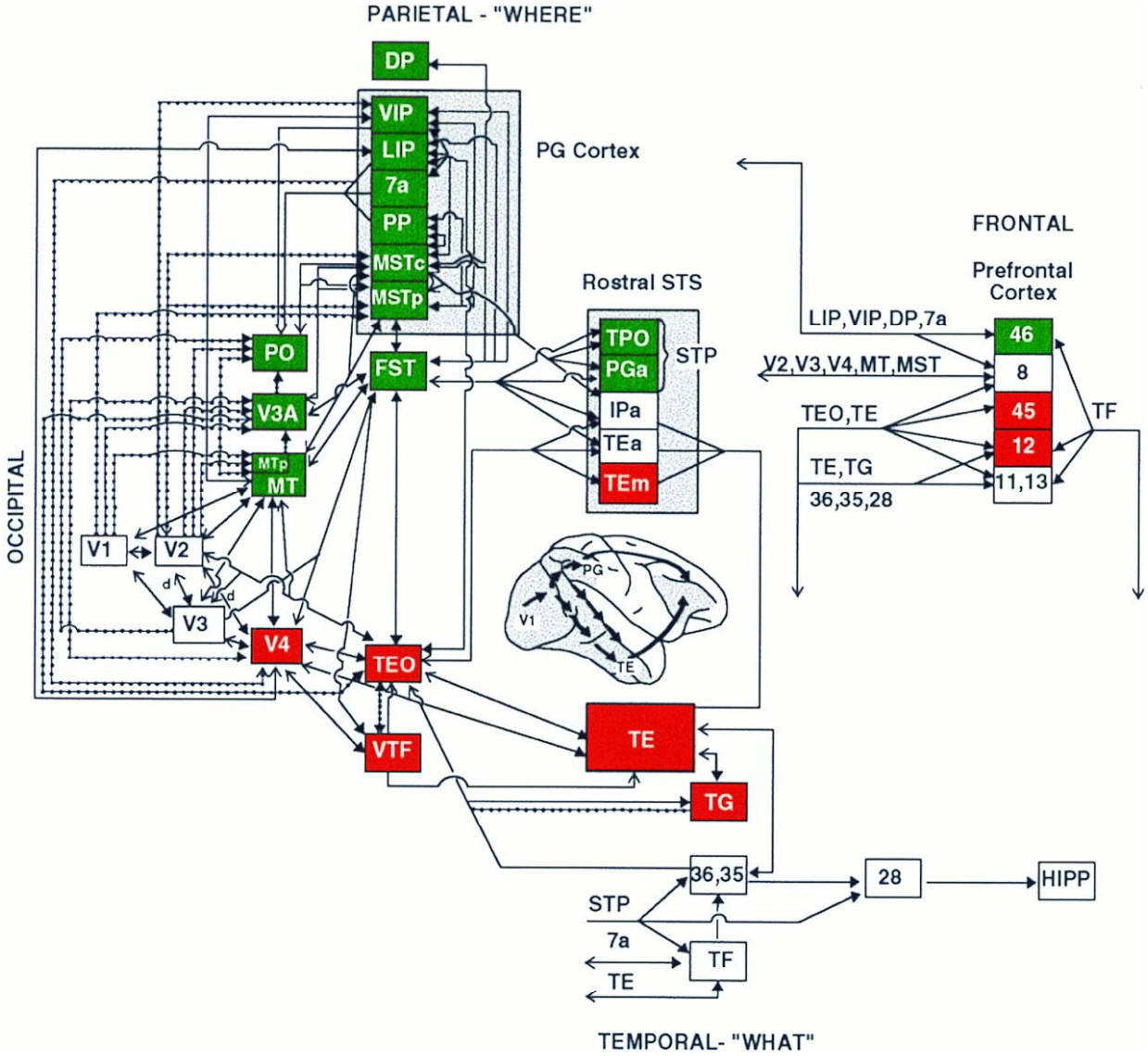
Retina



Hierachical Model of visual perception



Visual Pathway Scheme



Lewis & Van Essen, 2002; Leslie G. Ungerleider et al. PNAS 1998;95:883-890

Neural Correlate of Consciousness:

What are we looking for?

Definition:

Minimal neural mechanisms that are **sufficient** for any one conscious percept under constant background conditions (*Koch, 2004)*

When have we found it?

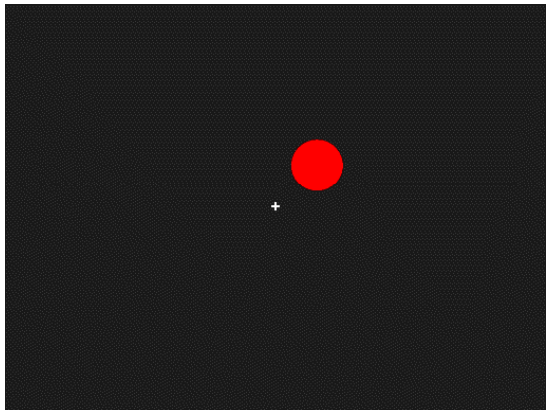
• Stimulating the relevant neuronal populations via non-invasive (TMS, tDCS) or invasive (microstimulation/pharmacological inactivation/optogenetics) etc. will give rise to a specific percept or disable it (Tononi & Koch, 2015)

Study questions:

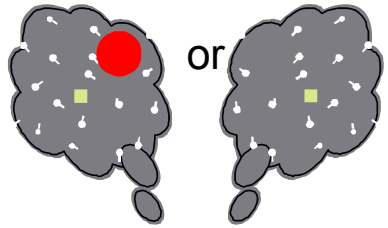
2. What does jointly ‚sufficient' mean in a reciprocally connected neural network?

3. What is the type of experimental evidence that would convince you of the NCC?

Perceptual Suppression Approaches (here: GFS)



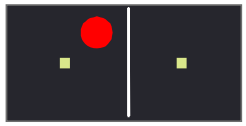
'Visible' 'Invisible'



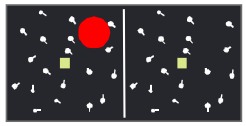
or

Fixation

Target On



Surround On



Lever release?

Reward

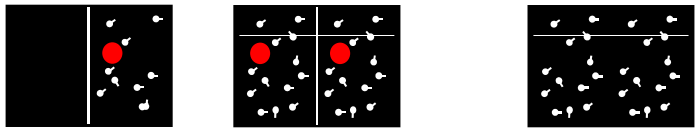
Ambiguous Period

0 300 1700 1700-3700

Time (ms)

