Coordinate-Based Meta-Analysis using Activation Likelihood Estimation (ALE)

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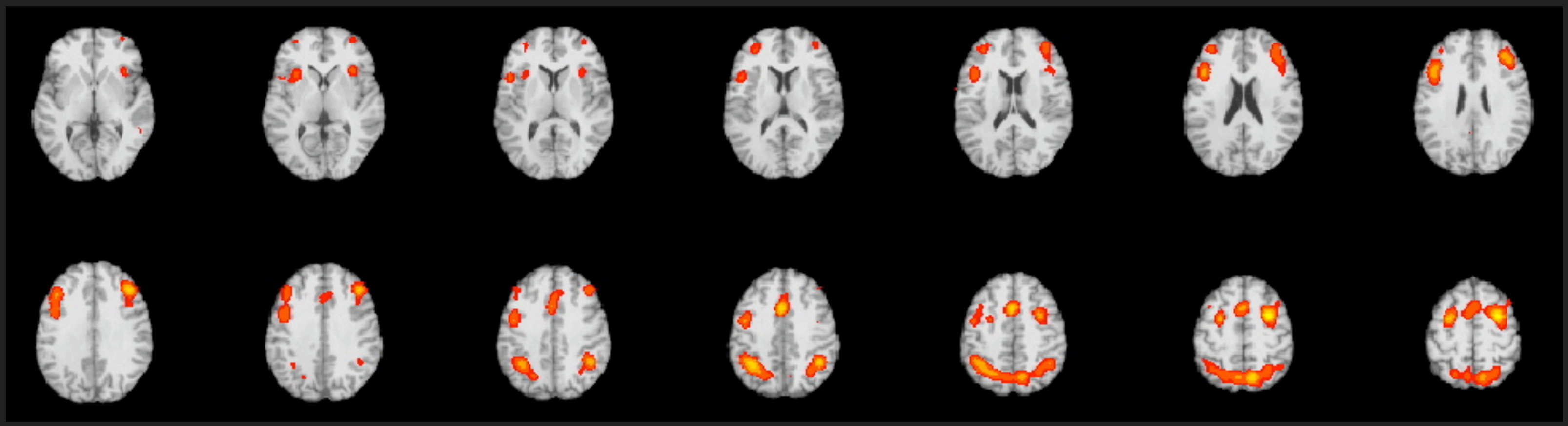
The BrainMap Project

a database of functional neuroimaging results

a comprehensive tool for ALE meta-analyses

http://brainmap.org

BrainMap: The Concept



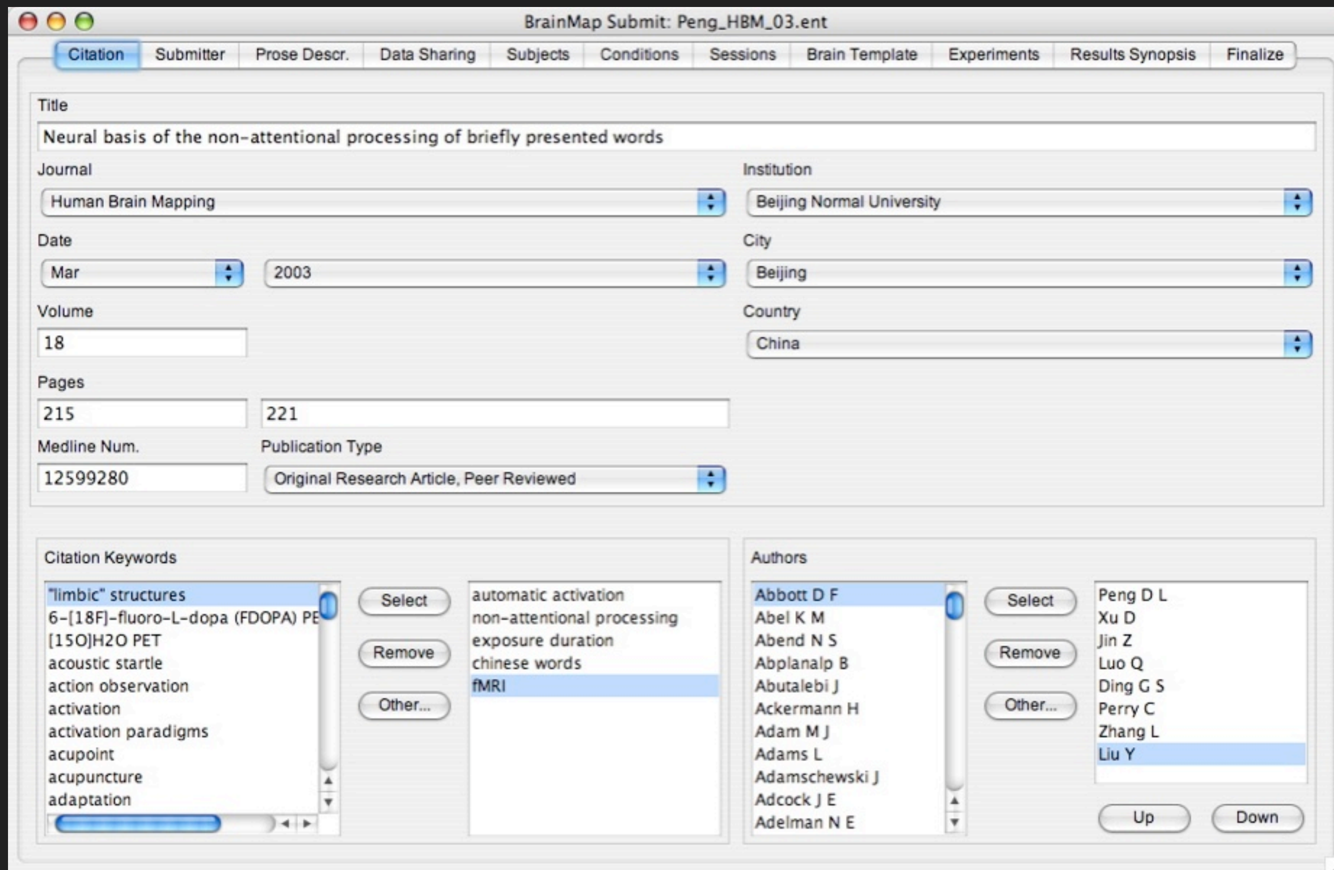
Database of functional neuroimaging studies

Archives coordinate data, not raw data, not SPIs

Searchable by paradigm, cognitive domain, subject groups, ROIs, anatomical labels, etc.

x	y	z
6	18	40
8	23	35
-4	14	35
0	15	41
-2	14	40
0	2	48
6	23	39

Reduced Data, Not Raw Data



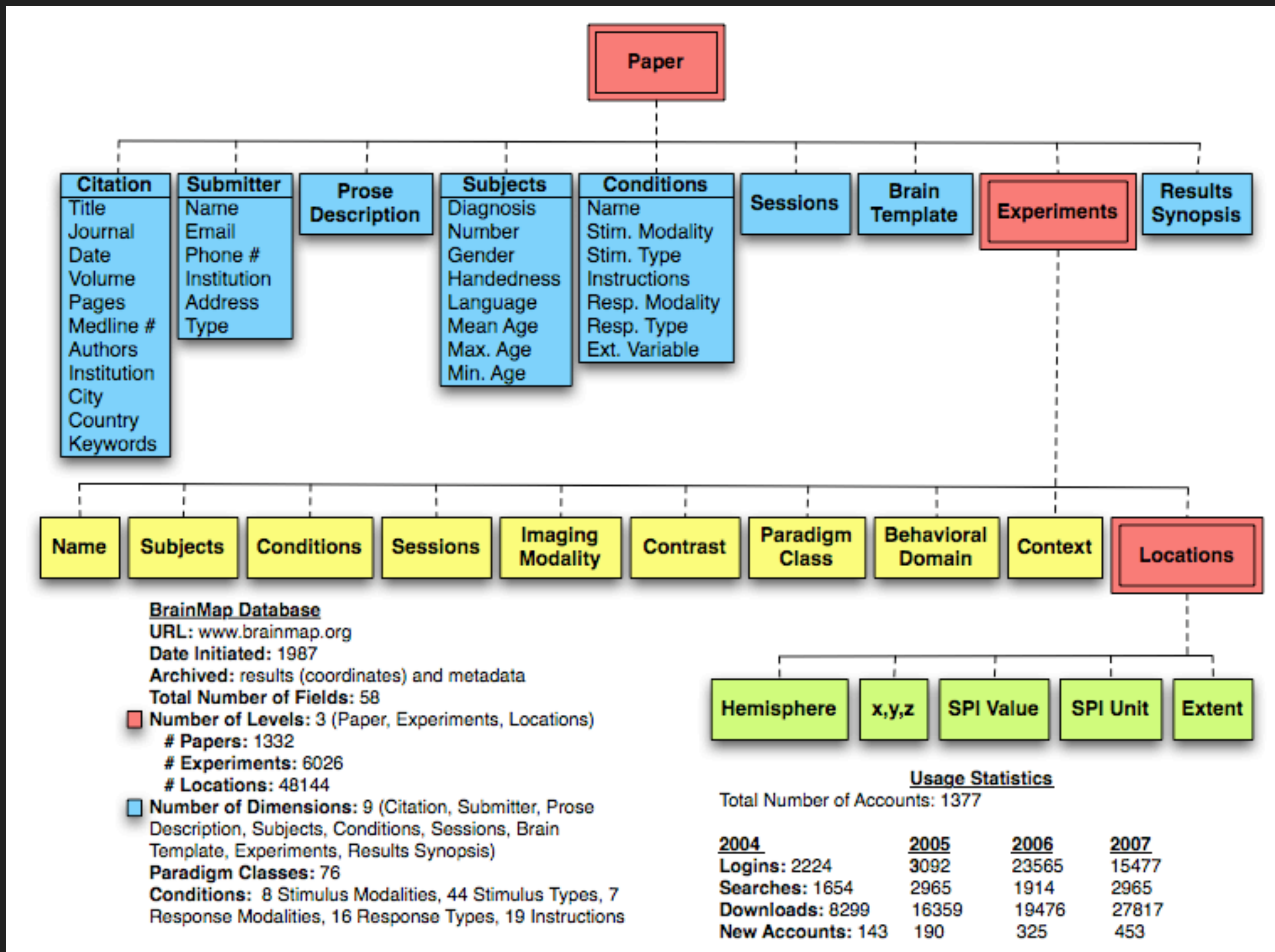
Coordinates: center-of-mass (x,y,z)

Extent (volume of activation in mm³)

