Neuroimaging of Behavior

Practical Implications of fMRI Data and the Independence of Verbal Operants

Outline

- Skinner and the Neurosciences
- Neuroscience literature in Behavioral Journals
- Why to integrate Neurosciences into Behaviorism
- Private events made public
- The procedures to study behavior in the brain
- The need to translate information from Neurosciences to Behaviorism and vice versa
- The critical role of Neuroimaging in translating the information
- The verbal operants in the brain: the neural basis of their independence
- Methods to directly modify behavior in the brain

Skinner and the Neurosciences

- Eventually we may expect the main features of a behavioral theory to have physiological significance.

As the science of physiology advances, it will ( ) be possible to show what is happening ( ) within the organism during particular behavioral events, and the theoretical systems of the two sciences may also be seen to correspond. ( )

- A similar day may come in psychology. ( ) But the eventual correspondence should not ( ) obscure the present need for a behavioral theory. The hypothetical physiological mechanisms ( ) are not acceptable as substitutes for a behavioral theory. On the contrary, because they introduce many irrelevant matters, they stand in the way of effective theory building.
- **Skinner, B.F. (1959). *Cumulative Record*, pp 354-355**

Skinner and the Neurosciences

- There is a tendency to [ ] insist on *compensating advantages.*
- It is argued that the solidity of the nervous system [can oppose] psychic fictions [better] than a purely behavioral theory.
- It is also thought to be a necessary intellectual crutch.
- Many people cannot think of the origination of an act without thinking of a motor center, or of learning without thinking of changes in synaptic resistance, or contemplate a derangement of behavior without thinking of damaged tissue.
- In any event an independent theory of behavior is not only possible, it is highly desirable, and such a theory is in no sense opposed to physiological speculation or research.

- **Skinner, B.F. (1959). *Cumulative Record*, pp 354-355**

Skinner and the Neurosciences

- We must wait to see what learning processes the physiologist will eventually discover through direct observation, rather than through inferences; meanwhile, the contingencies permit a useful and important distinction.
- Skinner, B.F. (1974) *About Behaviorism*, (pp 66-67)

Skinner and the Neurosciences

- The nervous system is much less accessible than behavior and environment, and the difference takes its toll.
- We know some of the processes which affect large blocks of behavior
- but we are still far short of knowing precisely what is happening when, say, a child learns to call an object by its name
- as we are still far short of making changes in the nervous system as a result of which a child will do these things.

Skinner, B.F. (1974) *About Behaviorism*, (pp.213-214)

Skinner and the Neurosciences

1. Eventually we may expect physiology to study events in the human brain and to produce [theories] that would meet behavioral ones

2. [But] hypothetical physiological mechanisms are not acceptable as substitutes for a behavioral theory.

3. [Even more] they may introduce many irrelevant matters and stand in the way of effective theory building.

4. Shortcomings are also accessibility and interpretability

5. There may be *compensating advantages.*

6. An independent theory of behavior is in no sense opposed to physiological speculation or research.

6. To be of use, brain processes have to be visible <u>through direct observation, rather than through inferences</u>;

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Cognitive Neuroscience from a Behavioral Perspective: A Critique of Chasing Ghosts with Geiger Counters

Steven R Faux, The Behavior Analyst 2002

Cognitive science has evolved into **Cognitive Neuroscience**, by embracing a variety of different disciplines

linguistics - Chomsky 1959
philosophy – Fodor 1975
connectionism - Grossberg 1988

And by using sophisticated brain imaging technology PET, MRI, and EEG-MEG, attractive to scientists and producing spectacular color plates that appear to take the reader a step closer to the "black box" of brain operations

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

Critical Points

1) It Produces inferences about unobserved neural mechanisms from overt behavior (Uttal 2001).

2) Many in cognitive neuroscience attempt to give a brain location to those unobserved processes using gross measures.

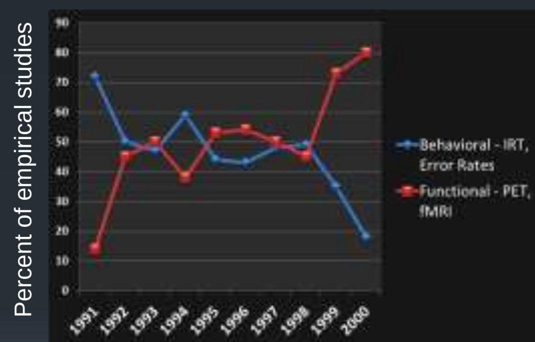
3) Still relies on mentalistic forms of explanation that either explicitly or implicitly appeal to an inner agent, "the ghost in the machine".

4) This paper updates an argument originally made by Skinner (1938/1991,1950,1953,1974) that superimposing unobserved mechanisms upon the brain, results in a "conceptual nervous system" with a great potential to misguide.

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

Major Dependent Variables in Journal of Cognitive Neuroscience



- **Cognitive science** has relied upon reaction time as its primary dependent variable, as indirect measure of mental chronometry (Posner 1986).
- **Cognitive neuroscience** now uses brain-imaging techniques (PET, fMRI, and ERP)

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

Methods in a particular PET scan study (Mellet, Tzourio, Denis, & Mazoyer, 1995)

- 8 subjects participate in three behavioral conditions, baseline, perception, mental imagery
- Mellet et al. presented regional cerebral blood flow (rCBF) results for all 8 individuals from 6 brain regions
- Positive rCBF values indicated brain activation (increased blood flow), and negative values indicated deactivation (decreased blood flow) relative to baseline
- In the "perception minus baseline“ data, primary visual cortex, superior occipital cortex, superior parietal and precuneus are activated consistent across all 8 participants.

Cognitive Neuroscience from a Behavioral Perspective
Steven R Faux, The Behavior Analyst 2002

Critical Points

Deactivation in the superior temporal and inferior frontal cortex. (Why brain regions are deactivated?)

Strong variability In the "imagery minus baseline“ data is seen across participants.

Misleading representation. Color coded data have the potential to mislead unless carefully analyzed.

Lack of consistency. no consistent pattems of anatomical activation would be evident in all volunteers.

Cognitive Interpretation. Despite large individual variability, the authors concluded that mental imagery is associated with activation of the superior occipital cortex.

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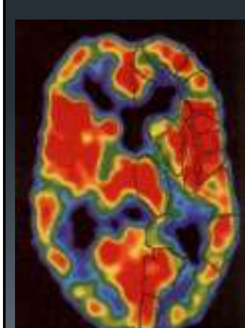
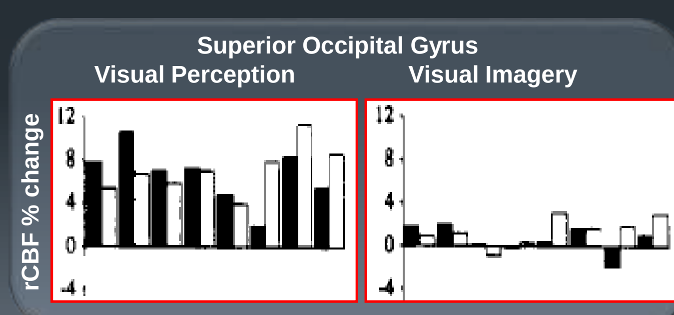
Misleading representation. Color coded data have the potential to mislead unless carefully analyzed. But in many activation areas in superior occipital cortex the same data in histogram form revealed very small rCBF values. Perceptually significant color differences in PET scan graphs do not necessarily equal physiologically important differences.





Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

This paper is not intended to be a general statement against the study of brain-behavior relations. Instead, this is a proposal that science progresses best when physical brain measurements are tied to overt behaviors.
As Skinner (1938/1991) stated, "Before ... [a neurological] fact may be shown to account for a fact of behavior, both must be quantitatively described and shown to correspond in all their properties".

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

Experimental Design: the Subtraction method

1. Identify a treatment task involving the cognitive process, *P.*
2. Identify a baseline task that is identical to the treatment task but does not involve the cognitive process, *P.*
3. Collect separate brain scans during the baseline and treatment tasks. Compute an average scan for each individual within each task.
4. Subtract average baseline scan results from average treatment scan results. Find brain regions with averages that are statistically different from zero.
5. Conclude that statistically significant brain regions account for cognitive process, *P.*

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Criticism 1: Cognitive Atoms Have Not Been Identified

It seems impossible that a treatment task could ever be designed differing from a baseline task by only a single brain operation. The *pure insertion problem* (Sartori & Umilta, 2000). "Even simple tasks, hypothesized to index selectively particolar aspects of language processing, often do not tap only one component of language processing but encompass a complex chain of processing" (Bavelier et al., 1997).
Like Smith (1997) states in a spatial working memory task: "Spatial working memory can be decomposed into a pure storage component (a spatial buffer) and a rehearsal component, ... the latter involv[ing] selective attention“. One must wonder how useful it is to break one vague construct into three vague constructs

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Criticism 2: Vague Cognitive Labels Do Not Elucidate Vague Anatomy

Cognitive neuroscientists have failed to justify why unobserved cognitive constructs make useful labels for particolar brain regions. While PET and fMRI reports assume that their data reveal brain areas that produce some *cognition,* PET or fMRI changes can exist simply because treatment and baseline involve different *behaviors* (Uttal, 2001).
Spatial Resolution: PET and tMRI can take us from not knowing what is happening in the whole brain to not knowing what is happening in some particolar gyrus. Brain-imaging procedures are sensitive only to large regional changes in activation, involving perhaps millions of neurons, while missing smaller regions of activation (Pitzpatrick 1999). Neurological significance is not necessarily that which is "large."

Cognitive Neuroscience from a Behavioral Perspective Steven R Faux, The Behavior Analyst 2002

Criticism 2: Vague Cognitive Labels Do Not Elucidate Vague Anatomy

PET and fMRI are not direct measures of neural activity, only blood flow (rCBF). It is an assumption that rCBF (a slow process of several seconds after a stimulus) reflects the most relevant neural regions of a behavior. It is a little frightening when one strings together the assumptions made in PET studies. PET investigators assume that increased gamma radiation indexes increased rCBF, which presumably indexes neural activity, which presumably indexes cognitive processing.

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Criticism 3: The "Cognitive" in Cognitive Neuroscience is Not Tested

Cognitive constructs are not directly tested in the subtraction method, because no brain-imaging result could ever refute a cognitive theory.
Instead, cognitive constructs are only "mapped."
There is no good reason to make cognitive terminology the de facto language of the neuroscience of complex behavior.
There is no indication of how one can go from brain maps to controlling or manipulating behavioral or neurologica! variables.
The goal of the research program appears to be to map and label the brain.

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Homunculus Resurrected: the Central Executive

Dennett (1991) has argued that a pervasive flaw of cognitive neuroscience models is that they "still presuppose that somewhere, conveniently hidden in the obscure 'center' of the mind/brain, there is a Cartesian Theater, a place where 'it all comes together‘ and consciousness happens“, a "central executive" (Baddeley, 1995), "willed action" (Badgaiyan, 2000), or "supervisory attentional systems" (Bayliss, 2000).

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Problem of Intrinsic Variability and Averaging

Brain-imaging experiments are not analyzed at the individual level, data are grouped and individual variability is obscured. Cognitive neuroscience accepts that large variation is intrinsic to the operations of the brain, and that experimental control of individual variation is not possible. As Sidman (1960) has argued, "Acceptance of variability as unavoidable or, in some sense, as representative of the 'real world' is a philosophy that leads to the ignoring of relevant factors" .

Cognitive Neuroscience from a Behavioral Perspective

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The Problem of Intrinsic Variability and Averaging

Unfortunately, in most PET, fMRI, and ERP studies total variability is mostly swept under the rug. Multiple brain-imaging measurements over time are averaged (a process called signal averaging) within an individual to determine the presence or absence of a neural response. Individual averages are then grouped to create grand averages. Individual results are rarely displayed, and brain maps are never displayed with error bars. Both intraindividual differences and interindividual differences are obscured (Raichle, 1996). With so much variation, it is reasonable to ask how well averages account for individual results.

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

The Problem of Statistical Tests

In PET and fMRI, thousands of measurements make up a single brain image. Further, a single brain scan will produce multiple brain slices several millimeters apart. Standard multivariate statistics are not possible because there are many more measurements than there are participants. Typically, studies use univariate statistical tests on each of the thousands of voxels (pixels) in a PET image.

Not only does Type I error inflate due to multiple correlated tests, but statistical significance, accurate or not, may have little direct relation to neurological significance.

Cognitive Neuroscience from a Behavioral Perspective

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The Problem of Replication

Given these problems, no surprise that replication is difficult in many brain-imaging studies of cognitive neuroscience. Intergroup replication, intrasubject replication, and intersubject replication are rare. The problem of replication is addressed by Cabeza (1997, 2000) reviewing 73 PET studies. Sixteen of those studies were categorized under the topic of attention, but used very different behavioral tasks. Even so, they concluded that attention "generally engages frontal and parietal cortices". Even when similar tasks were used the variability of findings was striking. For example, five of the studies used comparable versions of the Stroop task (color naming), but no single region of brain activation was common to all five studies.

Cognitive Neuroscience from a Behavioral Perspective

Steven R Faux, The Behavior Analyst 2002

Conclusions

Cognitive neuroscience is gaining in popularity because of its attempt to localize traditional cognitive constructs in neuroanatomy. However, too many proposed cognitive mechanisms are vague, unnecessarily complex, and amount to little more than inferred guesswork. Unobservable bebaviors of the mind, like volition, central executive function, and mental imagery, do not enhance understanding of empirical brain operations and such terminology obscures more than clarifies. The subtraction method creates significant problems, and brain images are incapable of refuting cognitive constructs. Instead, cognitive constructs are being used as labels to name the proposed functions of the cortex.

Relating Behavior and Neuroscience: Introduction and Synopsis Timberlake W JEAB 2005

Skinner and the Neuroscience

B. F. Skinner, in a chapter on ''Behavior and the Nervous System'' in his seminal work, The Behavior of Organisms (1938, pp. 418–432), expressed both strong interest in and considerable concern about relating behavior and what he termed ''neurology.'' On the positive side, he subscribed to a unified reductionist science: ''One of the objectives of science is presumably the statement of all knowledge in a single language.''
Skinner spoke strongly against ''proceeding from a behavioral fact to its neural correlates instead of validating the fact as such.'' His goal was first, to establish an independent science of behavior ( ) and then, to bridge the gap between behavior and neurobiology by a comprehensive integration.

Relating Behavior and Neuroscience: Introduction and Synopsis Timberlake W JEAB 2005

Skinner and the Neuroscience

Thirty-six years later in a chapter on ''What is Inside the Skin?'' in About Behaviorism (1974), Skinner again rejected attributing the cause of a behavior to a single neurobiological entity, whether it was a synapse, an anatomical structure, an emotion, or a motivation.
The possible exception he noted was appealing to neural events to fill inevitable gaps in an operant account. For example, because behavioral accounts of reinforcement are ''necessarily historical,'' they leave gaps between events that might be filled in by neural processes related to memory.

Relating Behavior and Neuroscience: Introduction and Synopsis

Timberlake W JEAB 2005

Skinner and the Neuroscience

In short, there is considerable evidence for the existence of independent sciences of behavior and of neurobiology, and there is research that combines aspects of both.

What is missing is the broad conceptual integration that Skinner began pointing toward in 1938.

The potential for integration will be greater as experimenters use causal manipulations and analyses that consider both neuroscience and behavior.

Relating Behavior and Neuroscience: Introduction and Synopsis

Timberlake W JEAB 2005

Bridging Levels of Analysis

Warning against skipping levels of analysis when invoking causal connections (Bechtel). Applied to reinforcement, his warning calls attention to the multiple levels of mechanism that are omitted when we attribute the reinforcement of lever pressing to, say, GABA release. Such a correlation, even if present, does not specify the mechanisms that connect the multiple levels of organization separating GABA release and lever pressing.

Aa an example consider accelerating a car. At the level of the driver it involves pressing down on the gas pedal. At the level of production of energy, the cause is the igniting of gasoline under pressure. In between are multiple events. The mechanisms differ at each level, and they all are necessary for the car to accelerate. We cannot expect links between behavior and neurobiology to be any less complex.

Relating Behavior and Neuroscience: Introduction and Synopsis

Timberlake W JEAB 2005

Drug effects on Operant Behavior

1) Facilitation of Operant **Extinction** by chlordiazepoxide, Leslie, JEAB 2005. Extinction was facilitated by drug injections of chlordiazepoxide (**GABA**ergic drug).

2) Dopamine in Reinforcement: Changes in reinforcement sensitivity induced by D1-type and nonselective dopamine receptor agonists, but not D2-type (Bratcher, JEAB 2005).

3) Morphine: General disruption of stimulus control? Ward, JEAB 2005.

Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

Schlund MW, Cataldo MF, JEAB 2005

Magnetic resonance imaging (MRI) can study a variety of brain-behavior relations:
(a) the size and position of discrete brain structures (i.e., structural MRI),
(b) changes in activation of specific brain regions under differing stimulus and/or performance conditions (i.e., functional MRI or fMRI),
(c) certain biochemical changes related to neurotransmitters (MR spectroscopy)
(d) the location and direction of neural activity along the fiber tracts that connect brain structures and regions (fiber tract mapping).

Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

Schlund MW, Cataldo MF, JEAB 2005

Neuroimaging and the Experimental Analysis of Behavior (EAB) can make at least two important contributions to the advancement of behavioral science.

1) A better understanding of the neurobiology of operant learning. Studies on the relation between operant learning and brain function have never been considered an unimportant or unnecessary pursuit, just difficult. Indeed, these relations are particularly important to understanding learning deficits as well as understanding the action of different therapeutic approaches, such as drug versus behavior therapy.

Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

Schlund MW, Cataldo MF, JEAB 2005

2) The degree of precision that the EAB can offer fMRI research. Despite its rapid development, fMRI research is not without its own unique methodological concerns, some of which stem from a lack of precision in arranging stimulus conditions or response repertoires. Thus the rigor in arranging environmental conditions to control behavior, typical of EAB, can make a significant contribution to imaging research on operant learning, particularly on discriminative stimulus control of human behavior.

Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

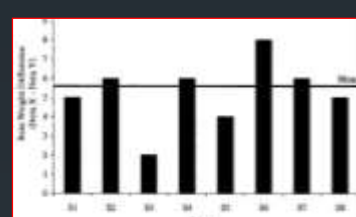
Schlund MW, Cataldo MF, JEAB 2005

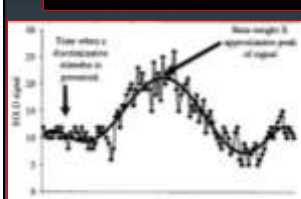
For example, Tremblay and Schultz (2000a) investigated responses of neurons in the caudate to different types of discriminative stimuli. Reinforcement contingencies were used to bring responding under the control of three different discriminative stimuli, each correlated with a different contingency: respond-reinforcer, no respond-reinforcer, and respond-no reinforcer. Orbitofrontal and caudate neural activity was consistently greater during the presentation of discriminative stimuli correlated with reinforcement.

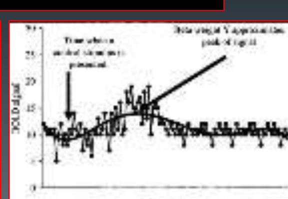
Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

Schlund MW, Cataldo MF, JEAB 2005

Activation correlated with differences in control of discriminative stimuli by learning histories with programmed contingencies







Integrating Functional Neuroimaging and Human Operant Research: Brain Activation and Discriminative Stimuli

Schlund MW, Cataldo MF, JEAB 2005

Two topics that may surface at some point within the EAB:
1) The place of human operant research in fMRI research: human operant research methods can be coupled successfully with fMRI designs in ways that can contribute to neuroscience research on operant learning processes.
2) Regarding contrast, the "cognitive subtraction method" compares activation from an experimental condition containing both a process of interest (X) and a second processe (Y) with a control condition containing only the second process (Y).
An alternative approach is to view results of contrasts as a difference between controlling variables rather than as a difference between additive, hypothetical processes.

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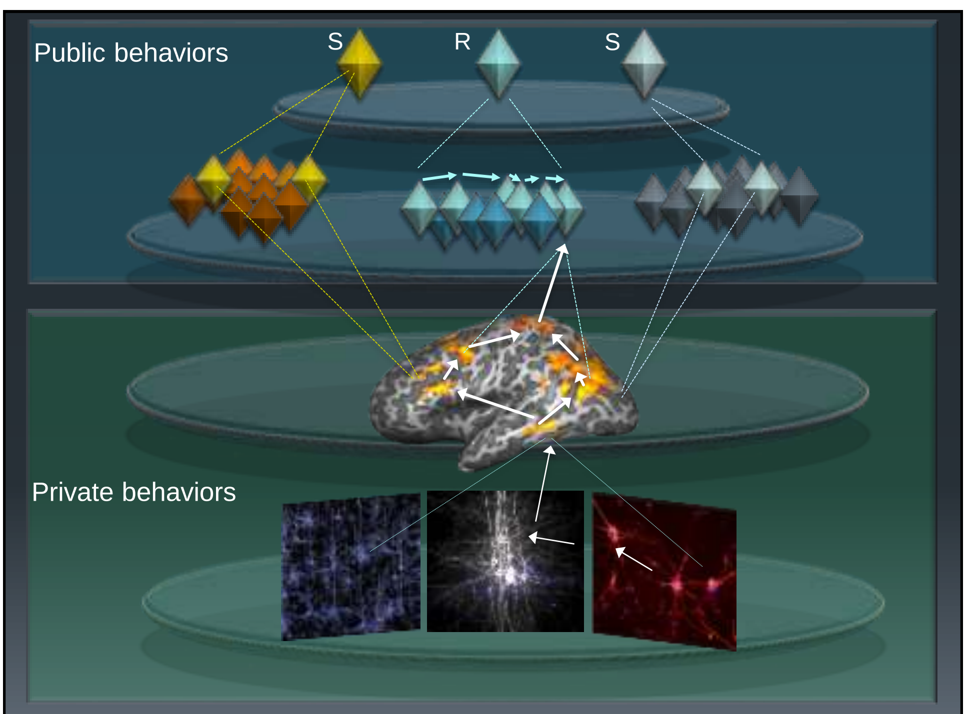
Behaviorism and Neurosciences

- The Science of Behavior has produced a conceptually sistematic analysis of public behaviors, able to explain them and to device high efficacy procedures to induce their modification
- All of this has been done without significant contributions from the Neurosciences
- What can Applied Behavior Analysis gain by sharing information with the Neurosciences?
- Is a constructive interaction between the two disciplines really possible?



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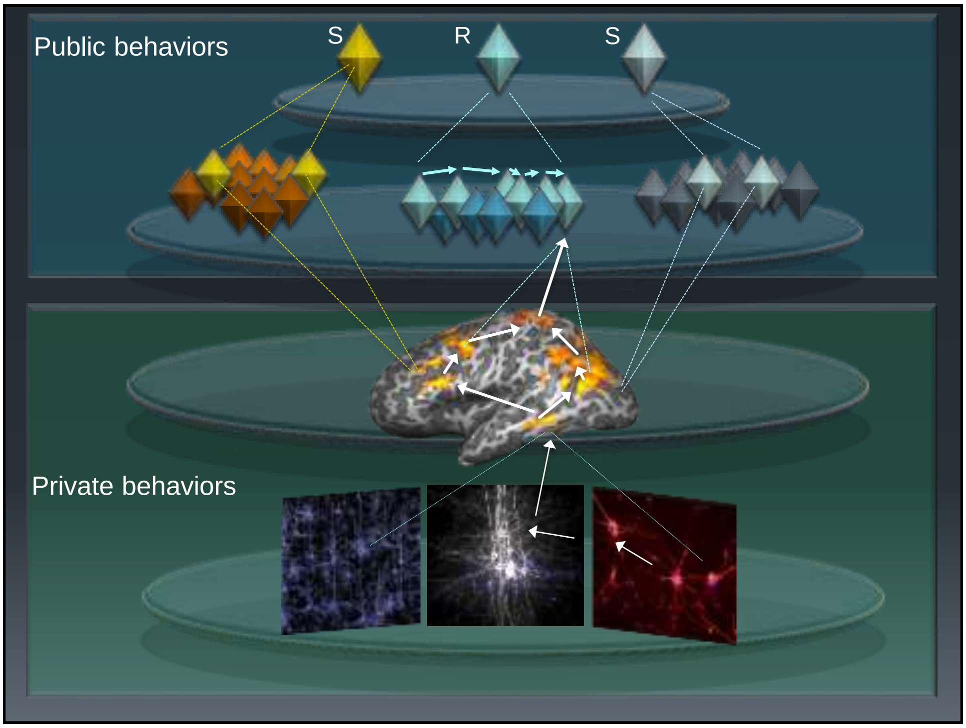
Behaviorism and Neurosciences

- Making private events public can increase the complexity of the observed responses up to a point where our understanding and the conceptual systematicity are difficult to preserve
- Increasing the complexity of observed behavior can produce a new level of understanding
- And new clinical approaches to diseases (ASD)



Outline

- Skinner and the Neurosciences
- Why to integrate Neurosciences into Behaviorism
- Private behaviors made public - increased complexity
- The procedures to study behavior in the brain
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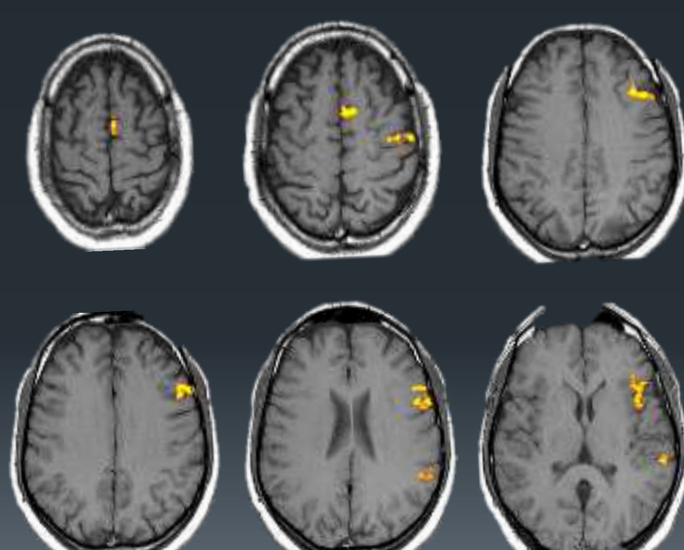
Private behaviors made public
The increased complexity

- The complexity of behavior depends on the level of observation we chose to take. Possible levels of observation of “private” events in the brain are:
- The points of the brain on neuroimages
- The cortical surface and/or its subdivisions
- The “unitary elements” of brain events, the neuronal columns
- The single neurons
- The single synapses

Brain pattern of activity in a verbal task identified by fMRI



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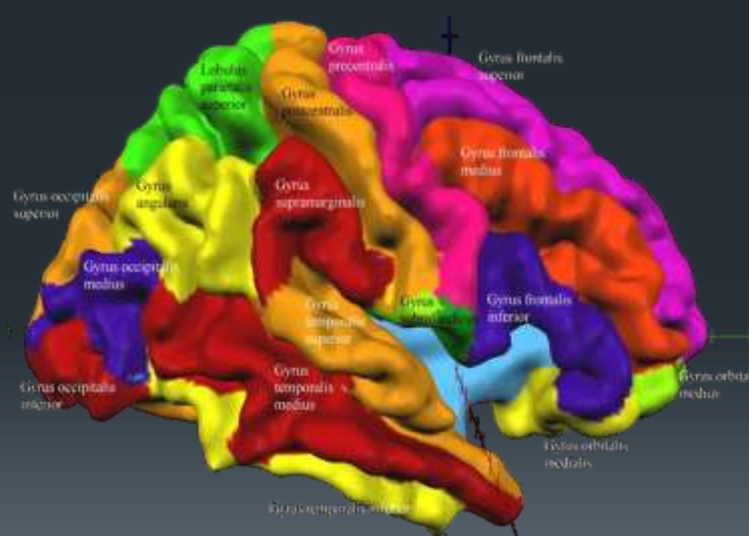
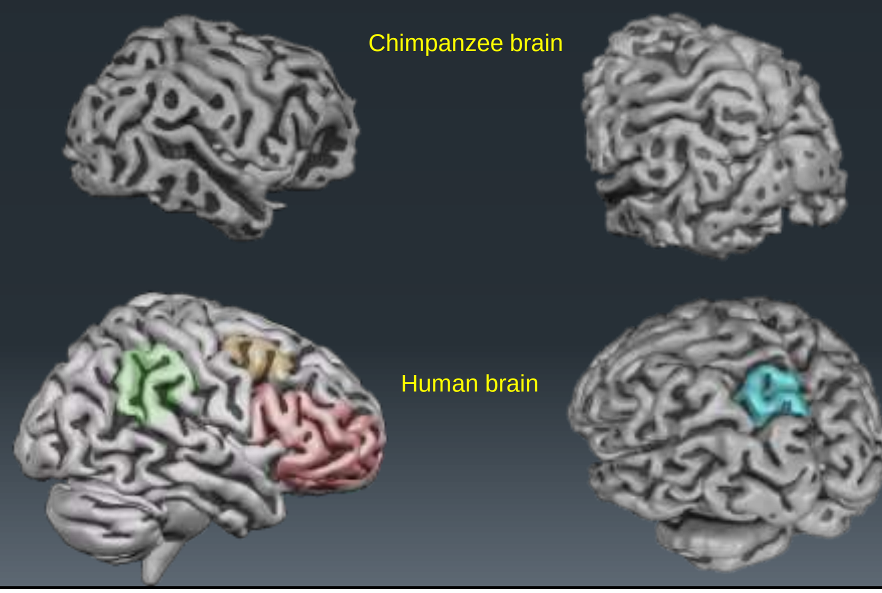
Neuroimaging of Brain cortex