Training (Catch) conditions

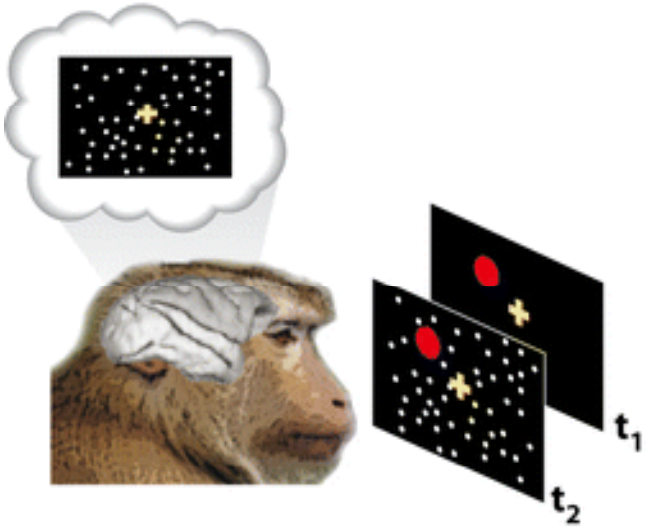
'No Suppression' **'Physical Removal'**

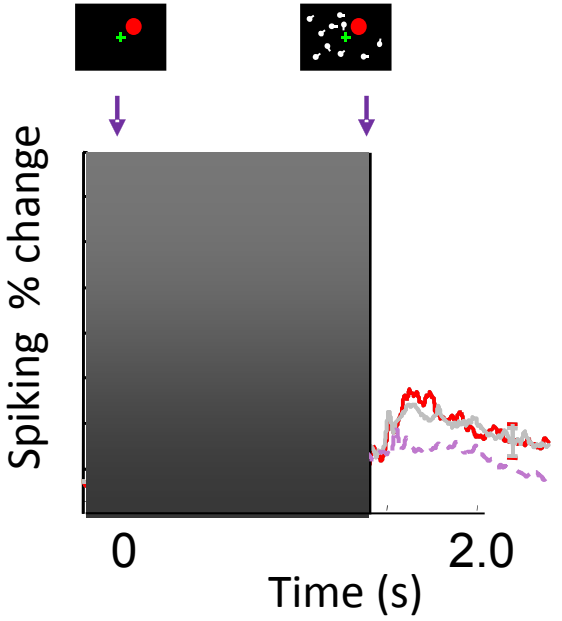


L_{eye} R_{eye} L_{eye} R_{eye} L_{eye} R_{eye}

Wilke, Logothetis & Leopold, Neuron 2003
Wilke, Logothetis & Leopold, PNAS, 2006

Firing rates in higher-order visual cortex reflect perceptual visibility



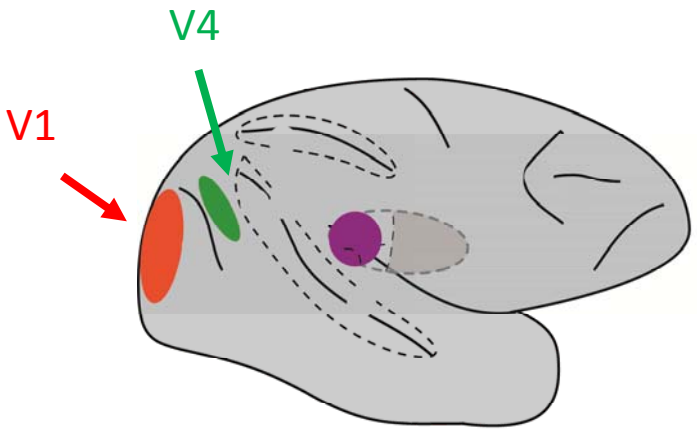


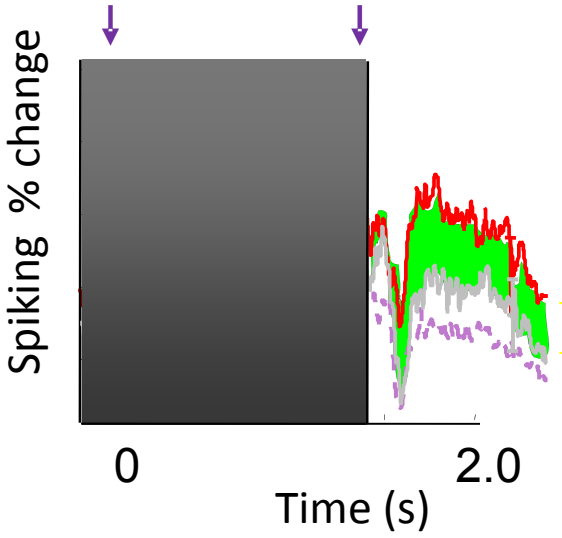
Area V1

Visible

Invisible

Physical removal



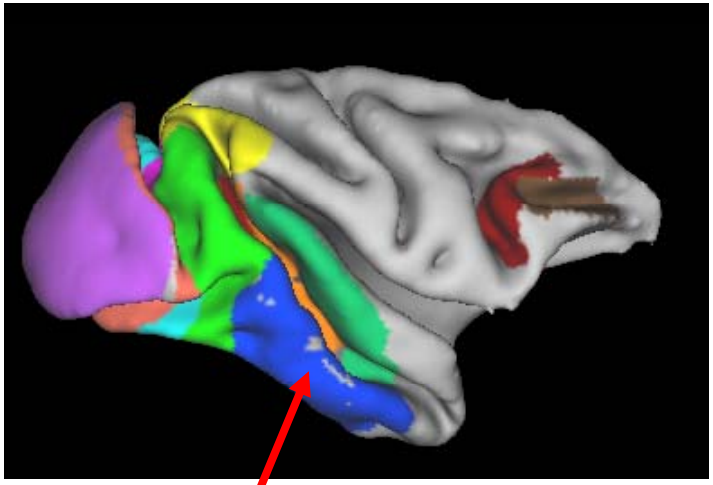


Area V4

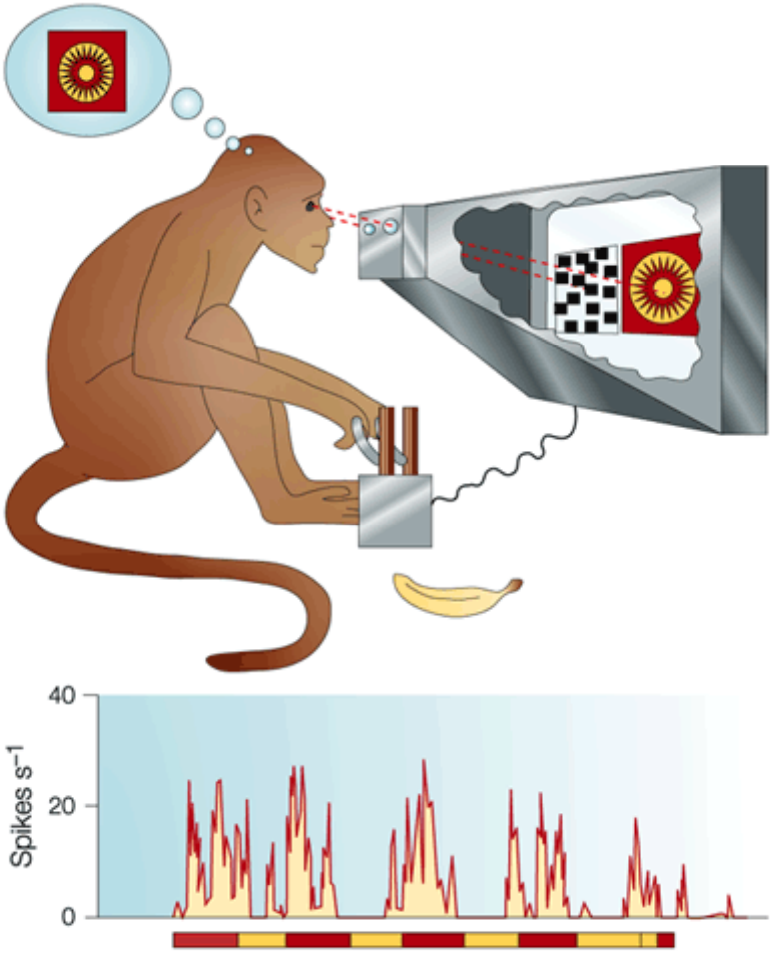
Visibility Modulation

Wilke et al., (2006) PNAS

Perceptual Modulation in higher-order visual cortex

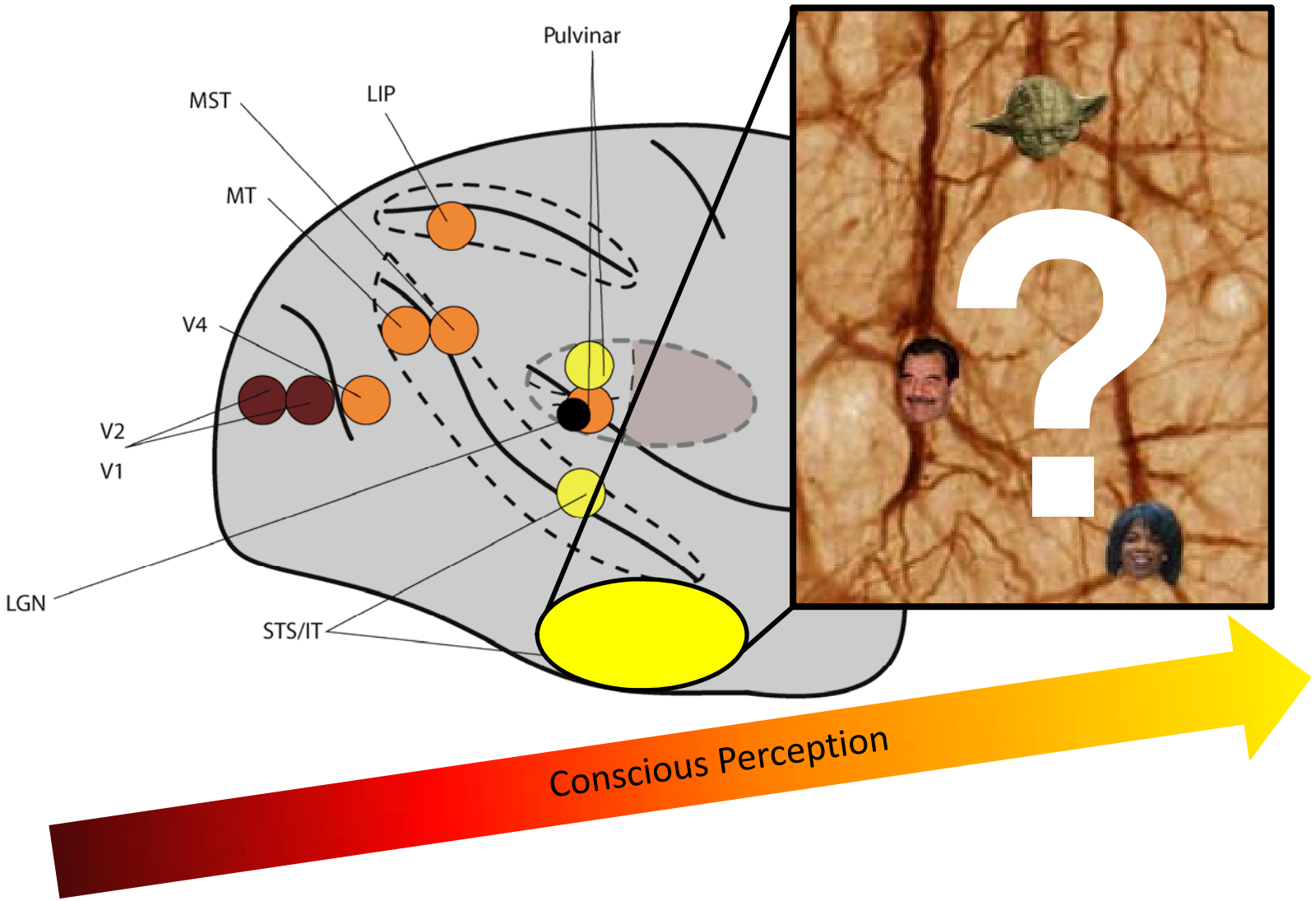


Inferotemporal Cortex

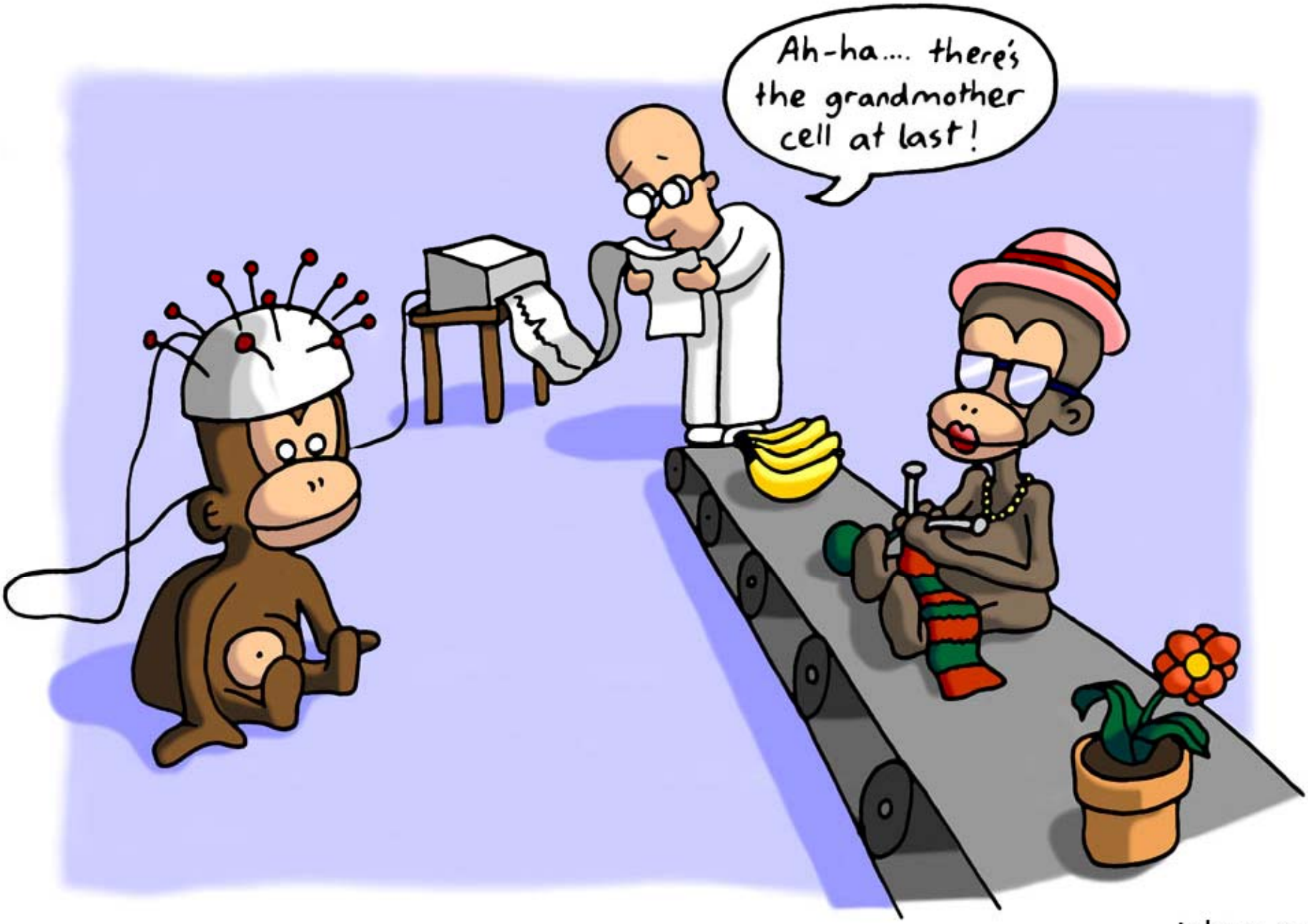


Sheinberg & Logothetis, 1997 (monkeys); Kreiman & Koch, 2005 (humans)

Single neurons: spike rates
Perceptual Modulation increases through visual hierachy



V1-V4 (Leopold et al., 1996; Gail et al. 2004; Wilke, Logothetis et al. 2006, **LGN/Pulvinar** (Lehky & Maunsell 1996; Wilke et al. 2009), **STS/IT** (Sheinberg and Logothetis 1997, **MT/MST** (Logothetis and Schall 1989; Williams, et al. 2003; Maier, Logothetis et al. 2007), **LIP** (Williams et al. 2003), **FEF**(Libedinsky and Livingstone 2011), ***LFPFC*** (Panagiotaropoulos et al. 2012).


Ah-ha.... there's the grandmother cell at last!
jolyon.co.uk

Hierachical model of conscious perception - does it make sense?

Notion: At the highest level, cardinal neurons integrate all the information and represent the percept

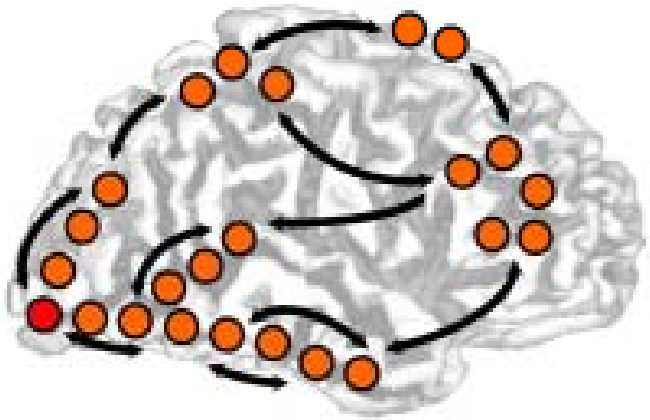
1. Information theoretical problem

- Actual number of possible percepts surmounts the number of neurons

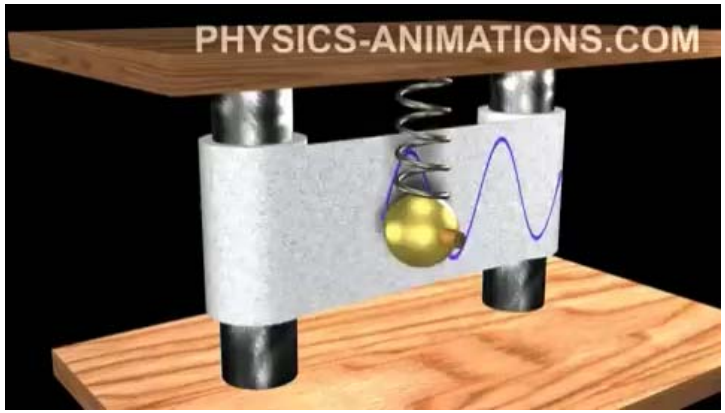
2. Contradiction by empirical findings

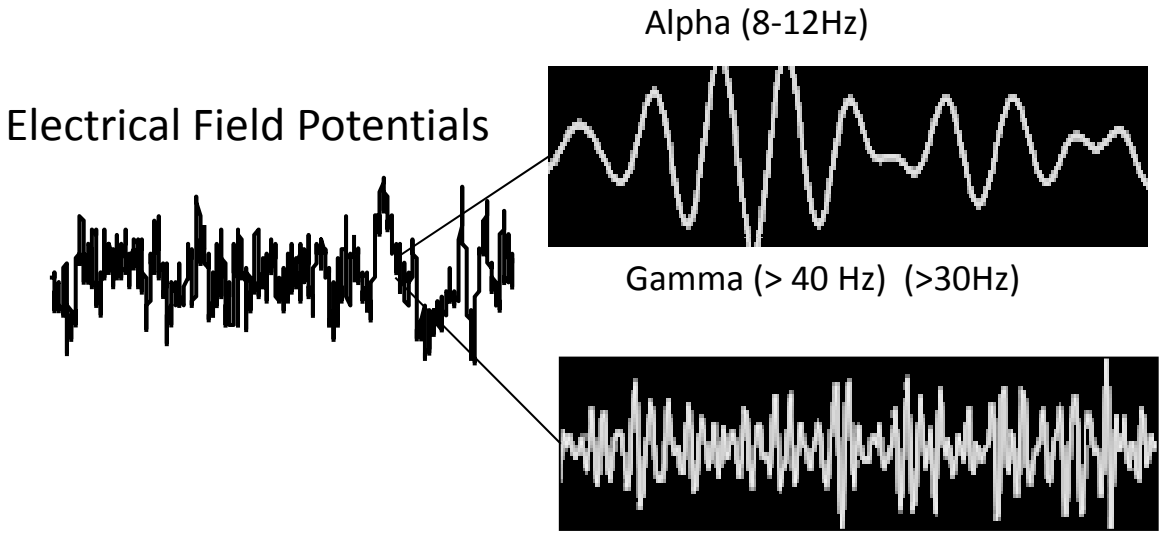
- Lesions in the temporal lobe lead to problems with object recognition **but** conscious experience is preserved

Perception and oscillatory synchrony



Dehaene & Changeux (2011), Neuron





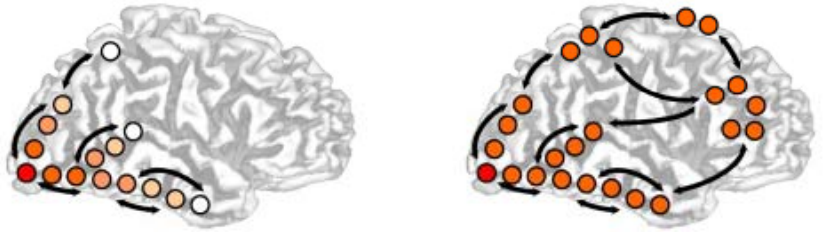
Presumed Correlates of Conscious Contents

Response Amplitudes

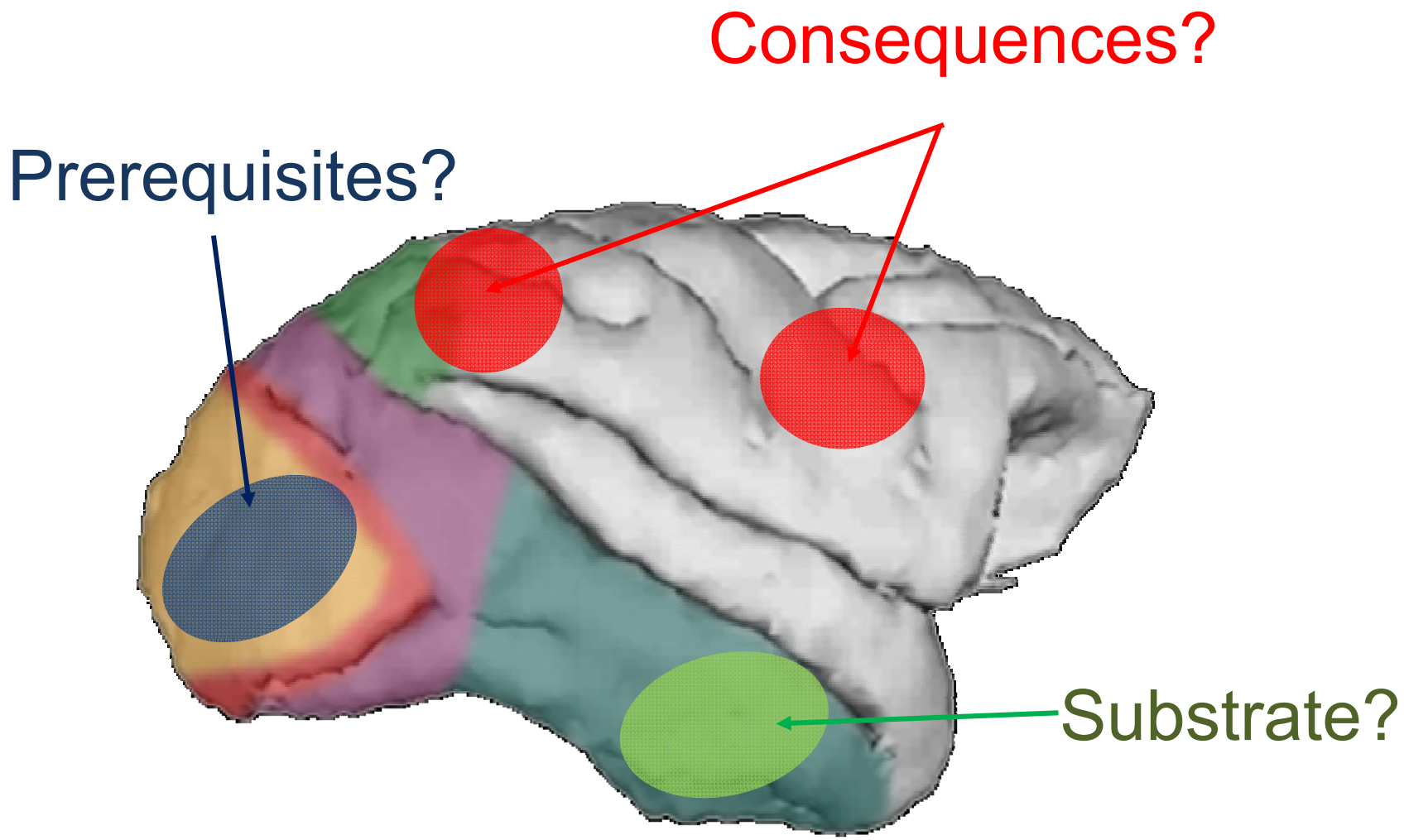
- Firing Rates of Neurons
- Neural Oscillations
(in specific structures/frequencies)

Communication

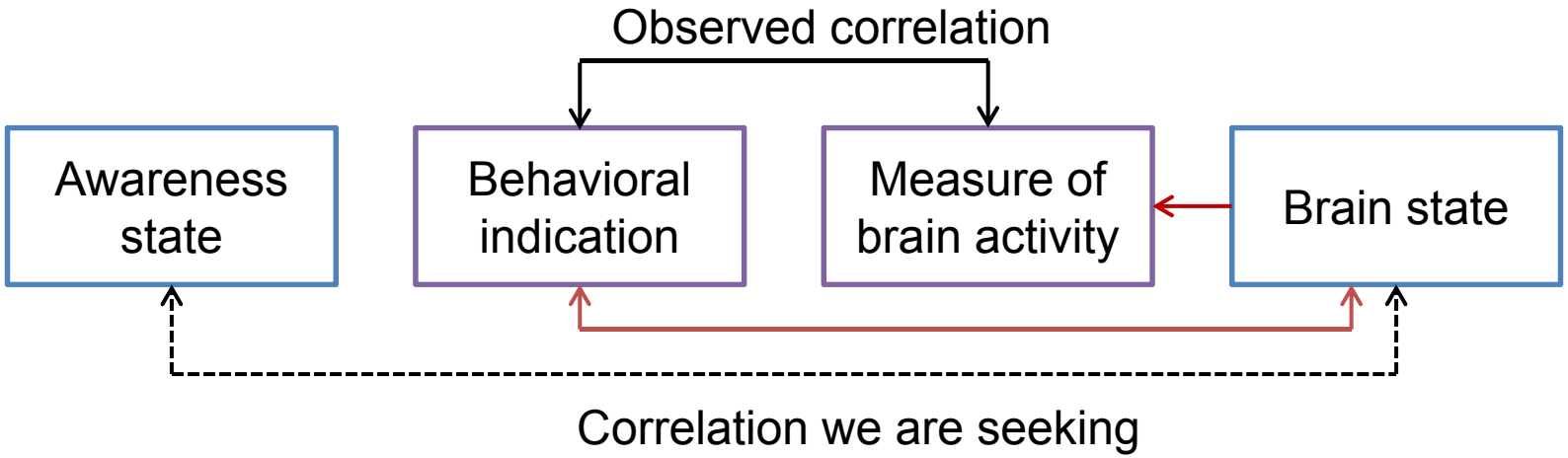
- Networks
(Coherency/Synchronicity)