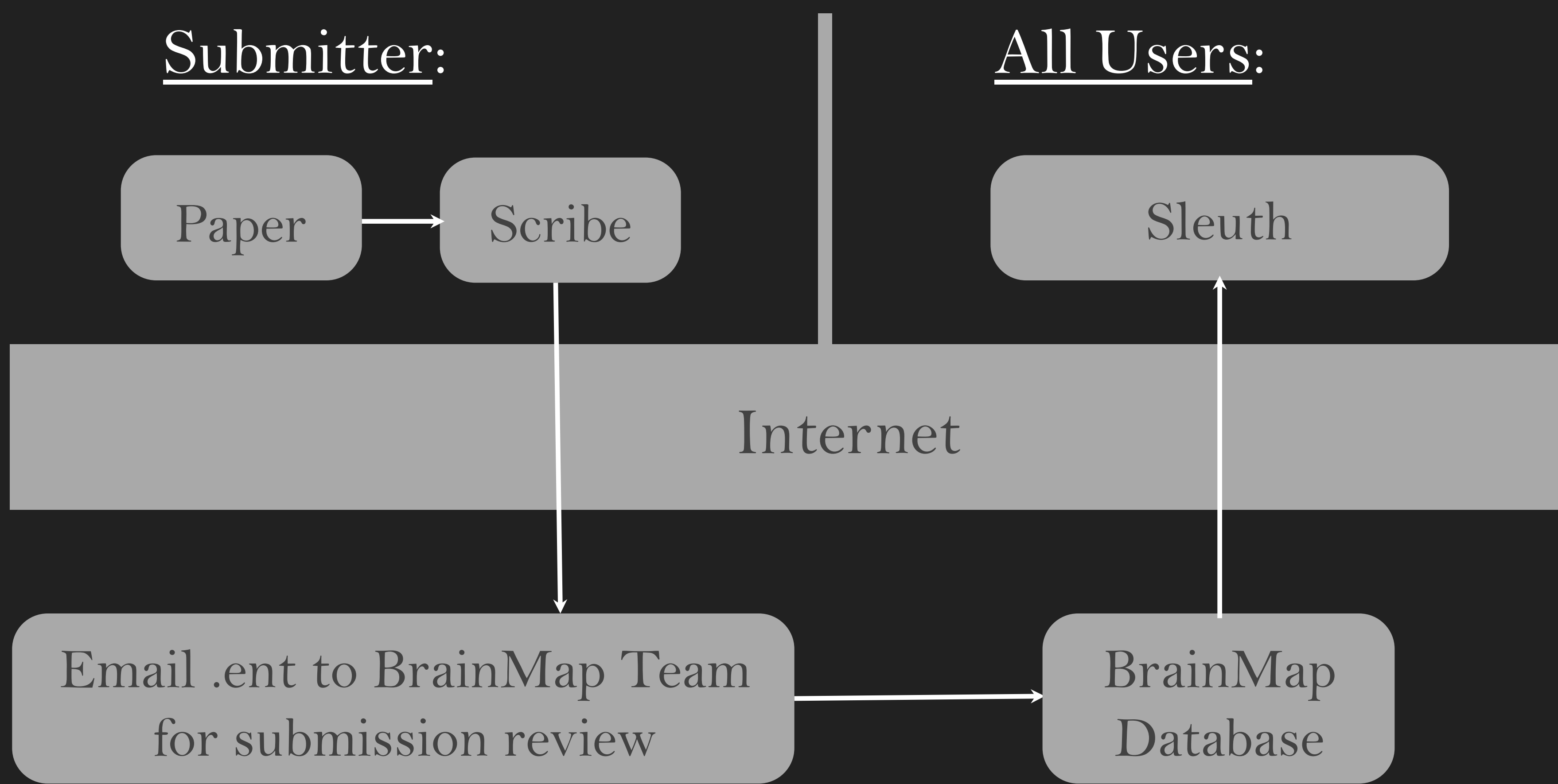
Standardized statistical parameters (Z, t, r, F)

Standard anatomical descriptor (Talairach Daemon)

BrainMap Coding Scheme

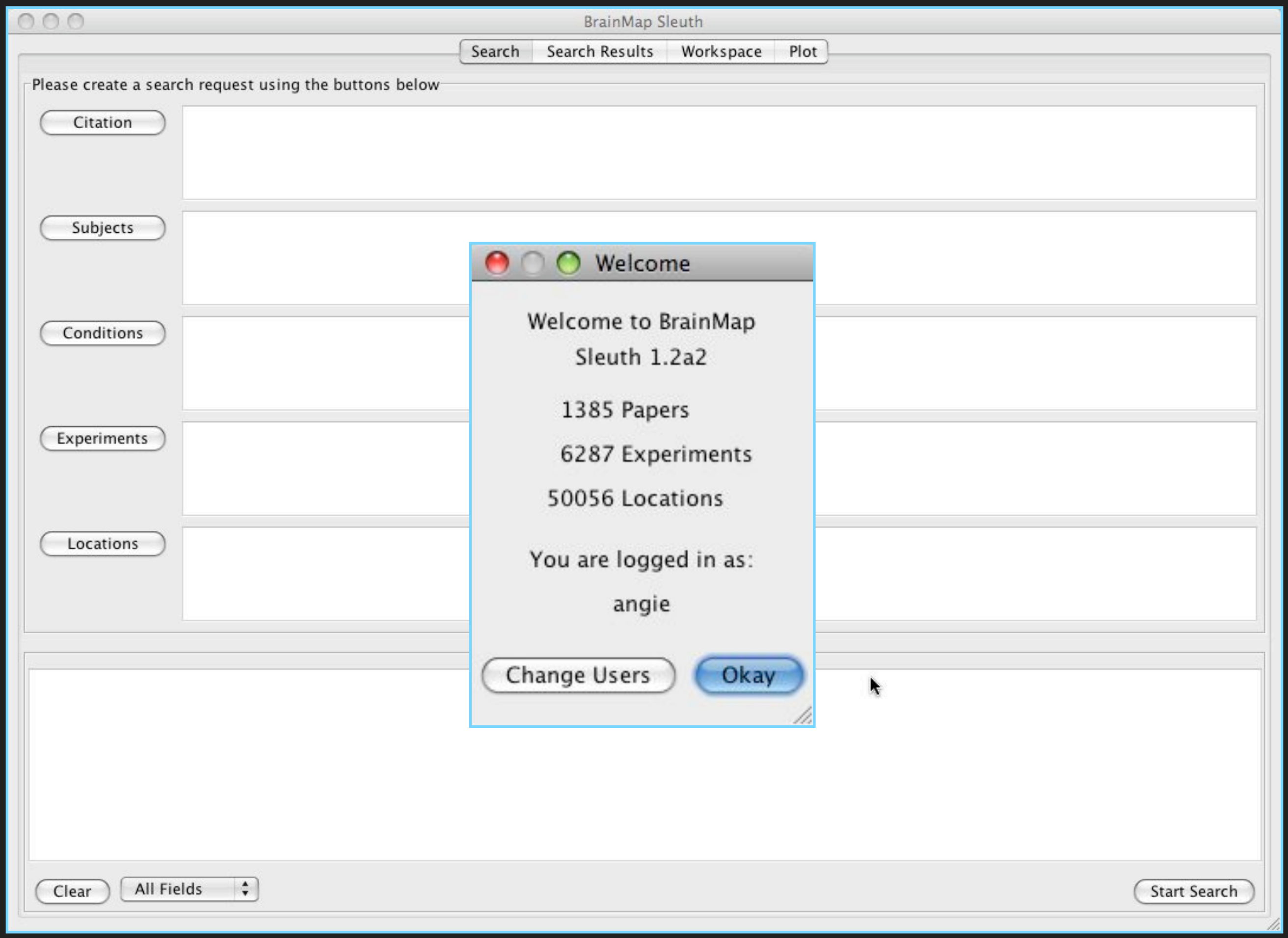


BrainMap Database Submission



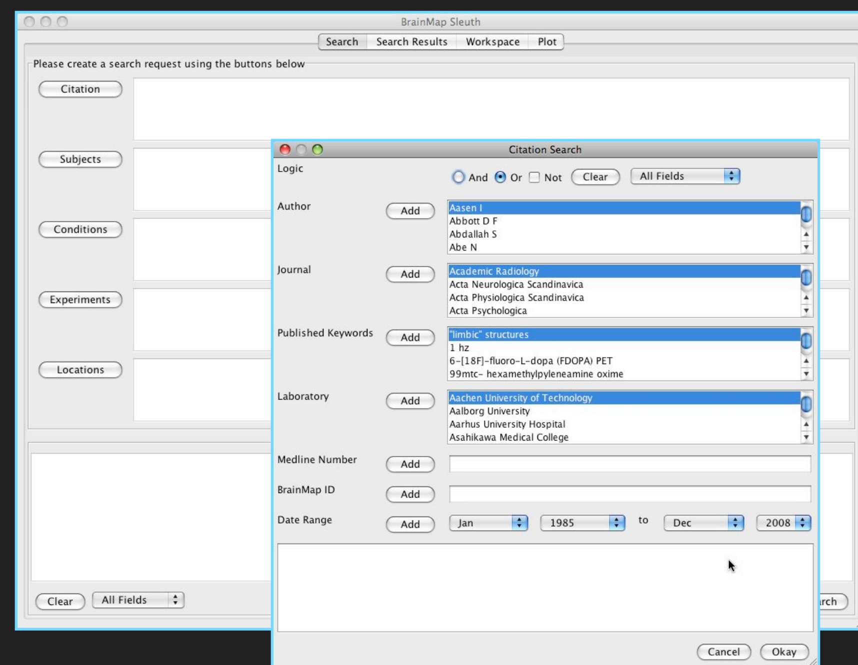
BrainMap Sleuth

Login to Sleuth to view database entries:

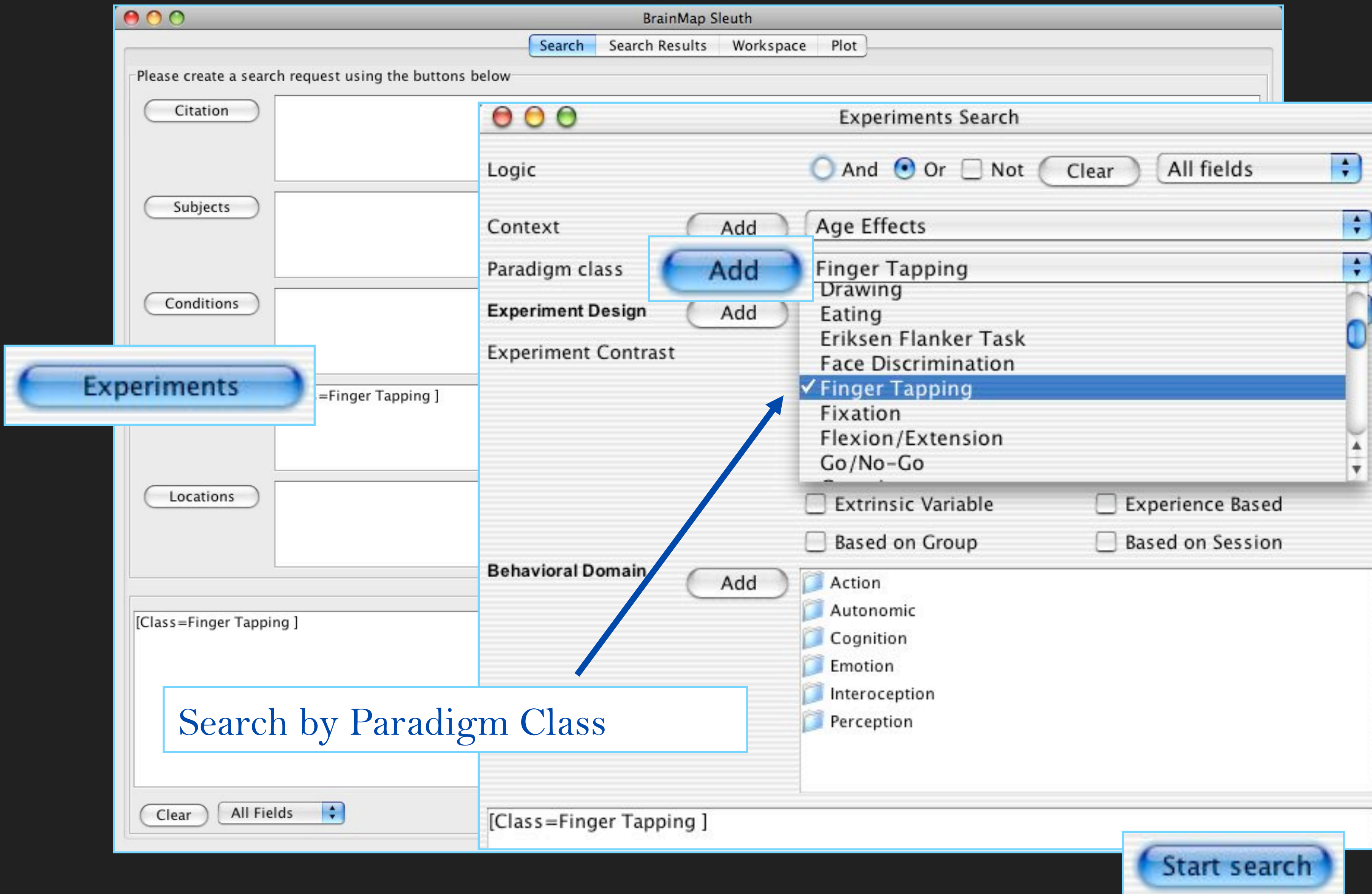


BrainMap Sleuth

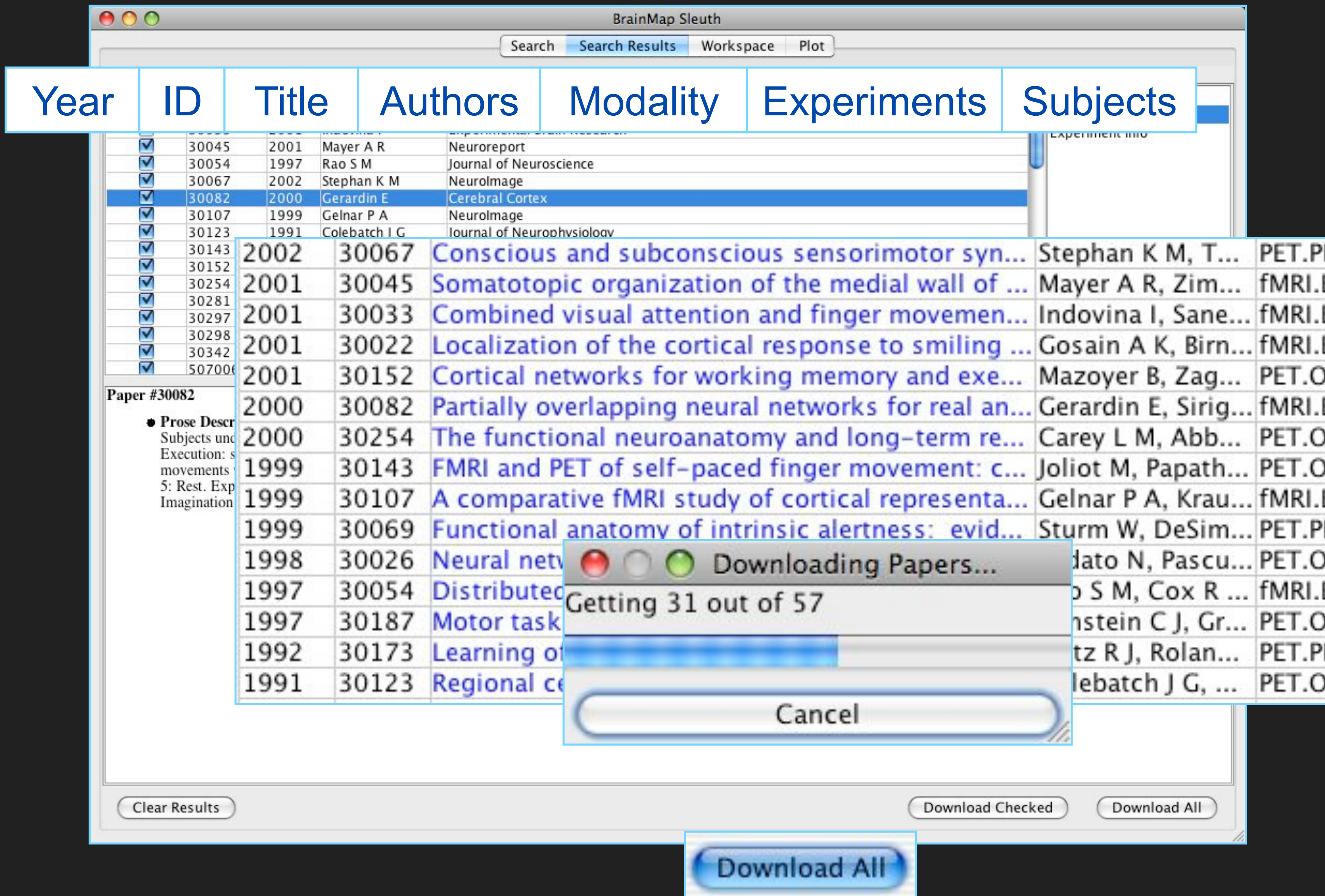
- Each button opens up a different search panel
- Search categories:
  - Citation
  - Subjects
  - Conditions
  - Experiments
  - Imaging Modality
  - Regions of Interest