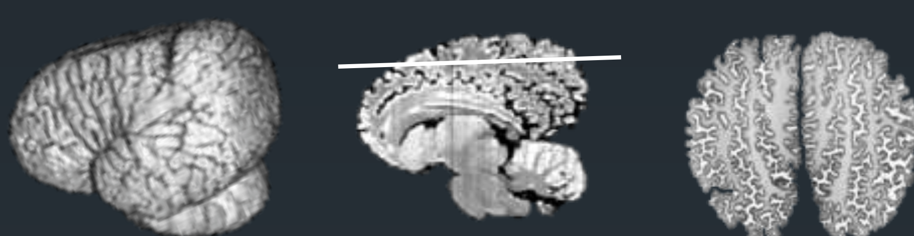
A brain atlas from a single volunteer



Regionally specific changes parallel the appearance of peculiar abilities in different species

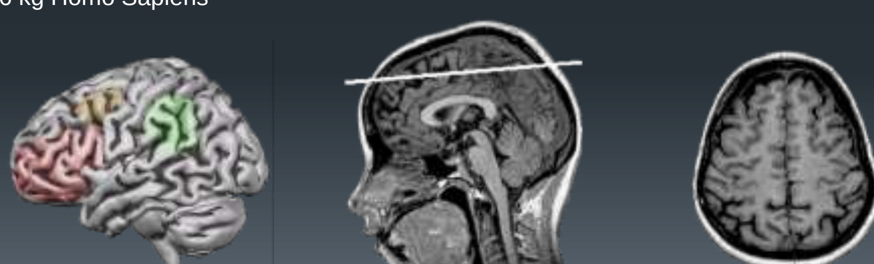


The incredible brain of Cetacea



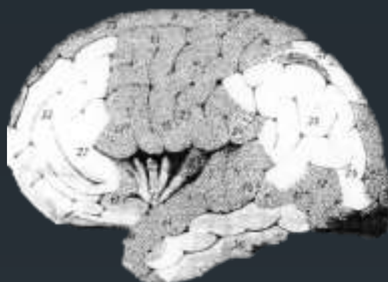
1.8 Kg Dolphin – 5.5 kg Orcinus Orca

1.6 kg Homo Sapiens

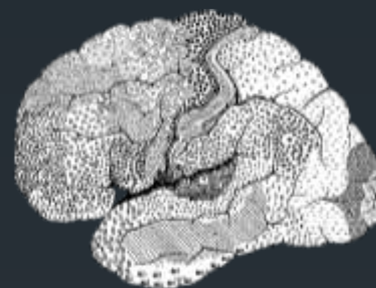


The Brain Surface and the need for landmarks

Cytoarchitectonic and behavioral dissection of brain cortex



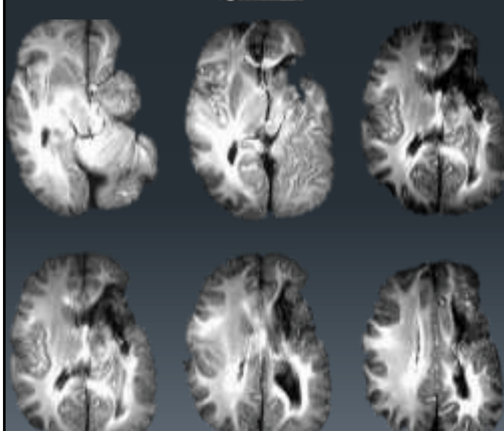
Flechsig (1904)



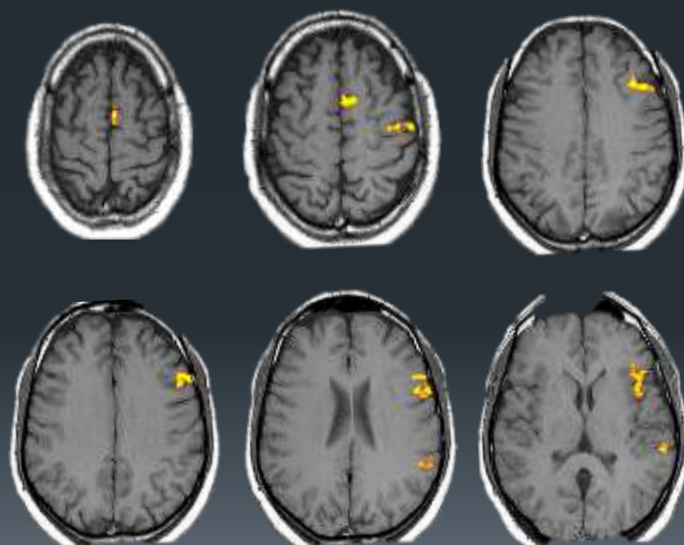
Broadmann (1909)

Von Economo and Koskinas (1925)
Galaburda and Sanides (1980)
Morosan et al. (2001)

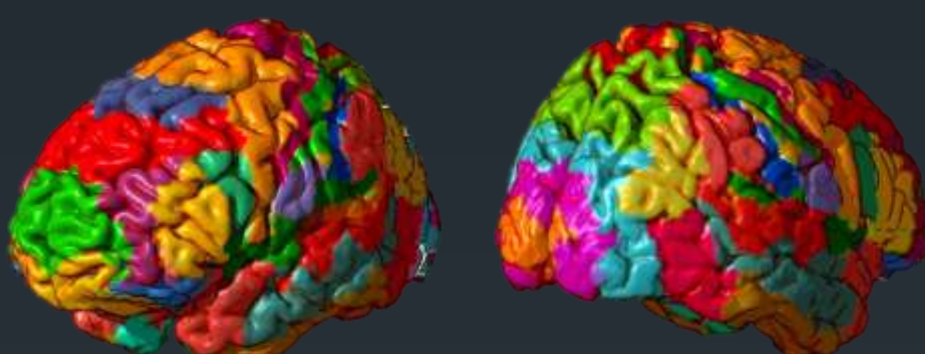
In search of a landmark



Brain pattern of activity in a verbal task identified by fMRI



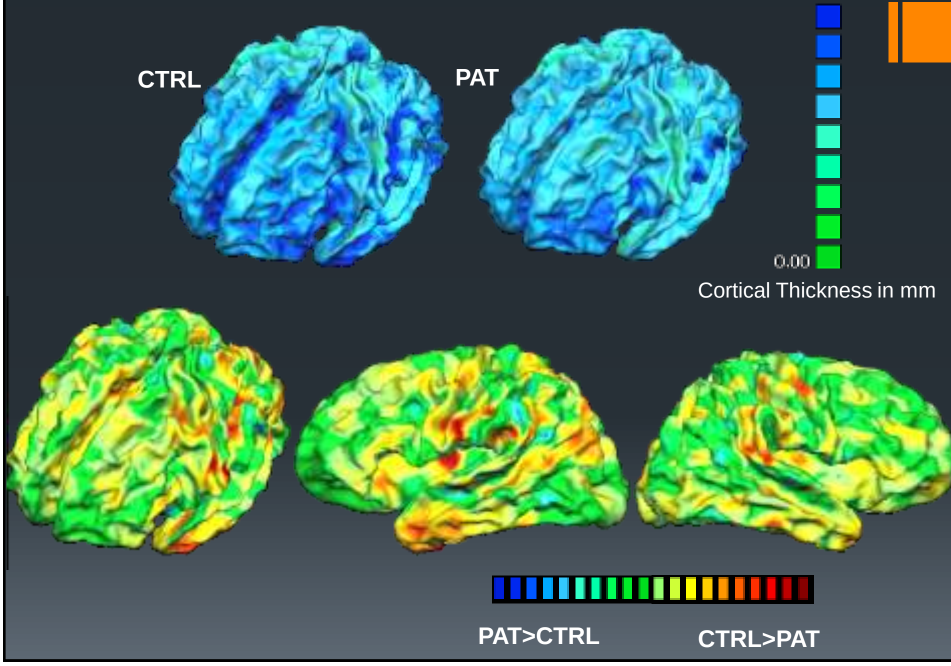
A behavioral dissection of brain cortex



Mark Dow, Brain Development Lab, University of Oregon

Neuroscience define a “Brain Area” as a unit of brain cortex having homogeneous cortical architecture and emitting a topographical response class, but the topographical similarity required is very generic (moving any part of the body, emitting any word etc.)

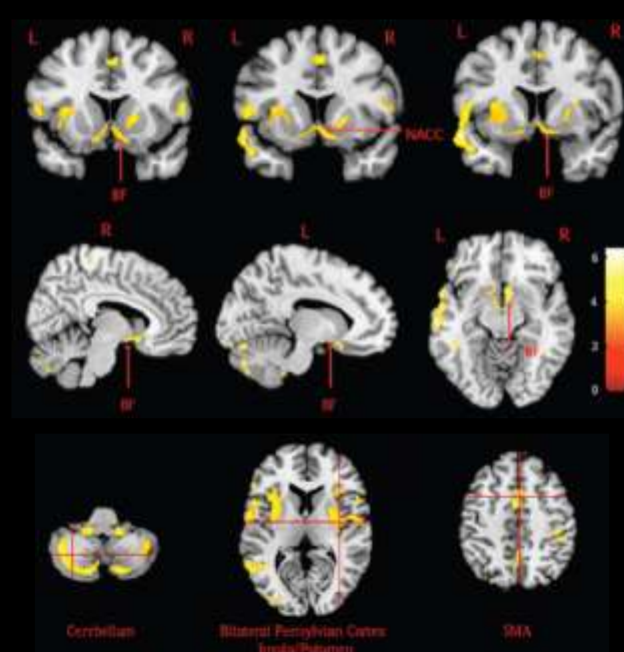
The Autistic Brain

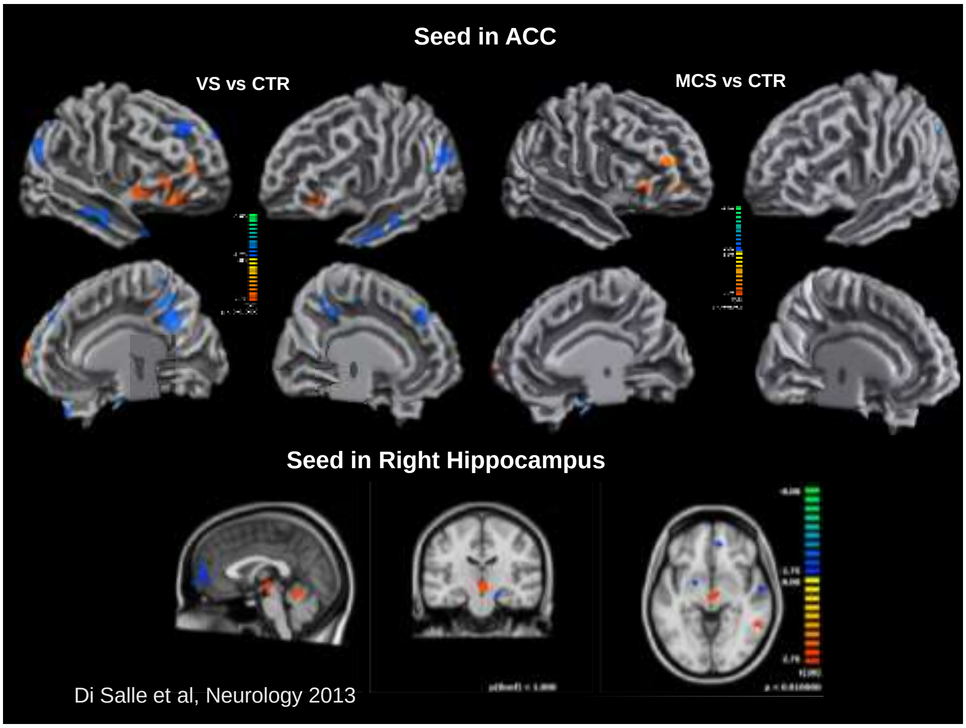


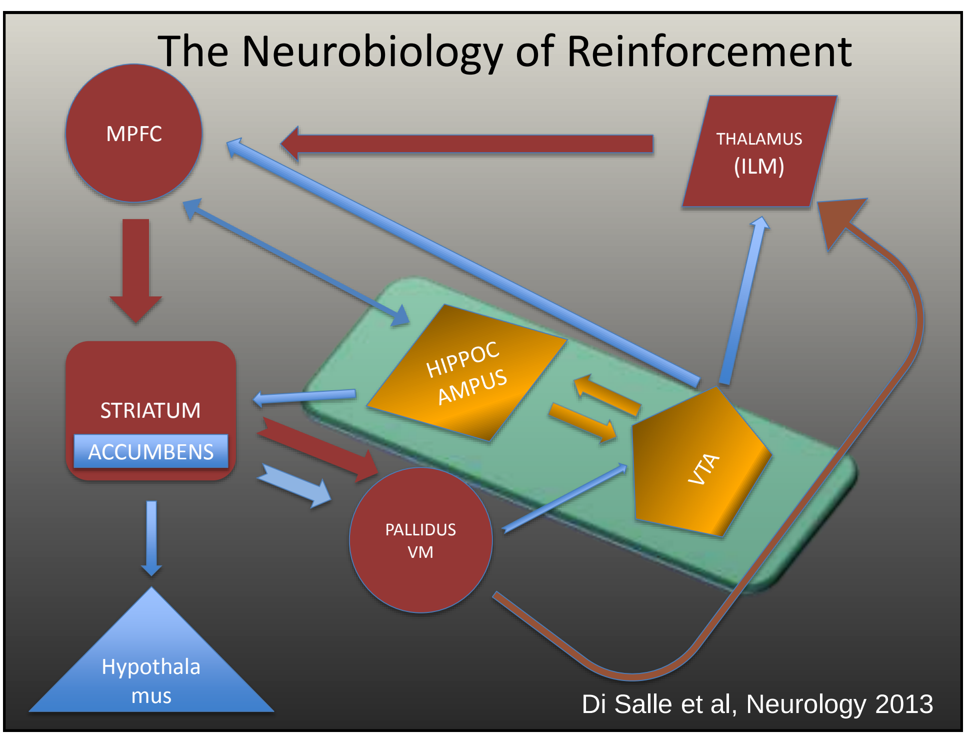
The Autistic Brain

Di Salle et al
Neuroradiology 2011

Ithe mesolimbic system

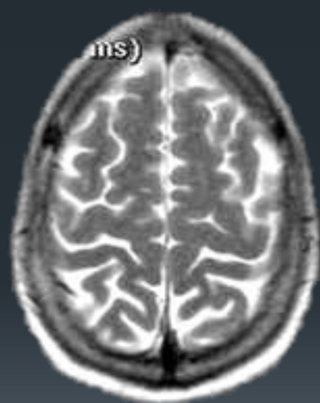



Seed in ACC
VS vs CTR
MCS vs CTR
Seed in Right Hippocampus
Di Salle et al, Neurology 2013

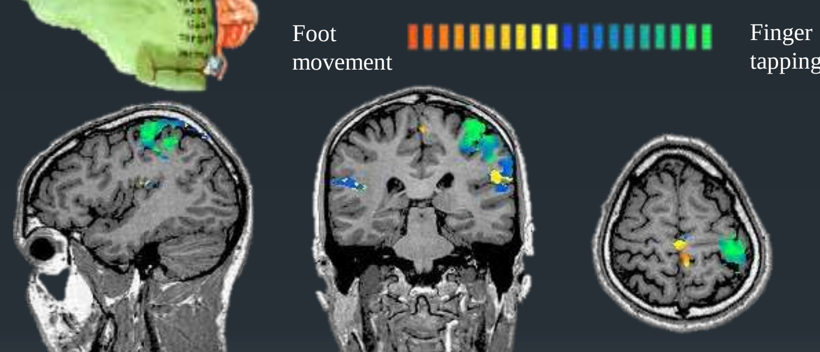

The Neurobiology of Reinforcement
MPFC
THALAMUS
(ILM)
HIPPOC
AMPUS
VTA
STRIATUM
ACCUMBENS
PALLIDUS
VM
Hypothala
mus
Di Salle et al, Neurology 2013

The landmarks on the surface of the Brain

Further subdivisions on a single gyrus

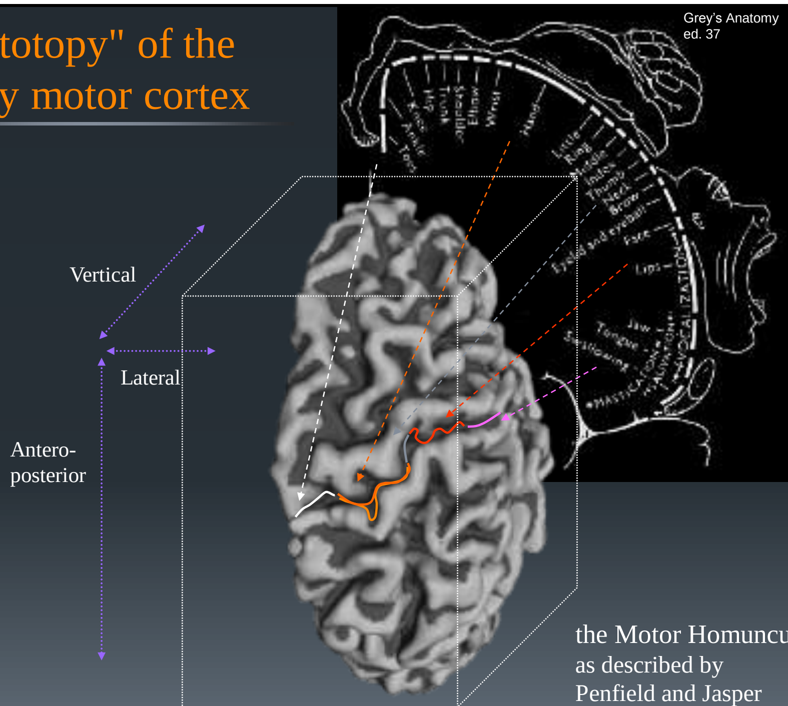


Motor cortex: Penfield's homunculus



More adherent to the concept of a topographical response class are the subdivisions of brain areas emitting more topographically homogeneous behaviors, like the hand, or the foot, or the face motor areas.

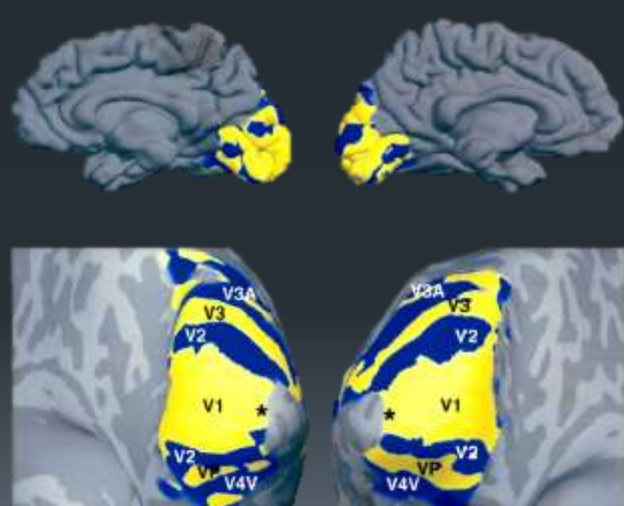
"Somatotopy" of the primary motor cortex



the Motor Homunculus as described by Penfield and Jasper

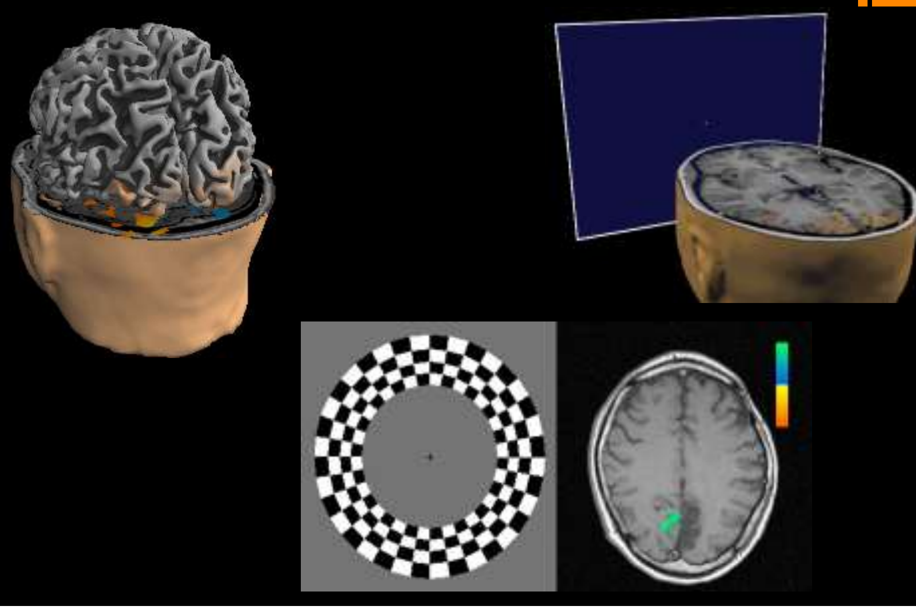
Borders of multiple visual areas in fMRI

Multiple neighbouring areas to respond to visual stimuli: Functional modularity to enhance the efficiency of responding?

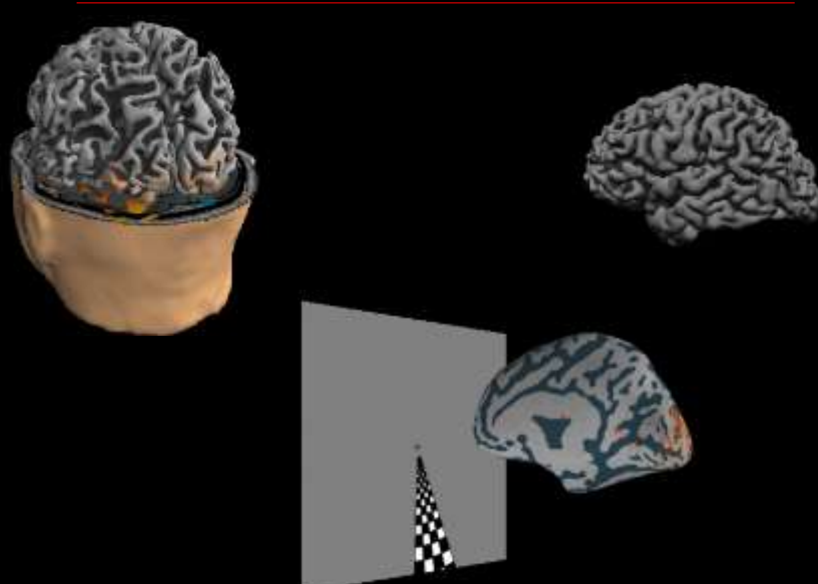


Tootell et al. PNAS 1998

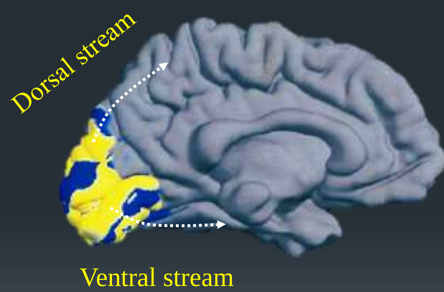
Multiple neighbouring visual areas to enhance the efficiency of responding?

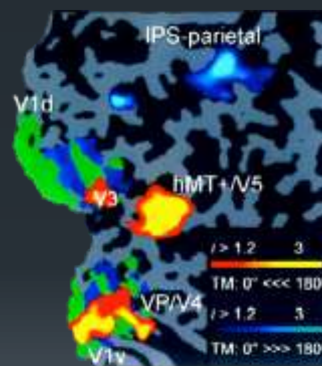


Multiple neighbouring visual areas to enhance the efficiency of responding?



Hierarchical responses to visual stimuli in ordered streams of processing

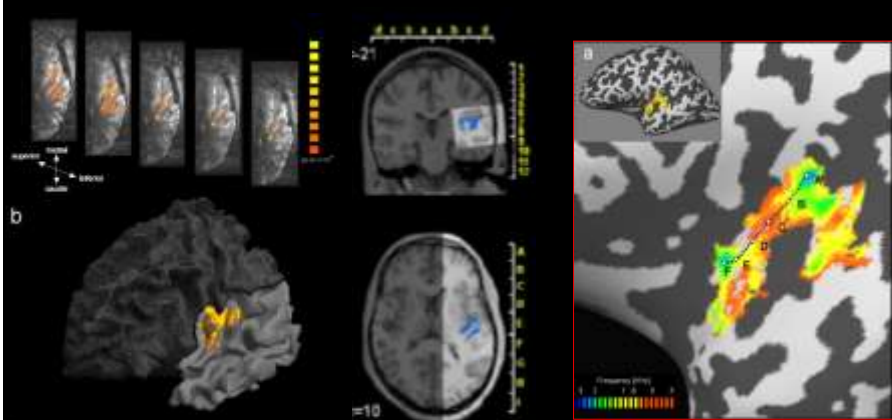




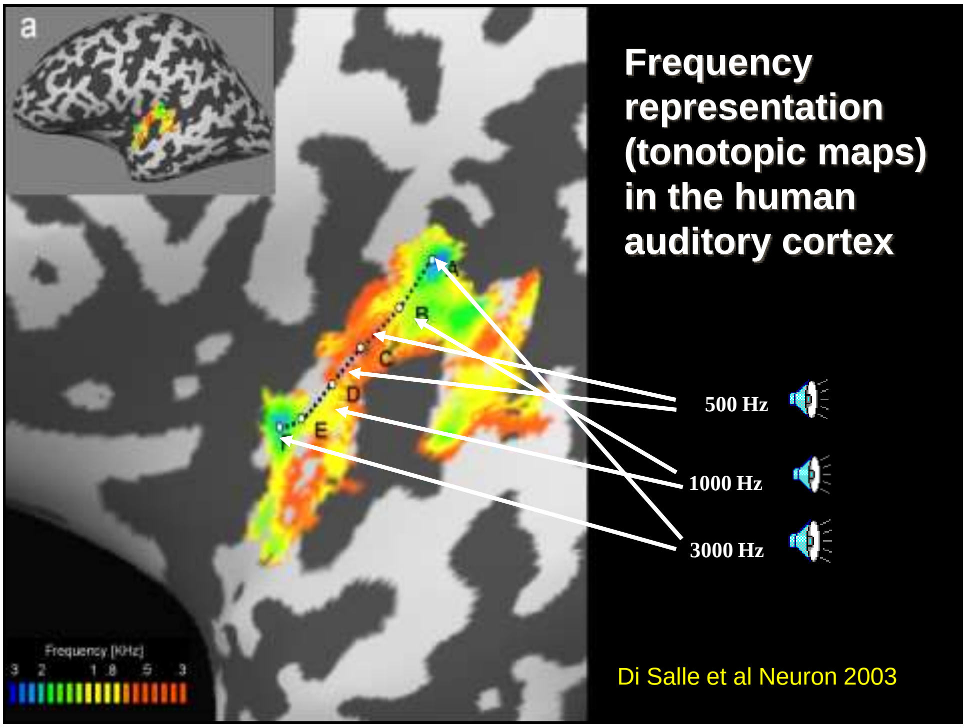
Muckli et al. Neuroimage 2002

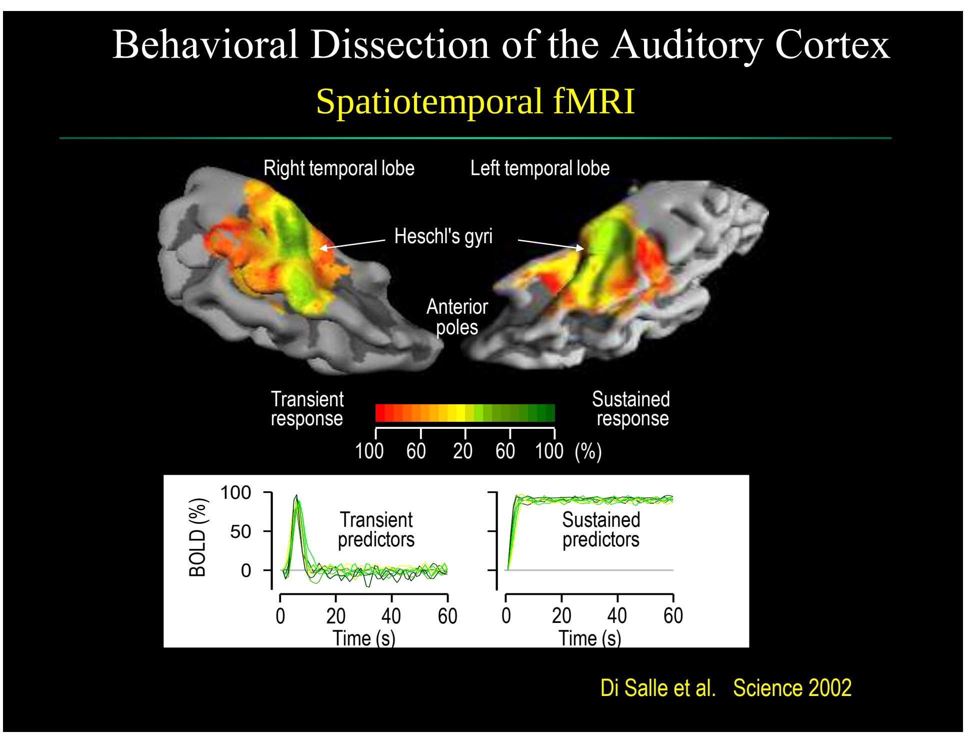
Behavioral Dissection of the Auditory Cortex

High field fMRI: 7T of the auditory system



Di Salle et al. Neuron 2003


a
Frequency representation (tonotopic maps) in the human auditory cortex
A
B
C
D
E
500 Hz
1000 Hz
3000 Hz
Frequency (KHz)
Di Salle et al Neuron 2003


Behavioral Dissection of the Auditory Cortex
Spatiotemporal fMRI
Right temporal lobe
Left temporal lobe
Heschl's gyri
Anterior poles
Transient response
Sustained response
100 60 20 60 100 (%)
BOLD (%)
100
50
0
Transient predictors
Sustained predictors
0 20 40 60
Time (s)
0 20 40 60
Time (s)
Di Salle et al. Science 2002