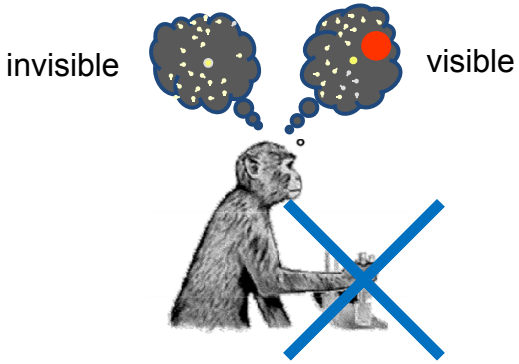
Overall scientific question:
Neural basis of visual awareness



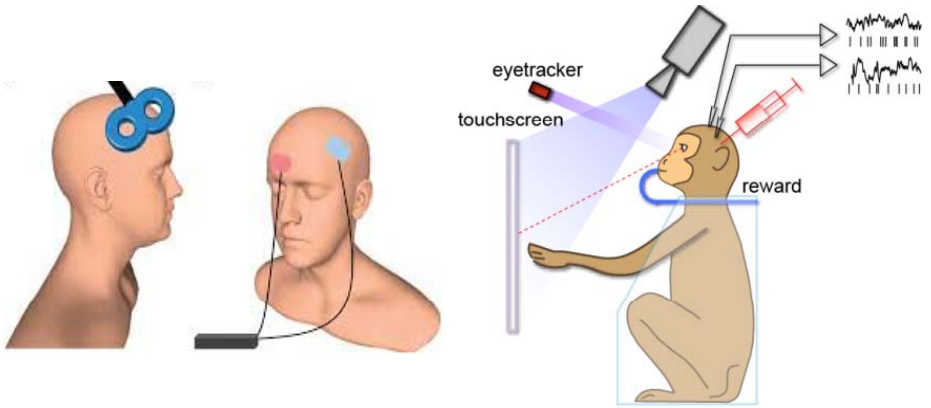
1.3. Disorders of Conscious Perception



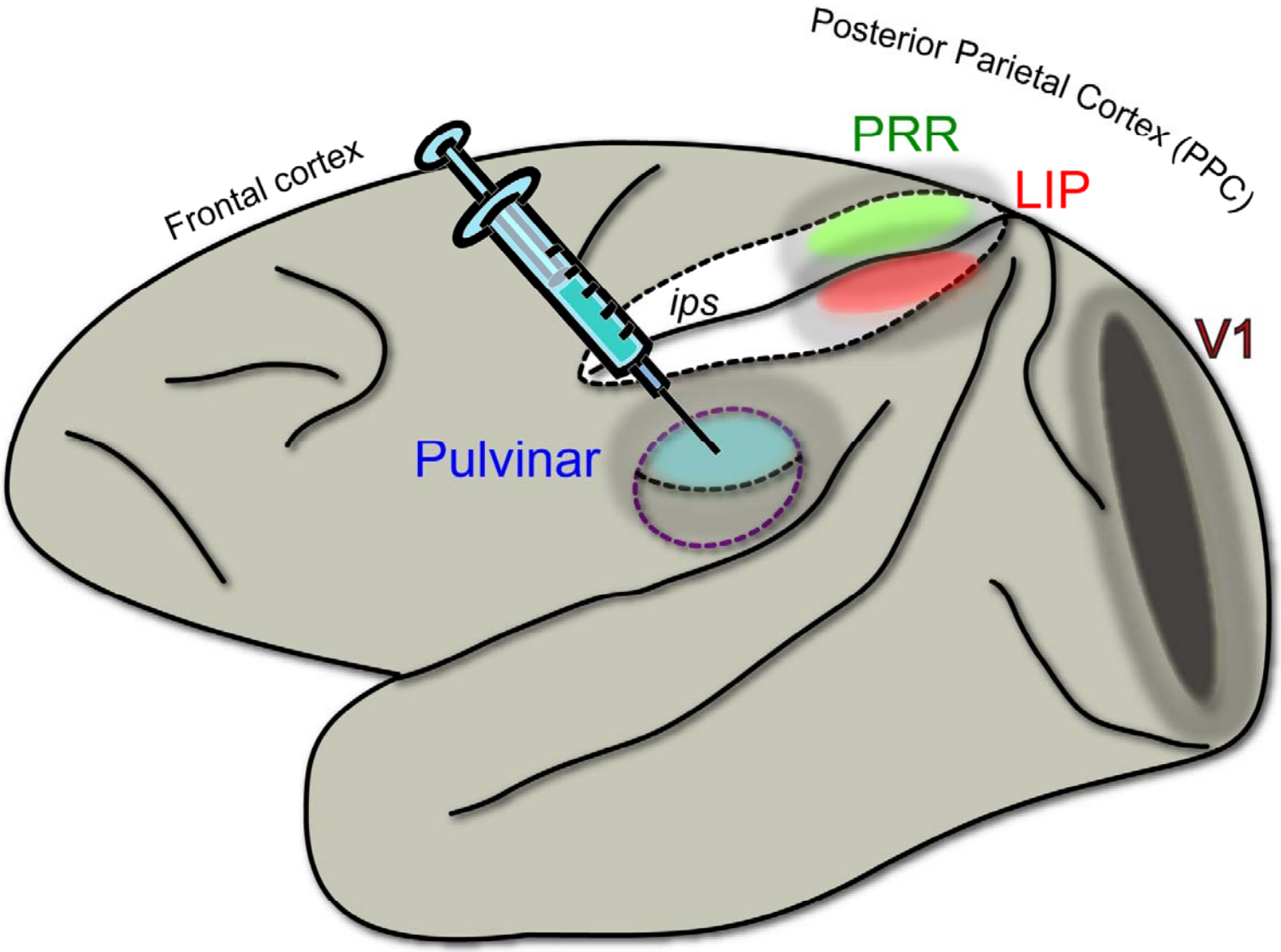
No report paradigms



Interfering with ongoing brain activity

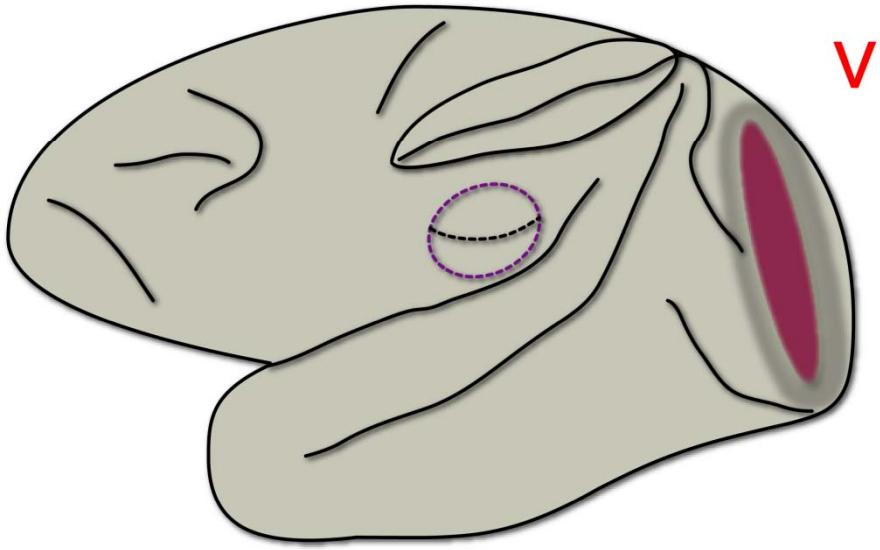


Brain areas of interest



Effect on perception/action following V1 lesions

Cortical blindness



Cortical blindness

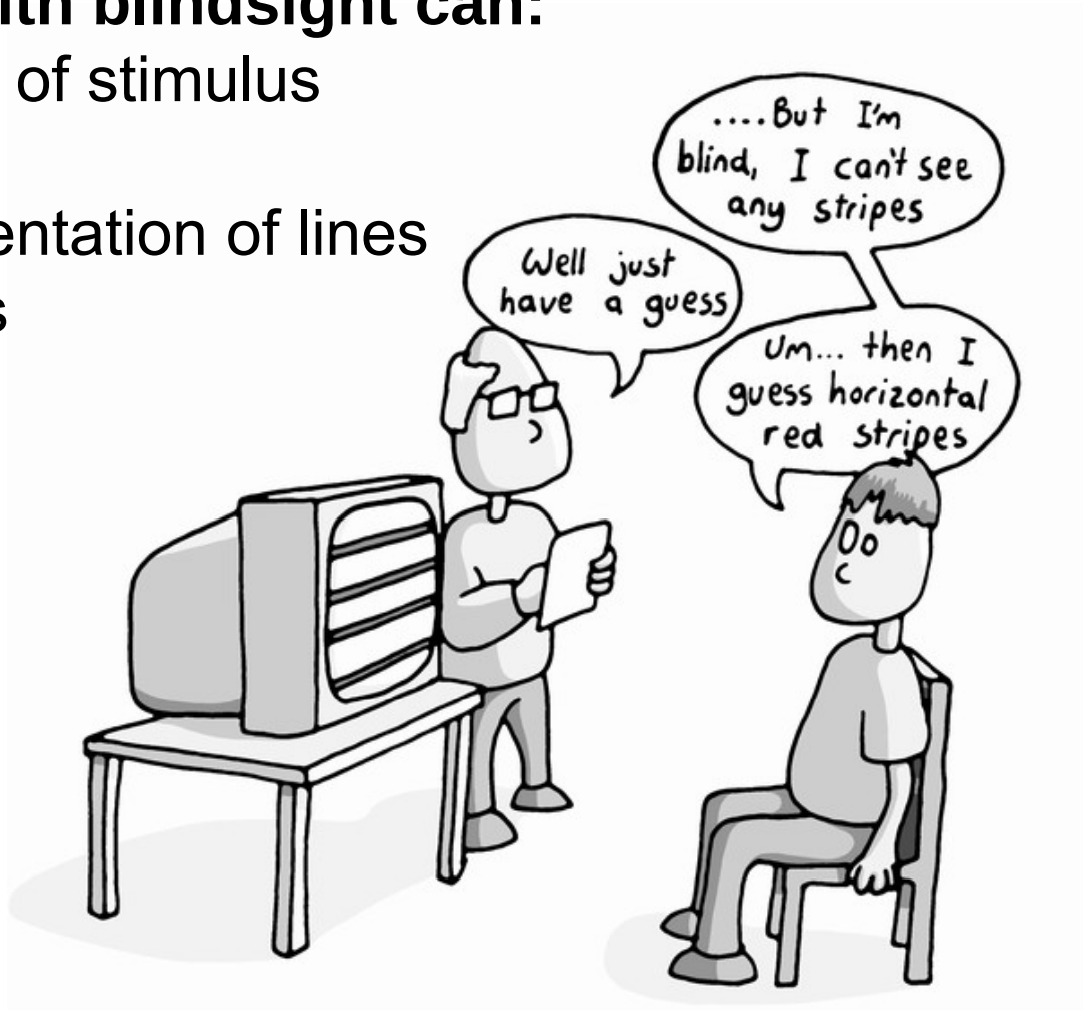
- What can you do without the primary visual cortex?

- Which visuomotor functions remain after visual consciousness is gone?

→ **Blindsight** is the ability of people who are cortically blind due to lesions in primary visual cortex (V1) to respond to visual stimuli that they do not consciously see.

V1-lesioned patients with blindsight can:

- point to the location of stimulus
- detect movement
- discriminate the orientation of lines
- discriminate shapes

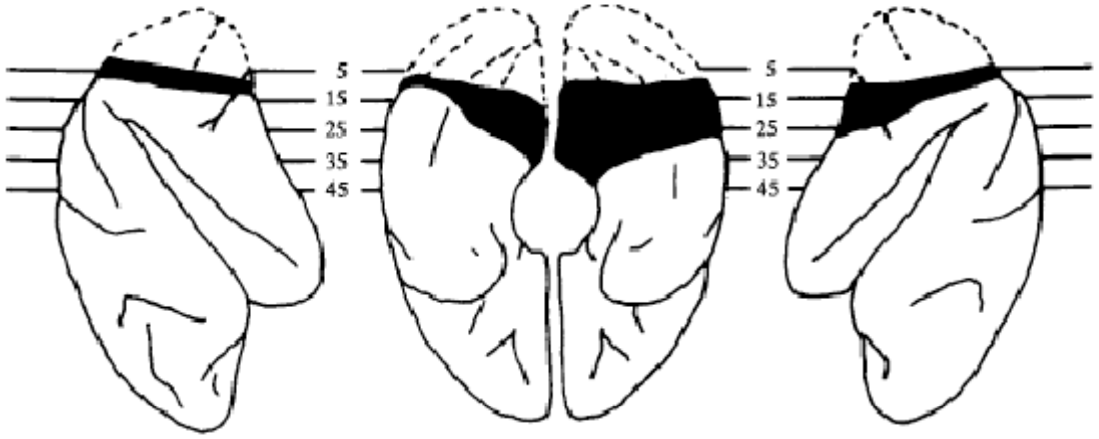


Study question

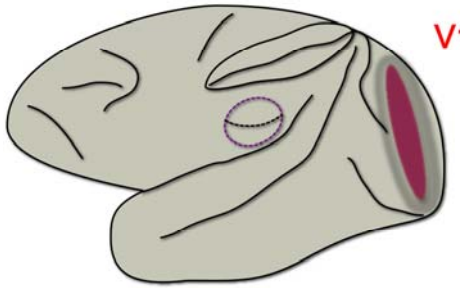
5. Glass half full vs. half empty:

If you find a patient who is not aware of a stimulus but manages to judge the location of a stimulus correctly in ~60% of the trials, is this evidence that consciousness is not needed to guide behavior?

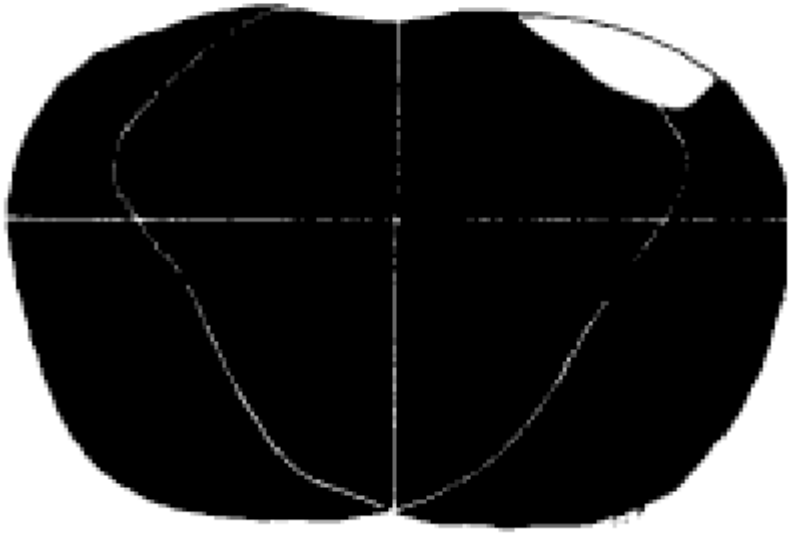
Helen the blindsight monkey



Reconstruction of Helen's brain



Probable extent of cortical field defect

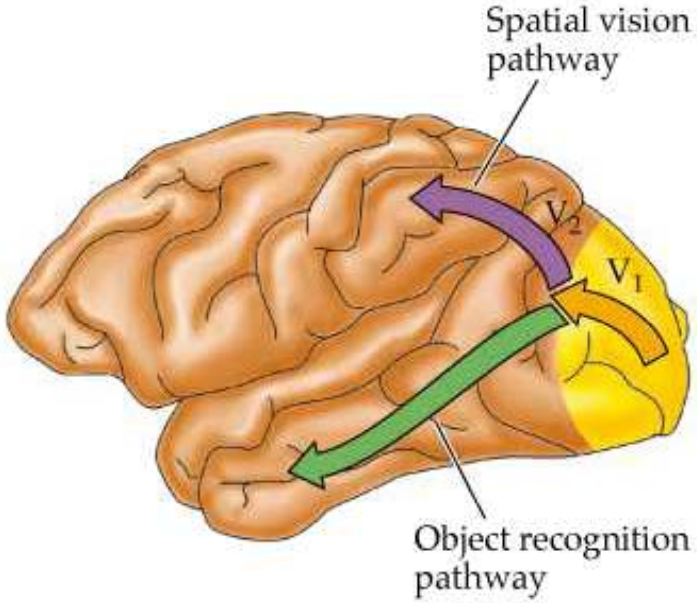


Humphrey N (1970).

Helen: the famous blindsight monkey

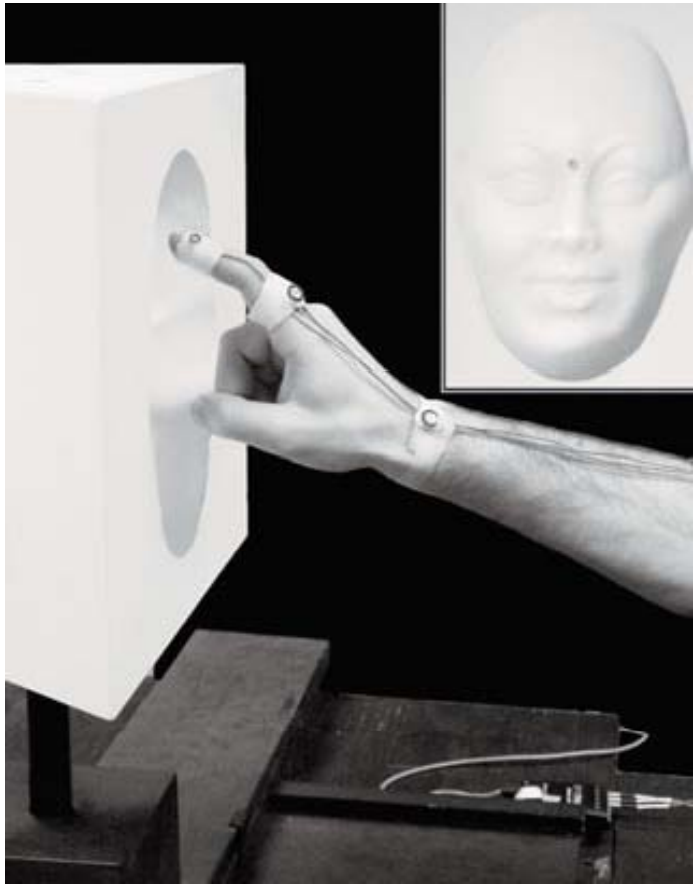
Humphrey N (1970).