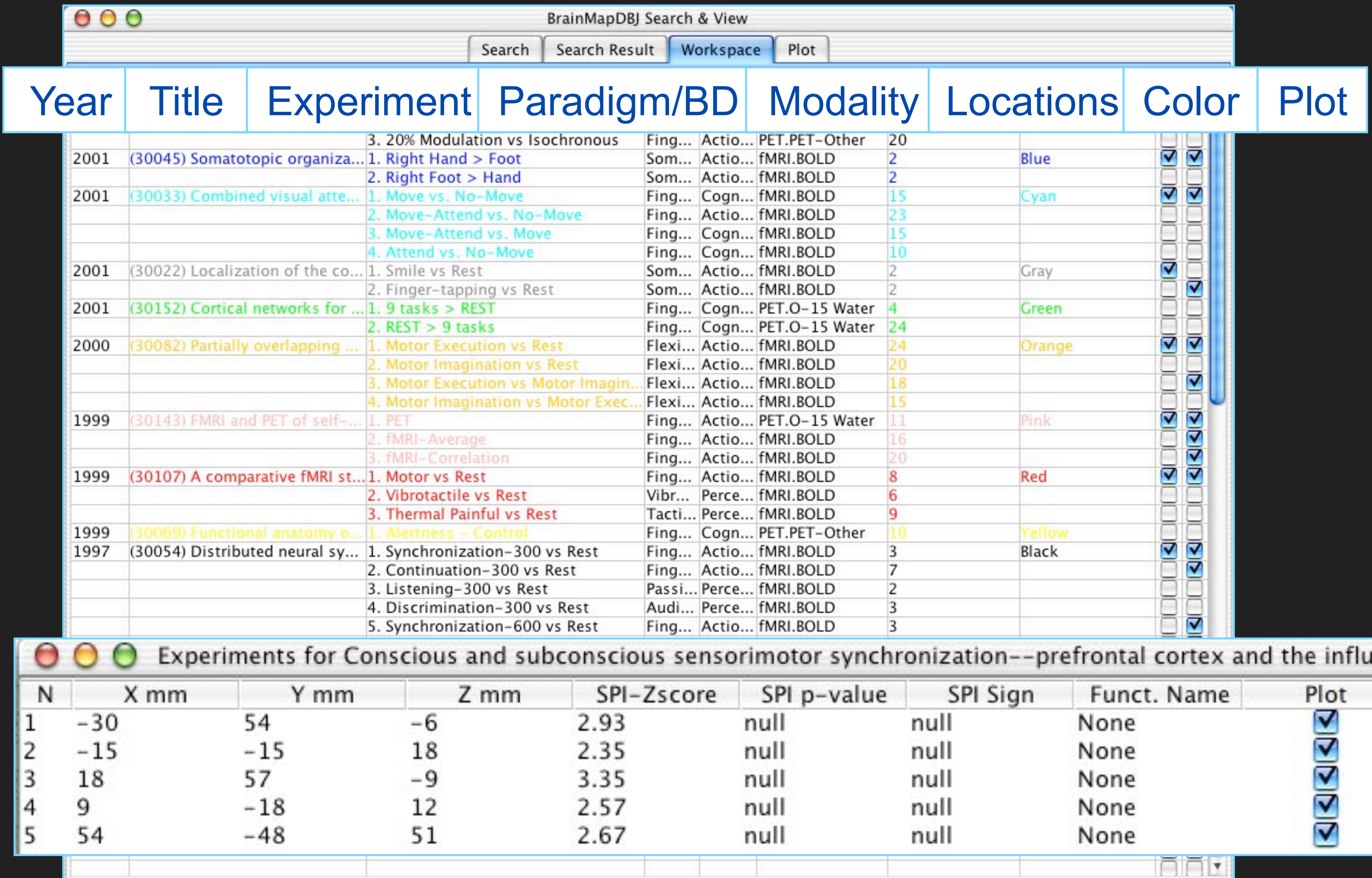
Sample Search: Finger Tapping



Search Results: Finger Tapping



Workspace: Finger Tapping

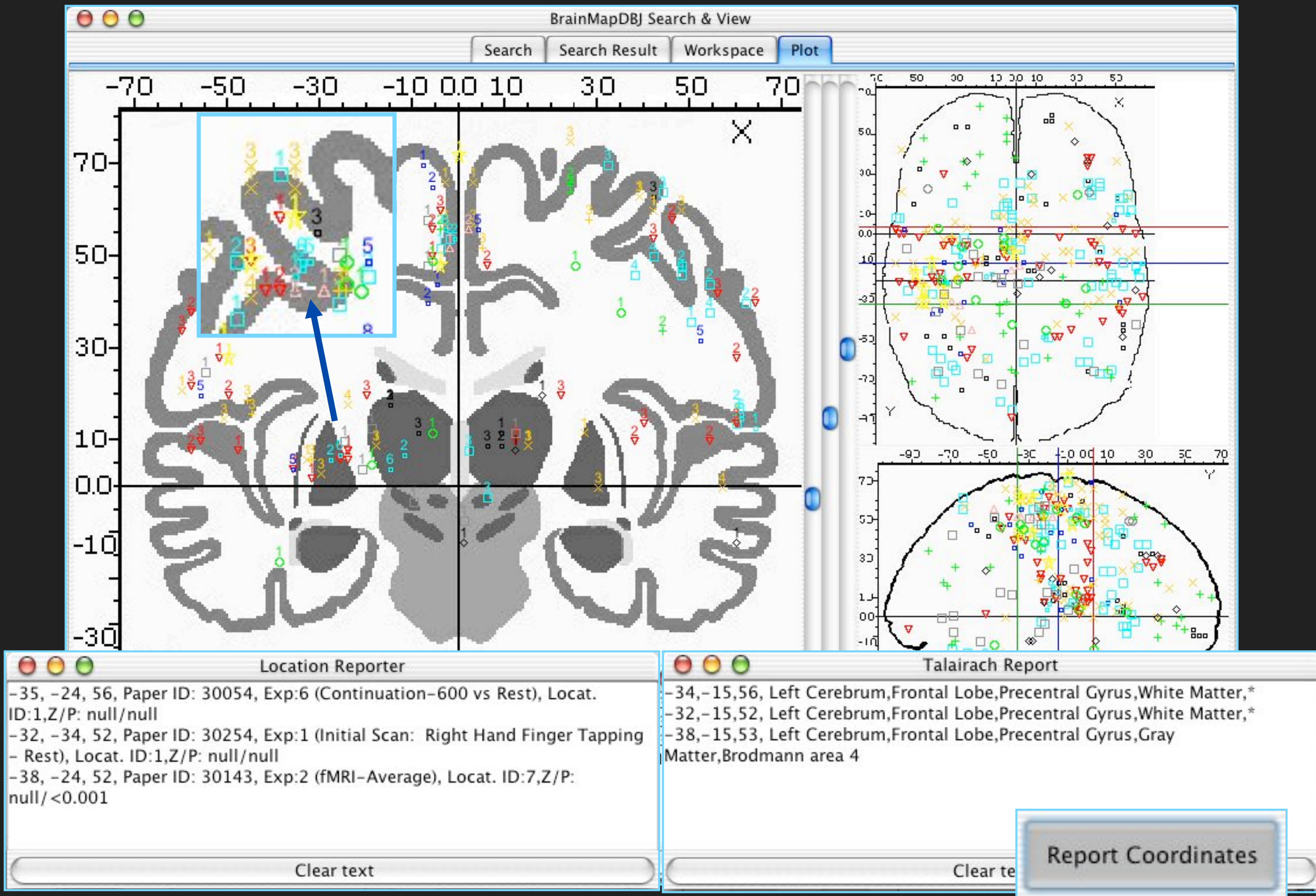


Year	Title	Experiment	Paradigm/BD		Modality	Locations	Color	Plot	
		3. 20% Modulation vs Isochronous	Fing...	Actio...	PET.PET-Other	20		☐	☐
2001	(30045) Somatotopic organiza...	1. Right Hand > Foot	Som...	Actio...	fMRI.BOLD	2	Blue	☑	☑
		2. Right Foot > Hand	Som...	Actio...	fMRI.BOLD	2		☐	☐
2001	(30033) Combined visual atte...	1. Move vs. No-Move	Fing...	Cogn...	fMRI.BOLD	15	Cyan	☑	☑
		2. Move-Attend vs. No-Move	Fing...	Actio...	fMRI.BOLD	23		☐	☐
		3. Move-Attend vs. Move	Fing...	Cogn...	fMRI.BOLD	15		☐	☐
		4. Attend vs. No-Move	Fing...	Cogn...	fMRI.BOLD	10		☐	☐
2001	(30022) Localization of the co...	1. Smile vs Rest	Som...	Actio...	fMRI.BOLD	2	Gray	☑	☐
		2. Finger-tapping vs Rest	Som...	Actio...	fMRI.BOLD	2		☐	☑
2001	(30152) Cortical networks for ...	1. 9 tasks > REST	Fing...	Cogn...	PET.O-15 Water	4	Green	☐	☐
		2. REST > 9 tasks	Fing...	Cogn...	PET.O-15 Water	24		☐	☐
2000	(30082) Partially overlapping ...	1. Motor Execution vs Rest	Flexi...	Actio...	fMRI.BOLD	24	Orange	☑	☑
		2. Motor Imagination vs Rest	Flexi...	Actio...	fMRI.BOLD	20		☐	☐
		3. Motor Execution vs Motor Imagin...	Flexi...	Actio...	fMRI.BOLD	18		☐	☑
		4. Motor Imagination vs Motor Exec...	Flexi...	Actio...	fMRI.BOLD	15		☐	☐
1999	(30143) FMRI and PET of self-...	1. PET	Fing...	Actio...	PET.O-15 Water	11	Pink	☑	☑
		2. fMRI-Average	Fing...	Actio...	fMRI.BOLD	16		☐	☑
		3. fMRI-Correlation	Fing...	Actio...	fMRI.BOLD	20		☐	☑
1999	(30107) A comparative fMRI st...	1. Motor vs Rest	Fing...	Actio...	fMRI.BOLD	8	Red	☑	☑
		2. Vibrotactile vs Rest	Vibr...	Perce...	fMRI.BOLD	6		☐	☐
		3. Thermal Painful vs Rest	Tacti...	Perce...	fMRI.BOLD	9		☐	☐
1999	(30069) Functional anatomy o...	1. Alertness - Control	Fing...	Cogn...	PET.PET-Other	10	Yellow	☐	☐
1997	(30054) Distributed neural sy...	1. Synchronization-300 vs Rest	Fing...	Actio...	fMRI.BOLD	3	Black	☑	☑
		2. Continuation-300 vs Rest	Fing...	Actio...	fMRI.BOLD	7		☐	☑
		3. Listening-300 vs Rest	Passi...	Perce...	fMRI.BOLD	2		☐	☐
		4. Discrimination-300 vs Rest	Audi...	Perce...	fMRI.BOLD	3		☐	☐
		5. Synchronization-600 vs Rest	Fing...	Actio...	fMRI.BOLD	3		☐	☑

Experiments for Conscious and subconscious sensorimotor synchronization--prefrontal cortex and the influe

N	X mm	Y mm	Z mm	SPI-Zscore	SPI p-value	SPI Sign	Funct. Name	Plot
1	-30	54	-6	2.93	null	null	None	☑
2	-15	-15	18	2.35	null	null	None	☑
3	18	57	-9	3.35	null	null	None	☑
4	9	-18	12	2.57	null	null	None	☑
5	54	-48	51	2.67	null	null	None	☑

Plot: Finger Tapping



Meta-Analysis: the *post hoc* combination of independently performed studies to better estimate a parameter of interest

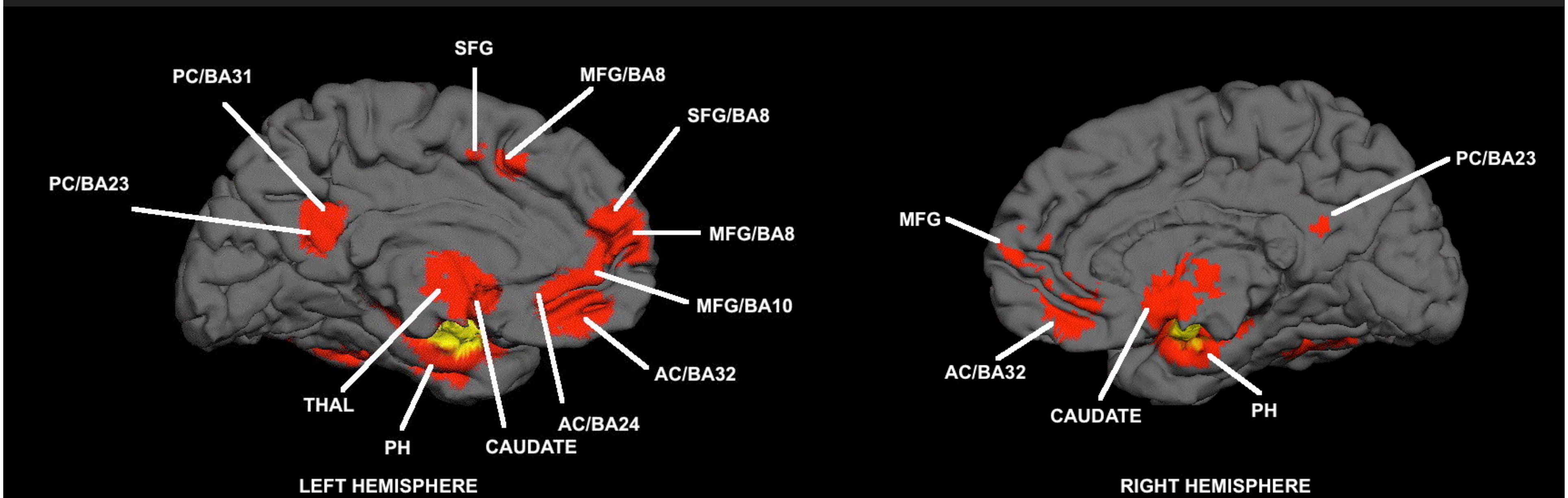
Location-effects: emerging as a tool for modeling neural systems