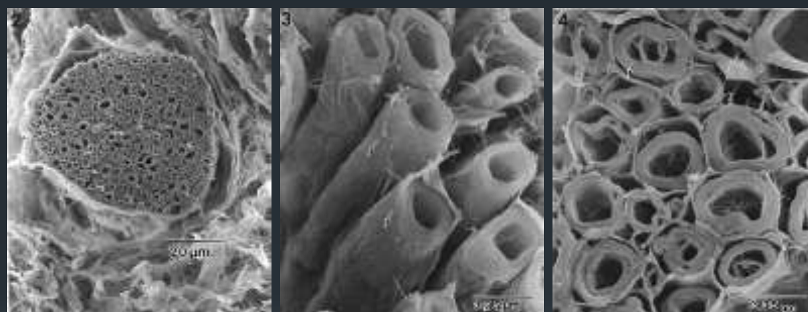
Behavioral specialization of brain areas

- Broadmann cytoarchitectonic areas reflect a functional specialization of brain areas
- Each area is selectively reached by special categories of stimuli and emits specific responses
- The selective distribution of stimuli in the brain is reached through a specific distribution, mainly governed by phylogenetic factors, of white matter connection fibers
- The specificity of responding is mainly governed by the nature of the stimuli that reach each area of the brain cortex

Connectivity Analysis

- **Anatomical Connectivity**
- **Functional Connectivity**
- **Effective Connectivity**

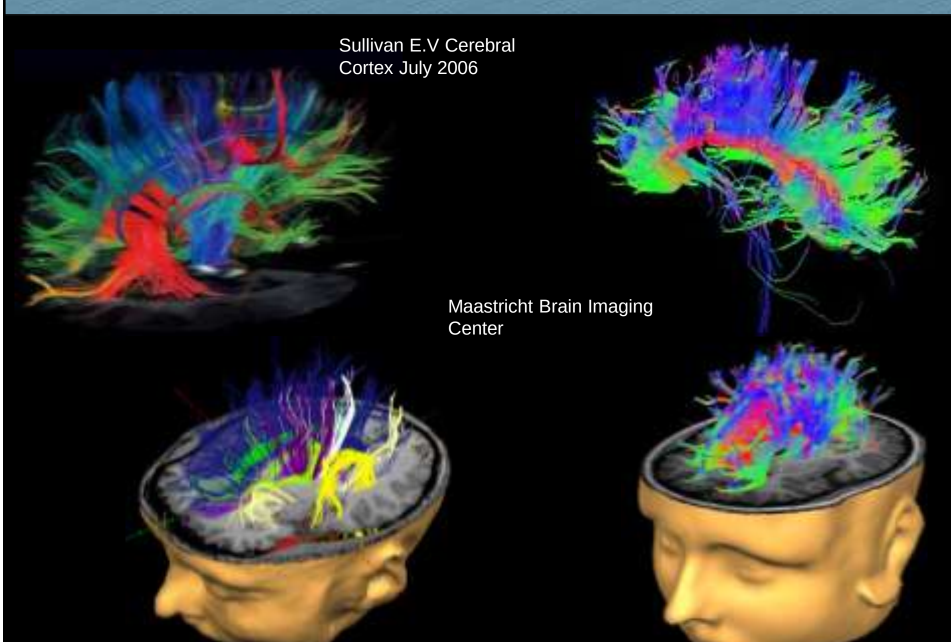
Intracellular diffusion is principal source in Diffusion Imaging

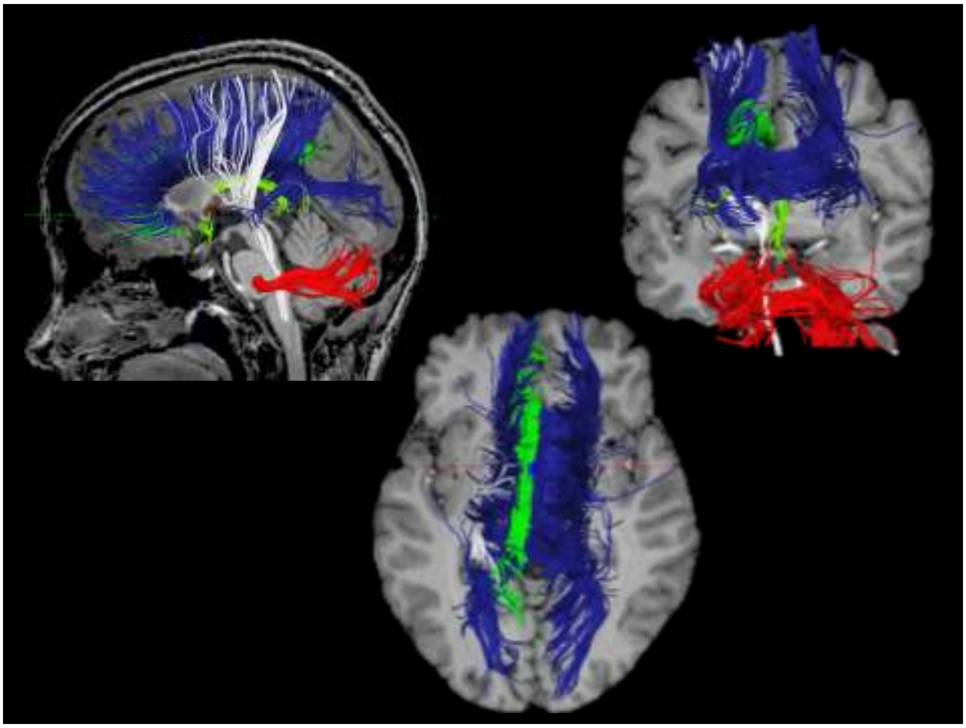


80% of space is taken up by intracellular, 20% extracellular

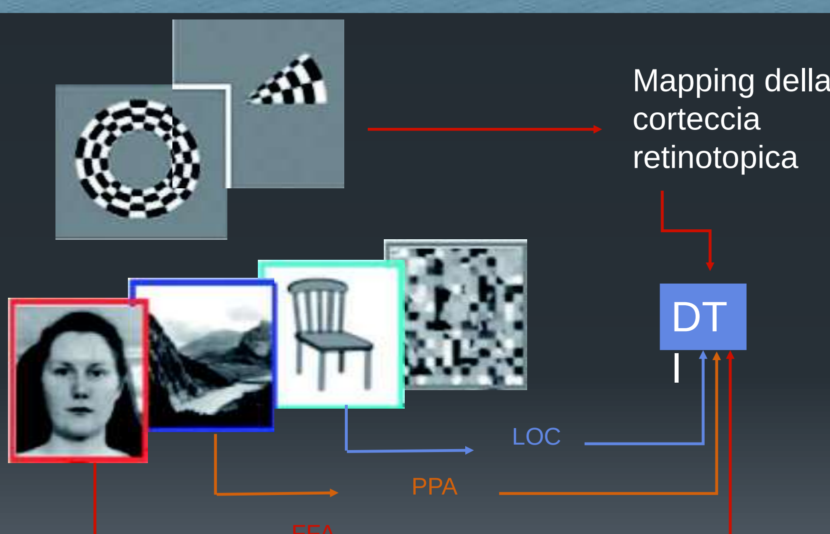
Most of the signal originates from *restricted water diffusion*

Fiber Tracking



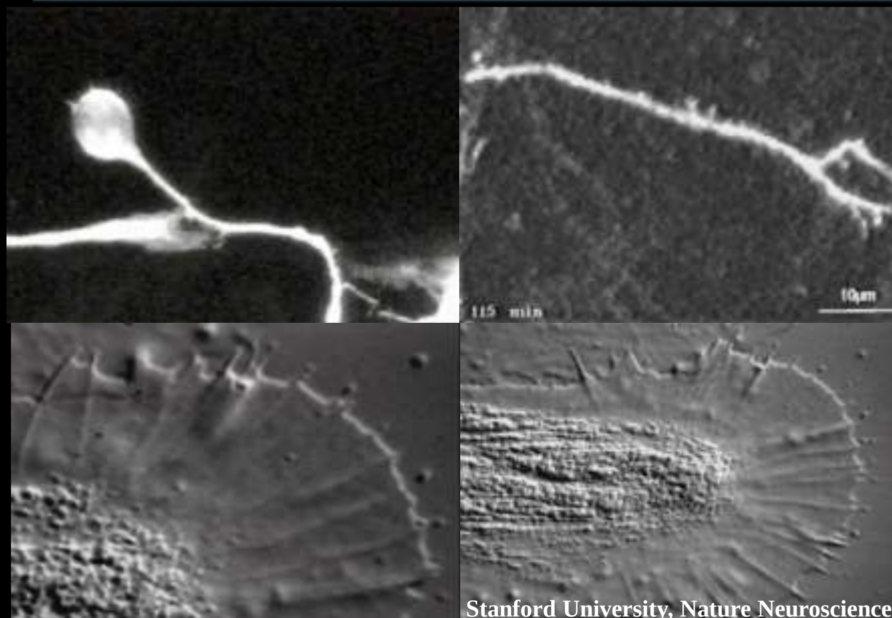


Connectivity regulates the discriminative value of stimuli

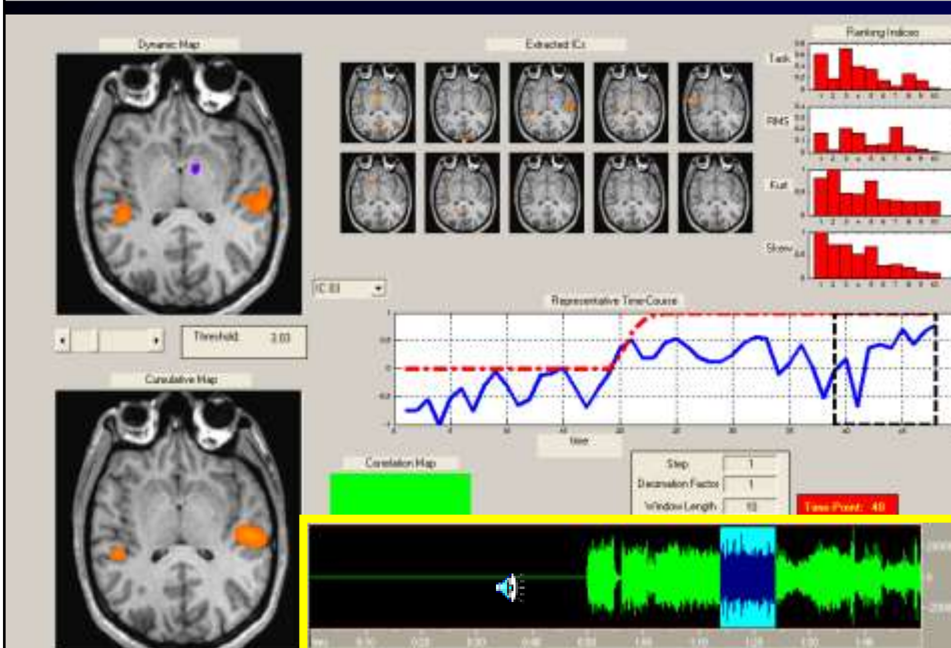


Anatomical correlates of brain functional organization Dae-Shik Kim - MRI 2006

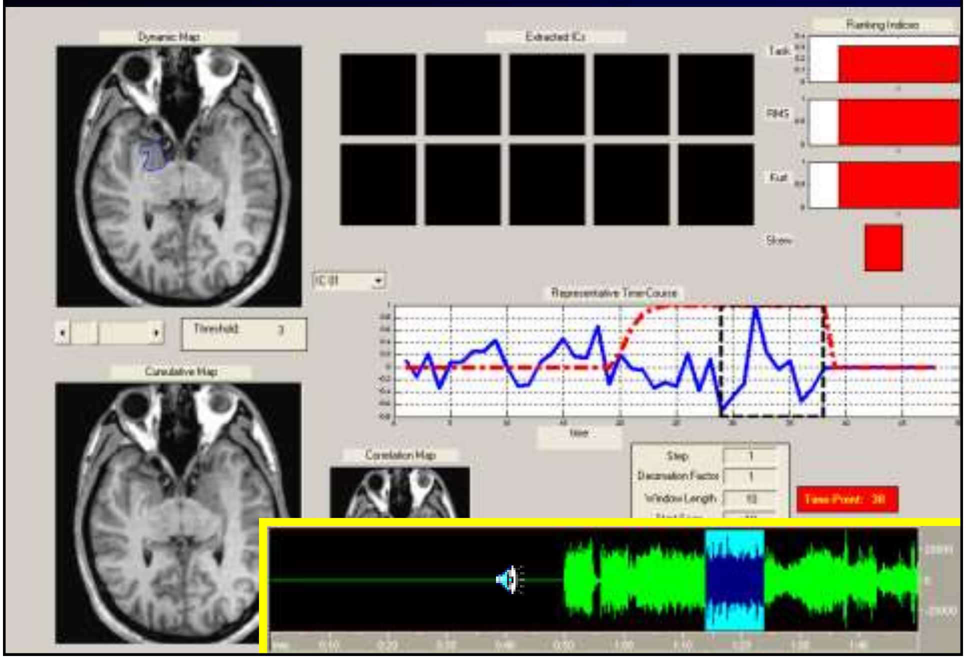
From Brain Activation to Connectivity



ICA in real-time fMRI during music hearing



ICA in real-time fMRI during music hearing

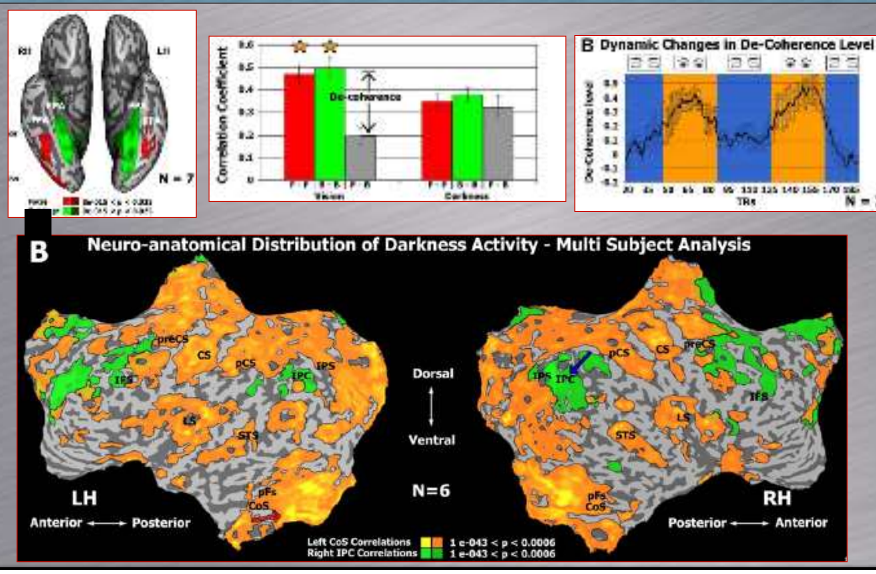


Independent component model of the default-mode brain function: Assessing the impact of active thinking

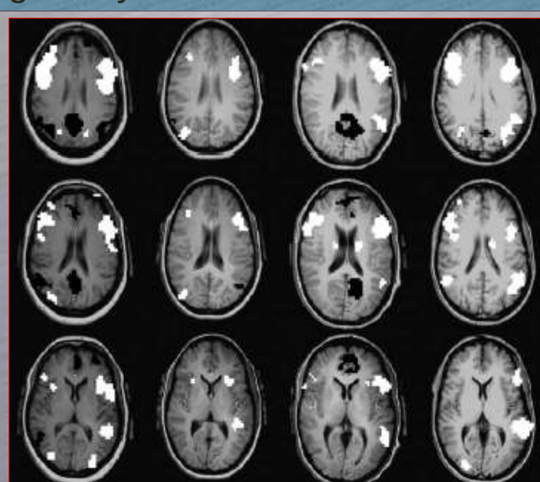
Di Salle F et al, BRB 2006

Widespread functional connectivity and fMRI fluctuations in human visual cortex in the absence of visual stimulation

Nir Y, Malach R, Neuroimage 2006



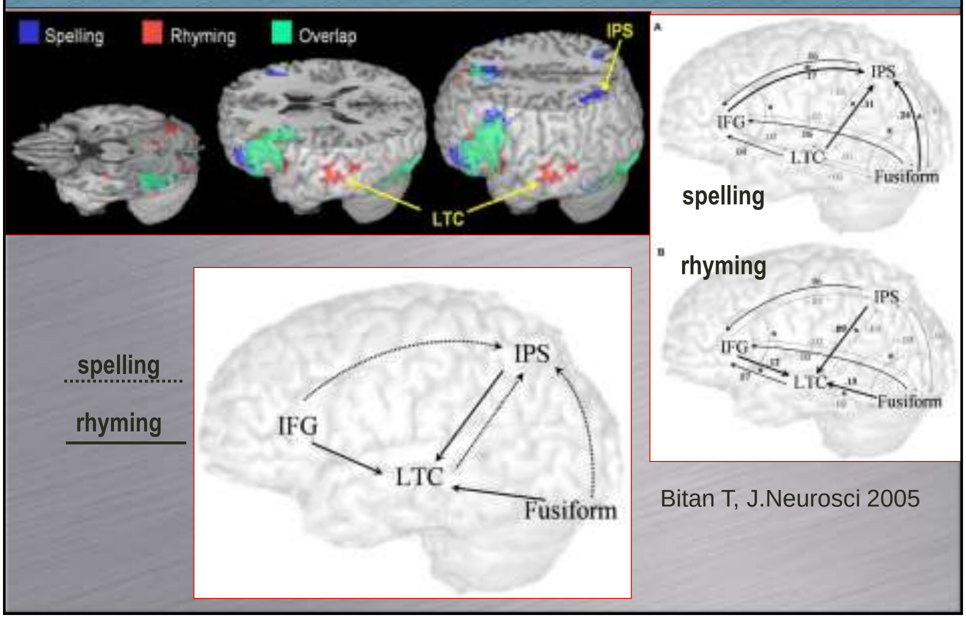
Connectivity–behavior analysis reveals that functional connectivity between left BA39 and Broca's area varies with reading ability



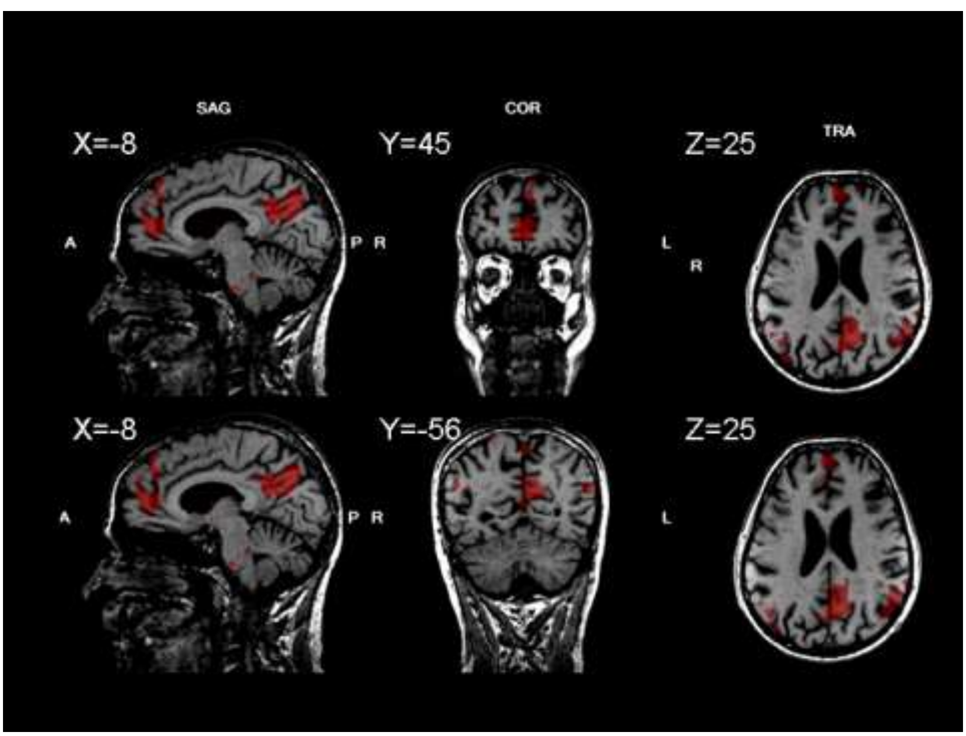
bad readers good readers

Hampson M., Neuroimage 2006

Shifts of Effective Connectivity within a Language Network during Rhyming and Spelling



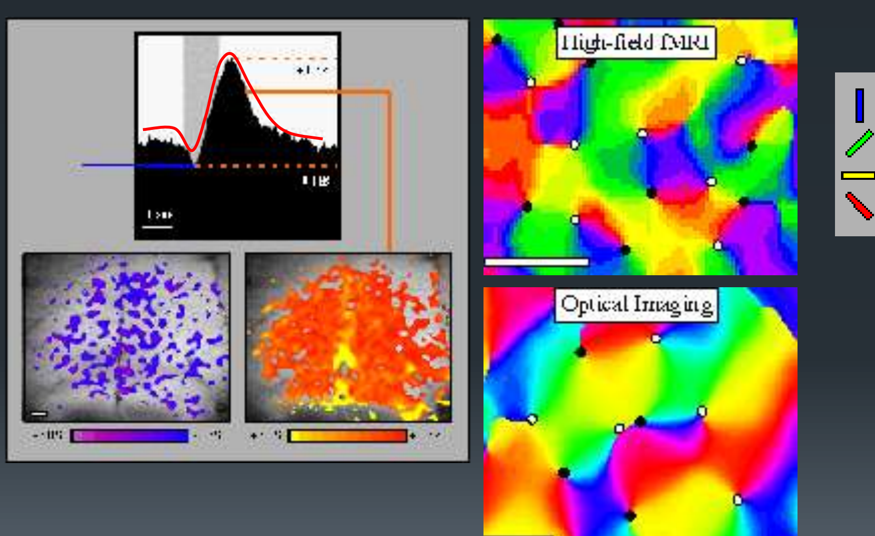
Bitan T, J.Neurosci 2005



Private behaviors made public
The increased complexity

- The complexity of behavior depends on the level of observation we chose to take. Possible levels of observation of "private" events in the brain are:
- The points of the brain on neuroimages
- The cortical surface and/or its subdivisions
- "Unitary elements" of brain activity, the neuronal columns
- The single neurons — 100 billion neurons
- The single synapses — 10 thousands per neuron

fMRI at the Columnar level



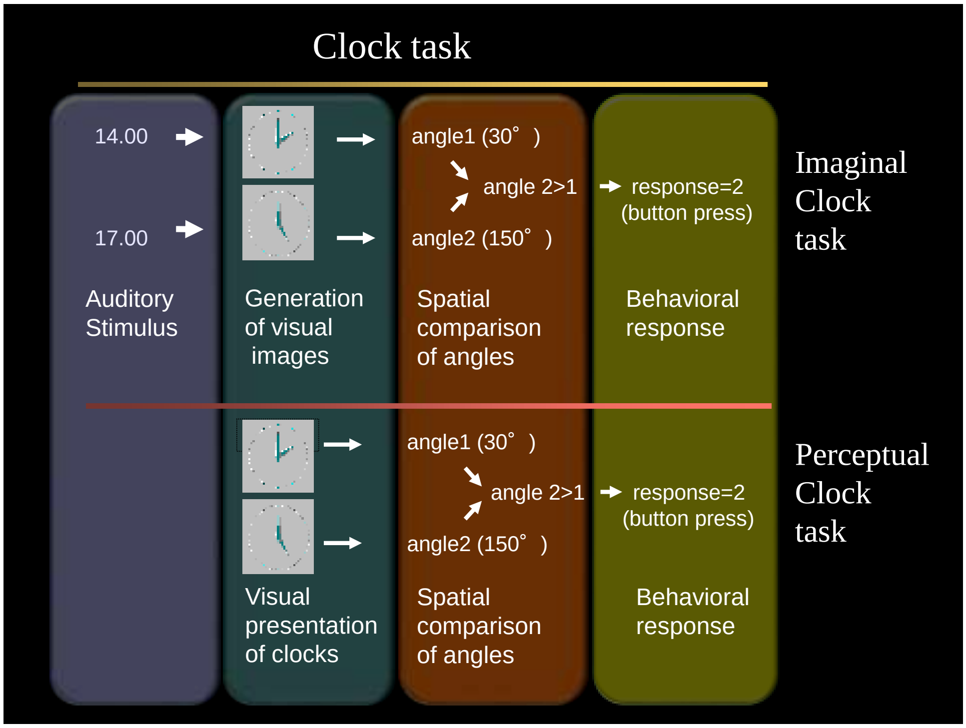
Dae-Shik Kim – Nature Neuroscience 2000

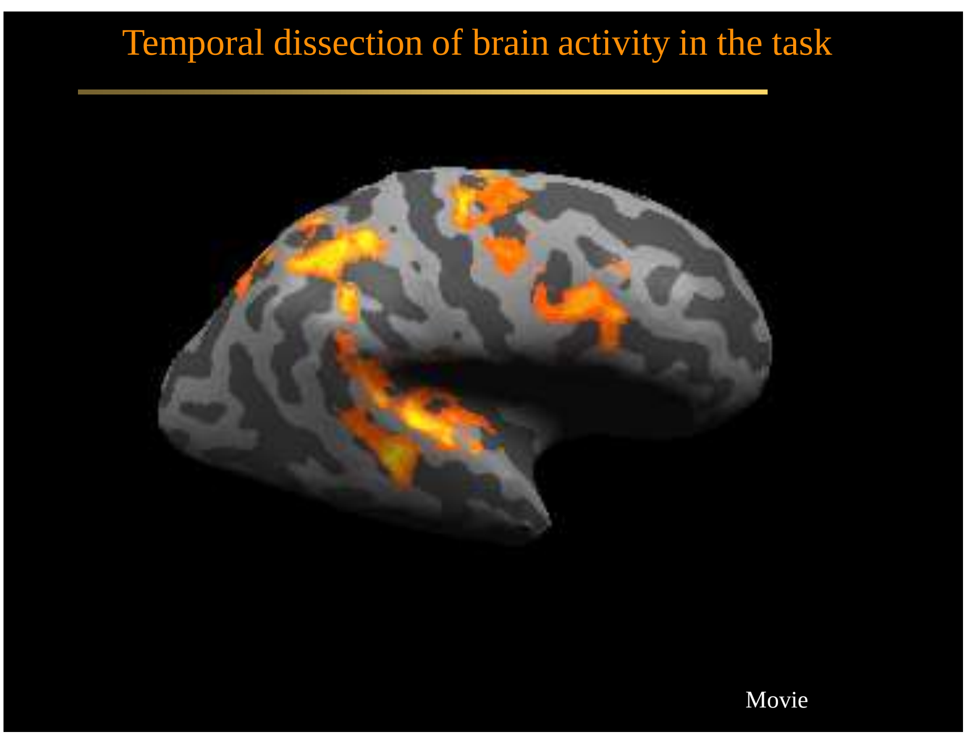
Outline

- Skinner and the Neurosciences
- Why to integrate Neurosciences into Behaviorism
- Private behaviors made public - increased complexity
- The procedures to study behavior in the brain
- The need to translate information from Neurosciences to Behaviorism and vice versa
- The critical role of Neuroimaging in translating the information
- The verbal operants in the brain: the neural basis of their independence
- Methods to directly modify behavior in the brain

The imaginal clock task

- **General purpose:** To trace the spatio-temporal pattern of brain activation during a single trial of a fMRI brain (mental) chronometry framework.
- **Design:** Time-resolved event-related fMRI; correlation of reaction times with BOLD delay in different brain areas.
- **Paradigm:** The "mental clock task" (Paivio, 1978, *J Exp Psychol HumPerc*, **4**, 61-71).
- **Specific purpose:** Investigate hemispheric specialization in the posterior parietal cortex (PPC) for generation and analysis of mental images.
- **Details:** Di Salle et al, (2002). Tracking the mind's image in the brain I. *Neuron*, **35**, 185-194.