Dissociation between Vision and Action



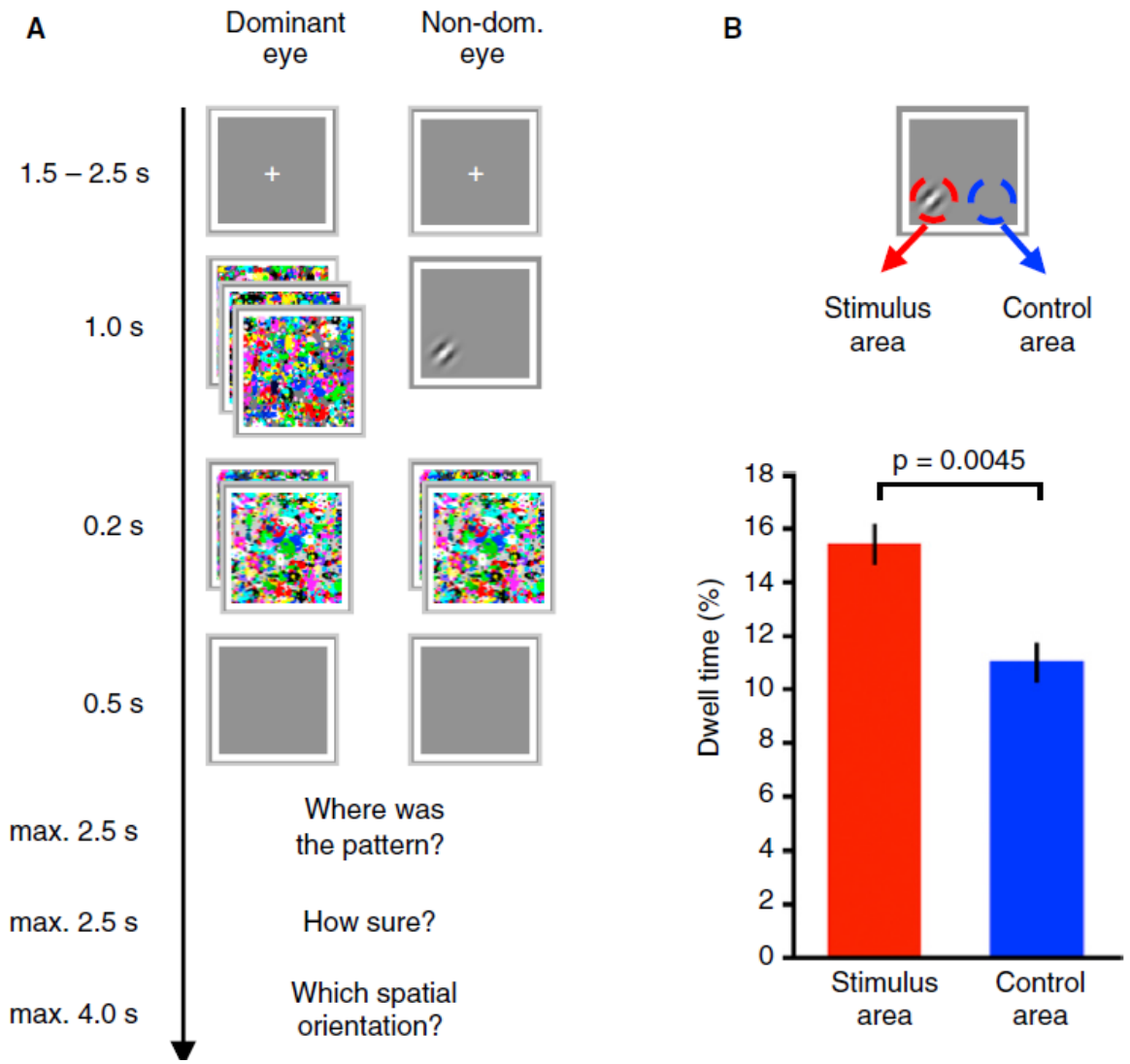
Optic Ataxia

Pointing does not fall for the visual illusion



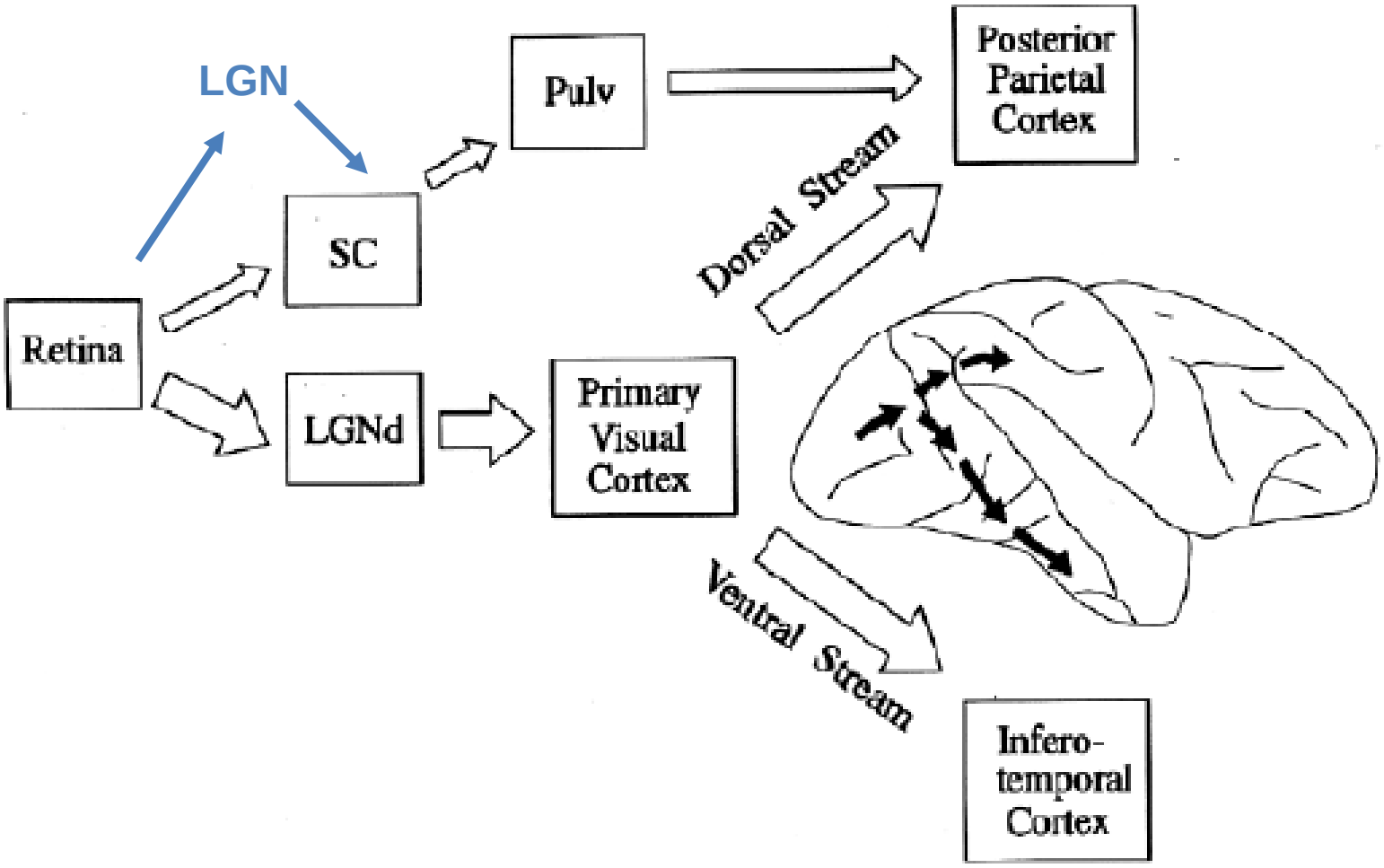
Kroliczak et al., 2006

Blindsight in healthy subjects: Dissociations between action and perception



Rothkirch, M., Stein, T., Sekutowicz, M. & Sterzer, P. (2012). A direct oculomotor correlate of unconscious visual processing. *Current Biology*

Proposed Blindsight (‚Action?‘) Pathway

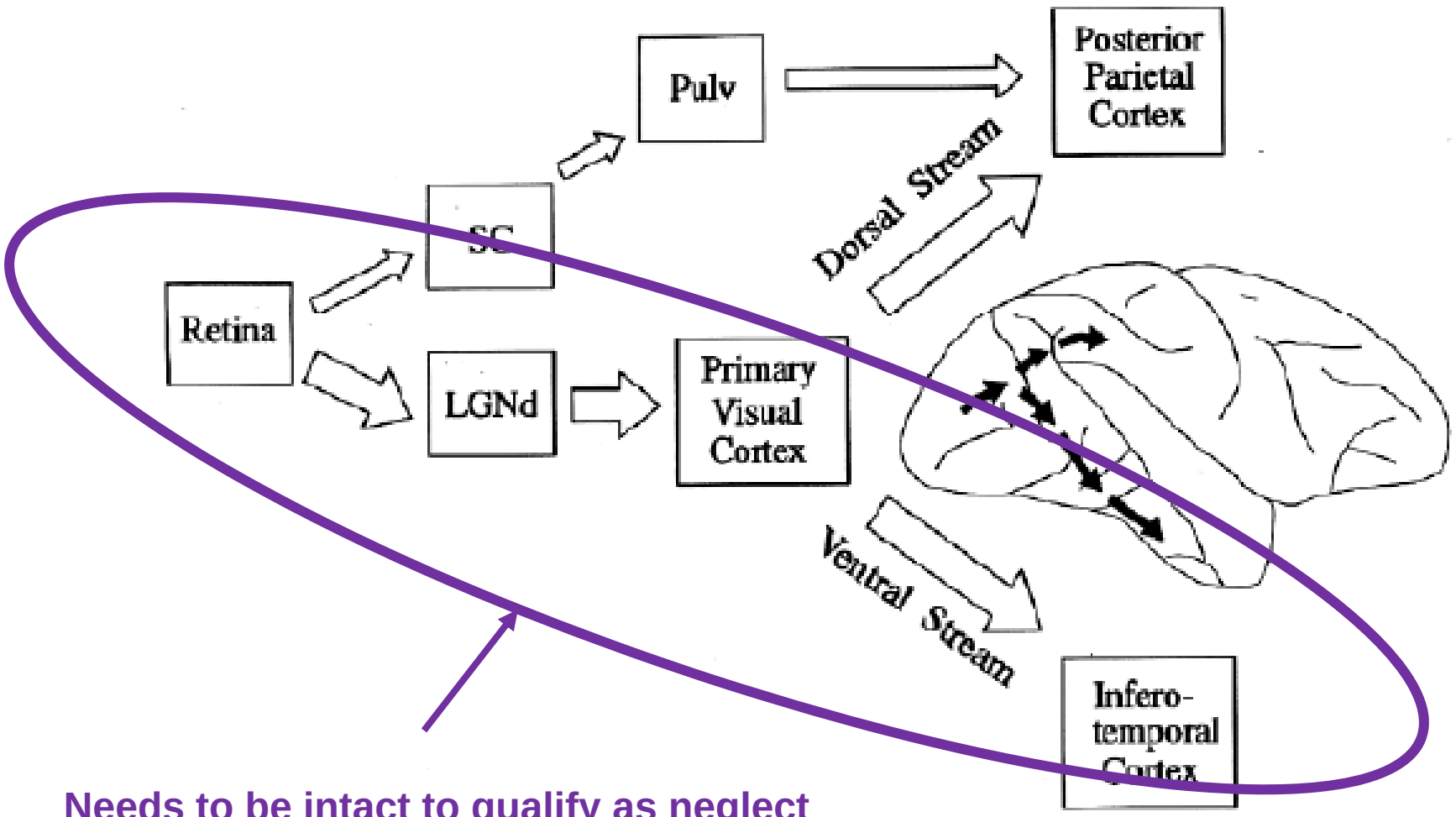


Cowey, 2012, Current Biology, Schmid et al., Nature, 2010

1. Neglect - Syndrome

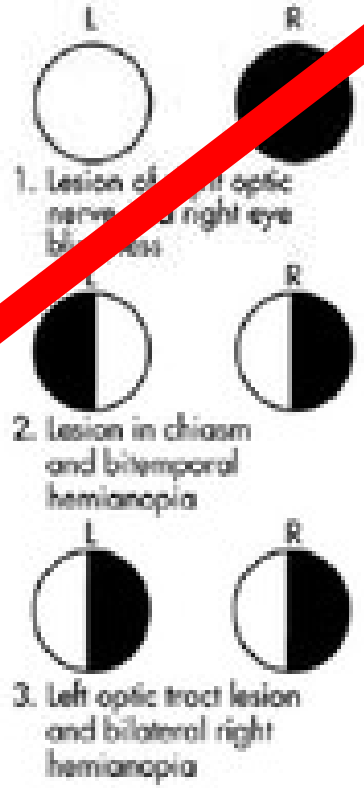
Extinction

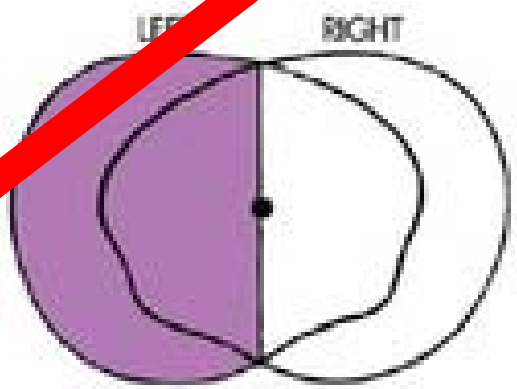
Spatial neglect and extinction

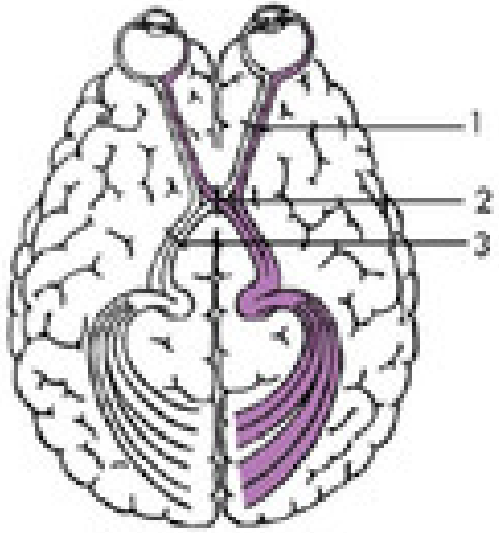


Needs to be intact to qualify as neglect

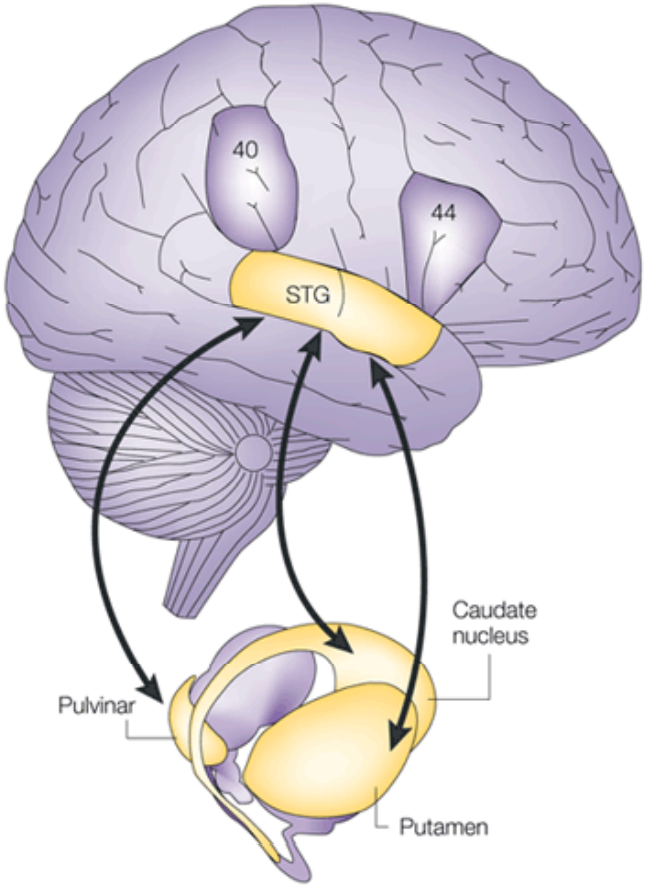
Neglect is *not*:
Differential Diagnosis: Cortical blindness