Combines statistically significant effects to create predictive models

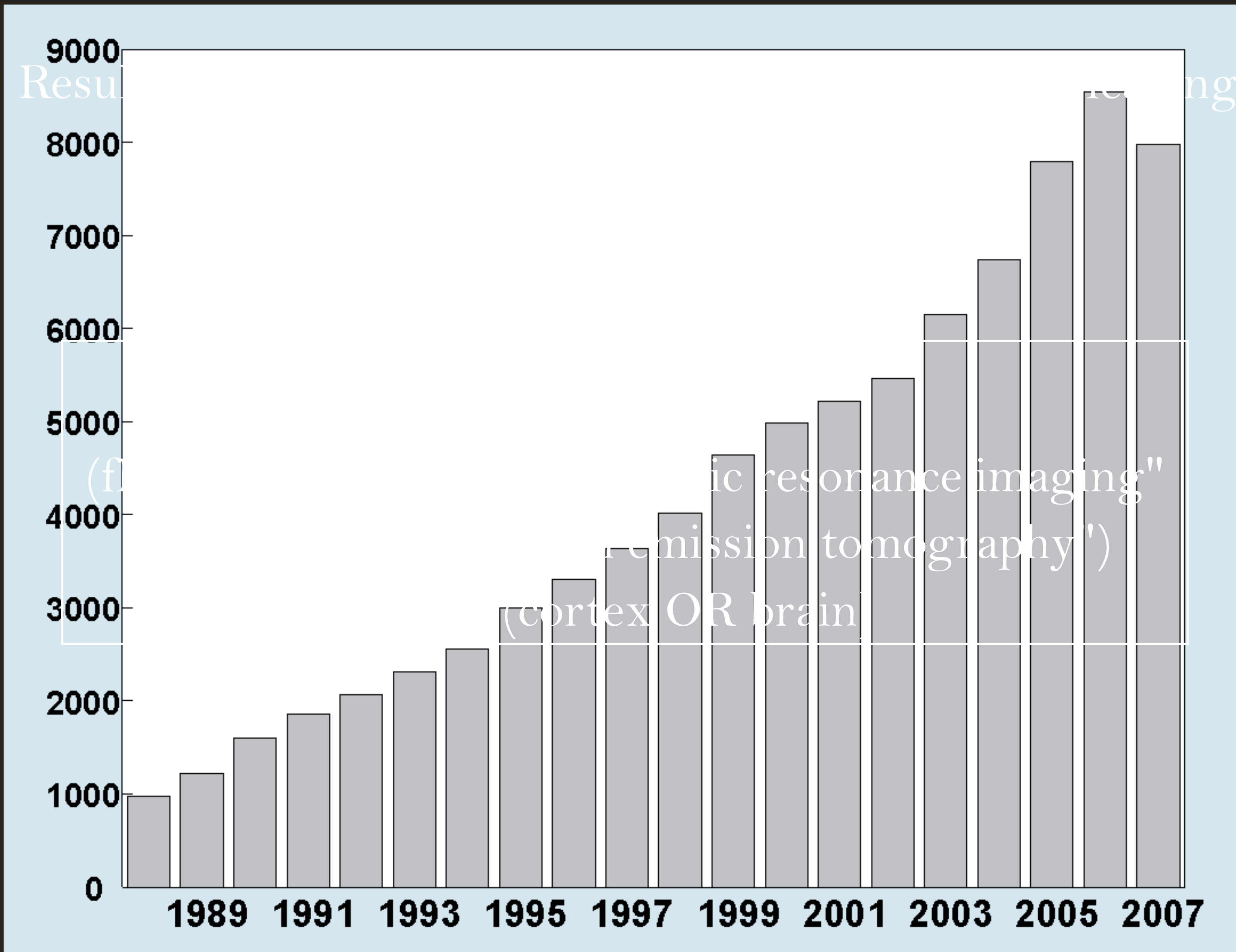
Why Meta-Analyses ?

fMRI and PET are powerful for localising brain functions

but …



Why Meta-Analyses ?



Forms of Meta-Analyses

cant left posterior MTL activation for words, and a significant bilateral posterior MTL activation for objects and faces. Direct comparisons between the two hemispheres revealed left>right activation for words and right>left activation for faces.

Whereas the previous studies all examined encoding of isolated words, objects, scenes, or faces, Aguirre et al. (1996) examined encoding of a complex spatial environment. In the encoding condition, participants actively explored the complex environment in order to remember it for a later test; in the control condition, they continually moved through a sparse circular corridor. Aguirre et al. (1996) reported activation of parahippocampal cortex bilaterally in the encoding condition compared to the control condition.

Retrieval Studies

Only a handful of fMRI experiments have provided evidence of MTL activations during memory retrieval. In addition to the experiment involving encoding scans described earlier, Gabrieli et al. (1997) also scanned subjects after they had studied line drawings of objects. Subjects were shown words and were asked to recall whether they had seen a drawing with that name. In one condition, most of the words were the names of previously studied drawings and in another condition most of the words were names of drawings that had not been presented. Retrieval of previously studied drawings was associated with an anterior MTL activation in the vicinity of the subiculum. In an attempt to increase the similarity between this retrieval study and the previously described picture encoding study, Gabrieli et al. (1997) ran an additional two subjects on a retrieval task in which pictures were presented and subjects attempted to recall previously studied words. They found greater activation in the subiculum during a retrieval condition in which pictures primarily corresponded to previously studied words compared to a retrieval condition in which pictures corresponded mainly to nonstudied words.

In contrast to these anterior MTL retrieval activations, three other studies have reported evidence of more posterior MTL activations during retrieval. In two related experiments (one using a blocked design, the other an event-related design), Schacter et al. (1997a) exposed participants to lists of semantically associated words. Subjects were then scanned as they made old/new recognition judgments about previously studied words or related lures (i.e., "false targets") that were semantic associates of the previously studied words but had not actually been presented during the study trials. Compared to a fixation control condition, recognition of previously studied words and false targets was associated with activation in the left parahippocampal cortex.

Aguirre et al. (1996) examined retrieval of a recently learned complex environment (as described earlier). Similar to their findings concerning encoding of the environment, Aguirre et al. (1996) reported bilateral parahippocampal activation during retrieval. Aguirre and D'Esposito (1997) scanned subjects while they attempted to recall different aspects of a "virtual town" that they had become familiar with 2 to 3 days prior to scanning. In the appearance condition, participants were shown a scene from the town and asked to indicate whether it matched a name that was provided. In the position condition, the same stimuli were presented, followed by an arrow and the name of another target location; participants were required to indicate the direction of the other target relative to the presented target. Compared to a control condition where subjects viewed scrambled visual scenes, there was significant bilateral parahippocampal activation in both experimental conditions.

SUMMARY OF FMRI FINDINGS

In summary, the findings from fMRI studies converge on the observation that posterior regions of the MTL, involving mainly the parahippocampal gyrus and caudal aspects of the hippocampus, play an important role in memory encoding processes. This finding has been obtained in studies using verbal materials (Fernandez et al., 1998; Wagner et al., 1998), nonverbal materials (Aguirre et al., 1996; Stern et al., 1996; Aguirre and D'Esposito, 1997; Gabrieli et al., 1997; Brewer et al., 1998), or both (Rombouts et al., 1997; Kelley et al., 1998); with a variety of analysis strategies, including subtraction (Aguirre et al., 1996; Stern et al., 1996; Aguirre and D'Esposito, 1997; Gabrieli et al., 1997; Rombouts et al., 1997; Kelley et al., 1998; Wagner et al., 1998), correlational techniques (Fernandez et al., 1998), and event-related procedures (Brewer et al., 1998; Wagner et al., 1998); and both when novelty detection processes are possible contributors to the observed activations (Stern et al., 1996; Gabrieli et al., 1997; Rombouts et al., 1997) and when they are not (Aguirre et al., 1996; Aguirre and D'Esposito, 1997; Brewer et al., 1998; Fernandez et al., 1998; Kelley et al., 1998; Wagner et al., 1998). Although some studies have also produced evidence of more anterior MTL activation during encoding (Stern et al., 1996; Rombouts et al., 1997; Wagner et al., 1998), all of the reviewed studies reported posterior MTL activation during encoding. By contrast, too few fMRI data are available concerning MTL activations during retrieval in order to permit any firm conclusions about their rostrocaudal location (for a schematic depiction of all encoding and retrieval foci, see Figure 1).

PET STUDIES OF ENCODING AND RETRIEVAL

The data from fMRI studies of encoding appear compelling and consistent. It thus may be surprising that Lepage et al. (1998) recently reported a meta-analysis of PET studies that appears to yield a different and perhaps opposite conclusion from the fMRI studies. Lepage et al. (1998) summarized results from a database of 52 PET studies that obtained evidence of 54 individual MTL activations during encoding or retrieval. They noted a highly consistent pattern of findings: MTL activations during encoding tended to fall in the rostral portions of the rostrocaudal axis,

object naming and color name generation both yielded posterior MTL activations. Compared to episodic retrieval of uncommon colors, color name generation yielded anterior MTL activation.

Beauregard et al. (1998)

In this study, incidental word encoding was compared to a lower level visual baseline. During word encoding, subjects decided whether words belonged to the category "tools." Compared to viewing a string of number signs (#####), word encoding resulted in left MTL activation.

N. Kapur et al. (1995)

In this study, both the encoding and the retrieval of facial stimuli were compared to a rest control. From these comparisons, Lepage et al. (1998) included a retrieval MTL activation. However, a posterior MTL activation resulting from encoding (elaborating on facial stimuli by making gender classifications) was not included.

Schacter et al. (1995)

Lepage et al. (1998) included data from a retrieval comparison in which subjects made recognition judgments about a block of previously studied "impossible" objects compared to a passive viewing condition. However, they did not include analogous data showing posterior MTL activation from a retrieval comparison in which subjects made recognition judgments about a block of previously studied "possible" objects compared to a passive viewing condition. In addition, Lepage et al. (1998) did not include a comparison that meets their elaborative encoding criterion, in which subjects made possible/impossible object decisions about new (i.e., previously nonstudied) objects. For impossible objects, the object decision versus passive viewing comparison yielded a significant posterior MTL activation; there was no corresponding activation for possible objects. As with the preceding six studies, this type of elaborative decision is similar to deep versus shallow encoding comparisons that were included by Lepage et al. (1998).

Bottini et al. (1994)

Participants were presented with sentences and decided whether (1) each sentence represents a plausible metaphor, or (2) whether each sentence is plausible at the literal level. Both of these tasks require considerable elaborative processing of the sentences. In the control condition, subjects viewed a sentence-like string of eight to nine words and were asked to judge whether one of the words is an orthographically legal non-word. Compared to the control task, the combined sentence processing conditions resulted in anterior MTL activation.