Clock task
14.00
17.00
Auditory Stimulus
Generation of visual images
angle1 (30˚)
angle 2>1
angle2 (150˚)
Spatial comparison of angles
response=2 (button press)
Behavioral response
Imaginal Clock task
Visual presentation of clocks
angle1 (30˚)
angle 2>1
angle2 (150˚)
Spatial comparison of angles
response=2 (button press)
Behavioral response
Perceptual Clock task

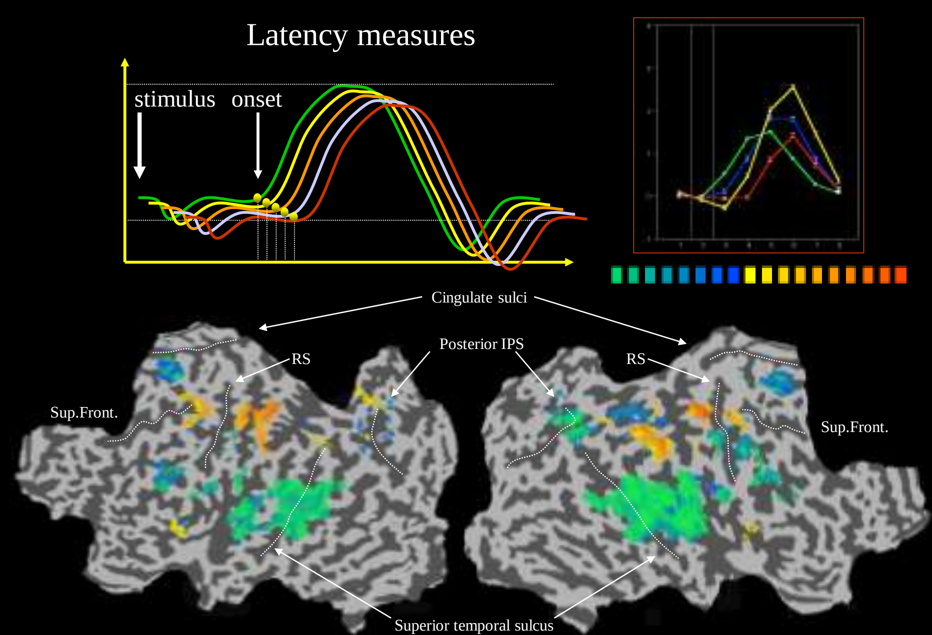

Temporal dissection of brain activity in the task
Movie

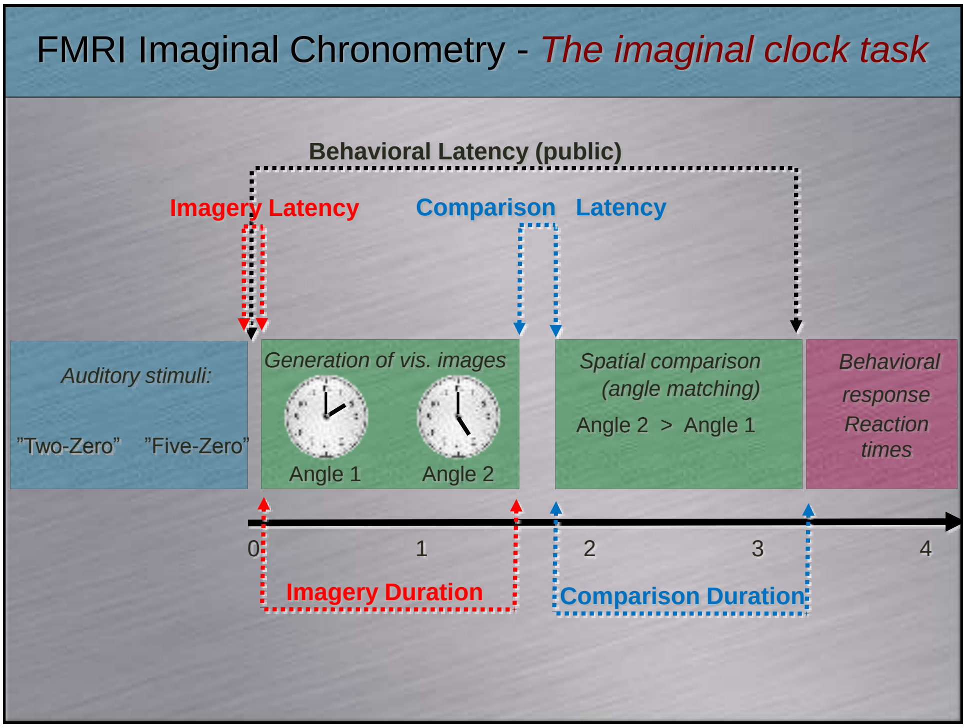
BOLD latency mapping

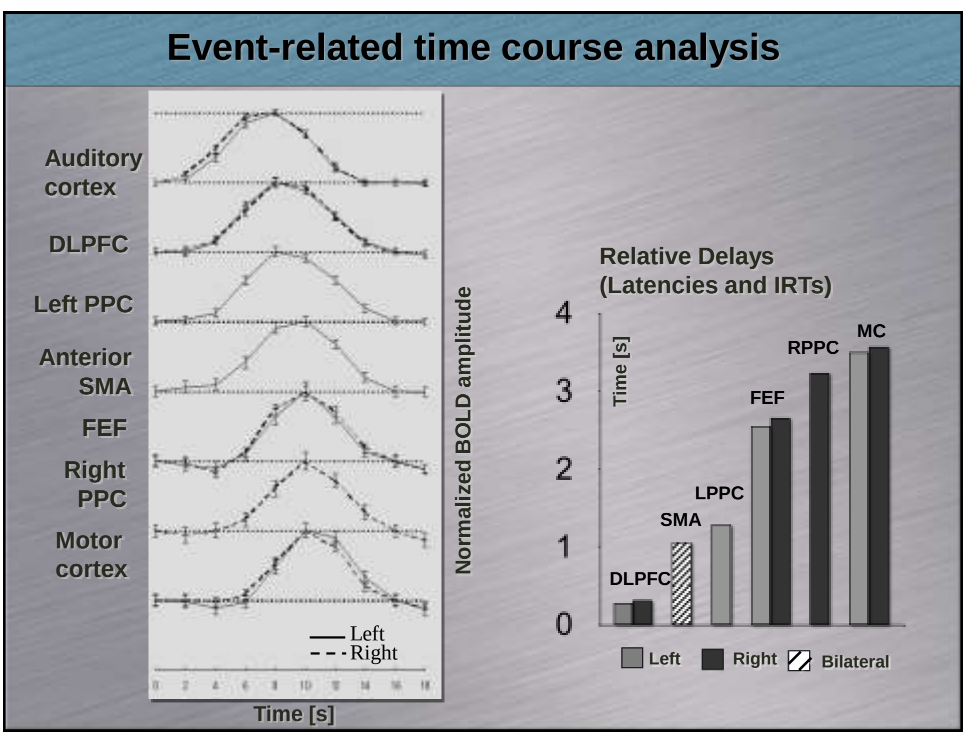
Separating physiological delays from "responding" latency

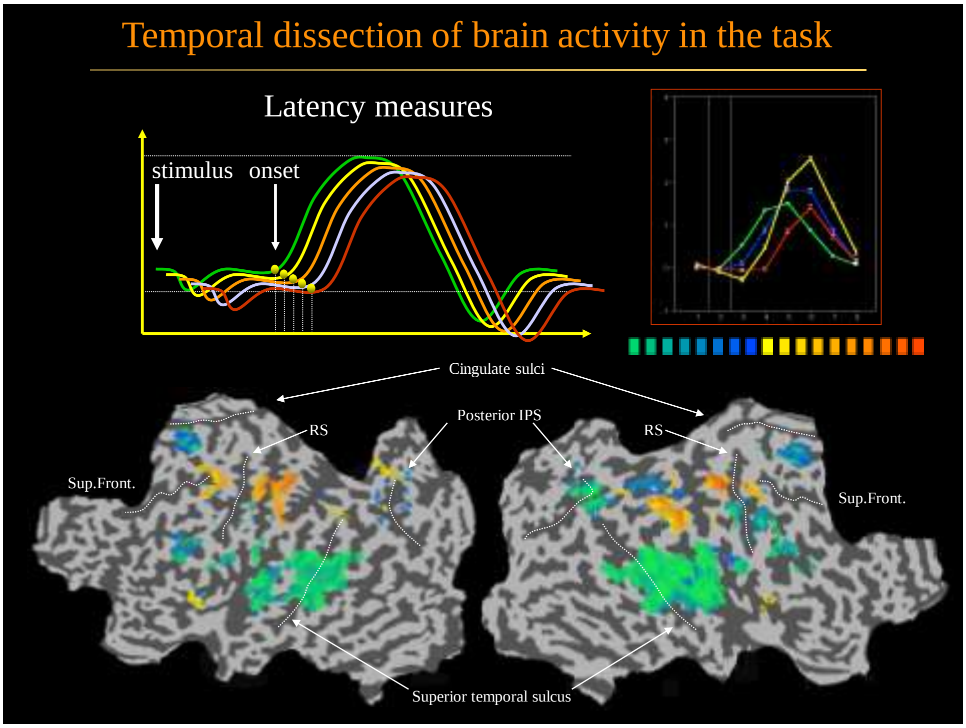
- Since hemodynamic properties remain constant within a brain area, any ***task-dependent change*** reflects responding timing effects.
- Task-dependent changes in timing can be revealed by correlation of single-trial BOLD latencies with reaction times, by changing the order of cognitive tasks etc.

Temporal dissection of brain activity in the task

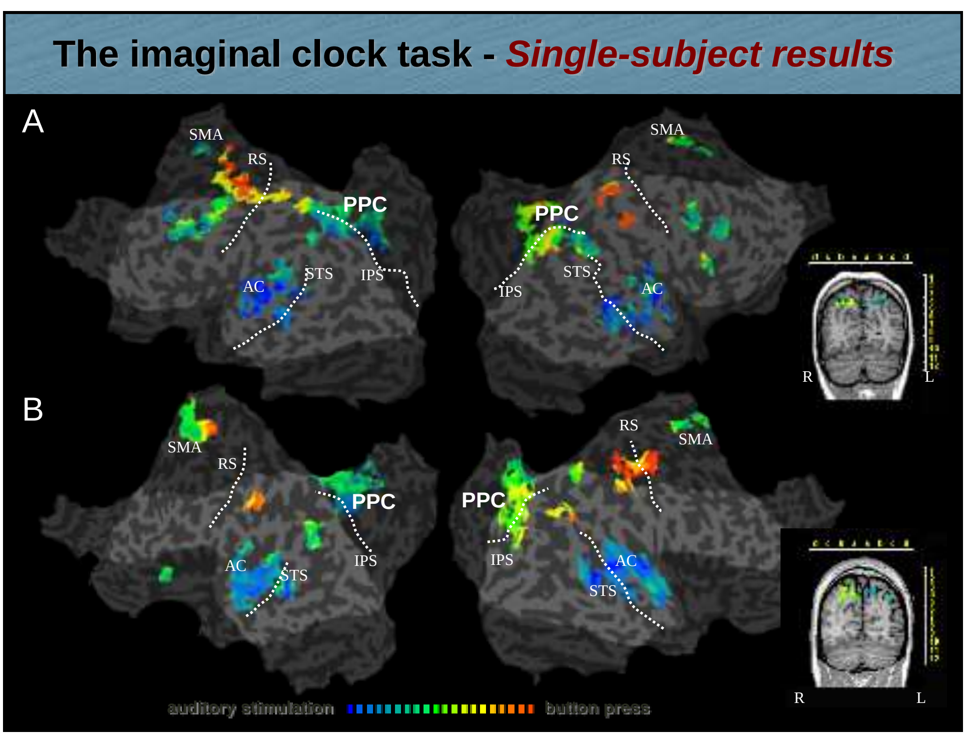



FMRI Imaginal Chronometry - The imaginal clock task
Behavioral Latency (public)
Imagery Latency
Comparison Latency
Auditory stimuli:
"Two-Zero" "Five-Zero"
Generation of vis. images
Angle 1
Angle 2
Spatial comparison
(angle matching)
Angle 2 > Angle 1
Behavioral
response
Reaction
times
0
1
2
3
4
Imagery Duration
Comparison Duration


Event-related time course analysis
Auditory cortex
DLPFC
Left PPC
Anterior SMA
FEF
Right PPC
Motor cortex
Left
Right
Time [s]
Normalized BOLD amplitude
Relative Delays
(Latencies and IRTs)
4
3
2
1
0
Time [s]
DLPFC
SMA
LPPC
FEF
RPPC
MC
Left
Right
Bilateral

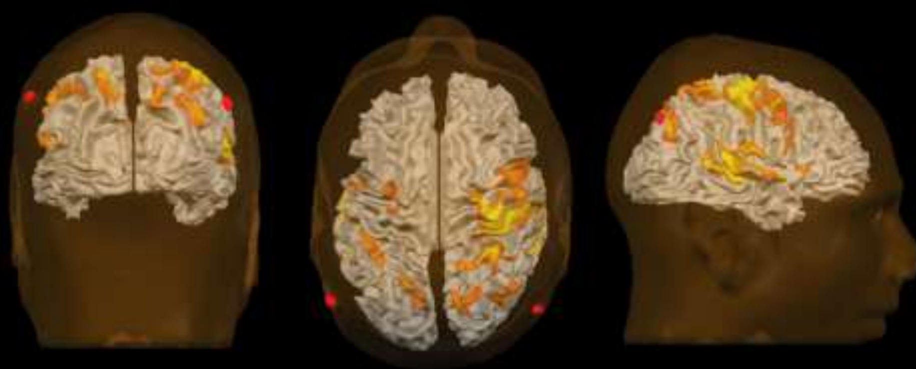


Temporal dissection of brain activity in the task
Latency measures
stimulus
onset
Cingulate sulci
Posterior IPS
RS
RS
Sup.Front.
Sup.Front.
Superior temporal sulcus



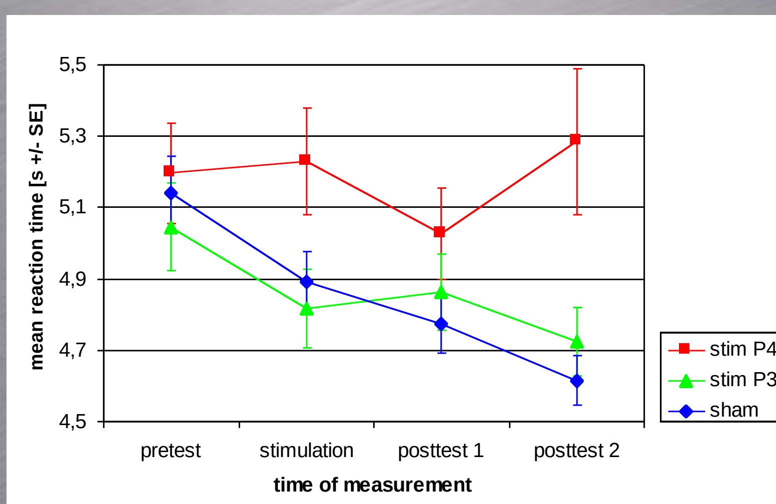
The imaginal clock task - Single-subject results
A
SMA
RS
PPC
STS
IPS
AC
SMA
RS
PPC
STS
IPS
AC
R
L
B
SMA
RS
PPC
AC
STS
IPS
RS
SMA
PPC
IPS
AC
STS
R
L
auditory stimulation
button press

Imaginal clock task - *Combined fMRI and rTMS*



Sack A, Di Salle F. et al., (2002), Tracking the mind's image in the brain II, *Neuron*, **35**, 195-204.

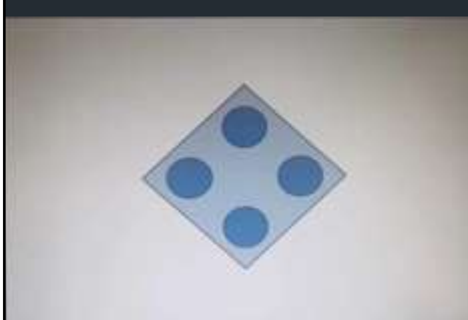
Imaginal clock task - *TMS results*



Brain Responses measured through the Continuous Measures of Behavior

The motor experiment

The motor experiment



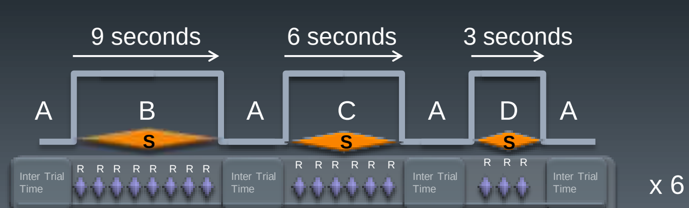
The Motor experiment

- Aim of the experiment was to: a) single out the brain area(s) were the motor behavior is emitted b) analyze the correspondence of Dimentional Quantities in the private and in the public motor behavior c) examine the presence of a chain of behaviors leading to the public motor behavior
- A visual Stimulus was active during the «treatment» periods (Motor Activity Trials), indicating which finger to move
- In the Baseline condition the Stimulus was replaced by a fixation cross and no Response was required
- The duration of trials was randomly varied from 3 to 6 and to 9 seconds, each condition repeated 6 times. The temporal resolution of the test was 800 milliseconds

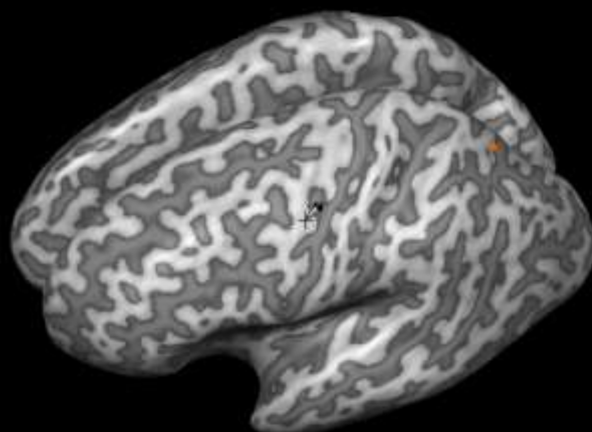
Design of the motor experiment

Conceptually a reversal/withdrawal experiment with many (n 18) applications and withdrowals of the Independent Variable

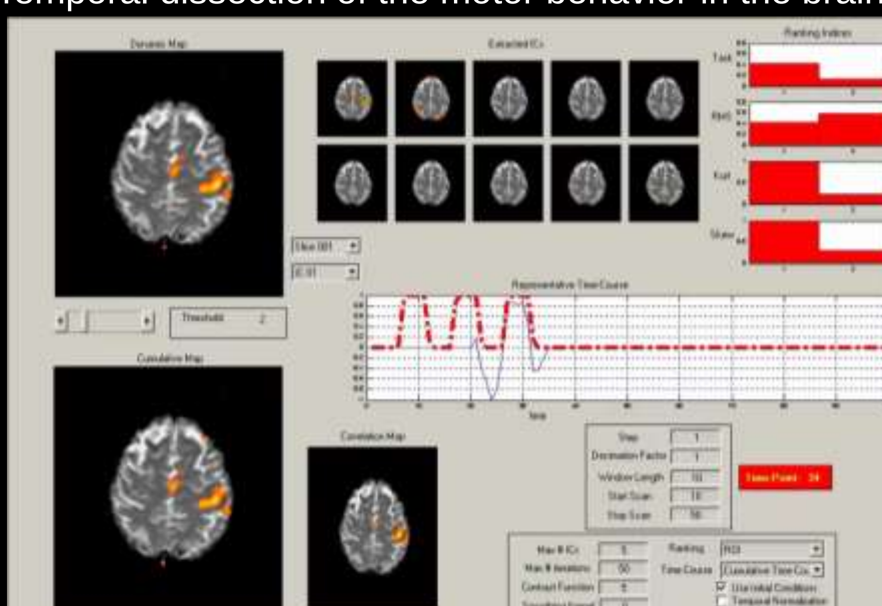
3 conditions of the Independent Variable are tested, differing for the duration of each trial, (motor episodes lasting 3,6,9 seconds)



Results of the motor experiment
Temporal dissection of the motor behavior in the brain

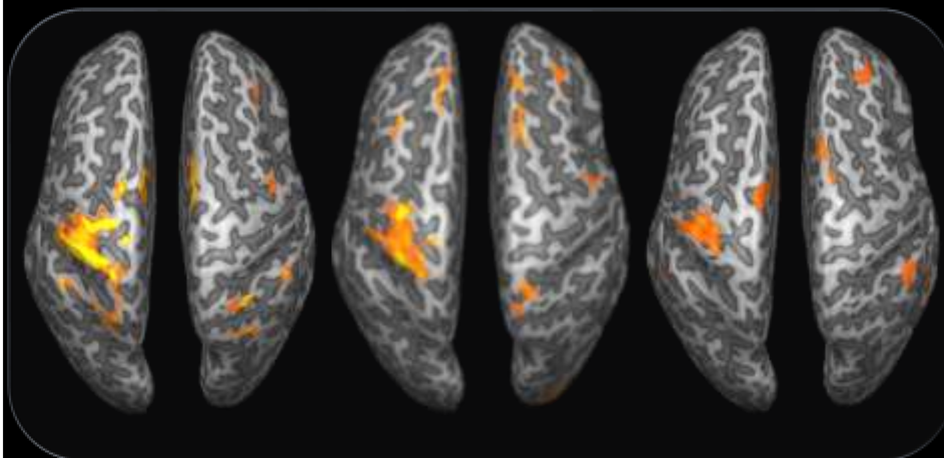


Results of the motor experiment
Temporal dissection of the motor behavior in the brain



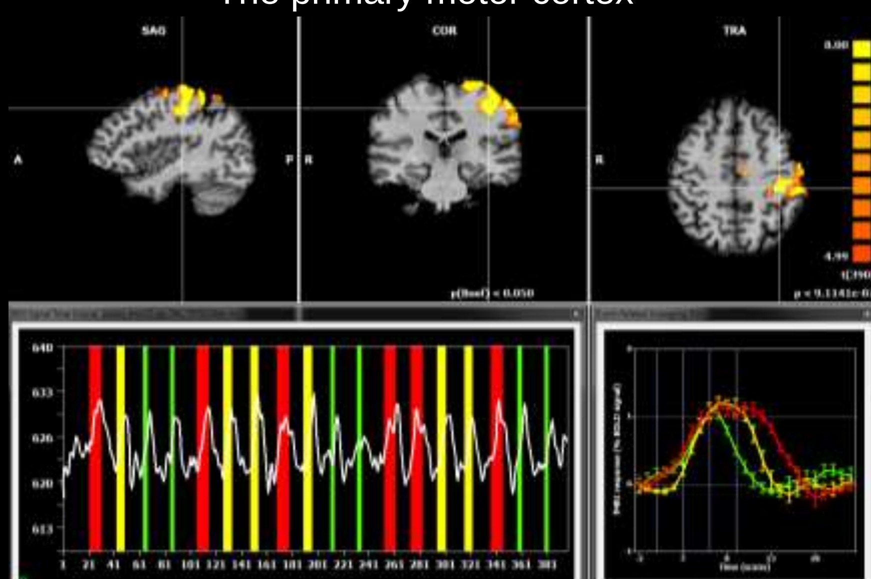
Motor Responses in the Rolandic Cortex

Reproducibility across subjects



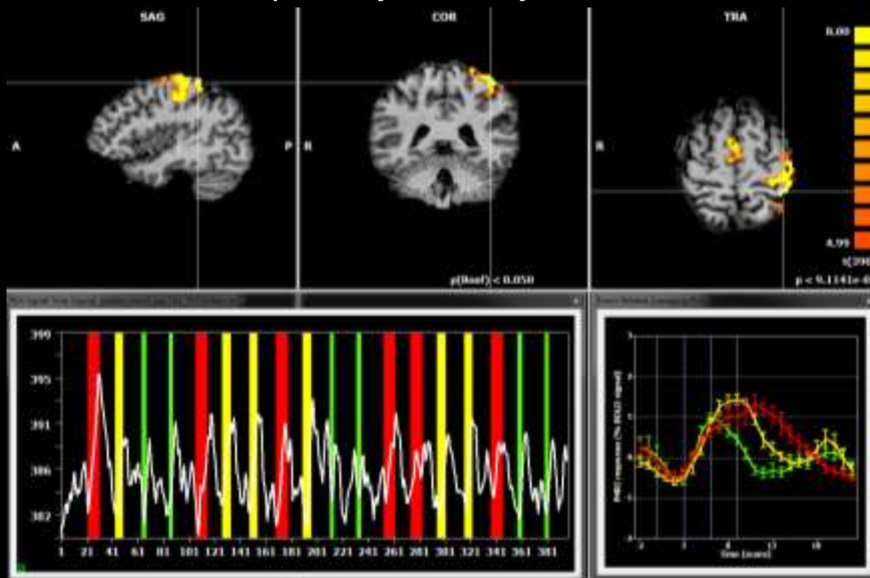
Results of the motor experiment

The primary motor cortex



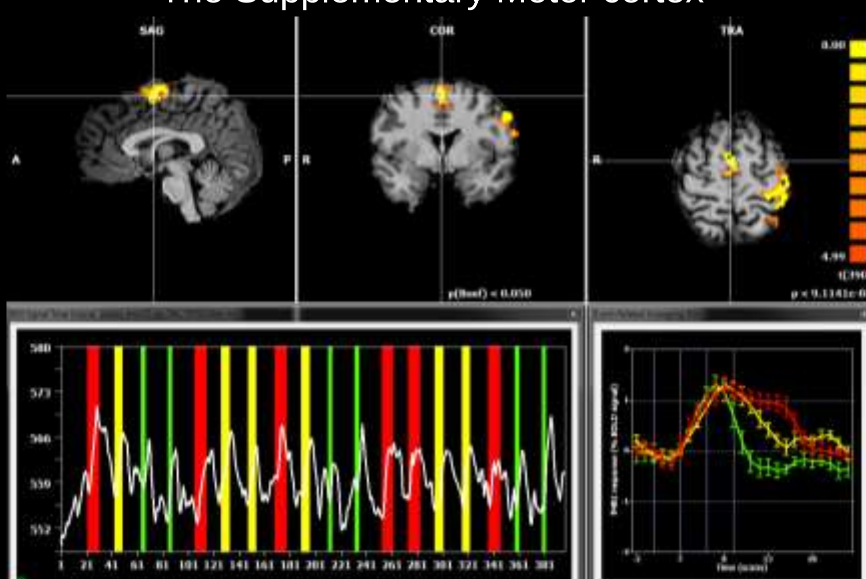
Results of the motor experiment

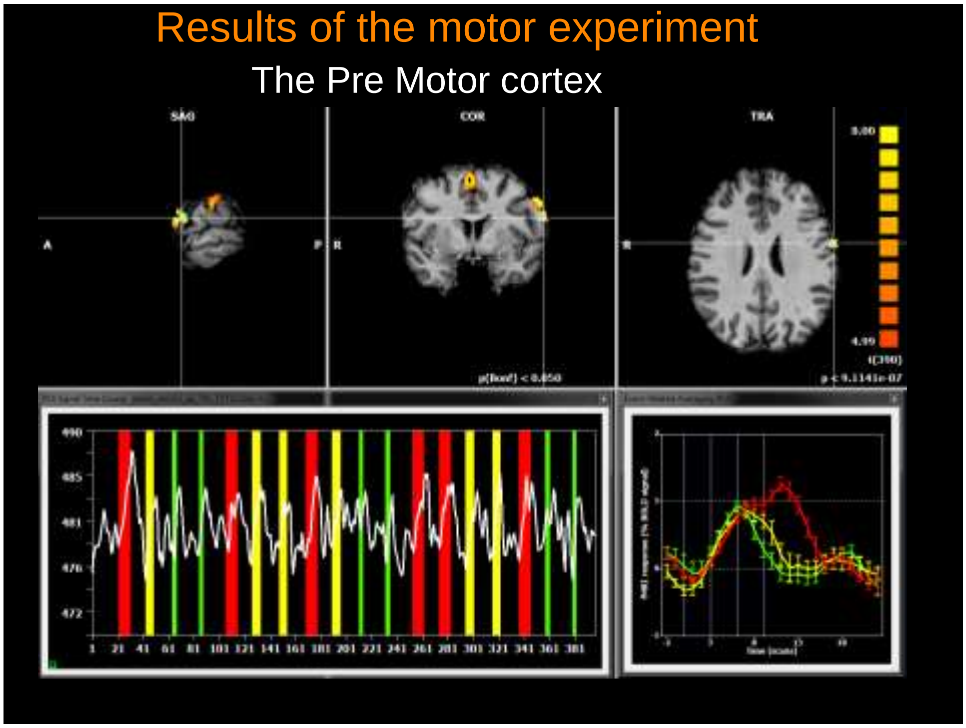
The primary sensory cortex

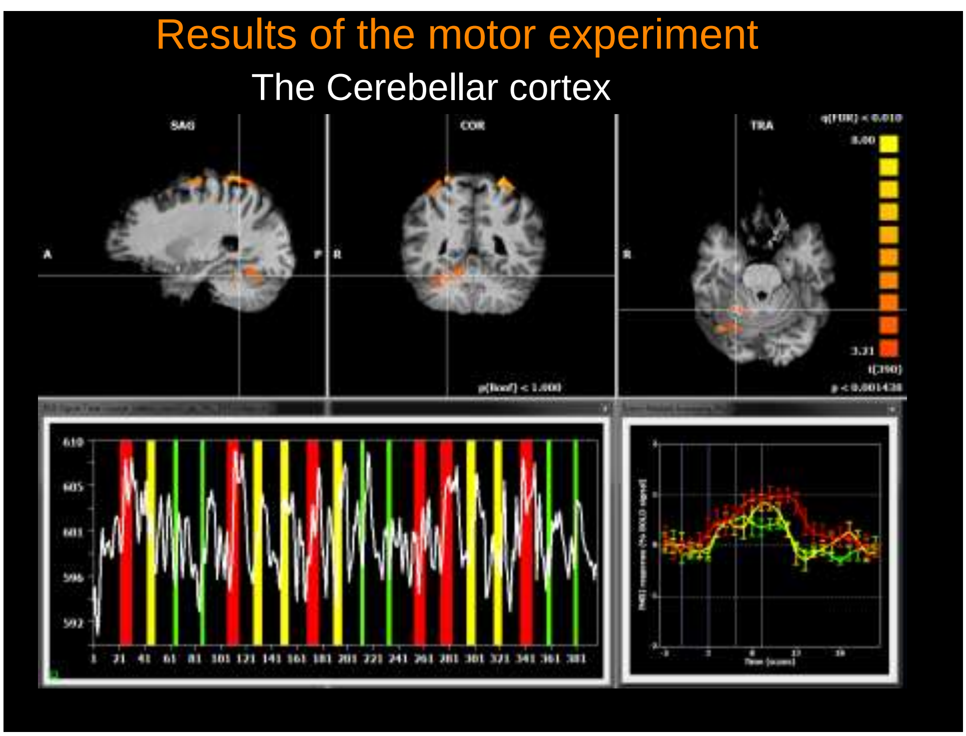


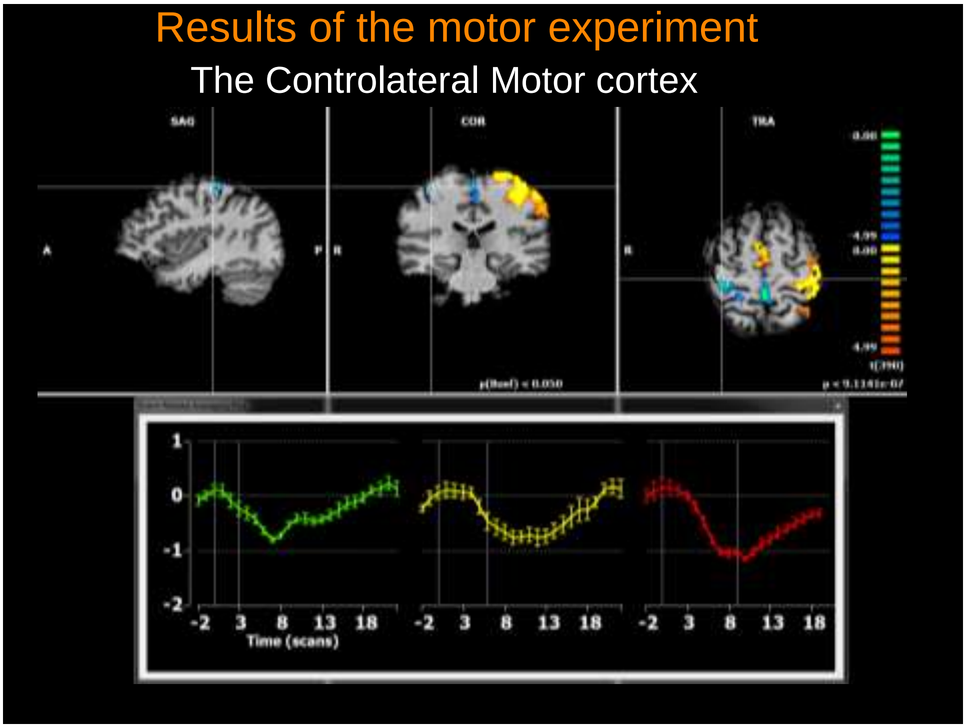
Results of the motor experiment

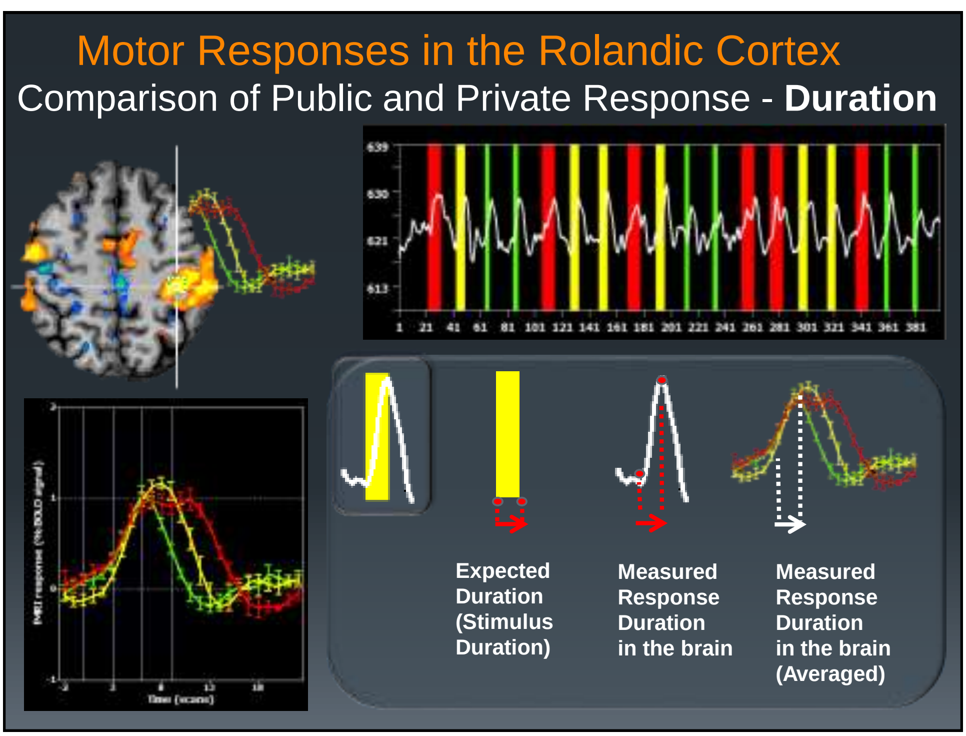
The Supplementary Motor cortex




Results of the motor experiment
The Pre Motor cortex
SAG
COR
TRA

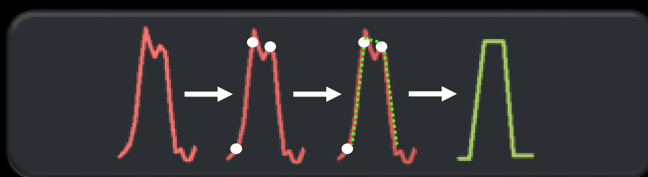

Results of the motor experiment
The Cerebellar cortex
SAG
COR
TRA


Results of the motor experiment
The Controlateral Motor cortex
SAG
COR
TRA
A
P
R
R
1
0
-1
-2
-2 3 8 13 18
Time (scans)
-2 3 8 13 18
-2 3 8 13 18