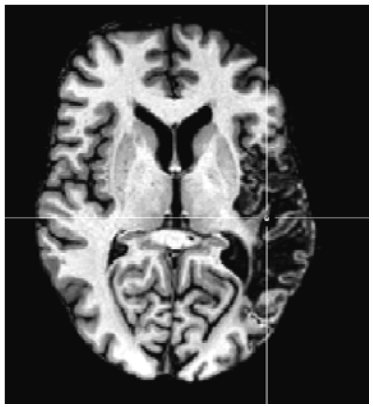




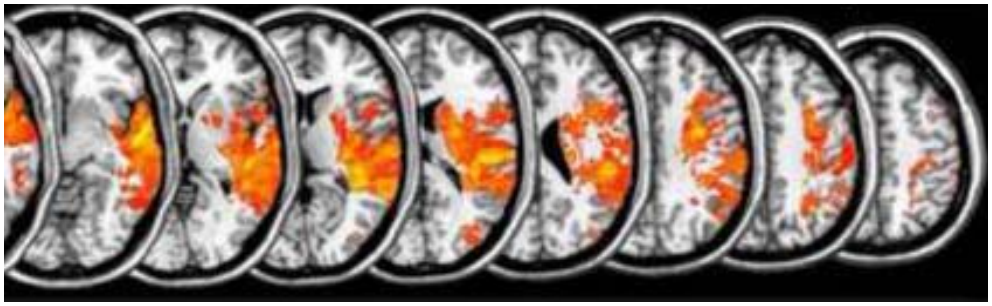


Brain areas involved in spatial neglect





Neglect patient
(7514 Hr H)



Karnath, Nature Reviews, 2001

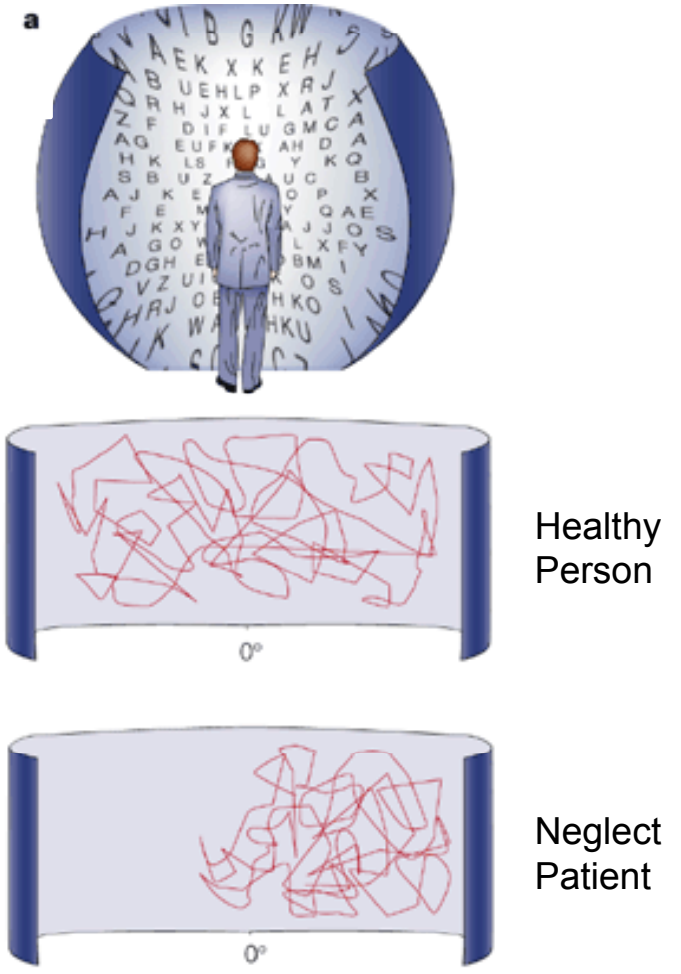
→ Lesions that lead to neglect form a large network that involves (mostly right) parietal, frontal and superior temporal cortical areas as well as subcortical structures.

Spatial neglect and extinction

Spontaneous orienting bias

Extinction

Ipsilesional exploration bias



Healthy Person

Neglect Patient

• Incidence: 40-60% after left and 50-70% right hemispheric lesions, most frequently after stroke

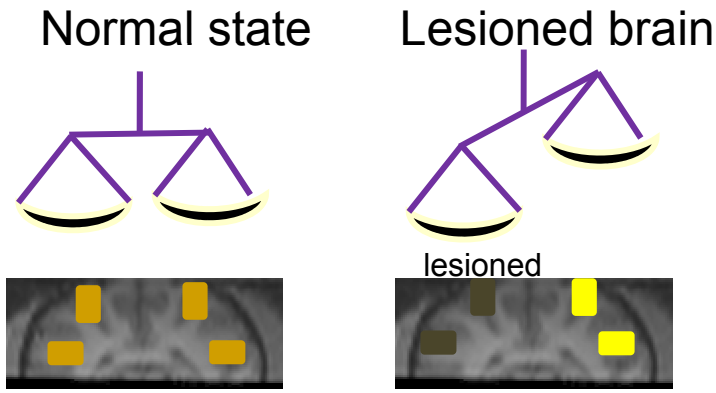
NEGLECT and EXTINCTION

CT SCAN

MRI SCAN

(Main) Theories of spatial neglect

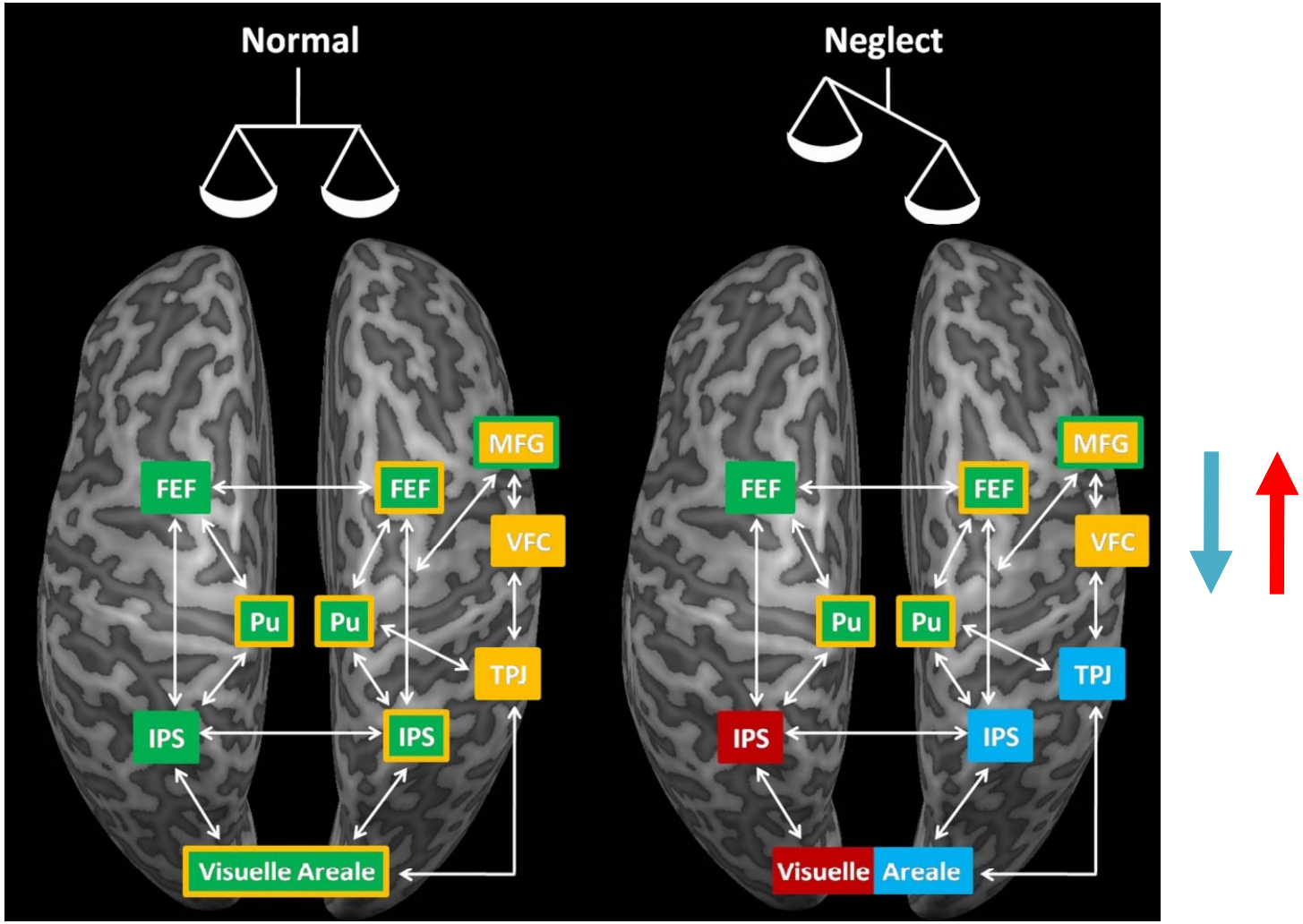
- Attentional Theory/
  Interhemispheric rivalry model



- Transformational Theory

Hemispheric Imbalance Model of Neglect

(Kinsbourne, 1977; Corbetta & Shulman, 2005)

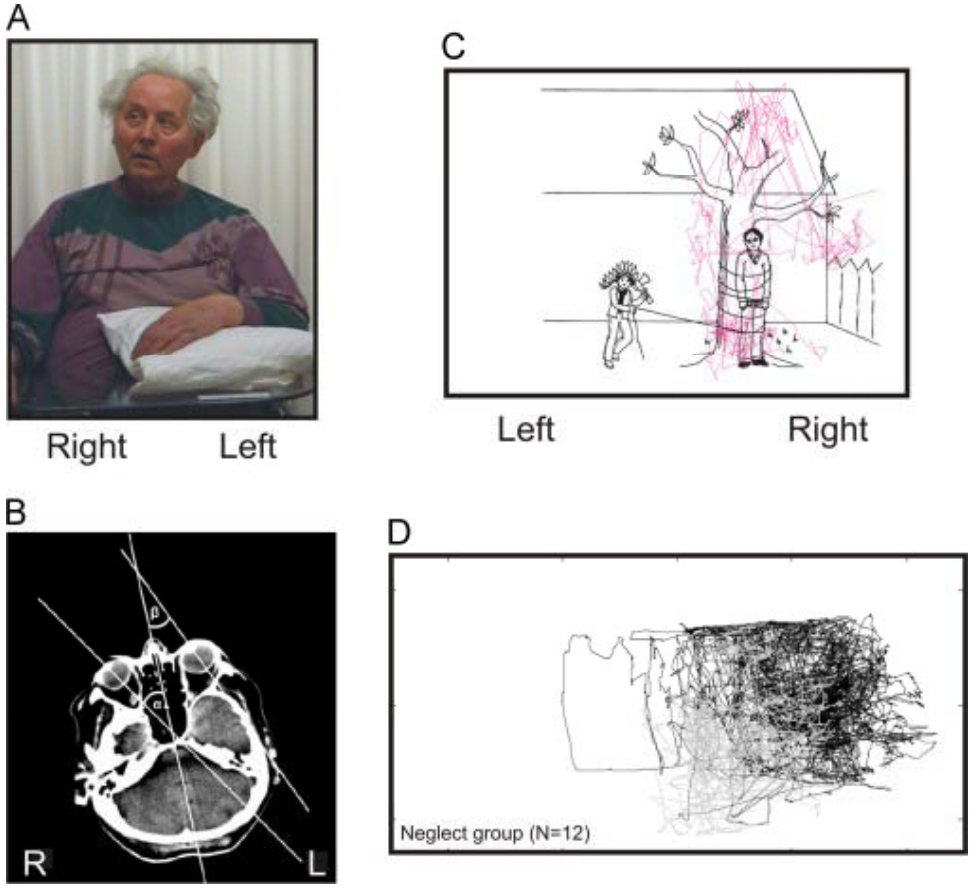


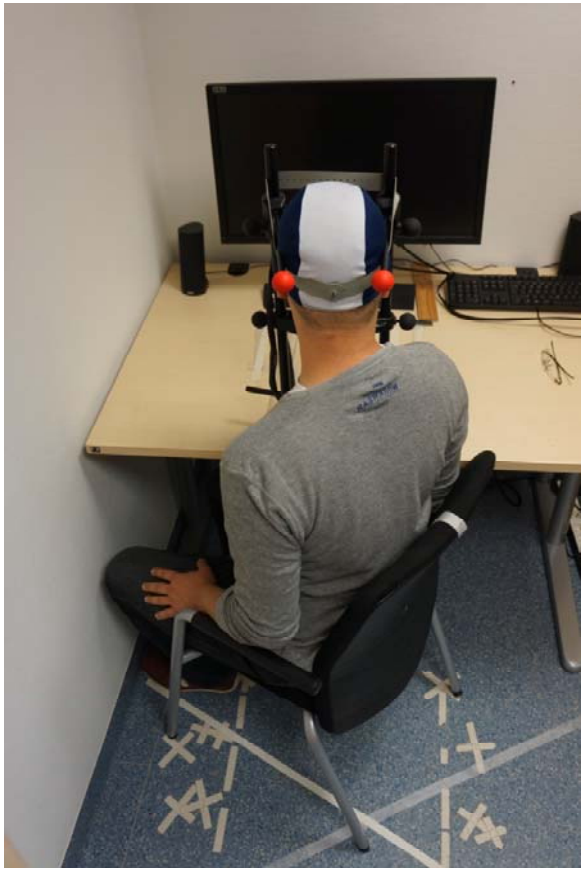
Modified from Grefkes & Fink, 2010

Awareness of Response Bias: Evidence:Shift of egocentric midline

Neglect Patient Behavior

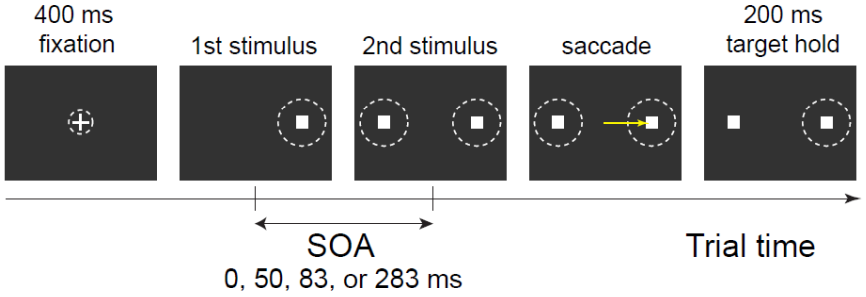
Improvement by Trunk Rotation

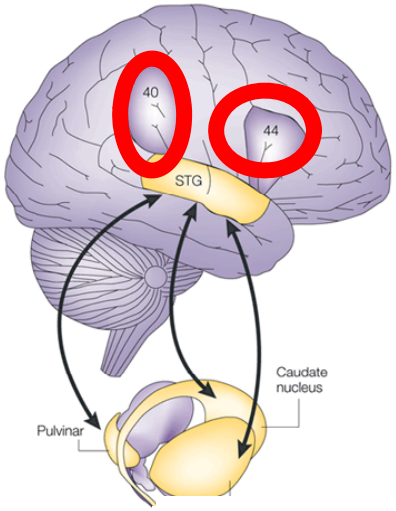


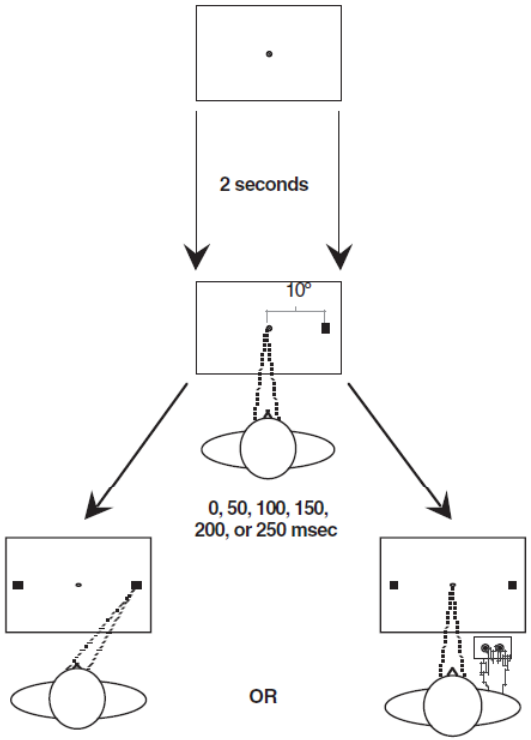


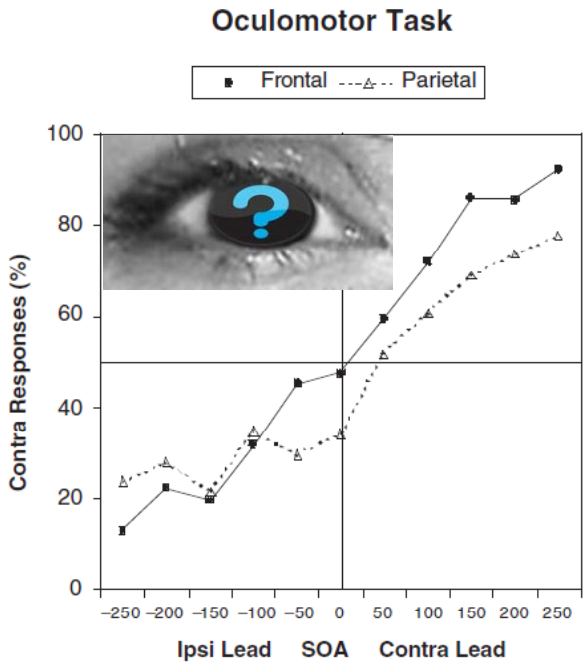
Karnath, 2015, Neuropsychologia, Paschke et al., 2015 (in revision)