Price et al. (1994)

In this study of word processing, participants performed three tasks: lexical decision on words and pseudowords, reading words aloud, and feature decision on false fonts. Across two versions of each task, the rate of stimulus presentation was varied; stimuli were presented for either 150 or 1,000 ms. At both presentation rates, compared to the baseline feature-detection task, lexical decision yielded posterior MTL activation. Lexical decision, which necessitates elaborative processing of each stimulus, is formally similar to the object decision task used in the Schacter et al. (1995) study. In addition to these foci, MTL activations related to word encoding were noted when word reading was compared to baseline. At both presentation rates, there was a more anterior MTL activation during the word reading condition. We have included these findings in our Table 2.[2]

Bookheimer et al. (1995)

Participants were presented words, drawings of common objects, and meaningless line drawings (similar in appearance to the false fonts of Price et al., 1994). Compared to visual scanning of the meaningless drawings, reading words aloud resulted in posterior MTL activation. Compared to the same baseline, silent object naming also yielded posterior MTL activation. Both of these comparisons are similar to the word reading versus baseline comparison of Price et al. (1994).

Martin et al. (1996)

In this study, participants passively viewed nonsense objects, named real objects from one of two categories (tools and animals), and viewed a visual noise field. As in a study by Martin et al. (1997; see below for discussion) that was included by Lepage et al. (1998), compared to the noise-field baseline, passive viewing of nonsense objects yielded anterior MTL activations. This comparison also revealed a posterior MTL activation in parahippocampal gyrus. In contrast to Martin et al. (1997) and Bookheimer et al. (1995), comparison of silent object naming to the low-level baseline did not result in differential MTL activation (although, as noted by Martin et al. [1997, p. 592], this comparison did yield activity medial and superior to the hippocampus (−14 −28 4).

Zelkowicz et al. (1998)

This study included four main conditions, each of which was compared to a fixation control: (1) viewing line drawings of common objects; (2) naming drawings of common objects; (3) viewing nonsense objects; and (4) speaking (saying "Hiya") while viewing nonsense objects. As in the studies by Martin et al. (1996,

[2]We thank M. Lepage for calling our attention to the Price et al. (1994) study. Note that, although the lexical decision condition in Price et al. (1994) clearly satisfies Lepage et al.'s (1998) encoding criteria, because Lepage et al. (1998) emphasized that encoding conditions involve either elaborative processing or intentional learning (or both), simple word reading may seem to violate these criteria. However, it is possible that word reading involves greater levels of encoding than does the control condition, and therefore inclusion of this comparison may be warranted (M. Lepage, personal communication). Similar considerations apply to the studies by Bookheimer et al. (1995), Martin et al. (1996), and Zelkowicz et al. (1998), as well as a study by Martin et al. (1997) that was originally included by Lepage et al. (1998).

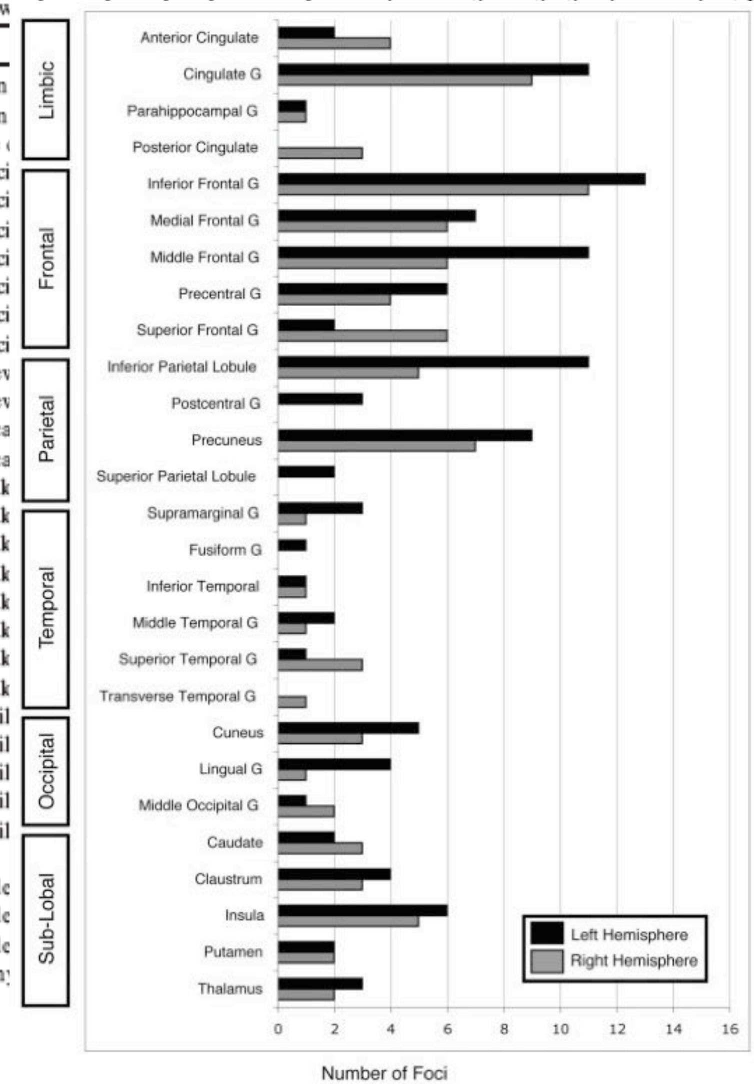
Textual Review

Schacteret et al., 1999

Forms of Meta-Analyses

Survey of neuroimaging studies on w... the left BA 44 and BA 45

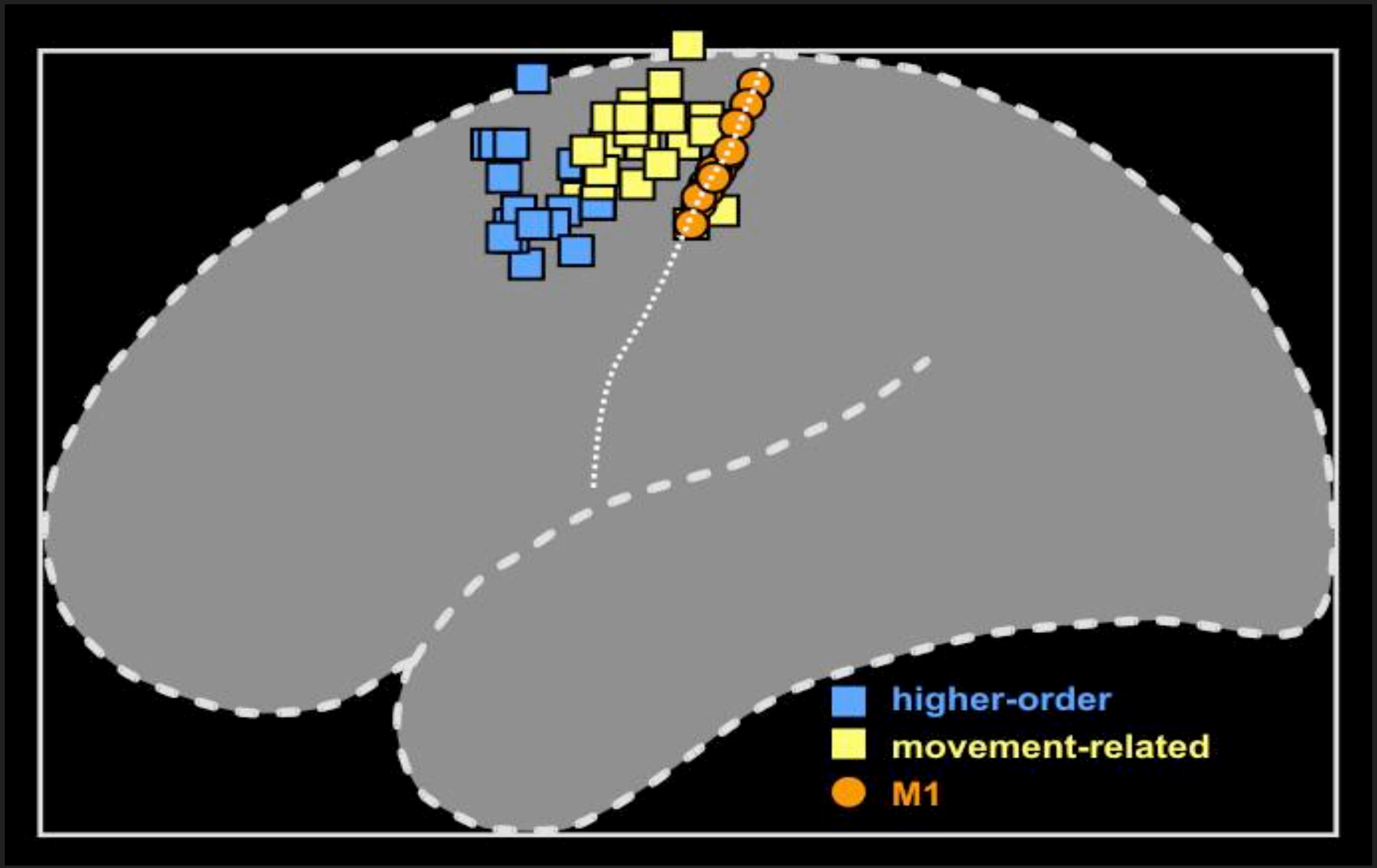
Study	Task	~BA	x	y	z
Ischebeck et al. [39]	Articulation	44	−50	10	23
Ischebeck et al. [39]	Articulation	44	−56	10	27
Chee et al. [12]	Letter case (	44	−31	6	18
Binder et al. [5]	Lexical deci	44	−40	17	2
Edwards et al. [19]	Lexical deci	44	−50	13	24
Fiebach et al. [24]	Lexical deci	44	−42	1	17
Fiebach et al. [24]	Lexical deci	44	−47	10	13
Rumsey et al. [61]	Lexical deci	44	−42	6	20
Rumsey et al. [61]	Lexical deci	44	−44	6	24
Xiao et al. [72]	Lexical deci	44	−51	15	14
Menard et al. [47]	Passive viev	44	−52	6	8
Menard et al. [47]	Passive viev	44	−43	7	0
Ischebeck et al. [39]	Phonologica	44	−53	15	4
Ischebeck et al. [39]	Phonologica	44	−53	11	10
Fiez et al. [27]	Reading (al	44	−49	11	11
Fiez et al. [27]	Reading (al	44	−49	11	10
Herbster et al. [35]	Reading (al	44	−48	6	0
Paulesu et al. [55]	Reading (al	44	−44	4	20
Rumsey et al. [61]	Reading (al	44	−42	6	20
Rumsey et al. [61]	Reading (al	44	−44	6	24
Tan et al. [67]	Reading (al	44	−51	15	7
Tan et al. [67]	Reading (al	44	−61	11	1
Joubert et al. [41]	Reading (sil	44	−47	12	18
Joubert et al. [41]	Reading (sil	44	−47	6	14
Mechelli et al. [46]	Reading (sil	44	−48	8	22
Mechelli et al. [46]	Reading (sil	44	−42	16	32
Mechelli et al. [46]	Reading (sil	44	−42	16	32
Xu et al. [73]	Rhyming	44	−52	10	12
Chee et al. [12]	Semantic de	44	−46	12	18
Chee et al. [12]	Semantic de	44	−46	9	31
Chee et al. [12]	Semantic de	44	−43	3	28
Booth et al. [8]	Spelling, rhy	44	−42	9	27
Dehaene et al. [17]	Viewing	44	−48	8	4
Mean coordinates		44	−47	10	15