Motor Responses in the Rolandic Cortex
Comparison of Public and Private Response - Duration
639
630
621
613
1 21 41 61 81 101 121 141 161 181 201 221 241 261 281 301 321 341 361 381
Time (scans)
Expected Duration (Stimulus Duration)
Measured Response Duration in the brain
Measured Response Duration in the brain (Averaged)

Motor Responses in the Rolandic Cortex

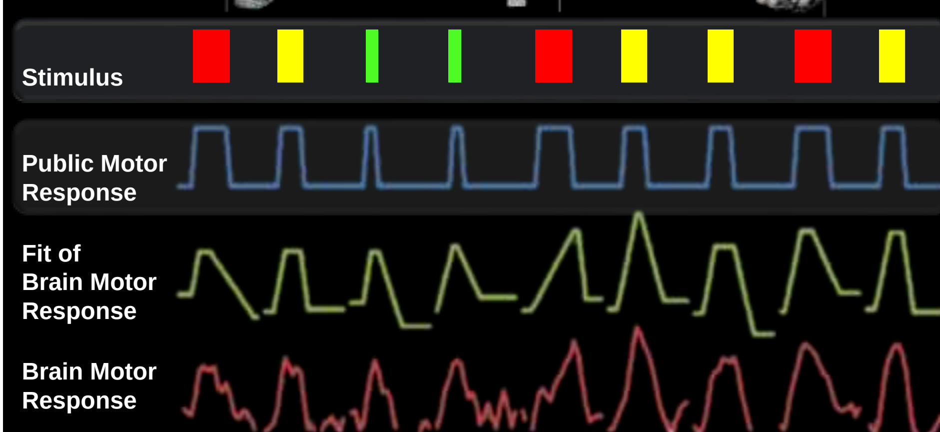
Comparison of Public and Private Dimensional Quantities - Trapezoidal Fitting

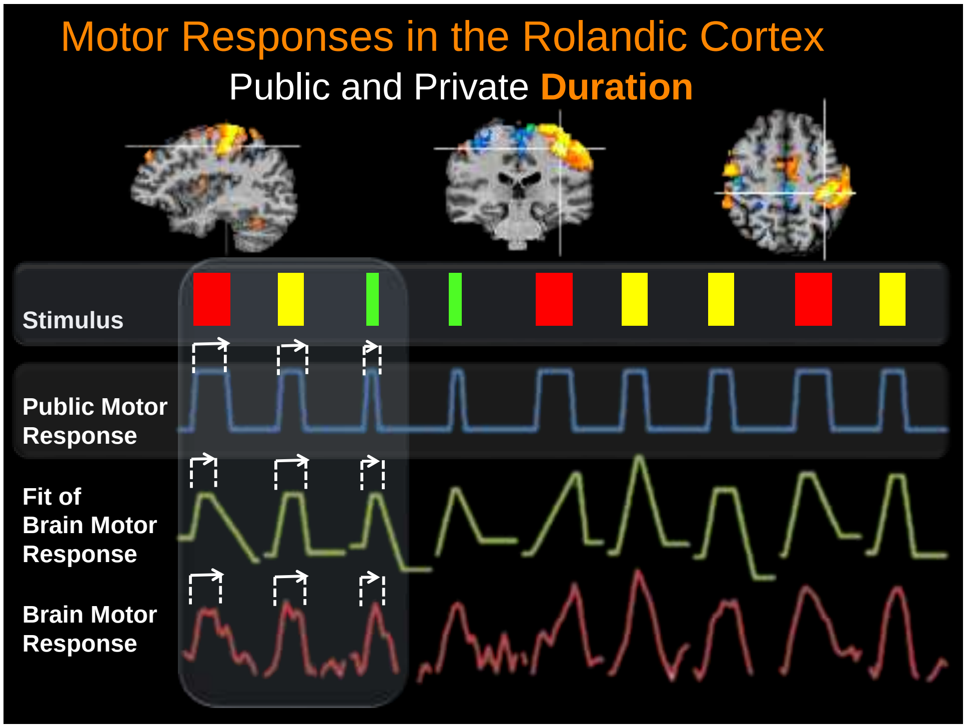


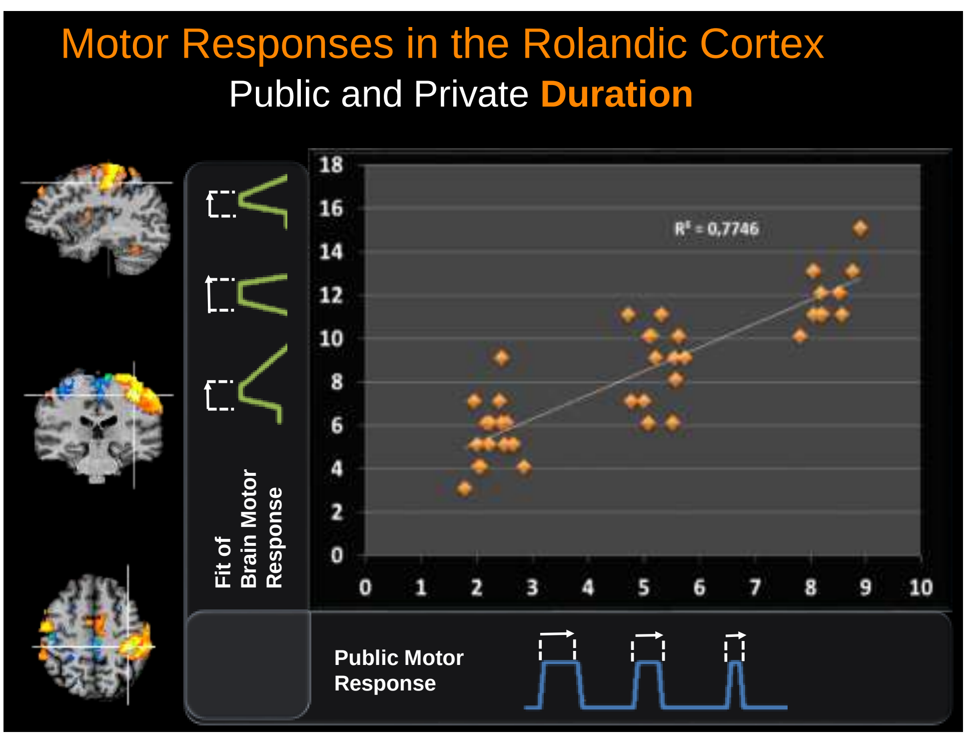
1) «Break Points» of the brain signal are automatically found
2) A trapezoid is fitted into the signal minimizing the RMS error
3) The trapezoid is then used as a simpler mean to measure brain signal in the single trials

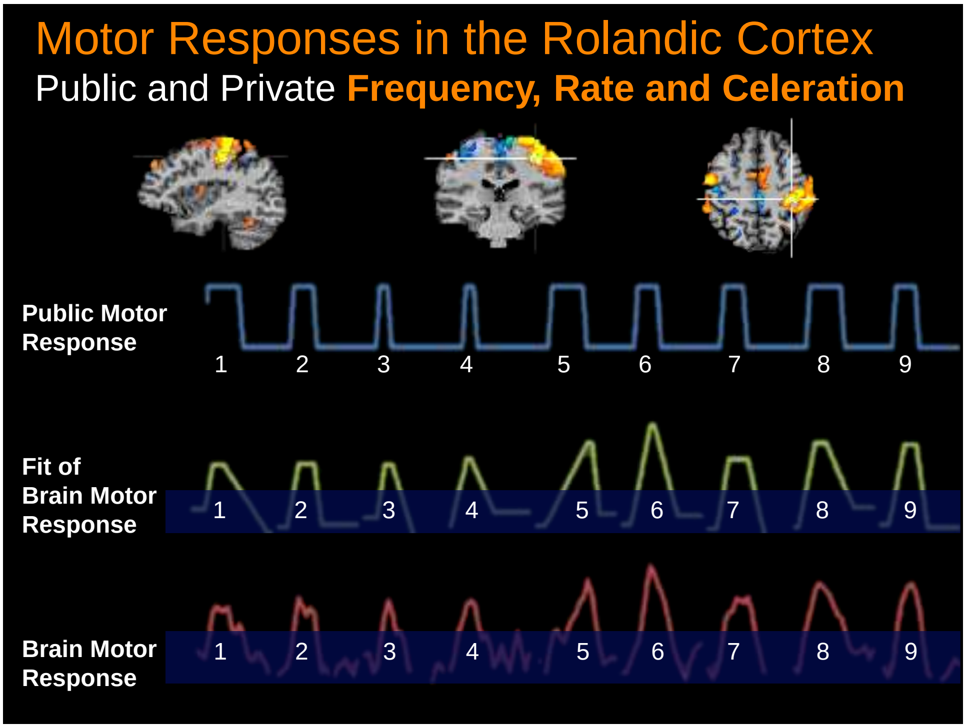
Motor Responses in the Rolandic Cortex

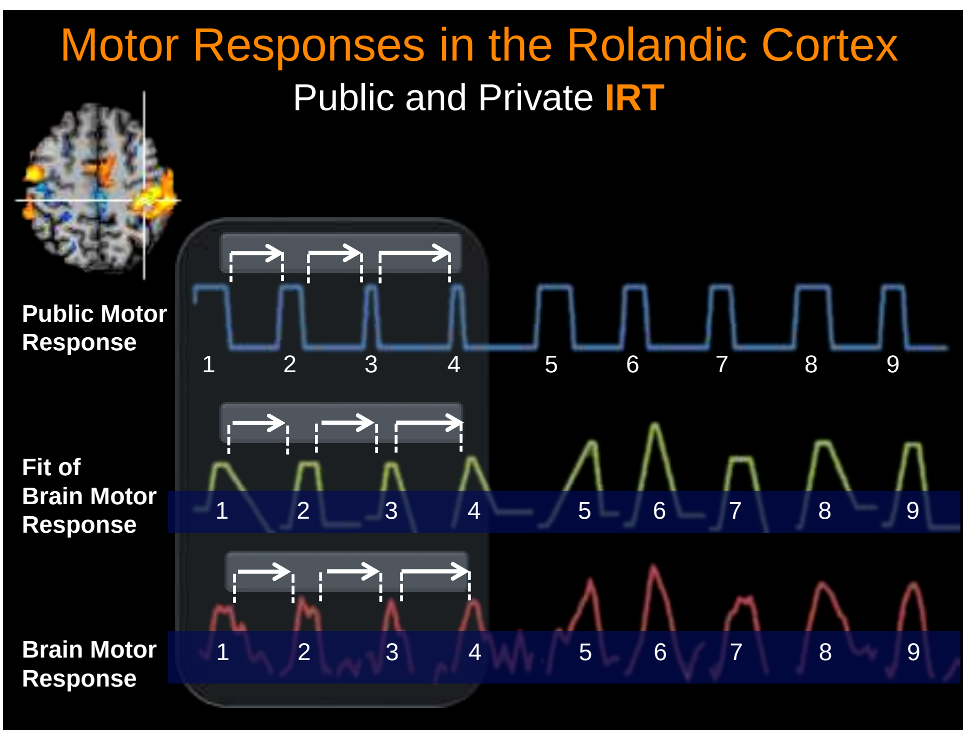
Public and Private **Response Duration**




Motor Responses in the Rolandic Cortex
Public and Private Duration
Stimulus
Public Motor Response
Fit of Brain Motor Response
Brain Motor Response

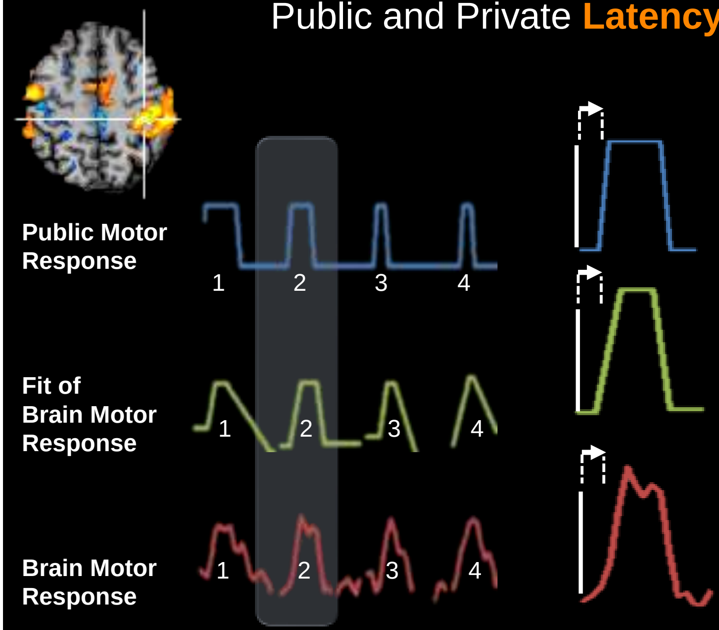

Motor Responses in the Rolandic Cortex
Public and Private Duration
Fit of Brain Motor Response
R² = 0,7746
18
16
14
12
10
8
6
4
2
0
0 1 2 3 4 5 6 7 8 9 10
Public Motor Response


Motor Responses in the Rolandic Cortex
Public and Private Frequency, Rate and Celeration
Public Motor Response
1 2 3 4 5 6 7 8 9
Fit of Brain Motor Response
1 2 3 4 5 6 7 8 9
Brain Motor Response
1 2 3 4 5 6 7 8 9


Motor Responses in the Rolandic Cortex
Public and Private IRT
Public Motor Response
1 2 3 4 5 6 7 8 9
Fit of Brain Motor Response
1 2 3 4 5 6 7 8 9
Brain Motor Response
1 2 3 4 5 6 7 8 9

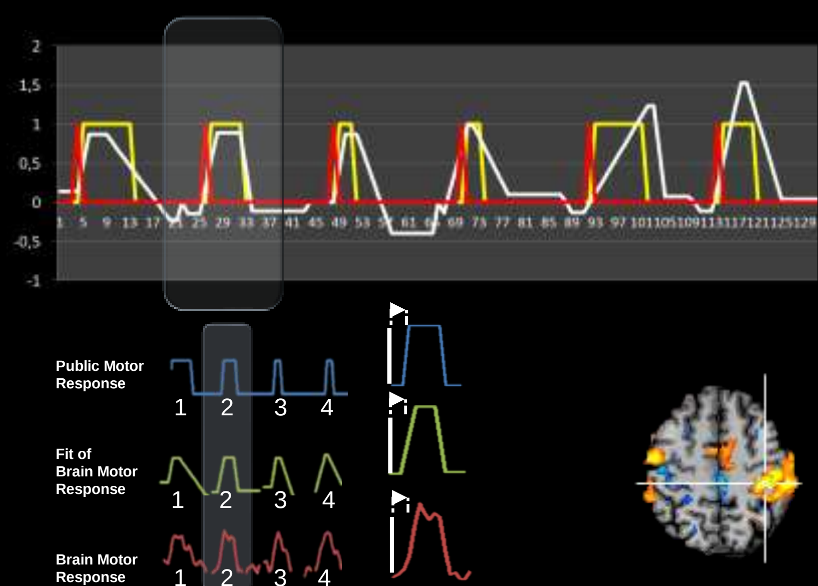
Motor Responses in the Rolandic Cortex

Public and Private **Latency**



Motor Responses in the Rolandic Cortex

Public and Private **Latency**



The Motor experiment
Conclusions

a) Brain areas where the private behavior was emitted were easy to single out and reproducible across subjects

b) Dimentional Quantities are well correlated, if not coincident, in the private and in the public motor behavior, and perfectly measurable in the single episodes

c) The temporal dissection of the motor episode in the brain showed a temporal succession of private behaviors from the IntraParietal sulcus to the Primary Motor, and to the Supplementary Motor regions.

Neural Activity in Verbal Operants

The Verbal Operants experiment

Aims

- Aims of the experiment were to:
- a) single out the brain area(s) were the brain behavior subserving the Verbal Operants (Echoic, Tact, Intraverbal and Textual) is emitted
- b) analyze the differences among the patterns of activity in search of a unique pattern for each Operant
- c) examine the differences in brain activity in conditions of private and public (overt) behavior and of private only (covert) behavior.

The Verbal Operants experiment

The Stimuli

1) In the Echoic condition the activity was evoked by vocal antecedent stimuli in the form of both words and not words
2) In the Tact condition half of the antecedent stimuli were in auditory and half in visual form
3) In the Intraverbal condition, half of the stimuli were in vocal and half in text form
4) In the Textual condition, half of the stimuli were words and half non words
5) In the Baseline condition no Stimulus was given to the subjects and no Response required.

The Verbal Operants experiment

Topography and Trials

1) For half of the trials, the topography was the same across all operants, in the remaining half the topography varied.
2) The duration of trials was of 20 seconds and each condition was repeated 12 times
3) in order to avoid additional activity, no consequence was given to the behavior

The Verbal Operants experiment

Topography and Trials

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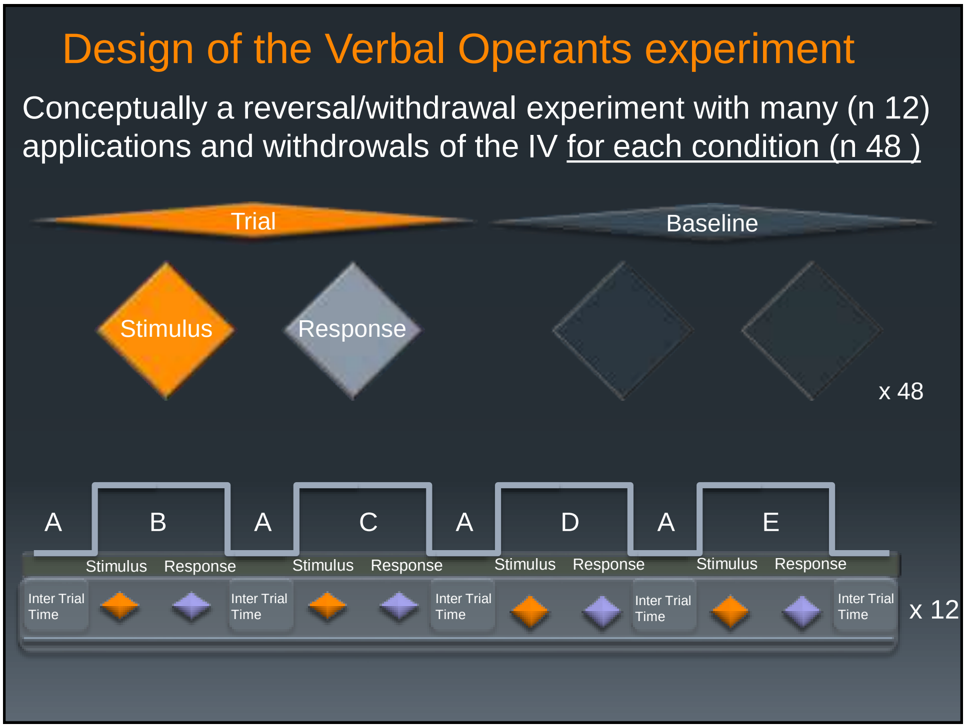
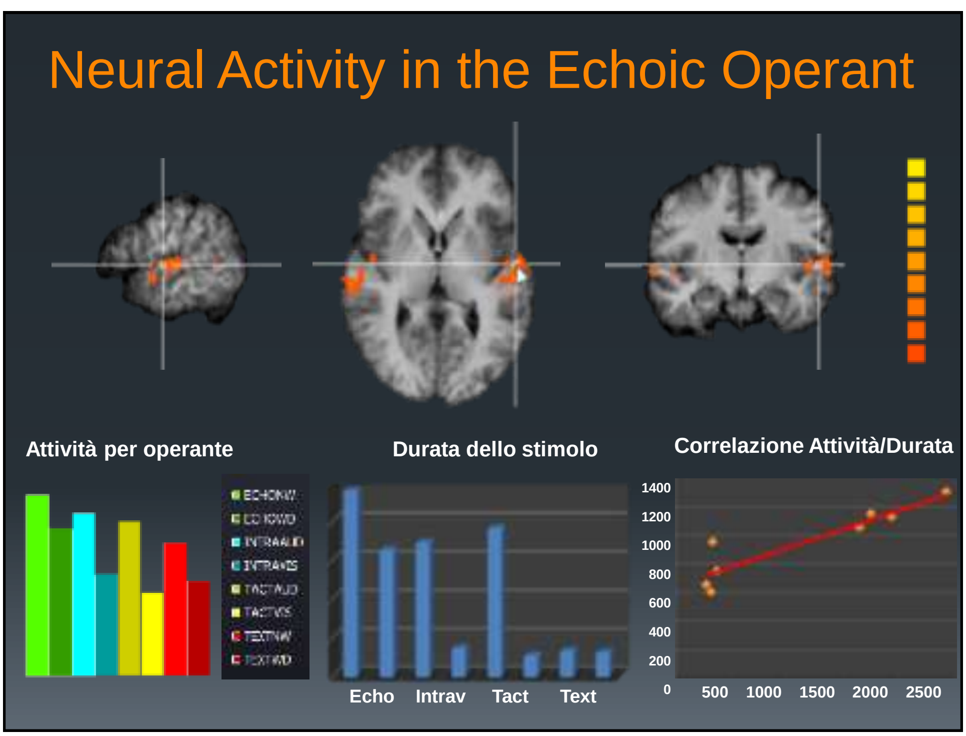
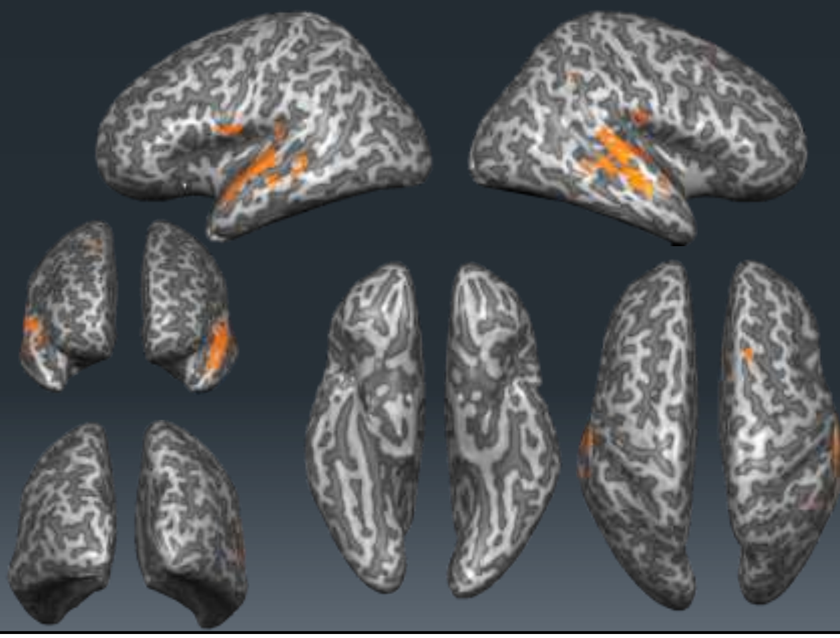
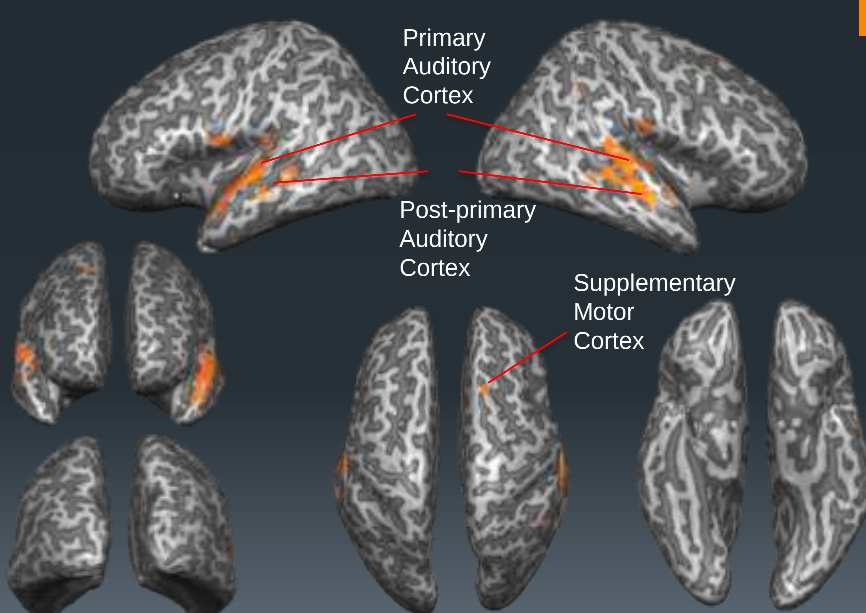

Design of the Verbal Operants experiment
Conceptually a reversal/withdrawal experiment with many (n 12) applications and withdrowals of the IV for each condition (n 48)
Trial
Baseline
Stimulus
Response
x 48
A
B
A
C
A
D
A
E
Stimulus
Response
Stimulus
Response
Stimulus
Response
Stimulus
Response
Inter Trial Time
Inter Trial Time
Inter Trial Time
Inter Trial Time
Inter Trial Time
x 12


Neural Activity in the Echoic Operant
Attività per operante
Durata dello stimolo
Correlazione Attività/Durata
Echo
Intrav
Tact
Text
1400
1200
1000
800
600
400
200
0
500
1000
1500
2000
2500