Report matters: Ipsilesional Biases in Saccades but not Perception after Lesions of the Human Parietal Lobe



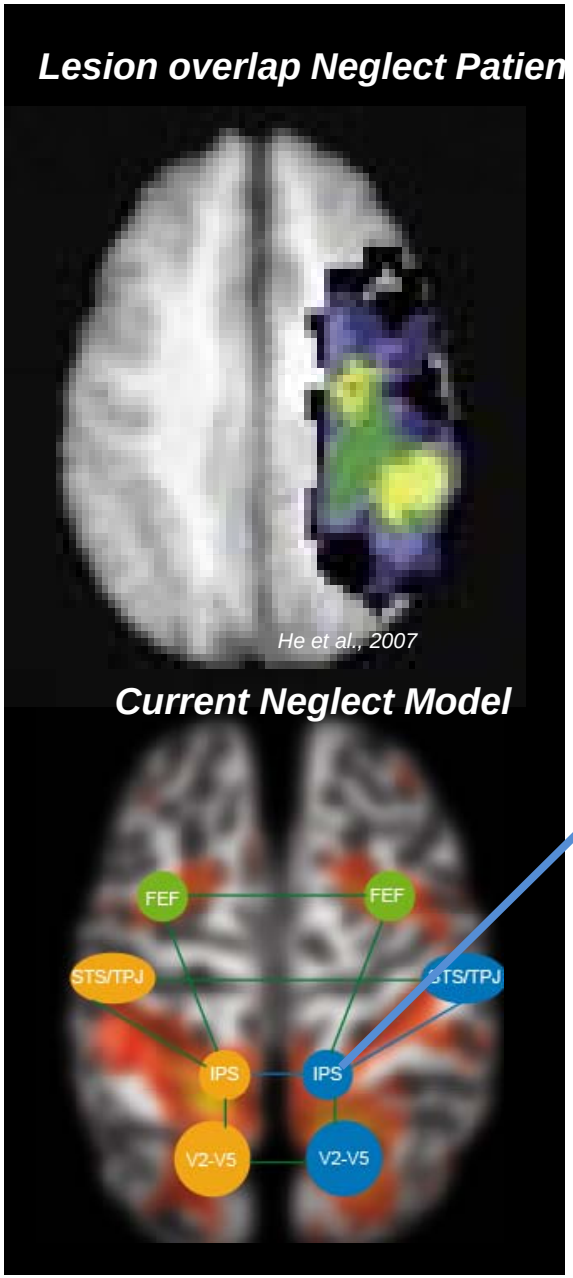






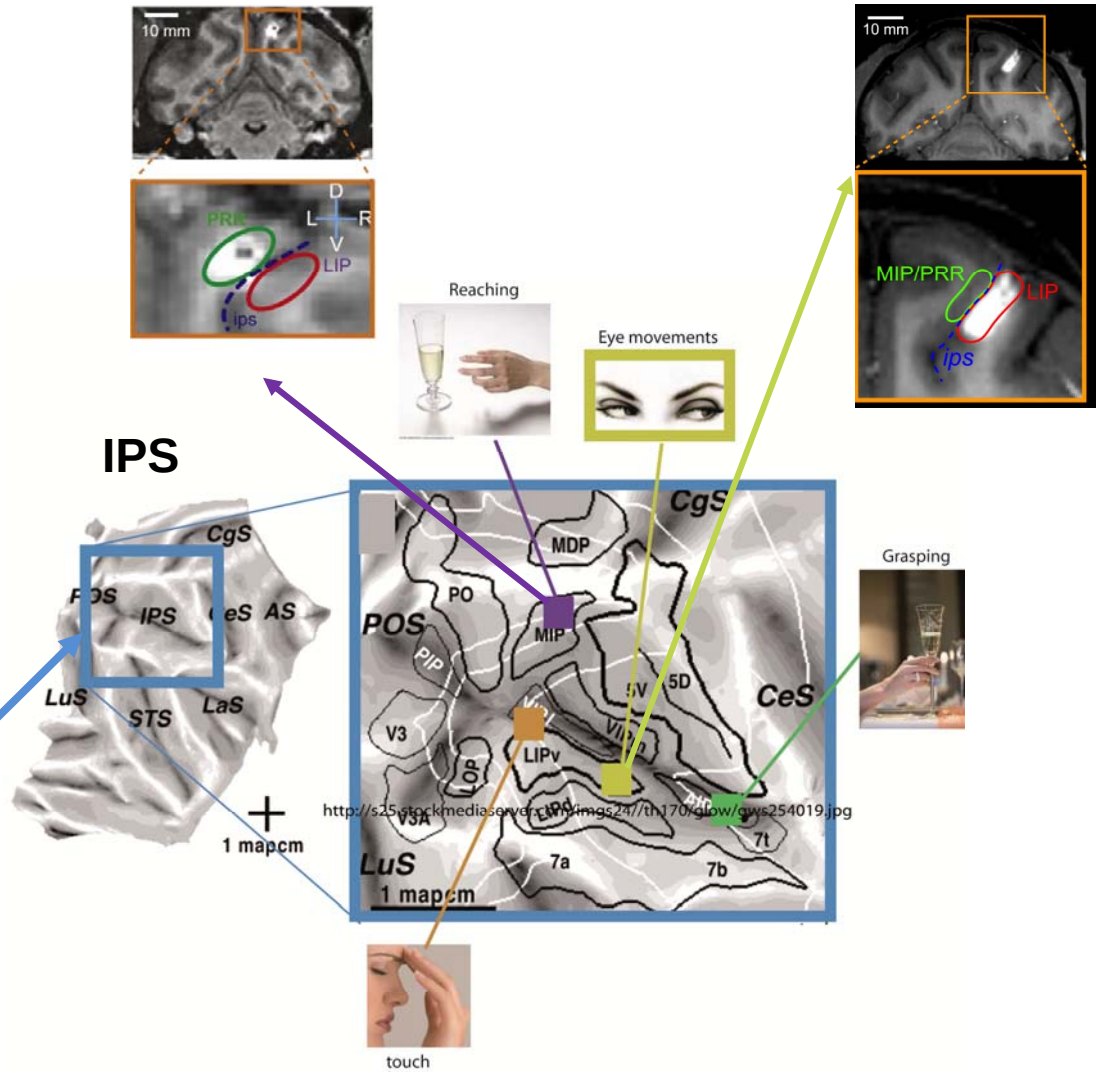
Ro et al., Journal of Cognitive Neuroscience, 2001

The parietal cortex: its own little universe



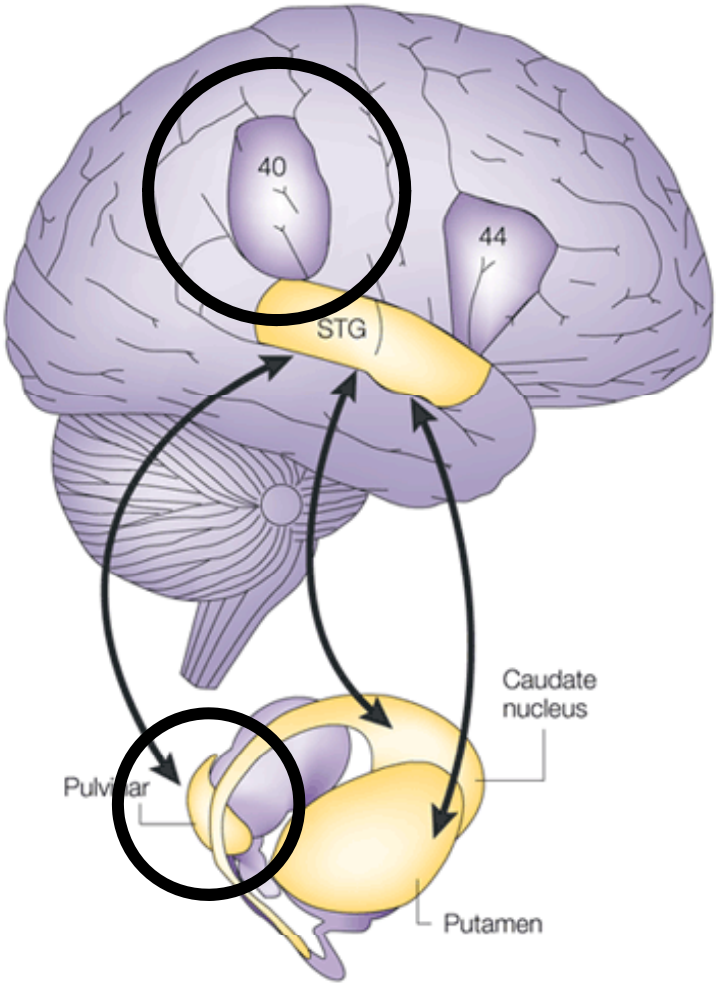
PRR
(Collab: E. Huang)

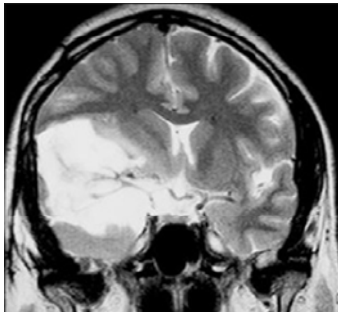
LIP

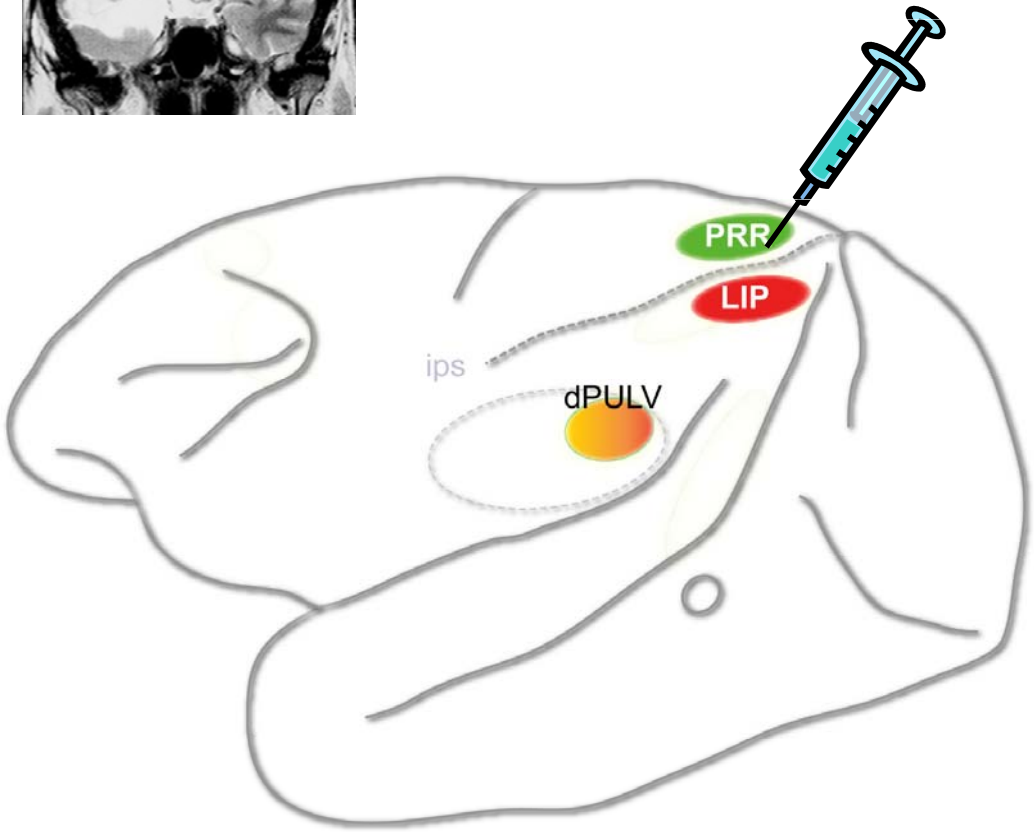


Wilke, Kagan* & Andersen, PNAS, 2012*
Hwang, Hauschild, Wilke & Andersen, Neuron, 2013

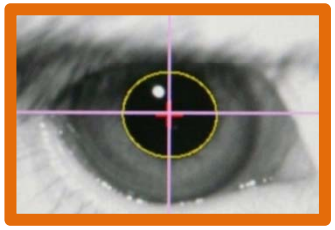
What is the functional contribution of individual brain regions to spatial awareness?