Review Tables

Heim et al., 2006
Laird et al., 2005

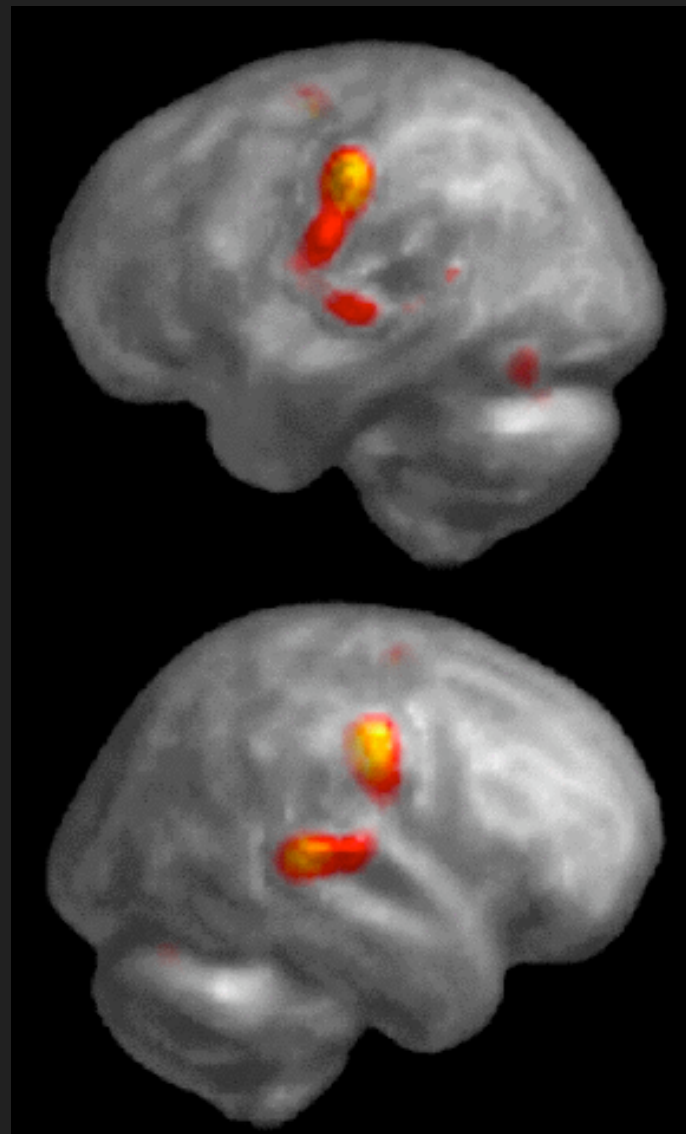
Forms of Meta-Analyses



Graphic Representation

Picard and Strick, 2001

Activation Likelihood Estimation



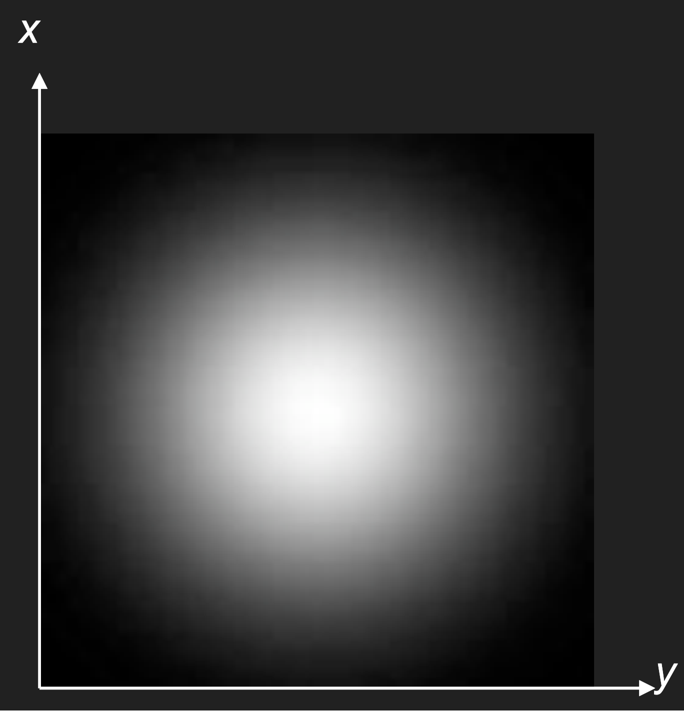
Quantitative
Coordinate-Based
Voxel-Wise
Meta-Analysis Method

originally developed by Turkeltaub et al. (2002), extended by Laird et al. (2005a)

Representation of Activation Foci

Reported coordinates are not treated as points but centers of probability distributions

Each reported activation is modeled by a 3D Gaussian distribution



ALE Meta-Analysis

Think of coordinate as center of probability distribution, not as a single point of activation

For multiple sets of coordinates, evaluate the union of these distributions for all brain locations to create a whole brain statistical map

Estimates the likelihood of activation for each voxel in the brain

X_i the event that the focus is in a given voxel

d_i Euclidean distance

σ standard deviation

$$\Pr(X_i) = \frac{\exp\left(-d_i^2 / 2\sigma^2\right)}{(2\pi)^{3/2}\sigma^3} \cdot \Delta V$$

Turkeltaub *et al.* Neuroimage 16: 765-780 (2002)

ALE Meta-Analysis

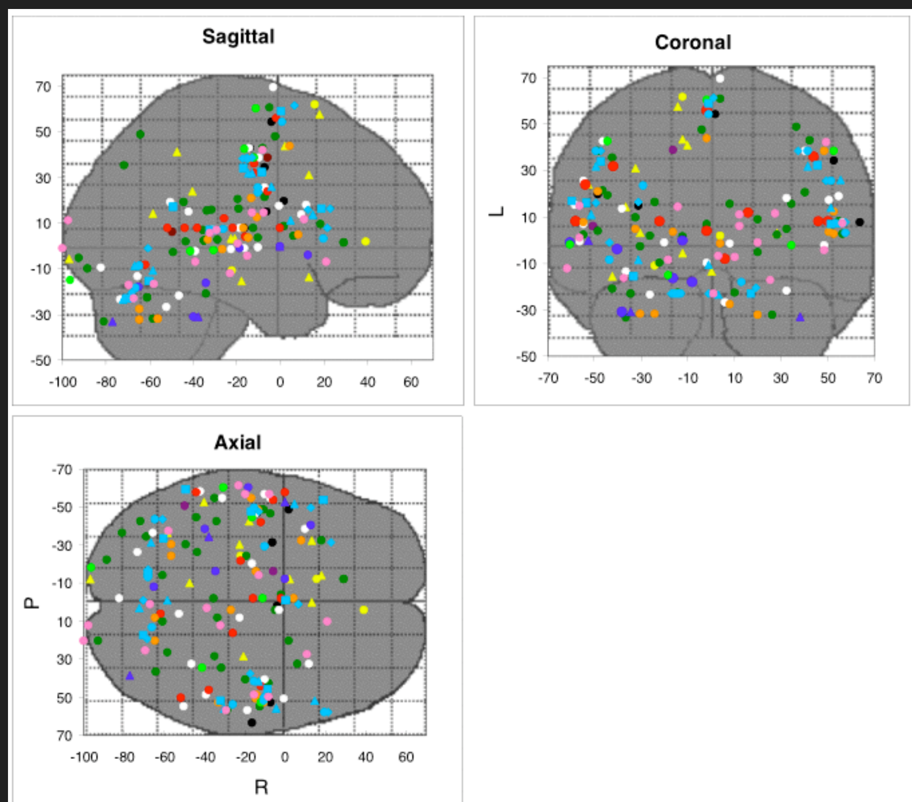
Single Word Reading (Turkeltaub et al., 2002)

Published Coordinates:

11 Papers

172 foci

Diffuse pattern of activation



Find studies of interest: MEDLINE, PubMed, review articles

Limit to those that report standardized coordinates

Contrasts: Activation Condition - Control Condition

Input coordinates to ALE software

Nonparametric permutation test to determine statistically significant ALE values

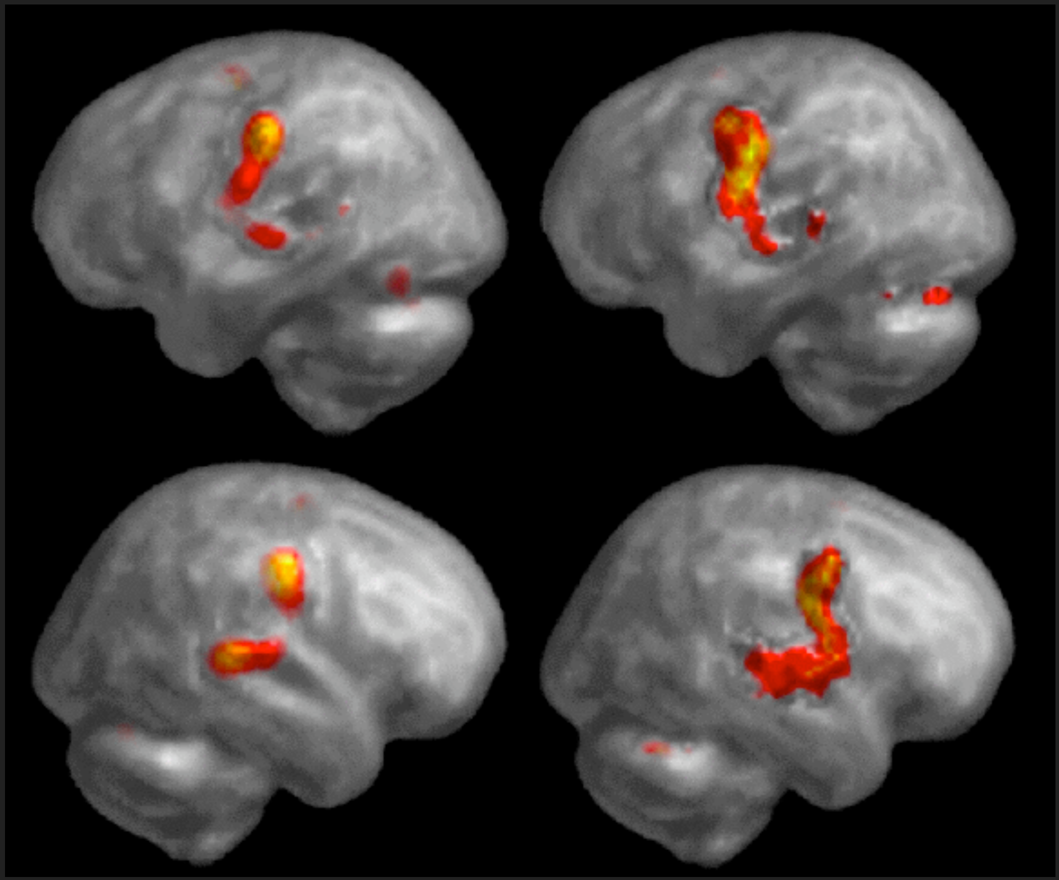
Interpret resultant map

ALE Results: Single Word Reading

Meta-Analysis   Validation (fMRI)