Neural Activity in the Echoic Operant

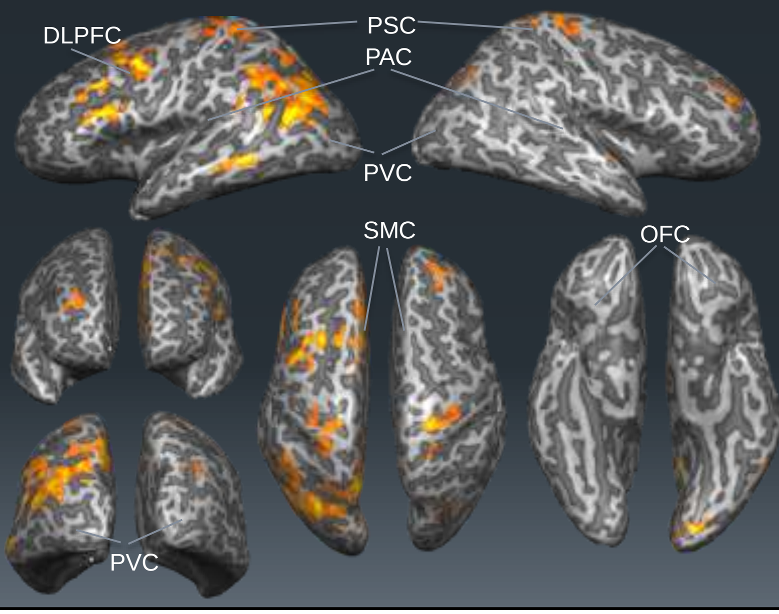


Neural Activity in Echoic behavior



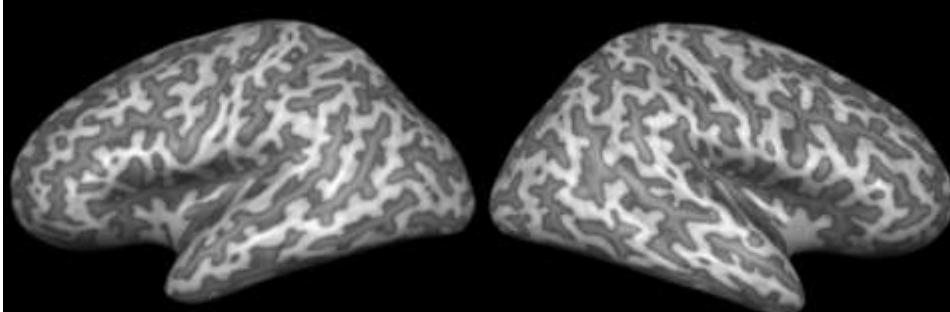
Neural Activity in the Intraverbal Operant

Boolean AND of IntraAud and IntraText



Results of the Verbal Operant experiment

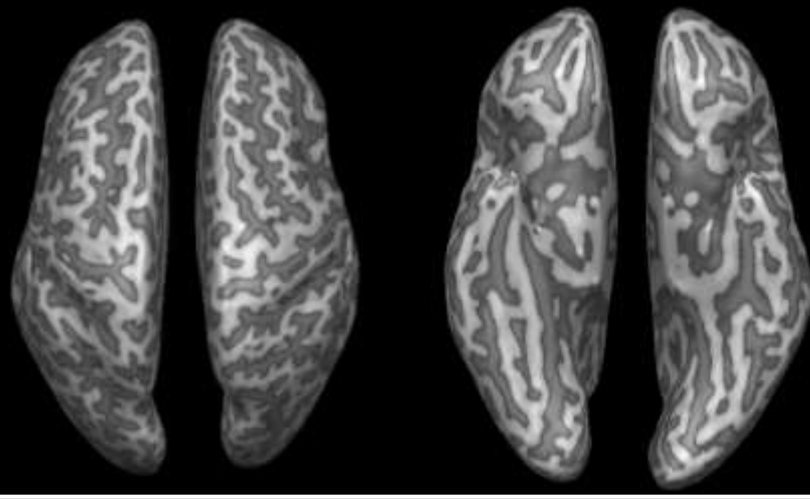
Temporal dissection of the Verbal Behavior in the brain



Echoic NW, Echoic W, IntraAud, IntraText, TactAud, TactVis, Text NW, Text W

Results of the Verbal Operant experiment

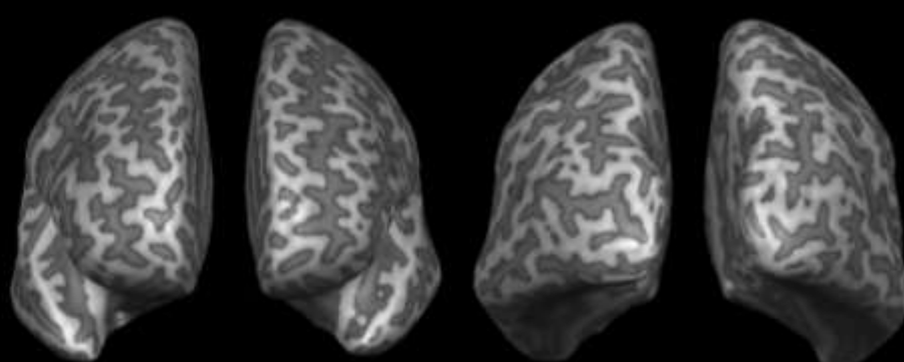
Temporal dissection of the Verbal Behavior in the brain



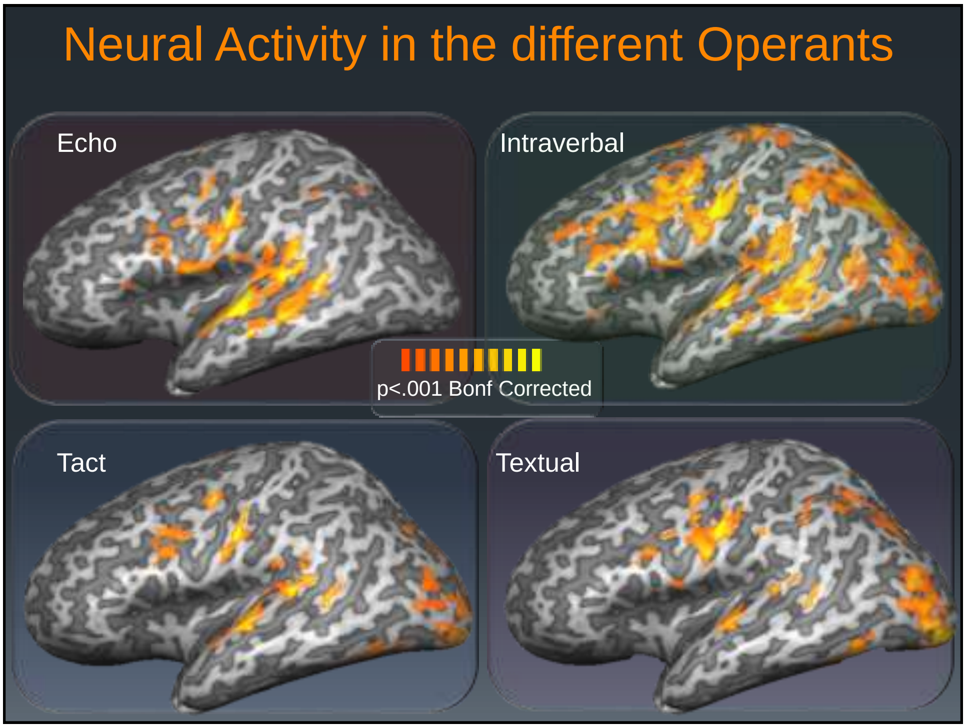
Echoic NW, Echoic W, IntraAud, IntraText, TactAud, TactVis, Text NW, Text W

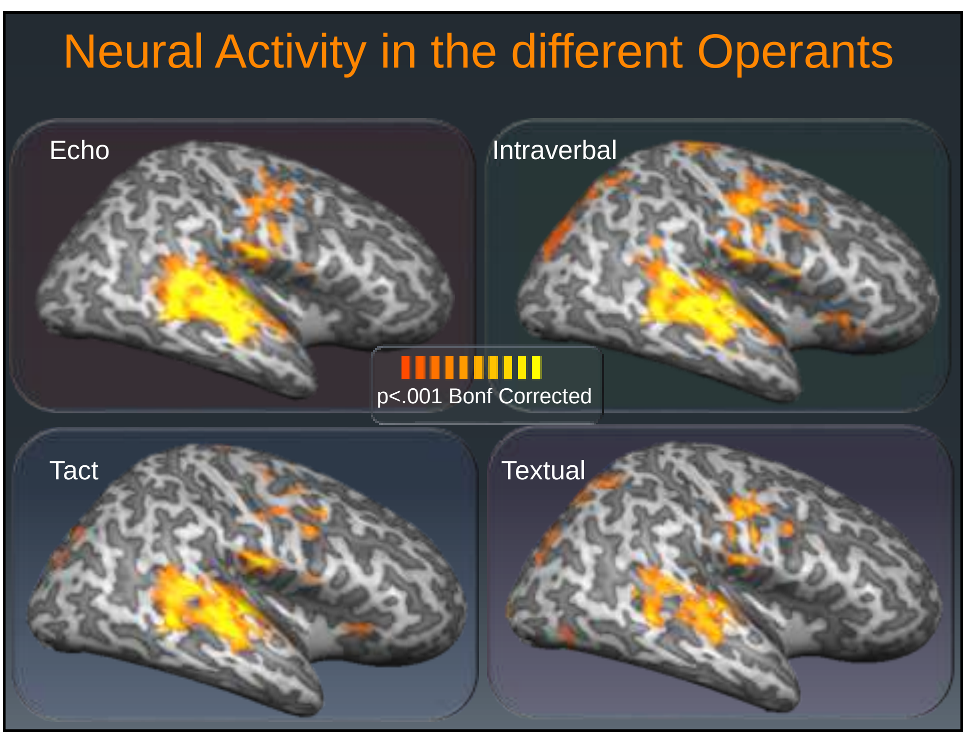
Results of the Verbal Operant experiment

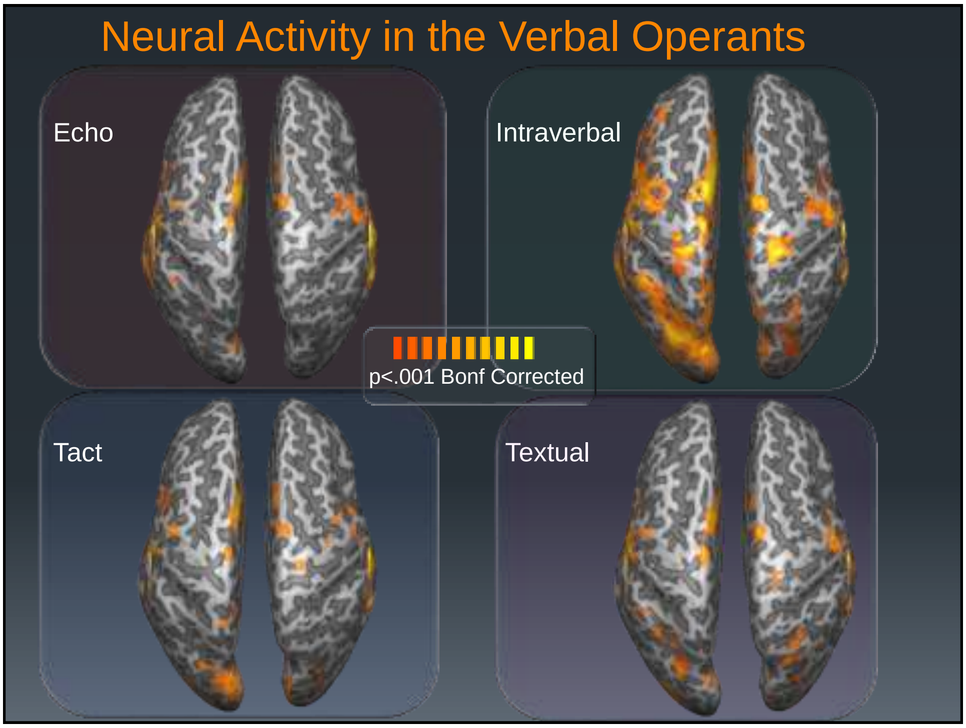
Temporal dissection of the Verbal Behavior in the brain

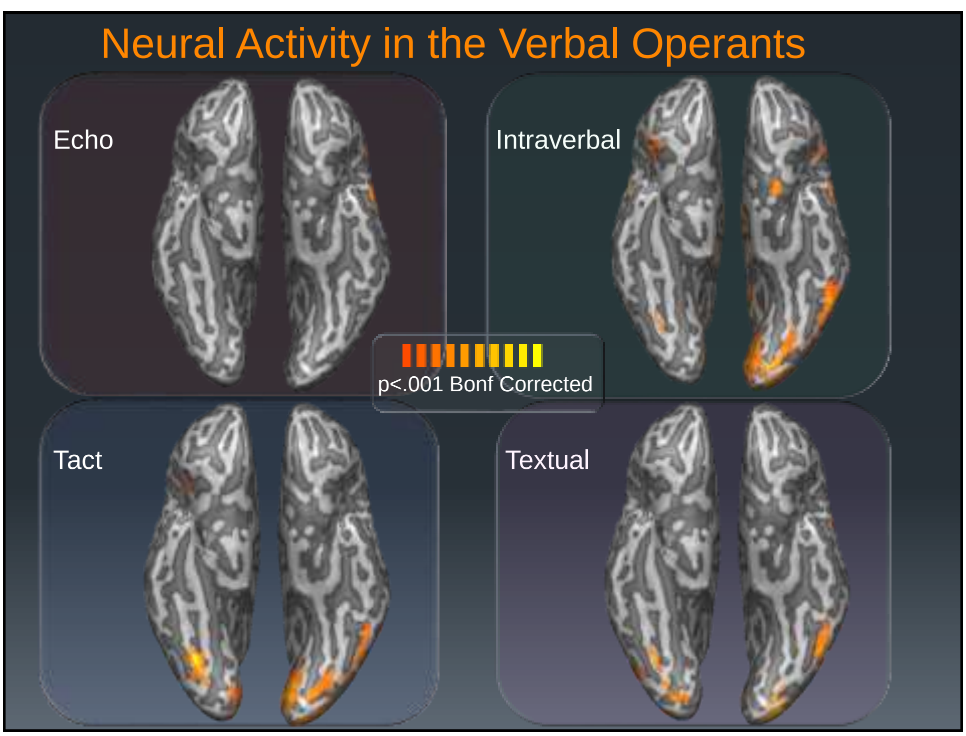


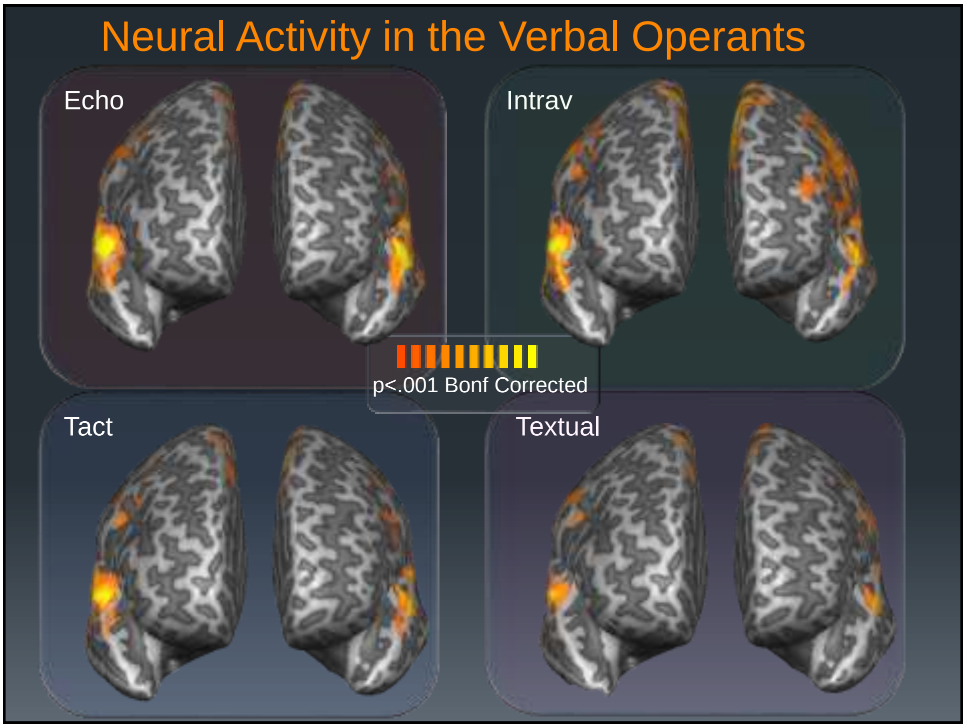
Echoic NW, Echoic W, IntraAud, IntraText, TactAud, TactVis, Text NW, Text W

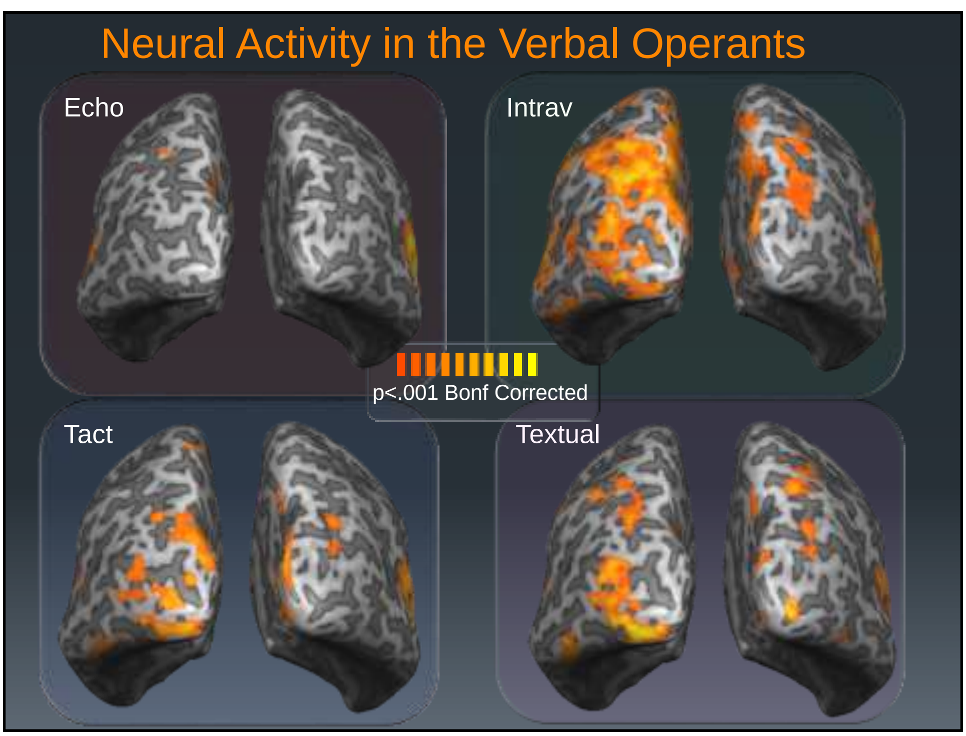

Neural Activity in the different Operants
Echo
Intraverbal
p<.001 Bonf Corrected
Tact
Textual

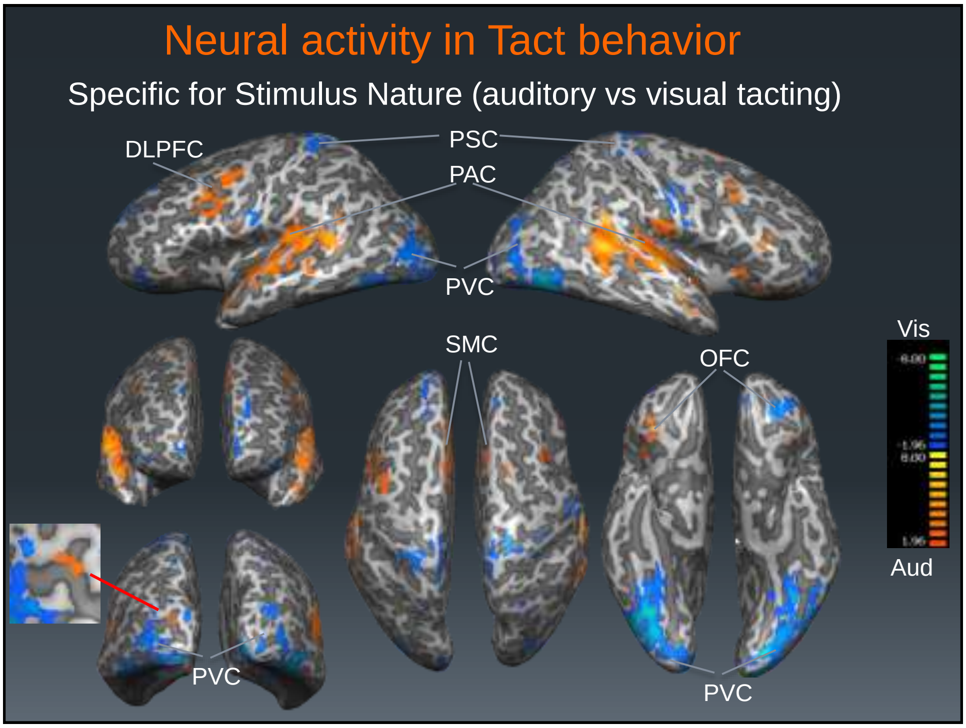

Neural Activity in the different Operants
Echo
Intraverbal
p<.001 Bonf Corrected
Tact
Textual

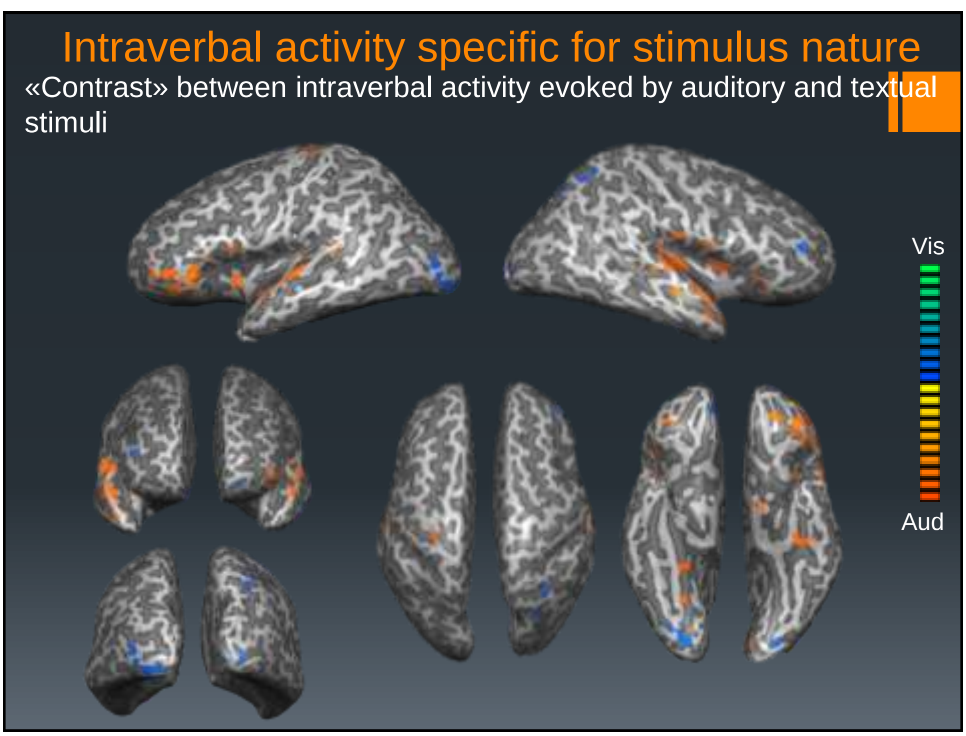

Neural Activity in the Verbal Operants
Echo
Intraverbal
p<.001 Bonf Corrected
Tact
Textual


Neural Activity in the Verbal Operants
Echo
Intraverbal
p<.001 Bonf Corrected
Tact
Textual


Neural Activity in the Verbal Operants
Echo
Intrav
p<.001 Bonf Corrected
Tact
Textual

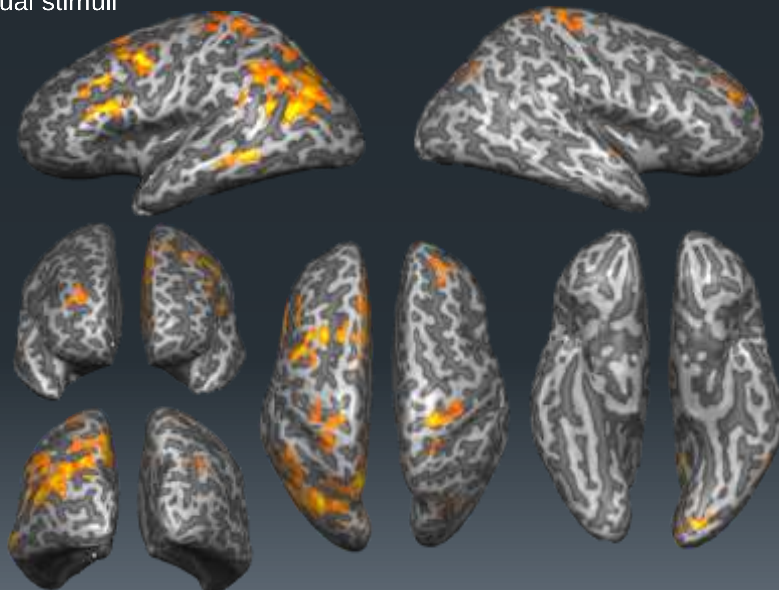

Neural Activity in the Verbal Operants
Echo
Intrav
p<.001 Bonf Corrected
Tact
Textual


Neural activity in Tact behavior
Specific for Stimulus Nature (auditory vs visual tacting)
DLPFC
PSC
PAC
PVC
SMC
OFC
Vis
Aud
PVC
PVC


Intraverbal activity specific for stimulus nature
«Contrast» between intraverbal activity evoked by auditory and textual stimuli
Vis
Aud

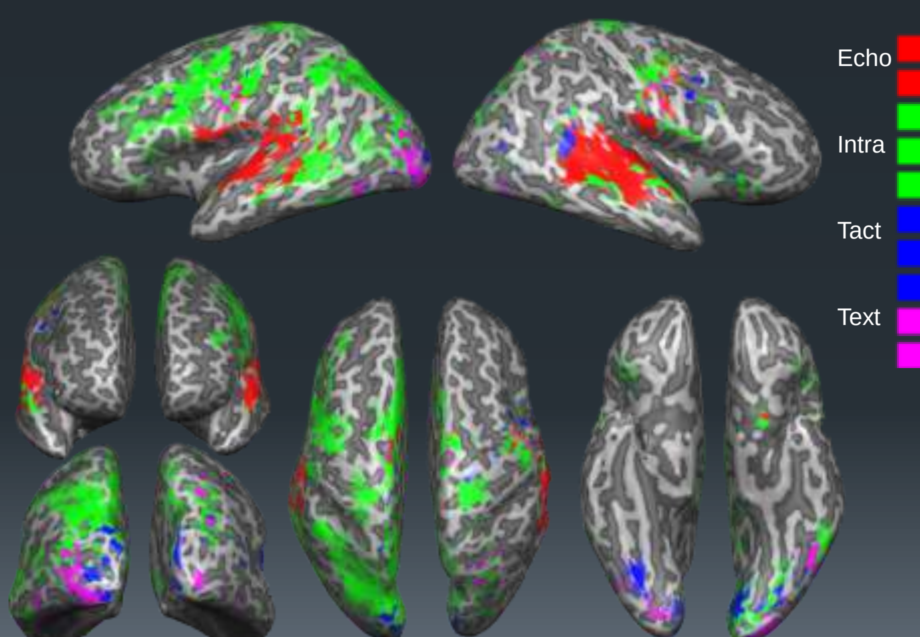
Intraverbal activity independent of stimulus nature

Brain activity in both (AND) intraverbal behavior evoked by auditory and textual stimuli