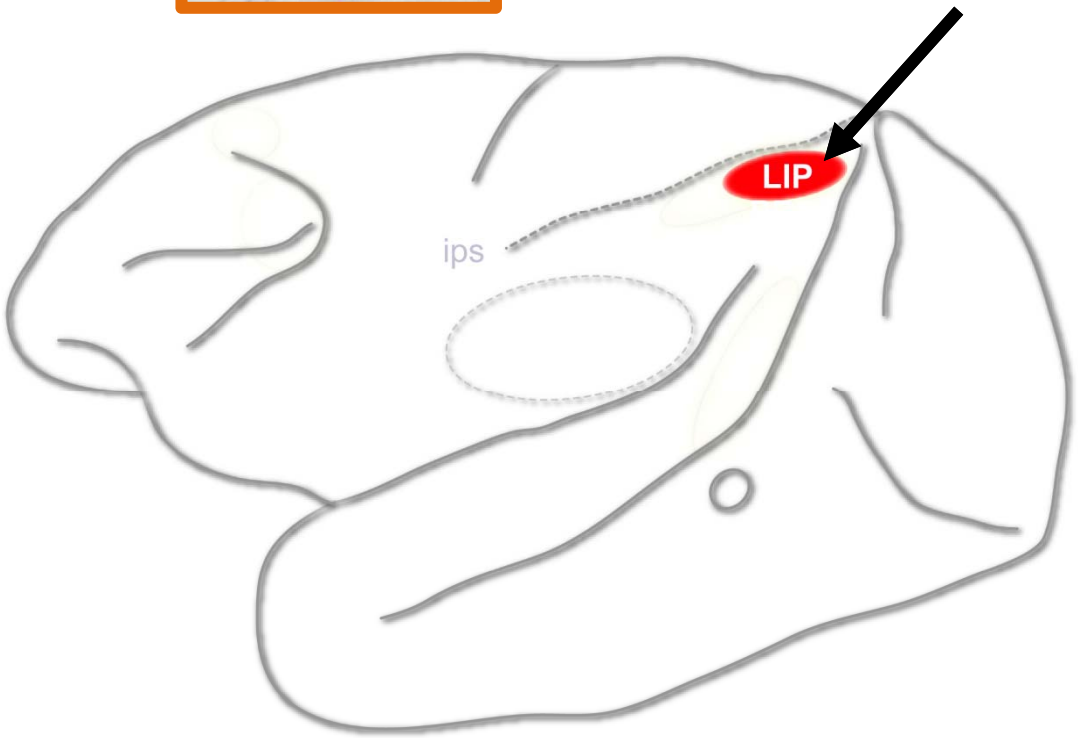


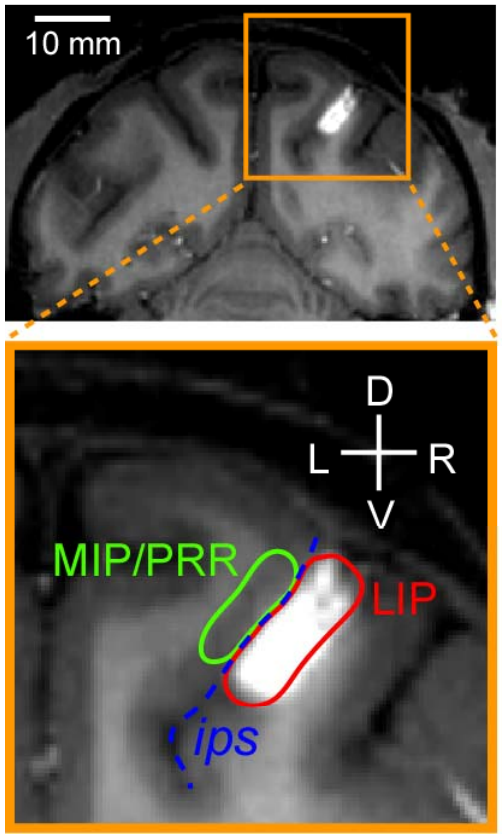


Inactivation of specific parietal regions: LIP

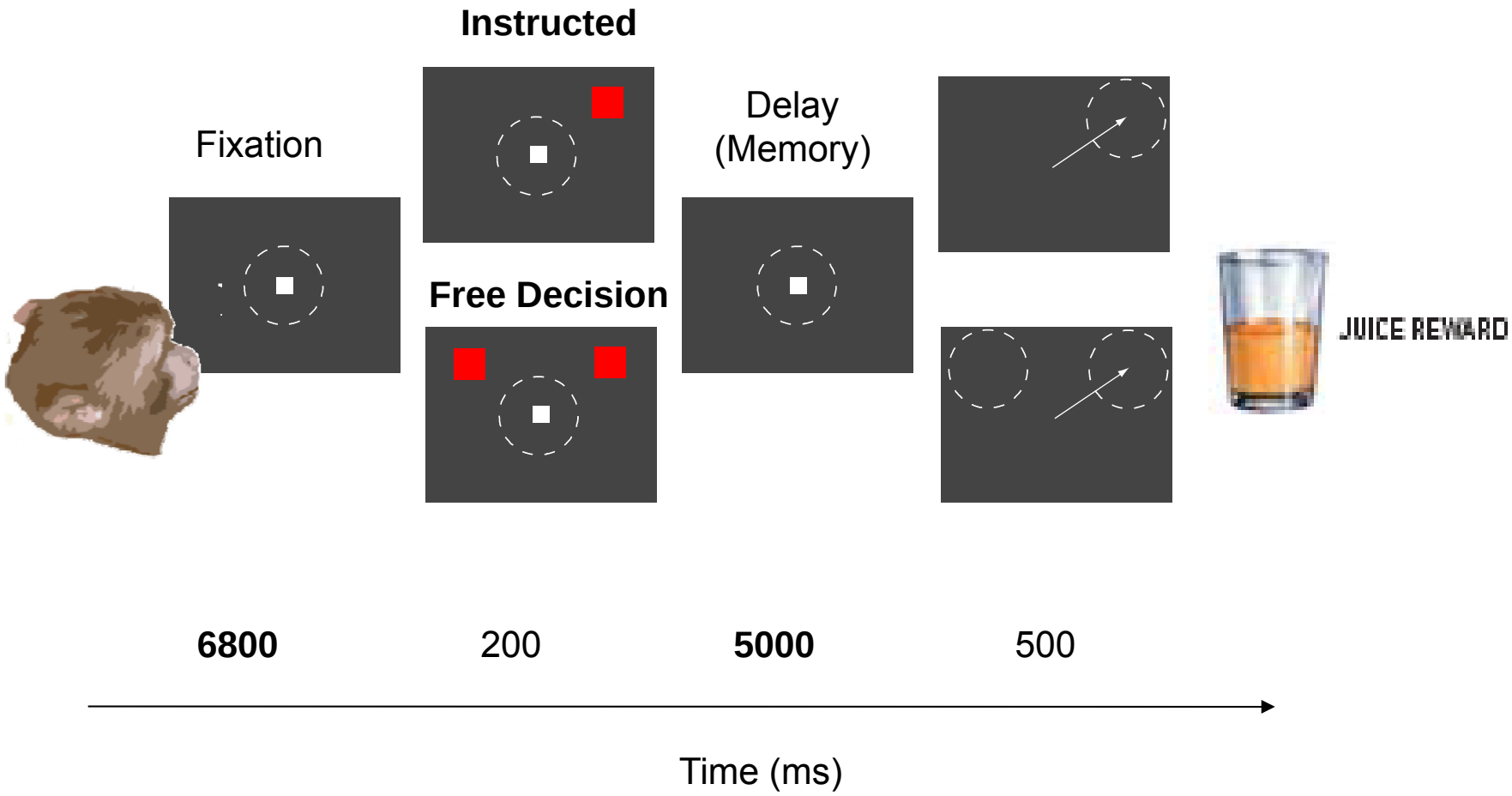


Lateral intraparietal area



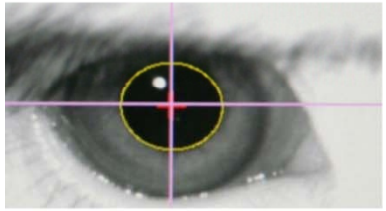


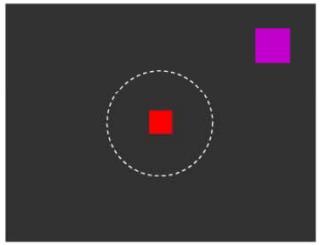
Wilke, Kagan* & Andersen, PNAS, 2012*

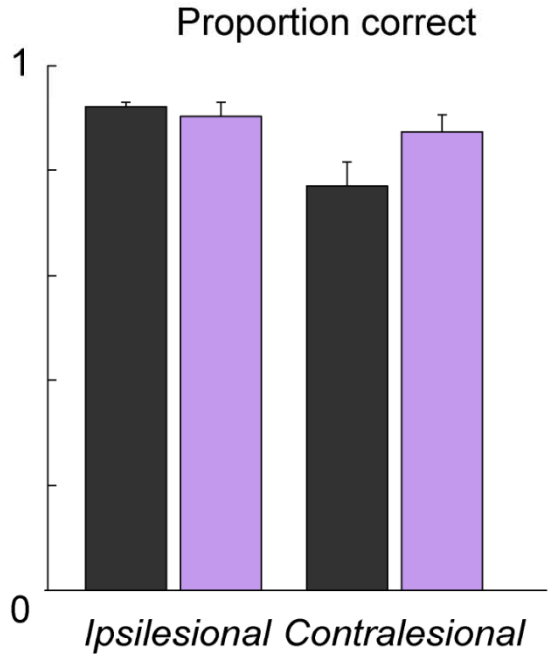

Instructed
Fixation
Delay
(Memory)
Free Decision
JUICE REWARD
6800
200
5000
500
Time (ms)

LIP inactivation biases saccades towards ipsilesional space

Performance in instructed trials

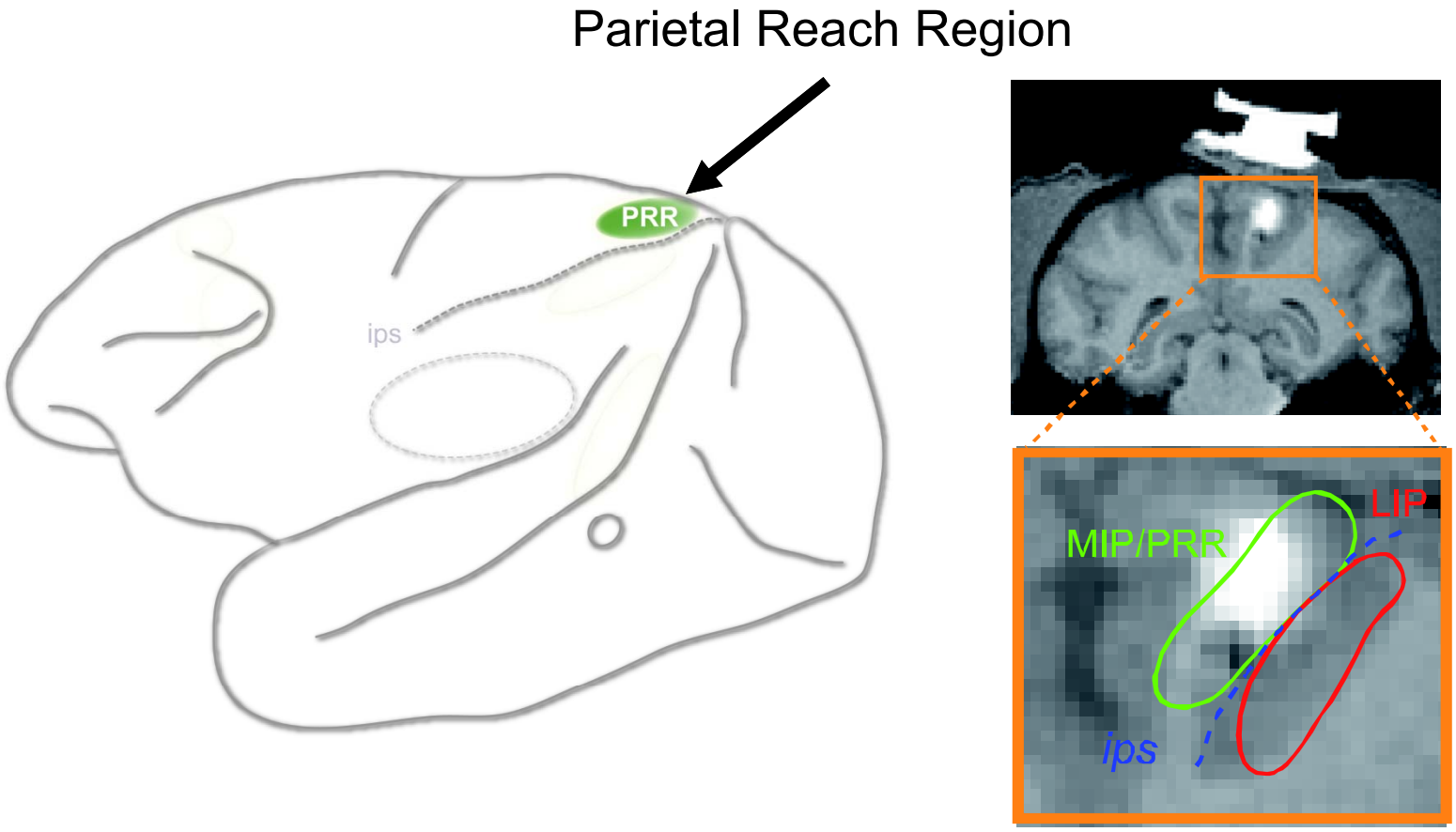






Wilke, Kagan* & Andersen, PNAS, 2012*

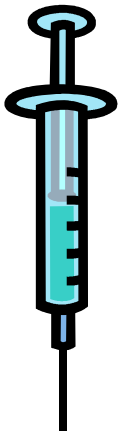
Inactivation of specific parietal regions: medial intraparietal sulcus

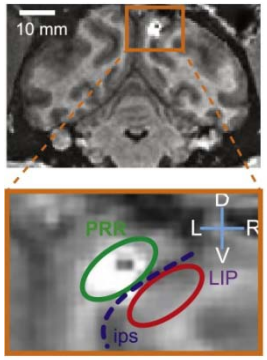


Hwang, Hauschild, Wilke & Andersen, Neuron, 2012

Parietal reach region (PRR) inactivation alters reach endpoints

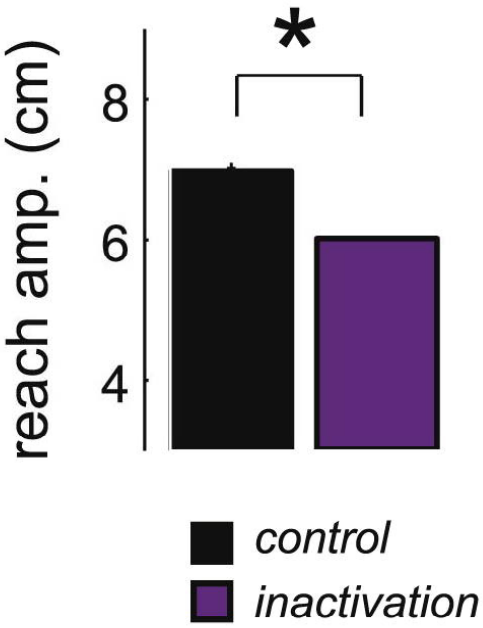
Inactivation sessions interleaved with control sessions
Muscimol (GABA-A agonist) injection



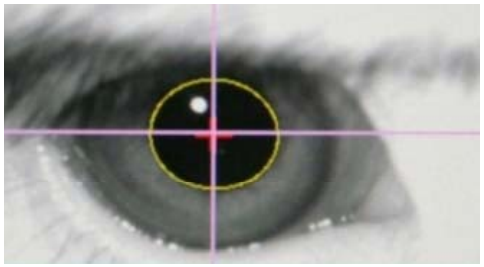


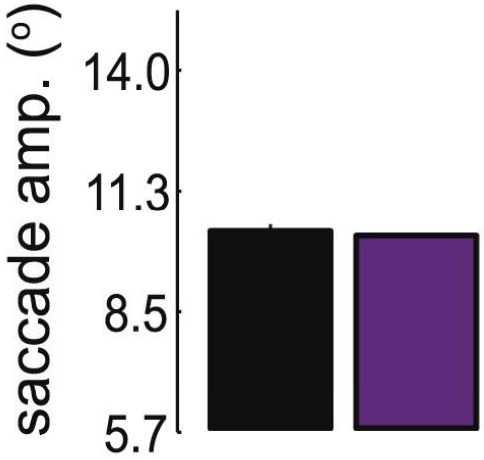
Dissociation between saccades and reaches in the parietal reach region

Reaching



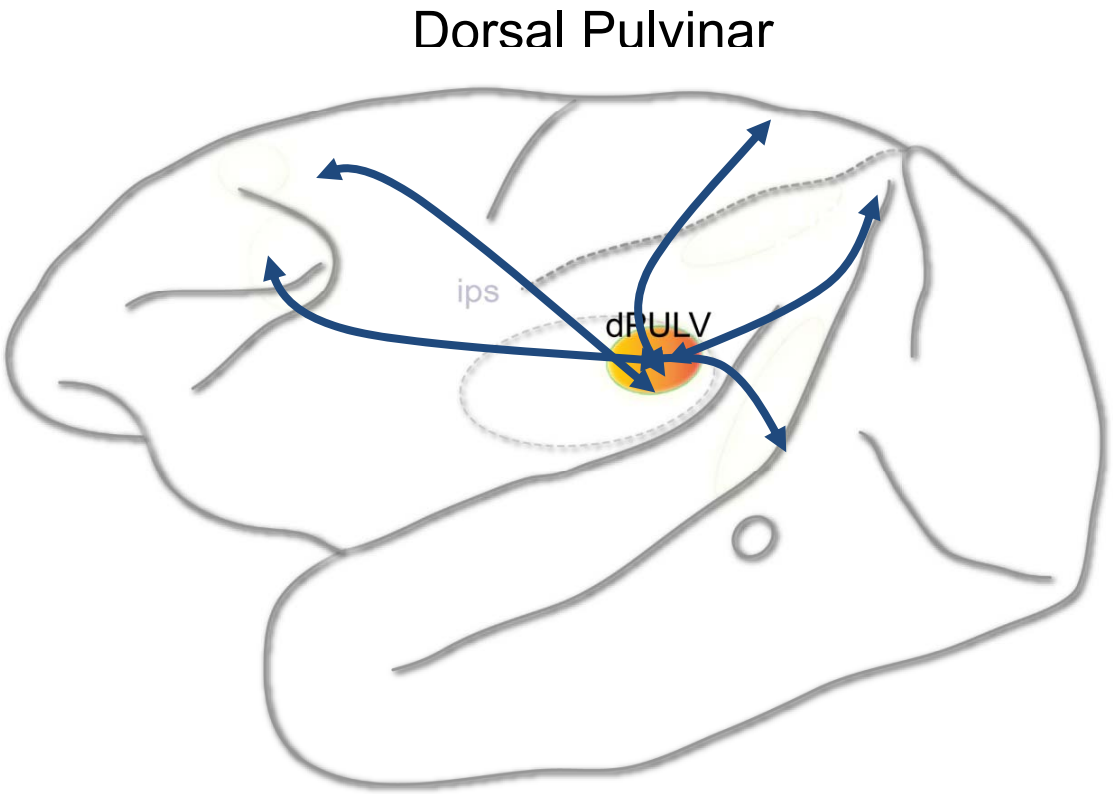
Saccade

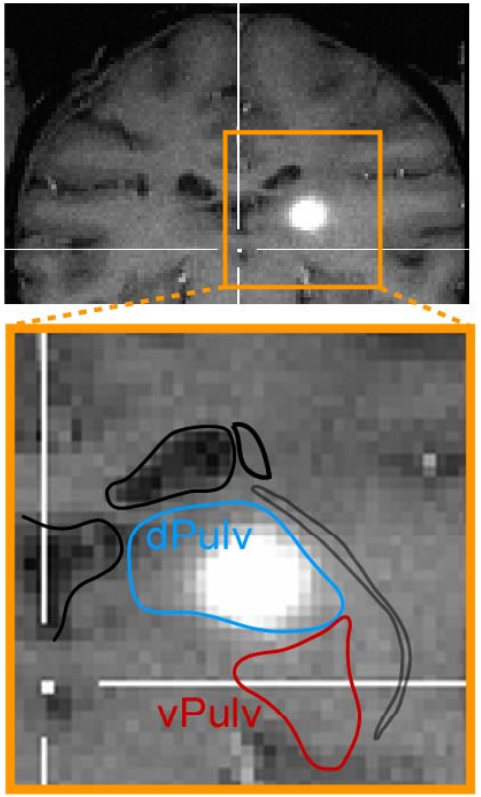




Hwang, Hauschild, Wilke & Andersen, Neuron, 2012

Inactivation of specific thalamic regions: dorsal Pulvinar

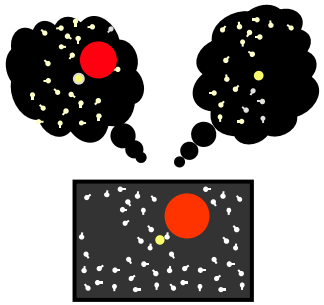




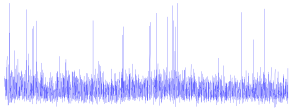
- receives its driving input from cortex
- projects to visual and visuo-motor areas

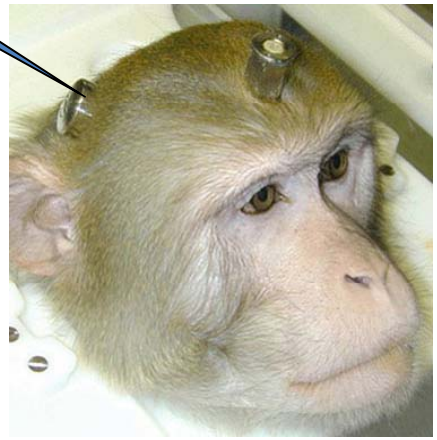
How to measure brain activity related to conscious perception?