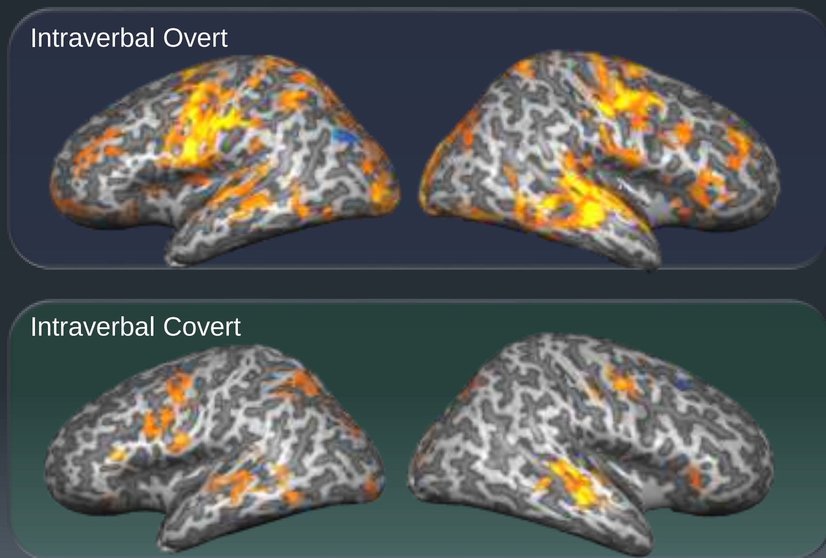


Winner Map

The prevalent operant in the pattern of activity

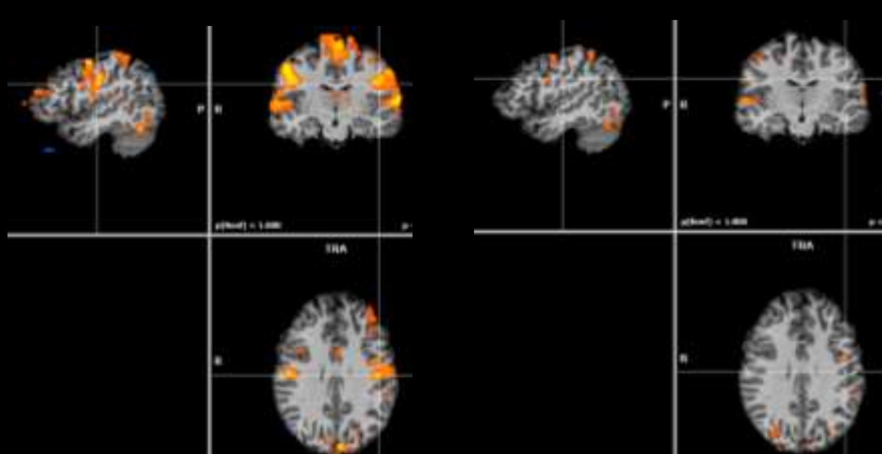


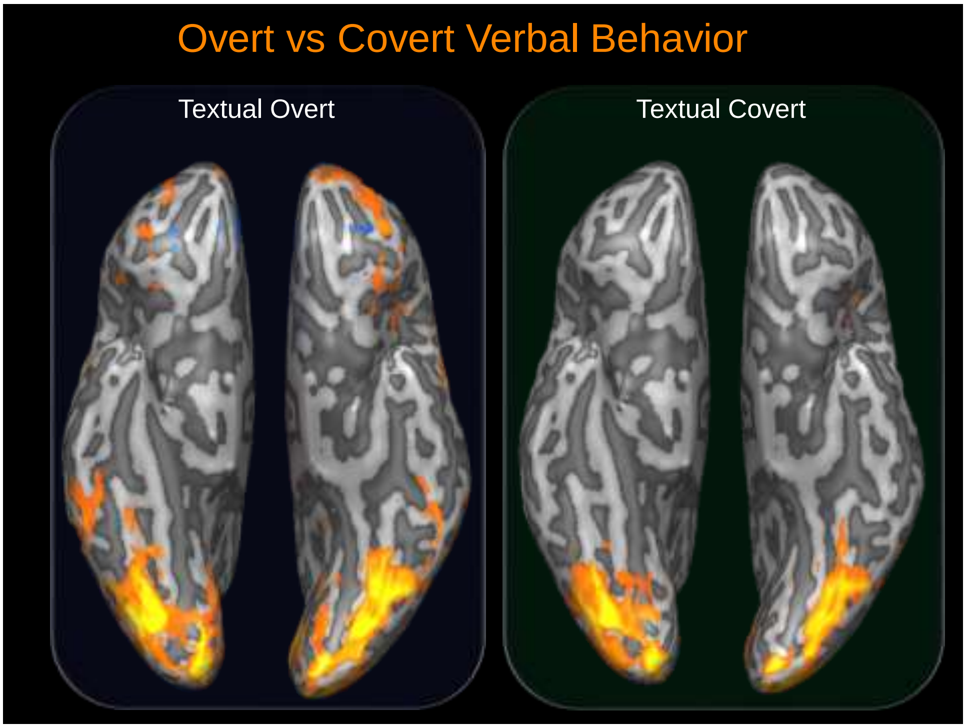
Overt vs Covert Verbal Behavior



Overt vs Covert Verbal Behavior

Brain activity in textual overt and covert behavior





The Verbal Operants experiment
Conclusions

a) The single Verbal Operants are associated to unique patterns of brain activity. It is possible to recognize what Operant a subject is emitting just from her/his brain activity pattern.

b) From a Neurobiological perspective, this implies that a specific learning process needs to be completed to use a given topography in a different Operant (Independence of Verbal Operants)

c) The Echoic Operant has the simplest pattern of activity, encompassing mainly temporal lobe (Auditory) regions

d) The Intraverbal shows by far the most complex pattern of activity, that includes massively parietal lobe regions, highly active in visual imagery, with implication for teaching Ivs

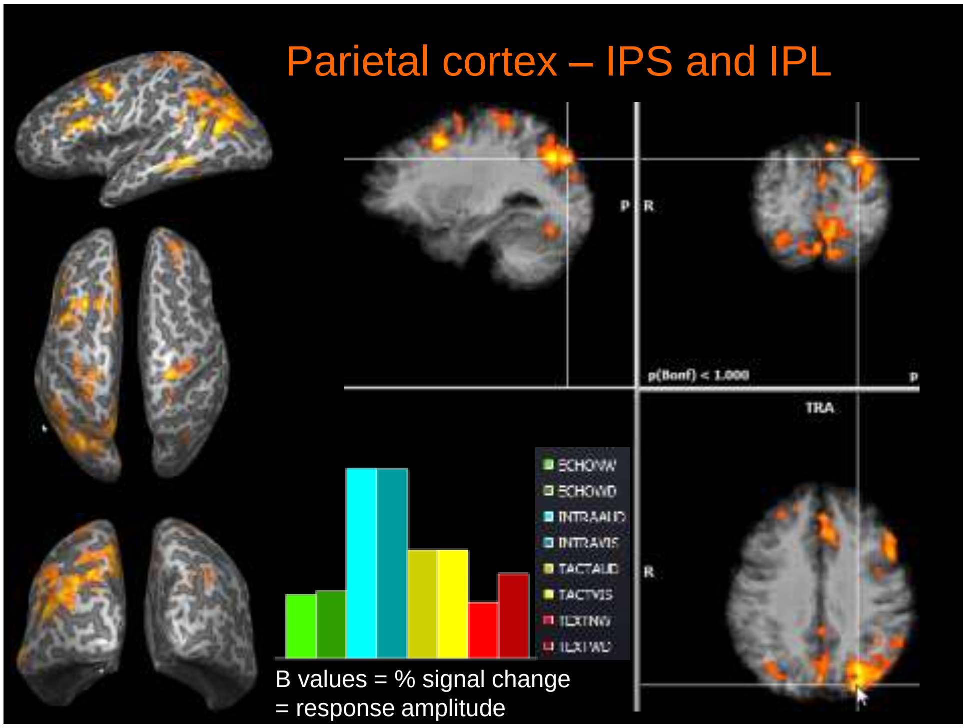
The Verbal Operants experiment
Conclusions

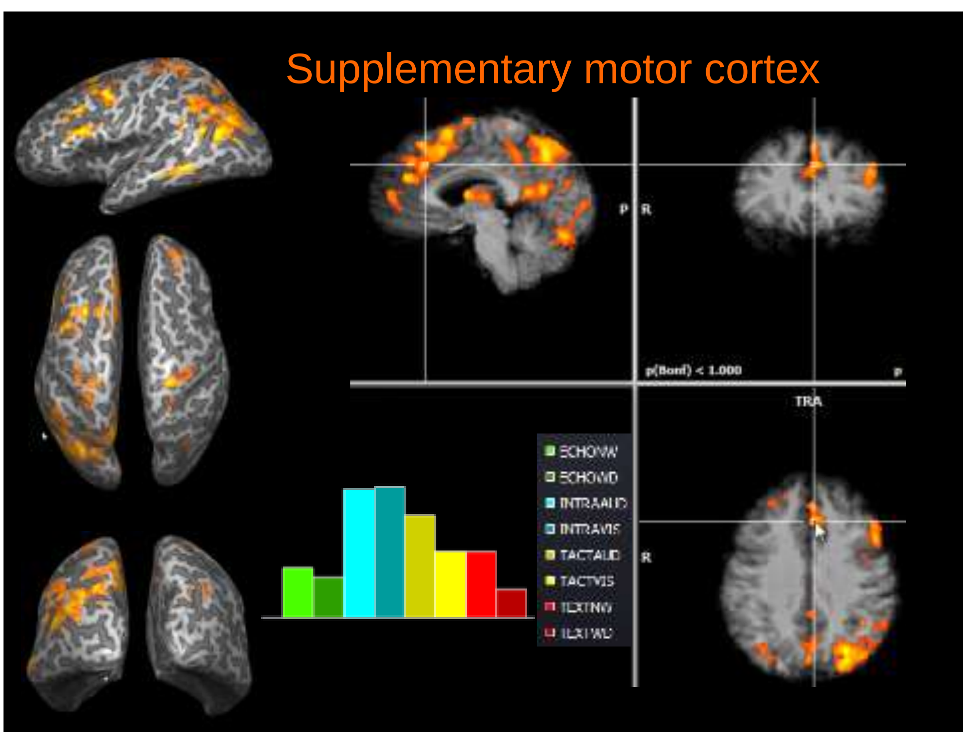
e) The Iv activity in the Occipital lobe is strongly similar to Tact-related activity

f) Both Tact-related and Textual-related activities use strongly visual regions, but differ in the Primary Visual Cortex, in the Occipital Pole, and in the Ventral Stream

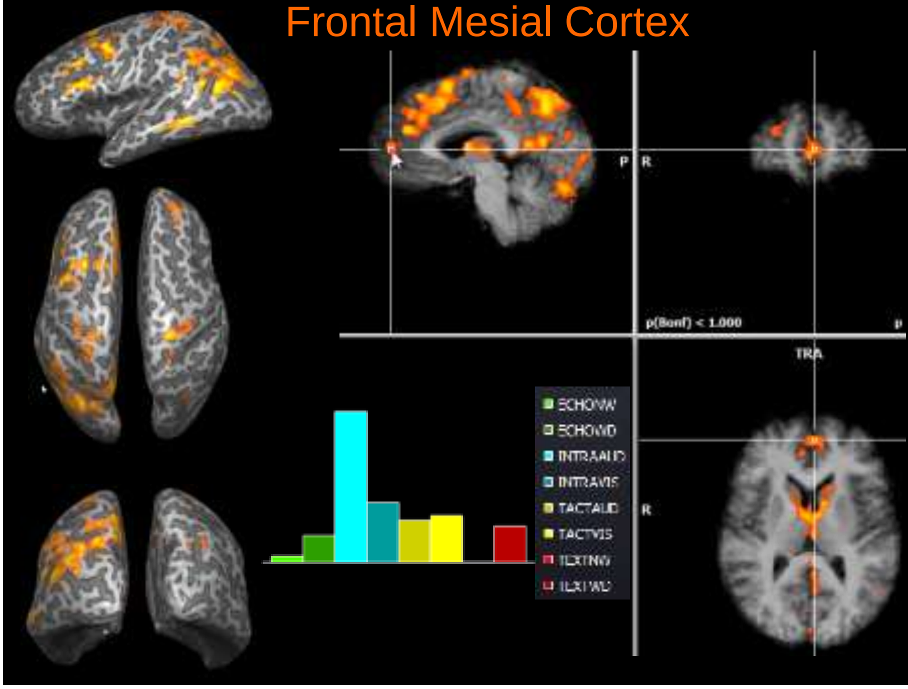
g) A common substrate of neural activity, though, is present in all Verbal Operants, e.g. in the auditory cortex and the supplementary motor region, possibly the neural basis for Stimulus Control transfer procedures

Neural Activity related to Verbal Operants in single brain areas


Parietal cortex – IPS and IPL
P R
p(Bonf) < 1.000
P
TRA
R
B values = % signal change
= response amplitude


Supplementary motor cortex
P R
p(Bonf) < 1.000
P
TRA
R

Frontal Mesial Cortex



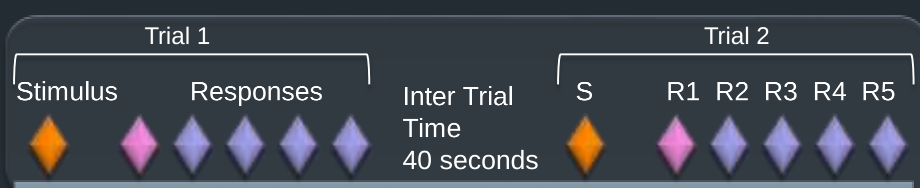
The Intraverbal Behavior time-course in the brain

The “word association” experiment analysed by the source of control of the associations

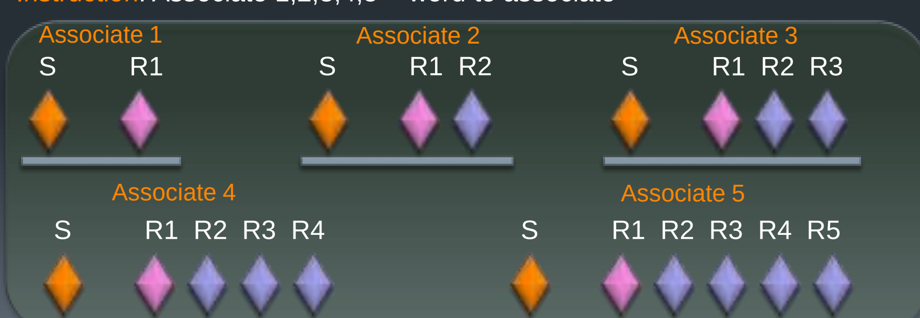
The “word association” experiment

- A word association in response to a verbal antecedent is Intraverbal Behavior (Skinner, Verbal Behavior p.72)
- The source of control: in a word association experiment is never only in the verbal antecedent
- The word association experiment has been reproduced in an fMRI environment in order to:
    - a) single out the brain area(s) were the behavior is emitted
    - b) analyze the source of control
    - c) identify the chain of behaviors that leads to the final behavior

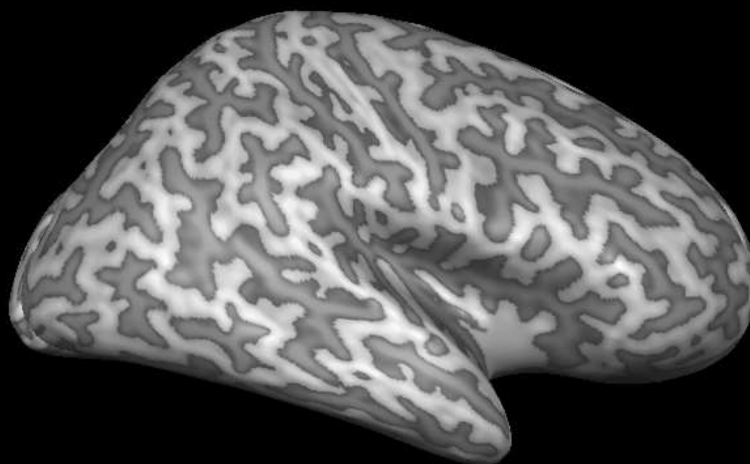
Design of the “word association” experiment



Five different types of Trials by the number of responses required
Instruction: Associate 1,2,3,4,5 + word to associate

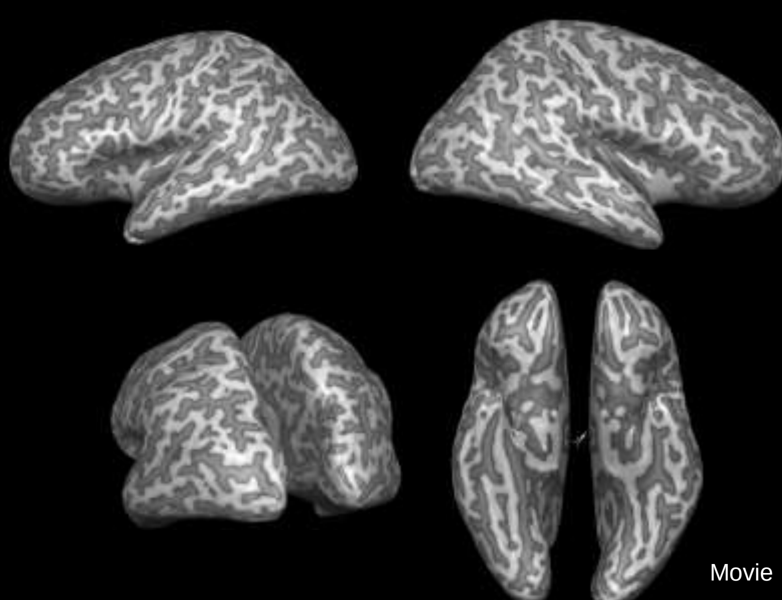


The “word association” experiment by number of word



Movie

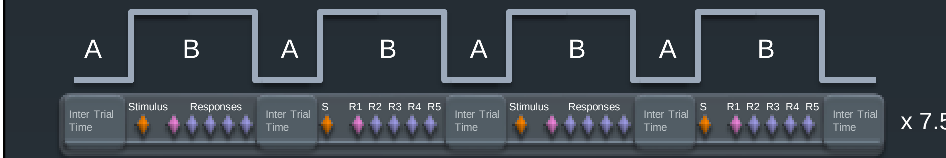
The “word association” experiment



Movie

Design of the “word association” experiment

Conteptually a reversal/withdrawal experiment with many (n 30) applications and withdrowals of the independent variable



Taking into account the number of responses required in each trial (1 to 5), 5 different conditions of the Independent Variable are tested

Sources of control identified “post hoc” from the responses

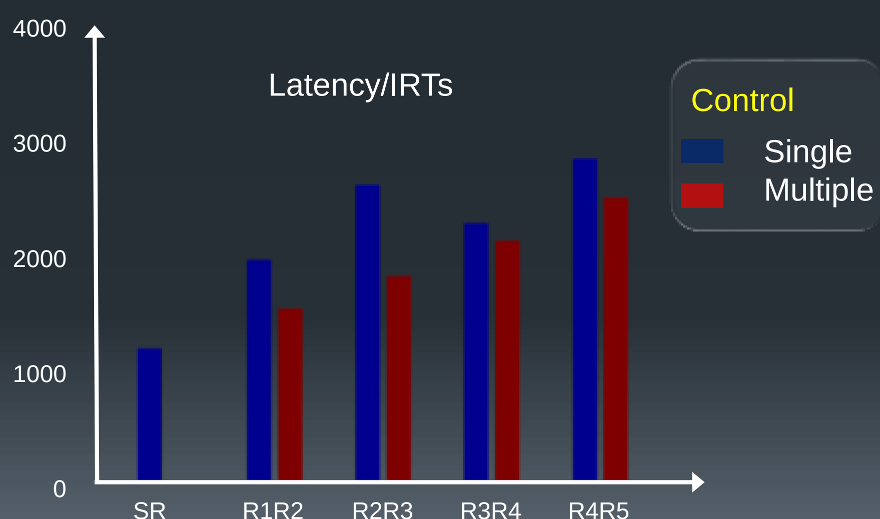
1. The initial Stimulus
2. The other words emitted previously in the same trial

The single trials are spaced enough in time (40 seconds) to reduce their strength as sources of control for the responces of the following trials

Categorization of the Responses by their source of control

1. The first word is controlled mainly by the initial stimulus and is categorized as "RS" (stimulus)
2. The following words can be controlled (mainly) by the initial stimulus, if no clear association can be derived "post hoc" with the previous words emitted, neither by the experimenter nor by the subject himself after the session. These responses are also categorized as "RS"
3. The following words can be controlled (also) by the other words emitted previously, as assessed by the experimenter and the subject himself after the session. These responses are categorized as "RM" (multiple)

Categorization of the Responses by their source of control



Categorization of the Trials by the source of control of their single responses

A trial-level analysis has been performed to comply with the difficulty of a response-level analysis

- The Trials are cathegorized as “S” if they contain only Responses type S (mainly controlled by the initial stimulus)
- The Trials are cathegorized as “SM” if they contain one or more Responses type S (except R1) and one or more Responses type M (partly controlled by previous Responses)
- The Trials are cathegorized as “M” if they contain only Responses type M and no Responses type S (except R1)

Categorization of the Trials by the source of control of their single responses

Examples

Trials type S

S	RS	RS	RS	RS
Close	**Door**	**Pack**	**Situation**	**Book**

Trials type SM

S	RS	RM	RM	RS	RM
Past	**Far**	**Girls**	**Friends**	**Future**	**Present**

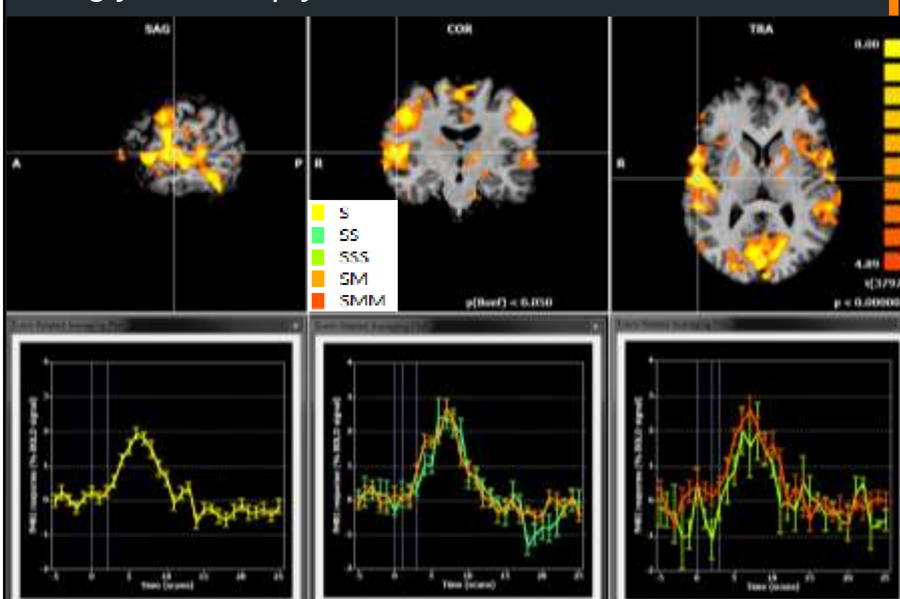
Trials type M

S	RS	RM	RM	RM	RM
Referee	**Match**	**Ball**	**Player**	**Goalkeeper**	**Goal**

Categorization of the Trials by the source of control of their individual responses

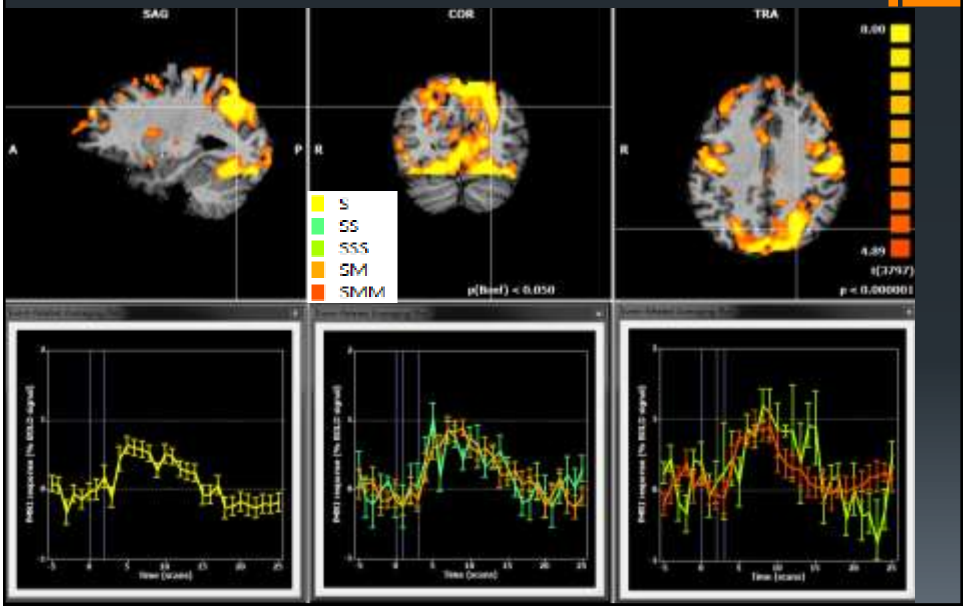
IV behavior in the Right Auditory Cortex

Singly vs Multiply controlled "word association" IVs



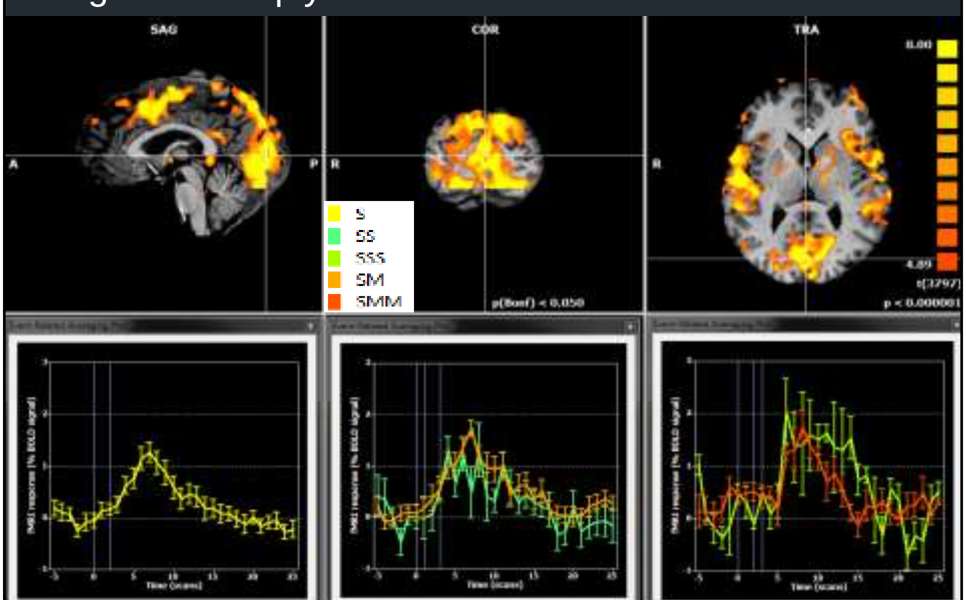
IV behavior in the IPS

Single vs Multiply controlled "word association" IVs



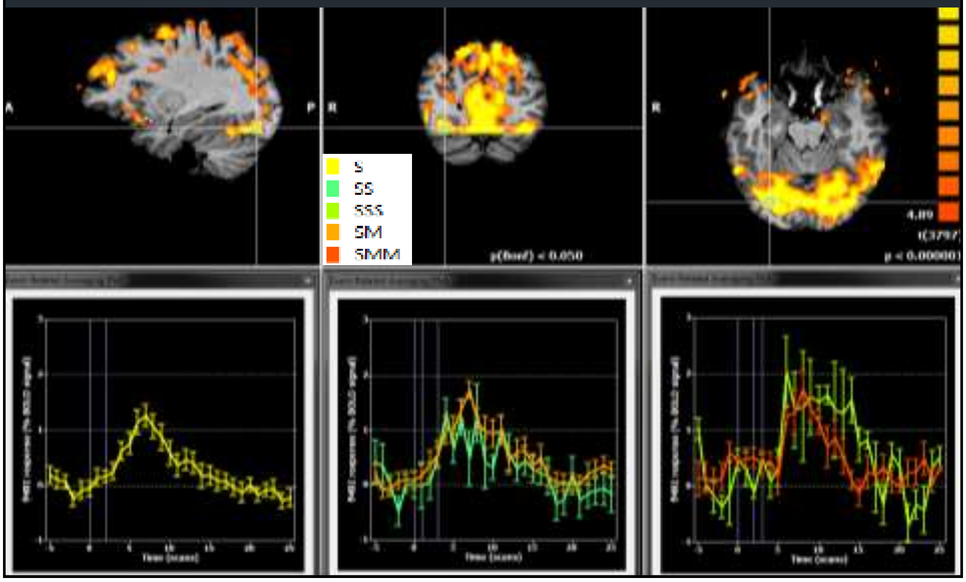
IV behavior in the Primary Visual Cortex

Single vs Multiply controlled "word association" IVs



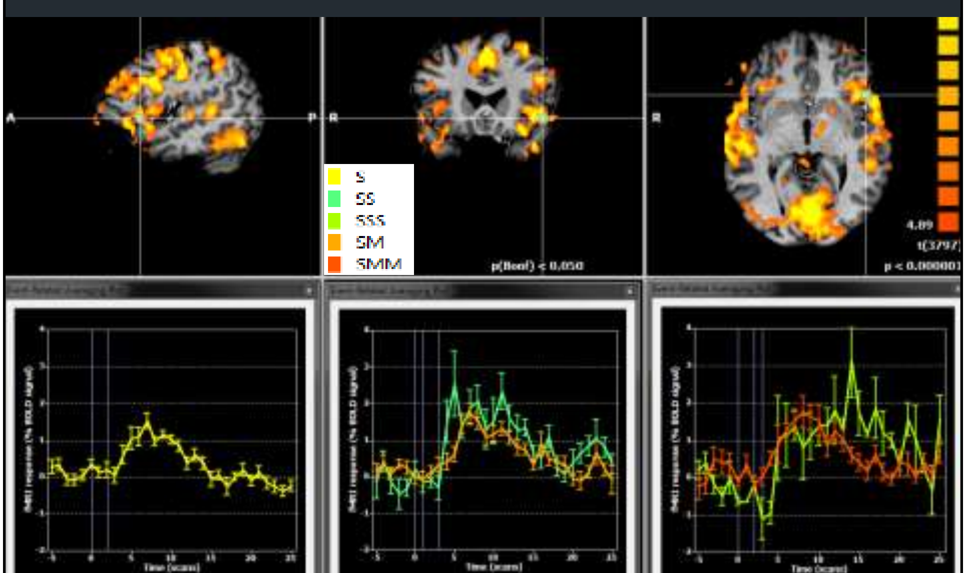
IV behavior in the Occipito-Temporal cortex

Single vs Multiply controlled "word association" IVs



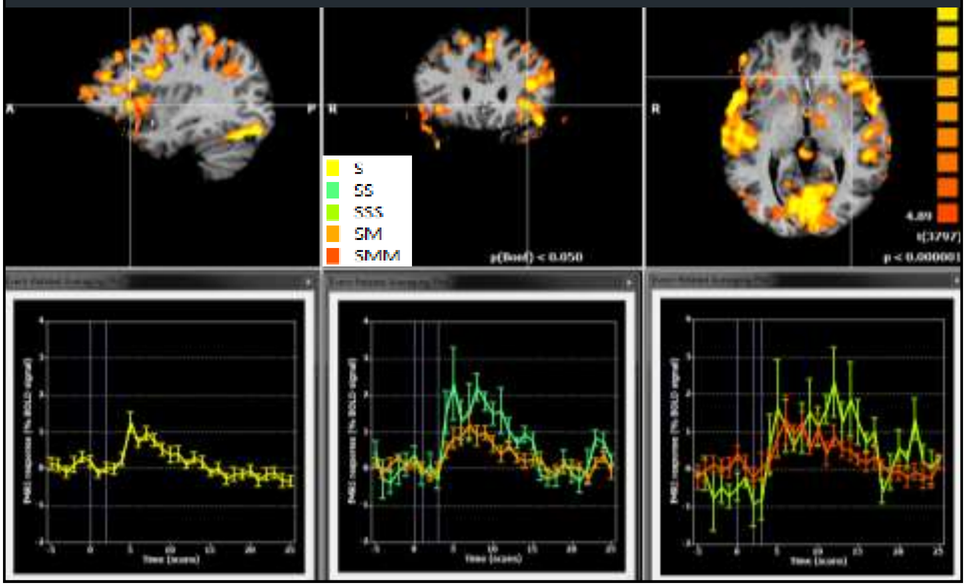
IV behavior in the Left Inferior Frontal