One Stimulus → Two Percepts

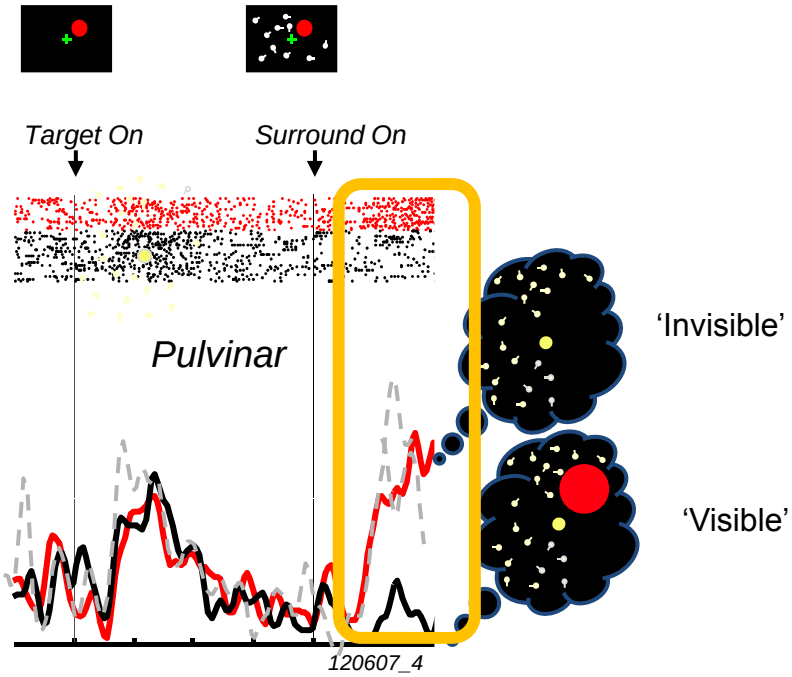


Spiking



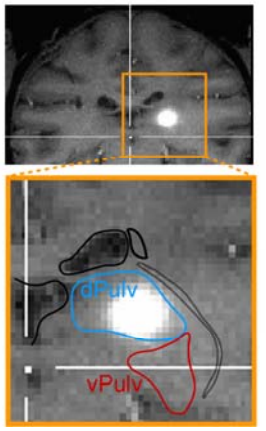


Pulvinar Single Neuron Response



Wilke, Müller & Leopold (2009) PNAS

Neglect symptoms after pulvinar inactivation



Pulvinar - Baseline

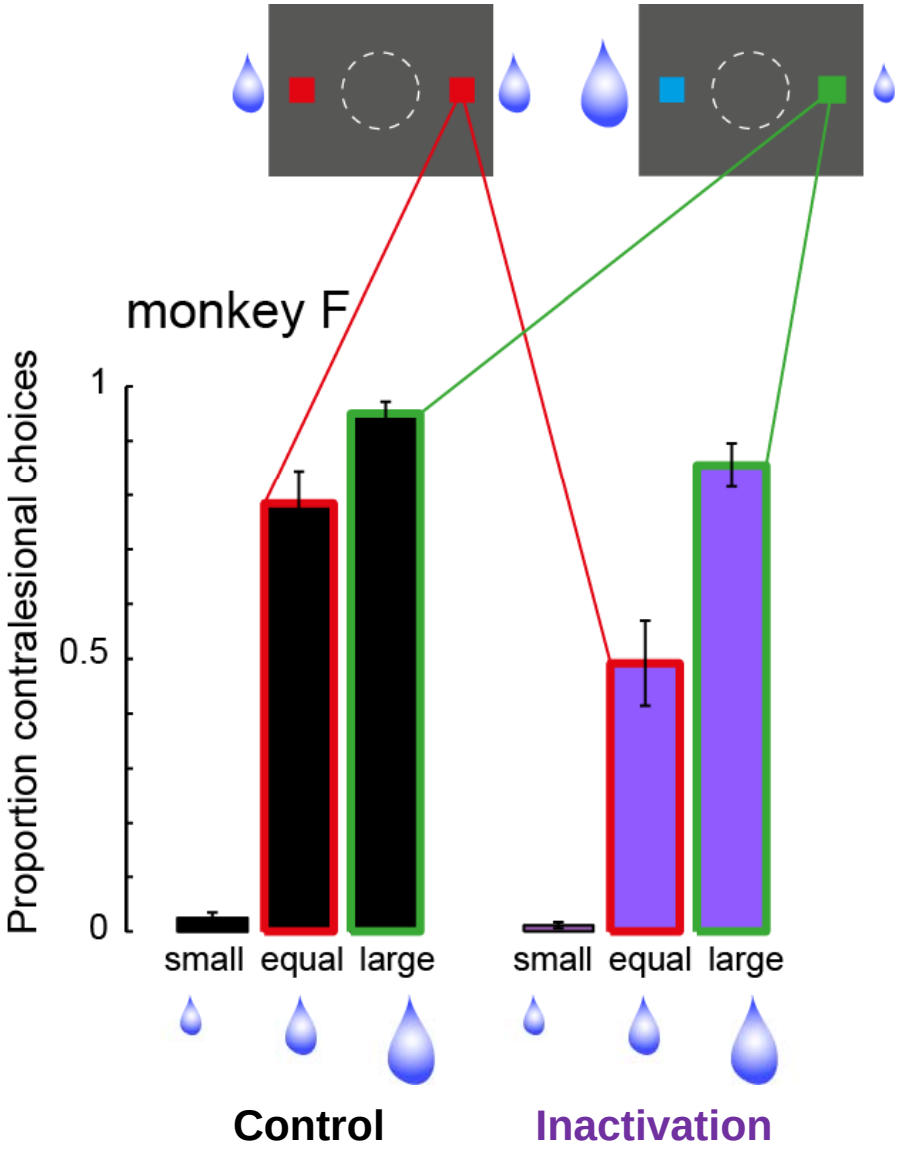
Pulvinar - Inactivation

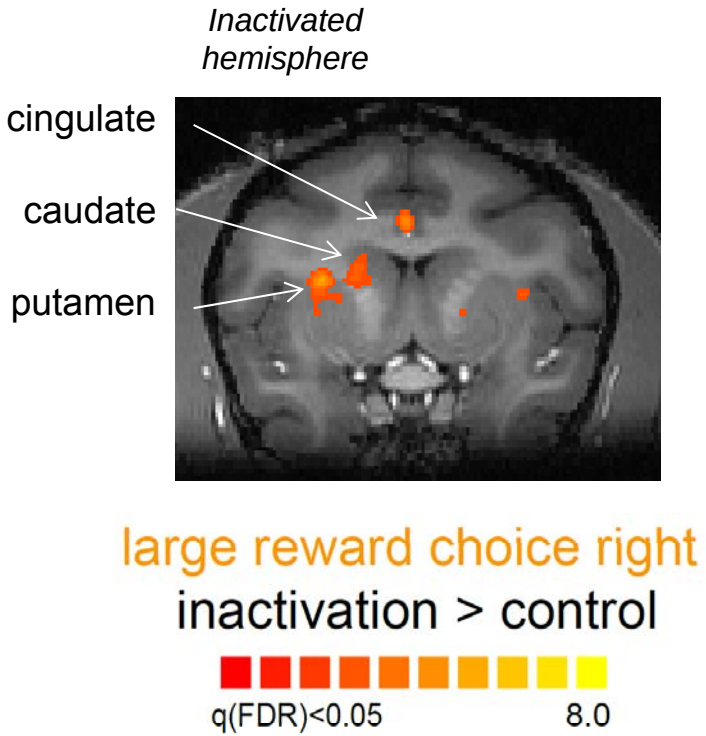
'contralesional'
('affected')

'ipsilesional'

Wilke et al., Journal of Neuroscience, 2010

Reward (partially) restores contralesional selection





Wilke et al., Journal of Cognitive Neuroscience, 2013
Wilke, Kagan* & Andersen, 2015, in revision*

How much emotional/reward information is processed in neglect?

Question: In which house would you like to live?

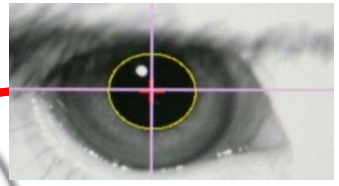
➡ Neglect-Patients may process visual stimuli in the contralesional unconsciously and guide their decisions

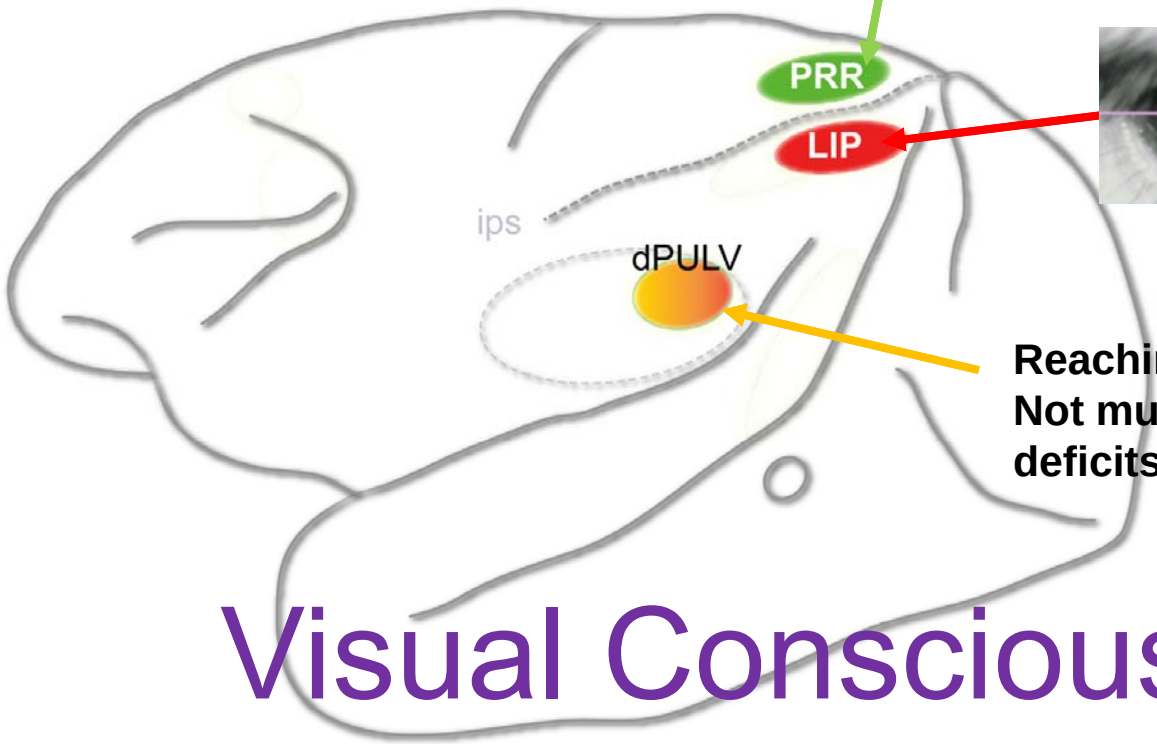
Quelle: Marshall & Halligan , 1988

Summary Inactivation Studies

Reaching Deficit: Optic Ataxia

Eye movement Bias



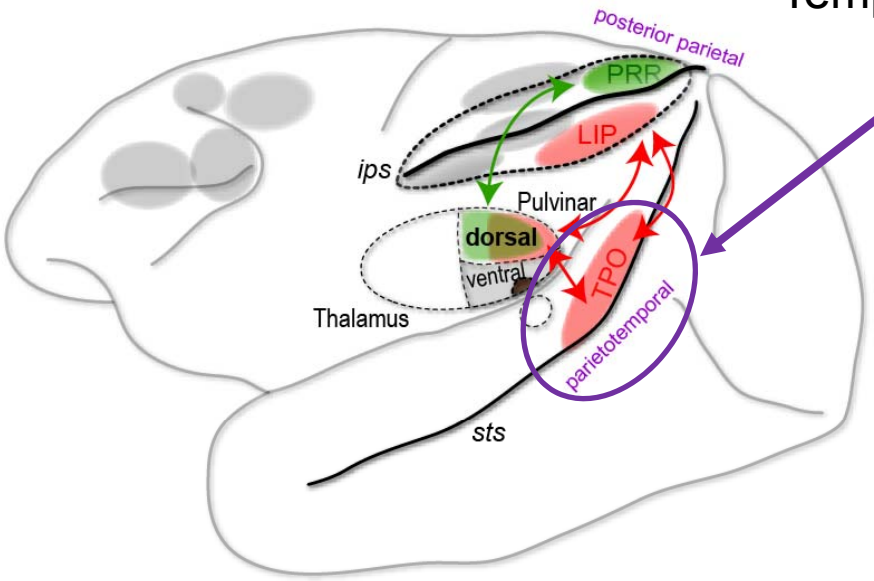


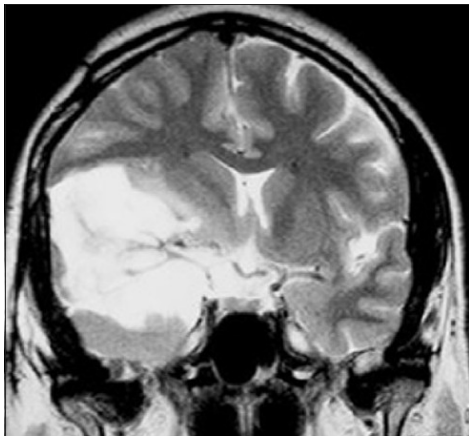
Reaching + Saccade Choice Deficit
Not much evidence for perceptual deficits however!

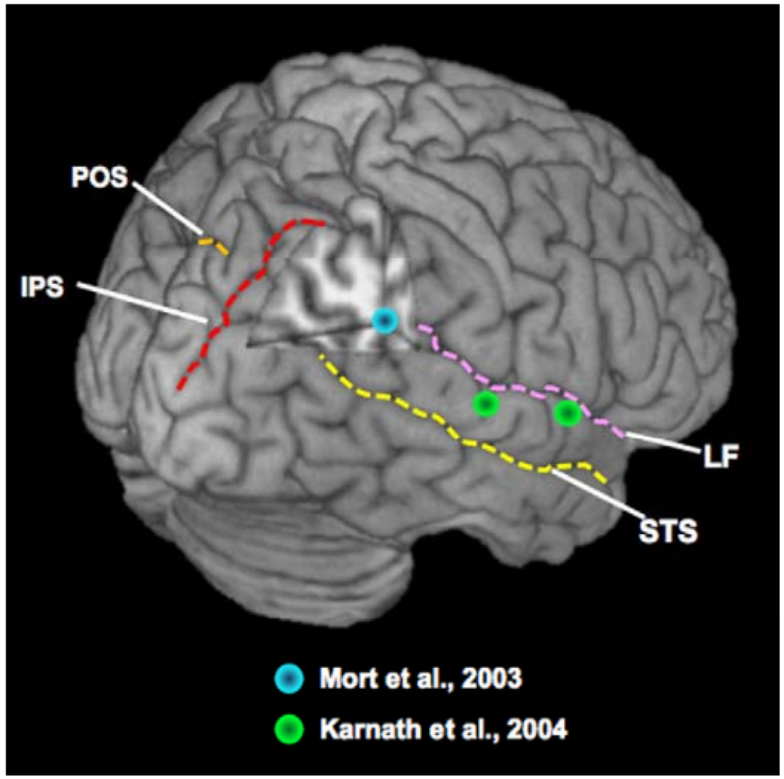
Visual Consciousness?

Have we looked in the wrong places?

Temporo-Parieto-Occipital Region (TPO)







- Several parietaltemporal regions have been implicated in the ability to attend and respond to visual events, impairments look often like visuomotor deficits.

Study question 6:

How do we best discriminate between visuomotor/ intentional and perceptual deficits?

Study question 7:

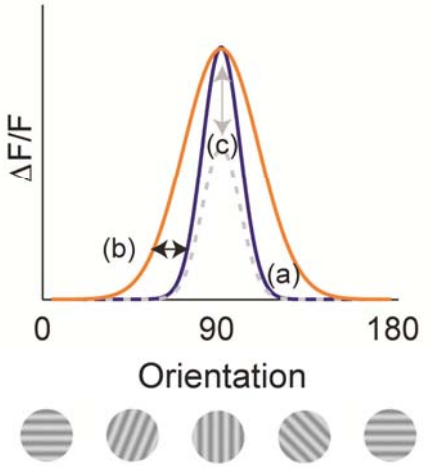
- Could visual consciousness be embodied in the visuomotor system and thus be effector specific?

Open Questions

• What is the contribution of report in our neural correlates of consciousness?

vs.

• How precise is the information encoded during perceptual suppression



• Are specific cell types (e.g., layers, astrocytes, connectivity etc.) more important for consciousness than others?

- Independent lesions of either V1 or parietal-temporal regions can greatly impair conscious vision, but no single visual area seems sufficient for visual awareness.

Study question 8:

- Does it mean we need to stimulate all areas simulatenously to prove the NCC?
- Does it mean we need to supply the higher-order areas with the precisely simulated input from V1?

Thank you!