Single vs Multiply controlled "word association" IVs



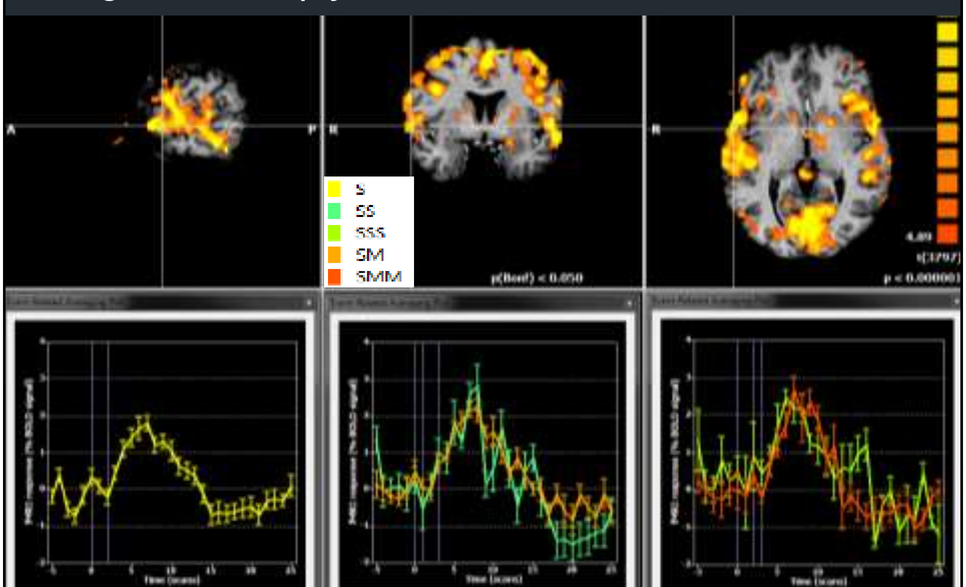
IV behavior in the Left Inferior Frontal

Single vs Multiply controlled "word association" IVs



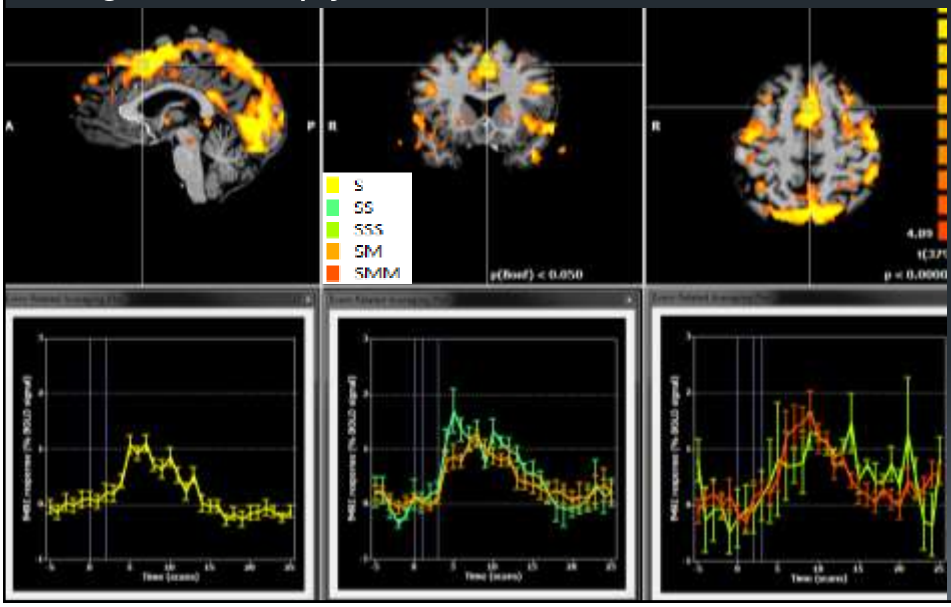
IV behavior in the Right Temporal Pole

Single vs Multiply controlled "word association" IVs



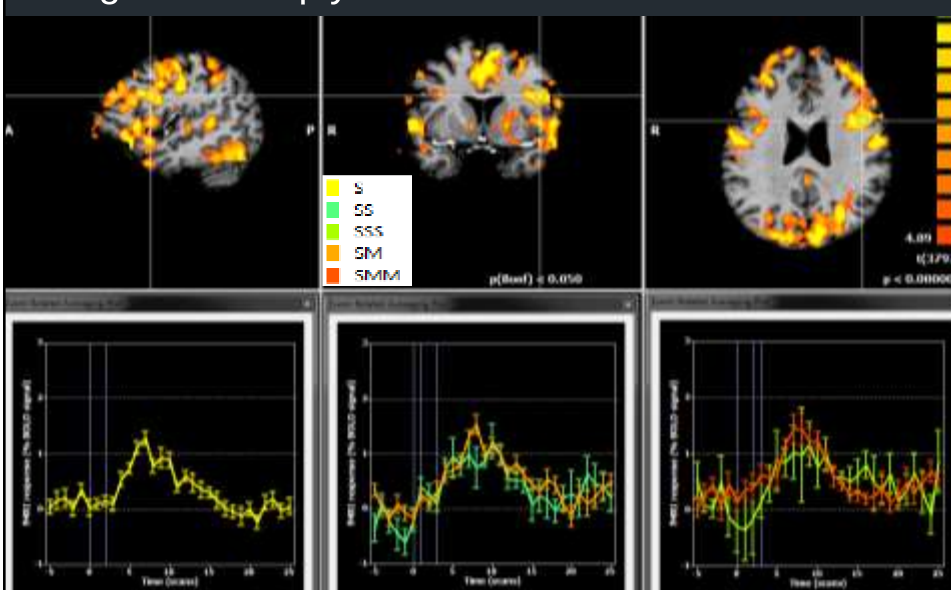
IV behavior in the SMA

Single vs Multiply controlled "word association" IVs



IV behavior in the left DLPFC

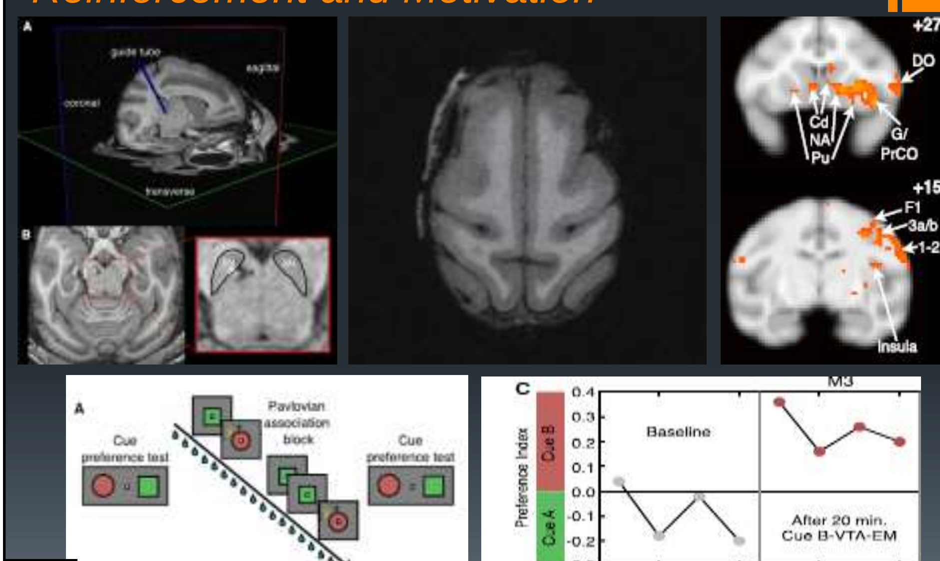
Single vs Multiply controlled "word association" IVs



Outline

- Skinner and the Neurosciences
- Why to integrate Neurosciences into Behaviorism
- Private behaviors made public - increased complexity
- The procedures to study behavior in the brain
- The need to translate information from Neurosciences to Behaviorism and vice versa
- The critical role of Neuroimaging in translating the information
- The verbal operants in the brain: the neural basis of their independence
- Methods to modify directly the behavior in the brain

The Primate Ventral Tegmental Area in Reinforcement and Motivation



Arsenault JT, 2014, Current Biology

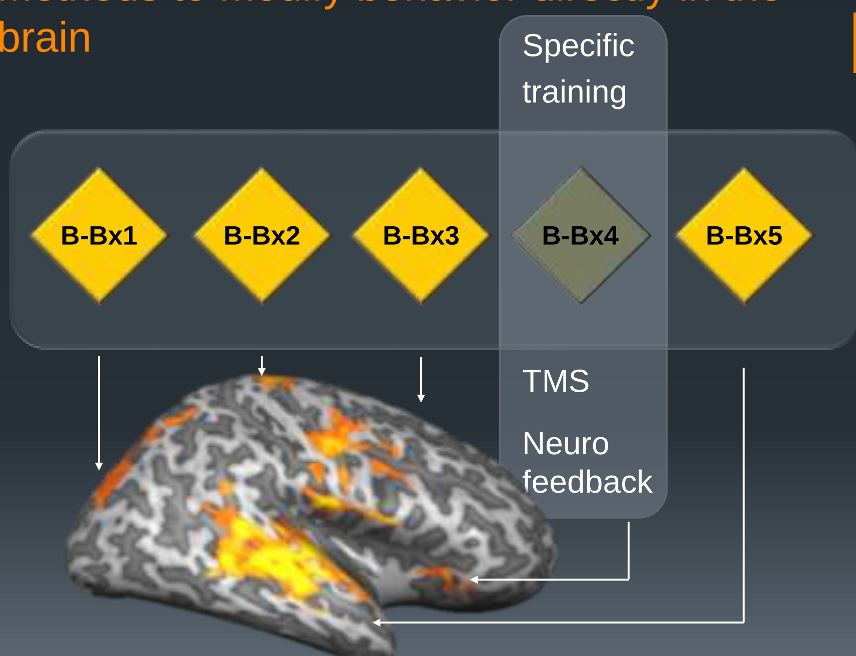
Methods to modify directly behavior in the brain

The focus of many discussions with friends Behavior Analysists has often been the possible application of knowing more about Behavior in the brain.

Beside the potential deriving from an expanded knowledge itself, which can be of substantial value, we can examine three possible ways to modify brain functioning directly with neuroscience derived methods, in a convergent action with Applied Behavior Analysis procedures:

a) Specific training
b) TMS (Transcranial Magnetic Stimulation)
c) Neurofeedback

Methods to modify behavior directly in the brain



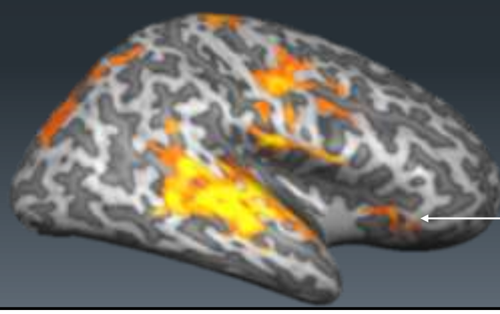
Methods to modify behavior directly in the brain

Specific training

Design Intervention that provide independent training of B-Bx 4 outside the behavioral chain

Return to teaching the chain when measures of B-Bx4 are substantially higher

B-Bx4



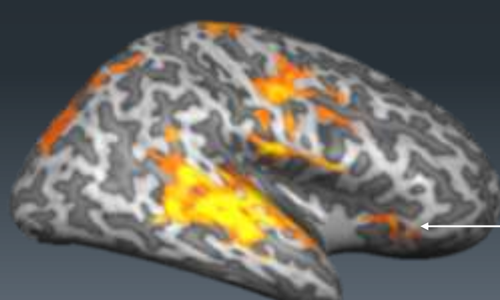
Methods to modify behavior directly in the brain

TMS

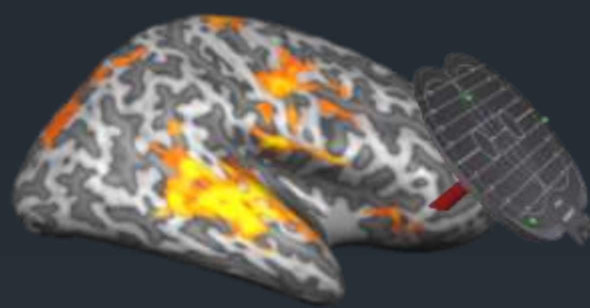
Apply «plasticity» paradigms of TMS, able to modify excitability of a specific brain area for a lasting time (hours)

Return to teaching the chain

B-Bx4



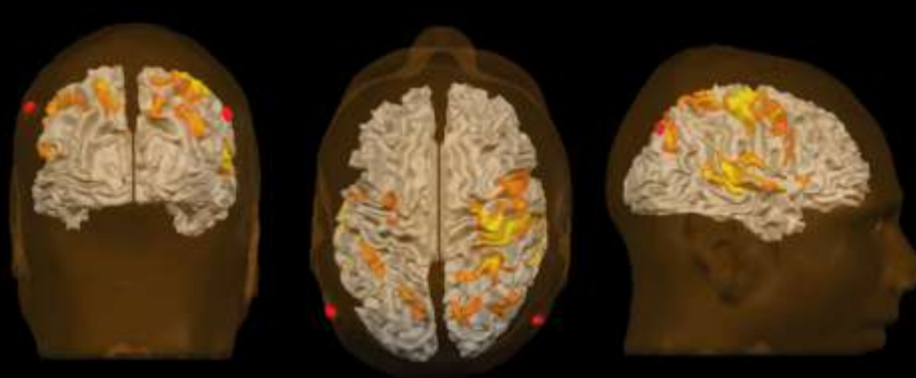
TMS – Transcranial Magnetic Stimulation



Release of brief magnetic pulses, often gathered in pulse trains, able to modify excitability of the specific brain area that is targeted through neuroimaging

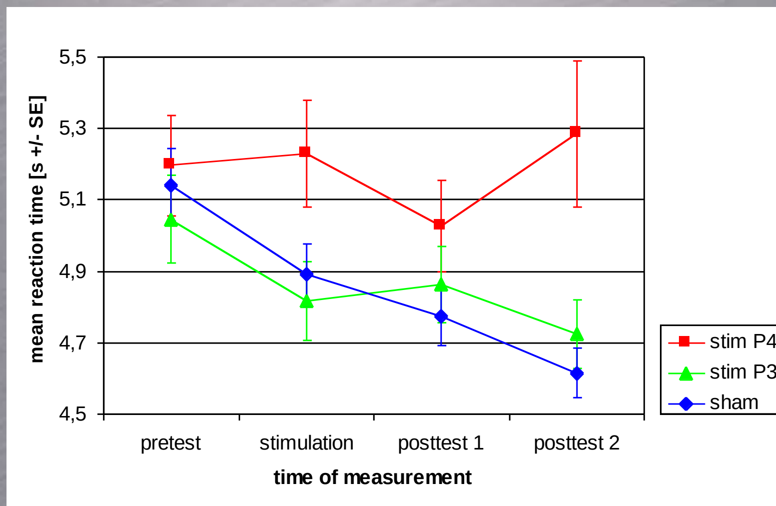
Extensively used since decades to study the conduction of motor information from brain cortex to neuromuscular perifery

Imaginal clock task - *Combined fMRI and rTMS*

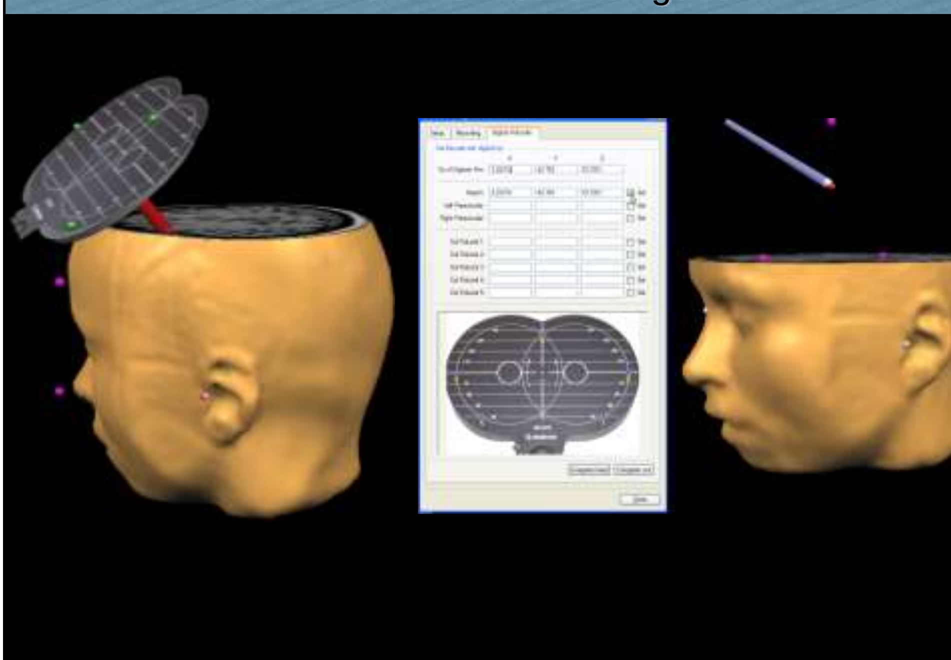


Sack A, Di Salle F. et al., (2002), Tracking the mind's image in the brain II, *Neuron*, **35**, 195-204.

Imaginal clock task - *TMS results*

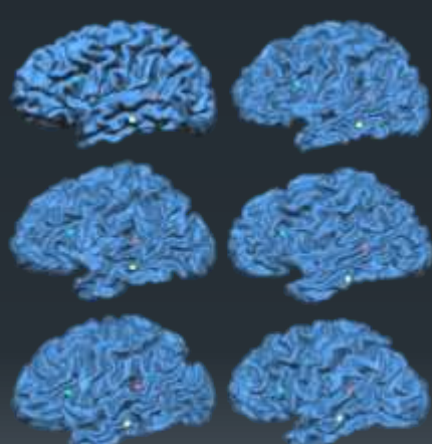


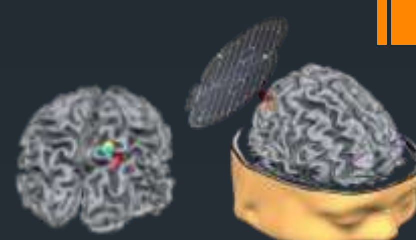
Real-Time TMS Neuronavigation

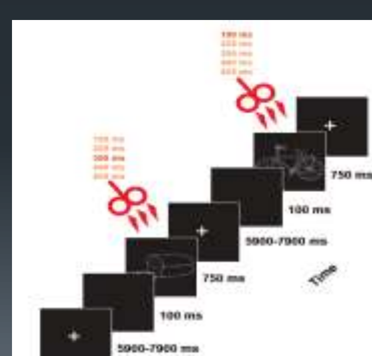


TMS Neuronavigation - *Example*

Functional Dissection of the neural network for verbal behavior

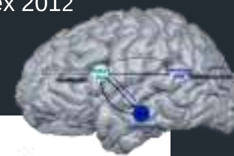


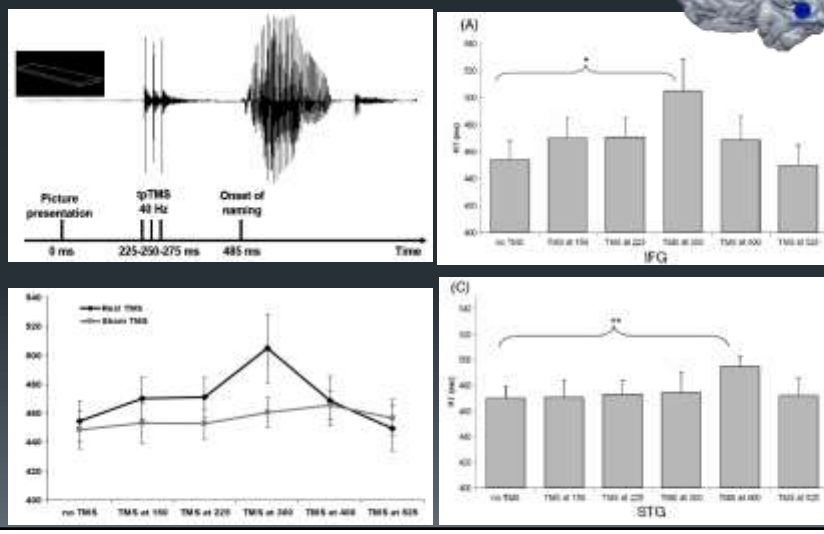




Speaking of Which: Dissecting the Network of Language Production in Picture Naming - Teresa Schuhmann – Cerebral Cortex 2012

Functional Dissection of the neural network for verbal behavior Schuhmann T – Cerebral Cortex 2012



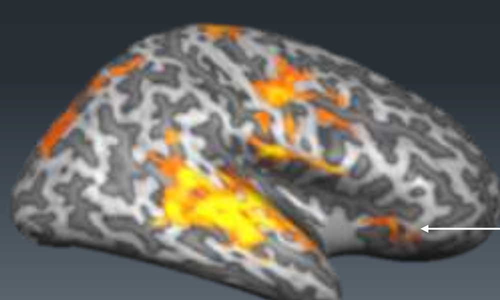


Methods to modify behavior directly in the brain

Neuro feedback

- The subject learns in time how to stimulate specifically a given brain region, having in real time a grafic feedback from its activity
- Already applied to brain pathologies
- Requires specific experience

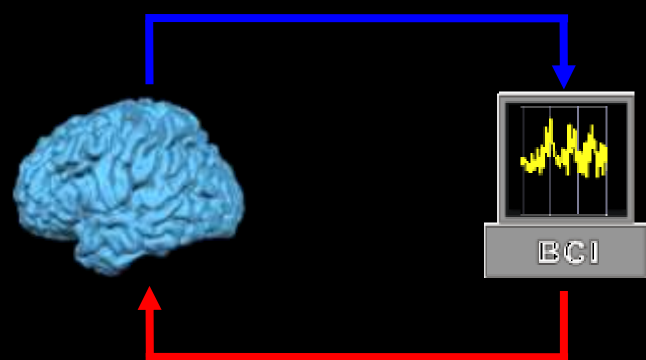
B-Bx4



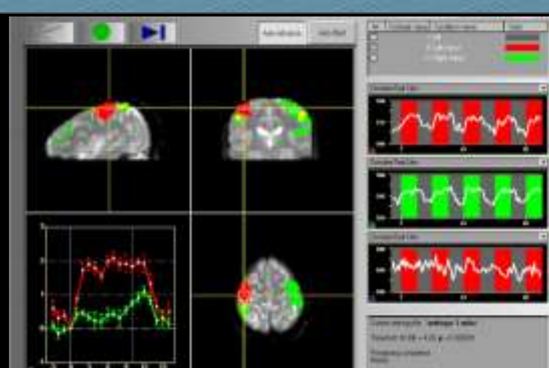
Neurofeedback

Creating a Brain-Computer Interface (BCI)

- Neural activity is transformed into digital code
- Feedback for learning of self-regulation of brain activity

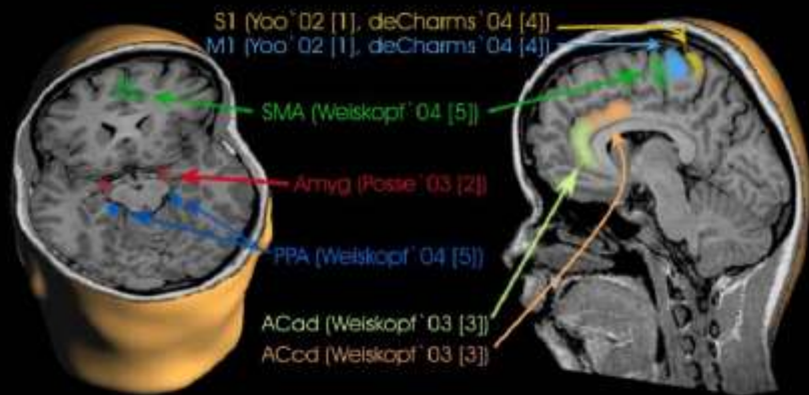


Real-time fMRI neurofeedback



- Real-time fMRI enables monitoring ***online*** changes in the activity of the brain area producing the response.
- The high spatial resolution of fMRI offers the possibility to investigate the control over ***localized*** brain regions.
- Subjects can learn to influence their own brain activity from ***one*** or ***multiple*** circumscribed brain regions.

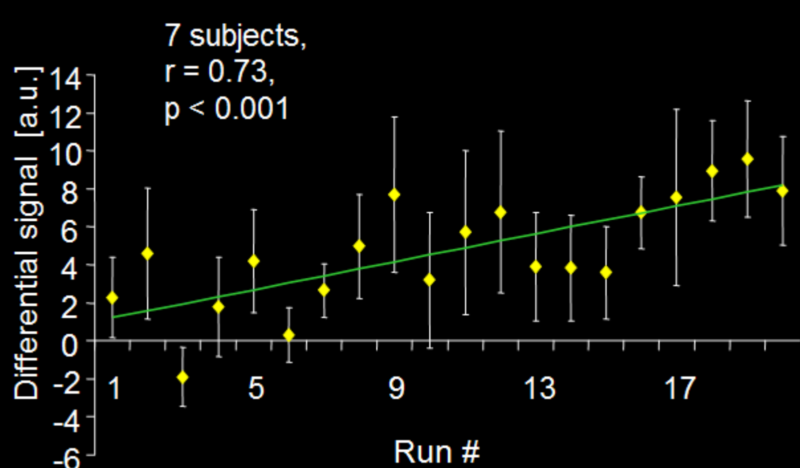
fMRI neurofeedback studies



fMRI neurofeedback studies have shown that we are able to modulate different brain areas using several strategies, such as visual or auditory imagery

FMRI neurofeedback

Differential modulation – Training effect



Clinical Implications (on the side of neuroscience)

fMRI Neurofeedback might be an important tool for clinical applications. It has been, for example, successfully applied to reduce pain perception (DeCharms et al., 2004).

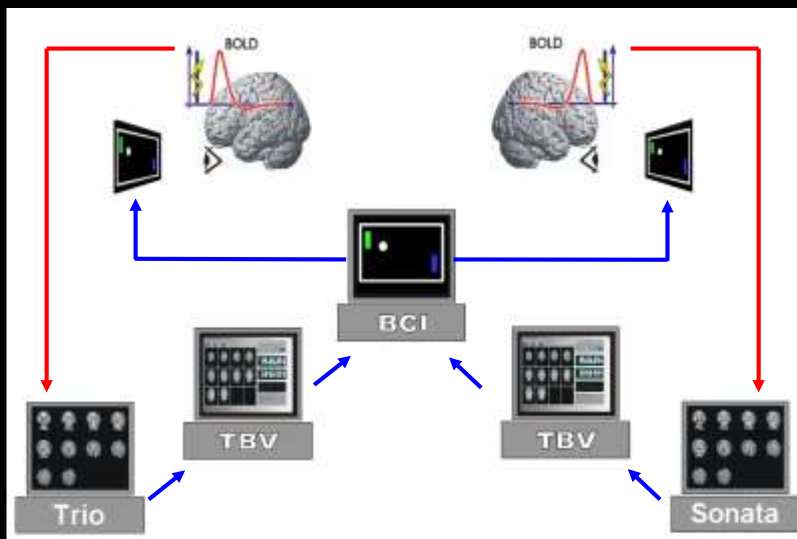
Other clinical applications might be the reduction of auditory hallucinations or the suppression of epileptic seizures or the treatment of phobia.

Synchro-Scanning and Neurofeedback

Is it possible to couple two brains ?
Can two subjects exchange information based on ongoing fMRI measurements?
How difficult is it to learn to handle the hemodynamic delay?
To what extent does this delay limit brain-brain interactions?
Proof of concept -> BOLD Brain Pong

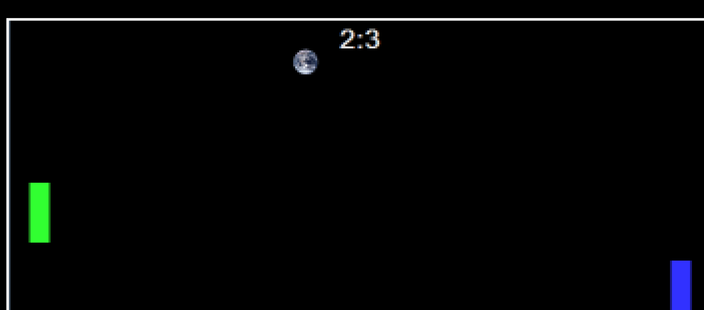
Interactive neurofeedback

Experimental Setup



Graded Control and Brain Pong

Results – Example game (real-time movie)



Conclusions

- Modern Neuroimaging has overcome many of the procedural weak points it presented at its beginnings
- It can complitely comply with the requisites Skinner posed over the use of Neuroscience data, regarding precision, reliability, reproducibility and interpretation.
- Neuroscience does not need to be cognitive. Neuroimaging is using a pure anatomical analysis of results
- New knowlege can be derived by a marriage between the Science of Behavior and the Neuroscience, even in an applied perspective.
- It is not, though, pure knowledge, powerful methods to modify the brain directly are available