L Hem

R Hem



Bi primary motor
Sup frontal gyrus
Bi sup temporal sulci
L fusiform gyrus
Bi cerebellum

ALE score

-- 0.015289

-- 0.00572

Turkeltaub et al., 2002

Activation Likelihood Estimation (ALE)

Illustration: meta-analysis on cortical activation in finger tapping studies

BrainMap Database Search

38 papers

73 experiments

347 subjects

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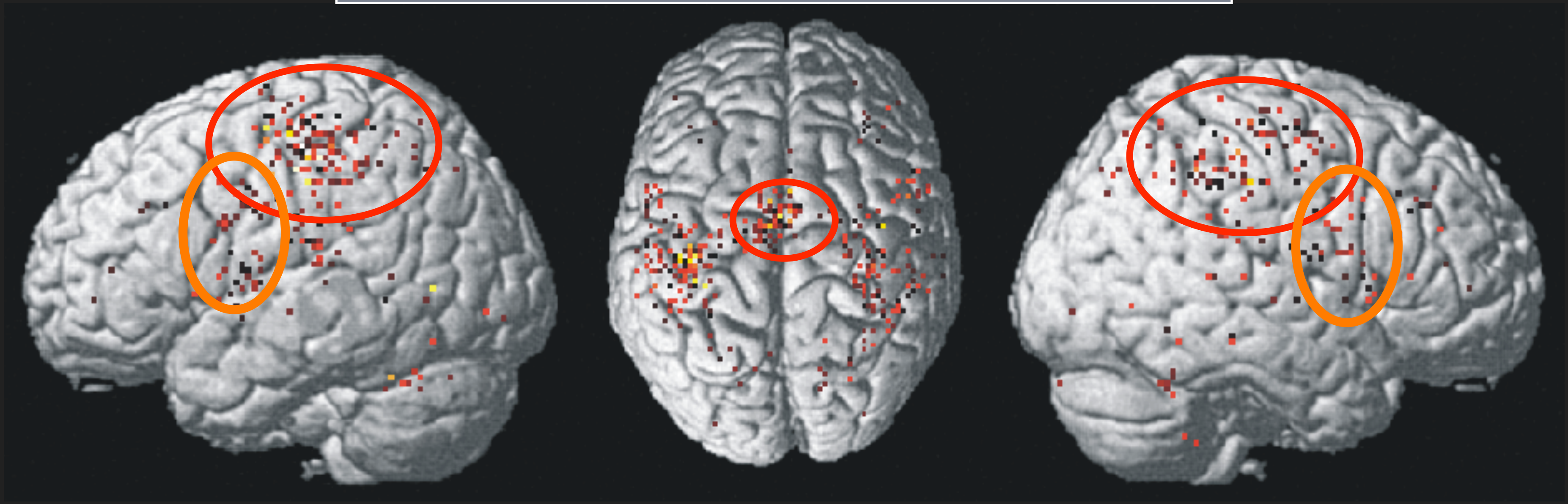
663 activation foci

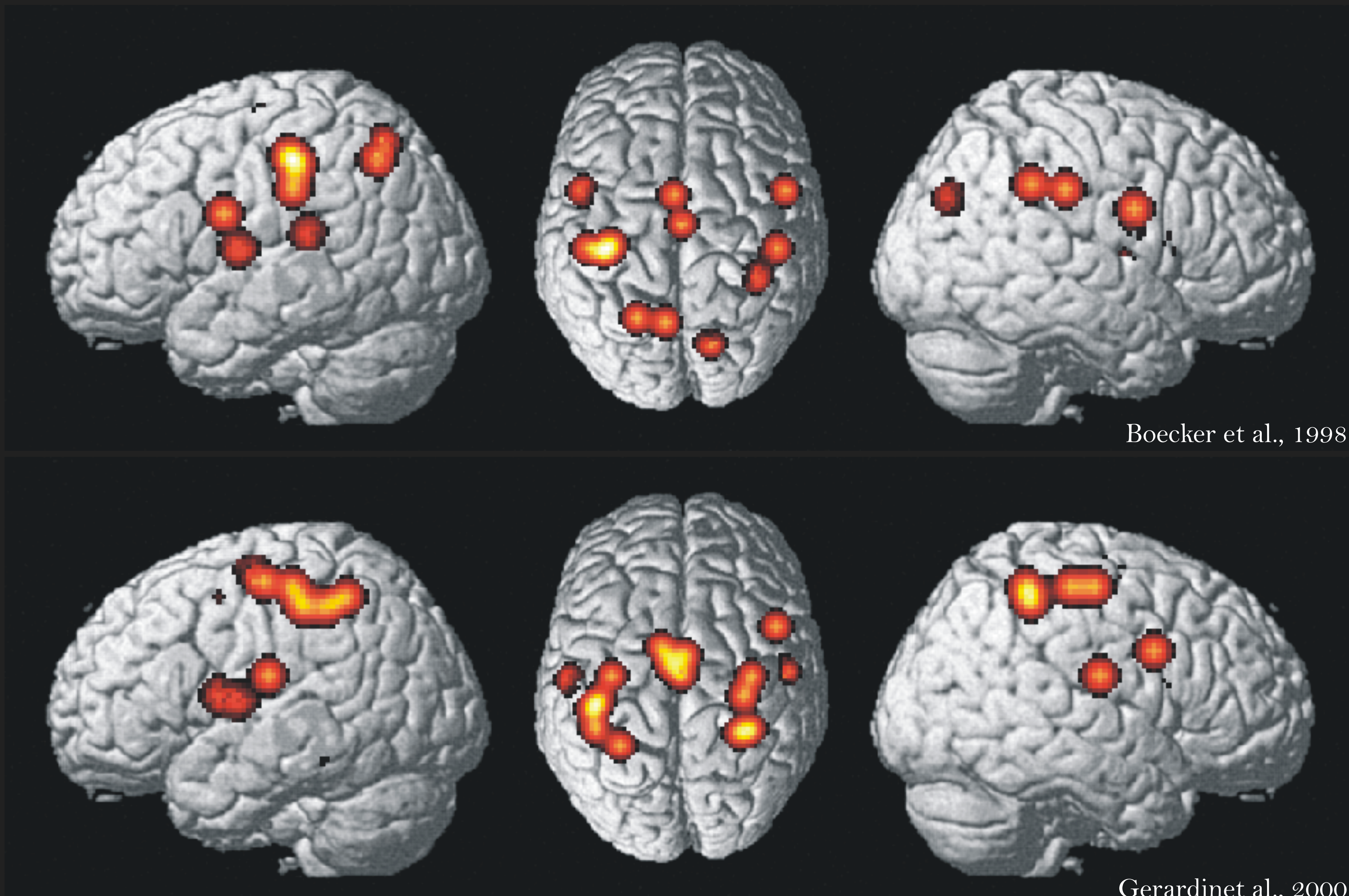
Meta-Analysis on Finger Tapping

Location of activation foci



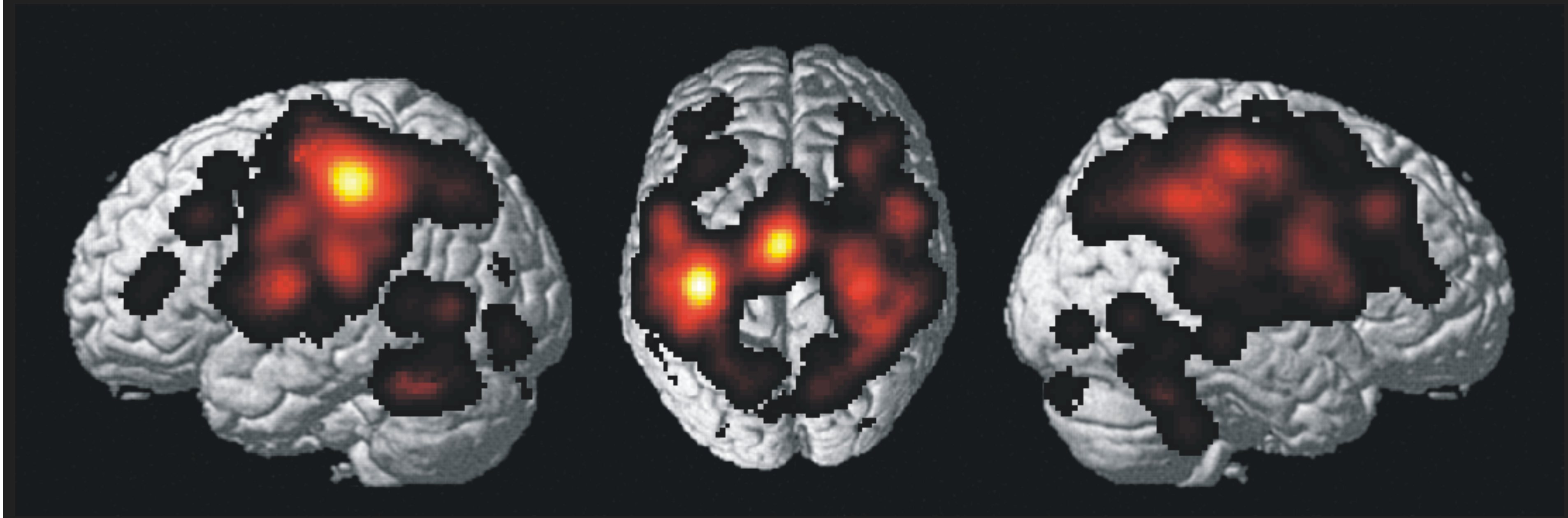
Where do the reported foci converge ?

Gaussian Representation of Activations



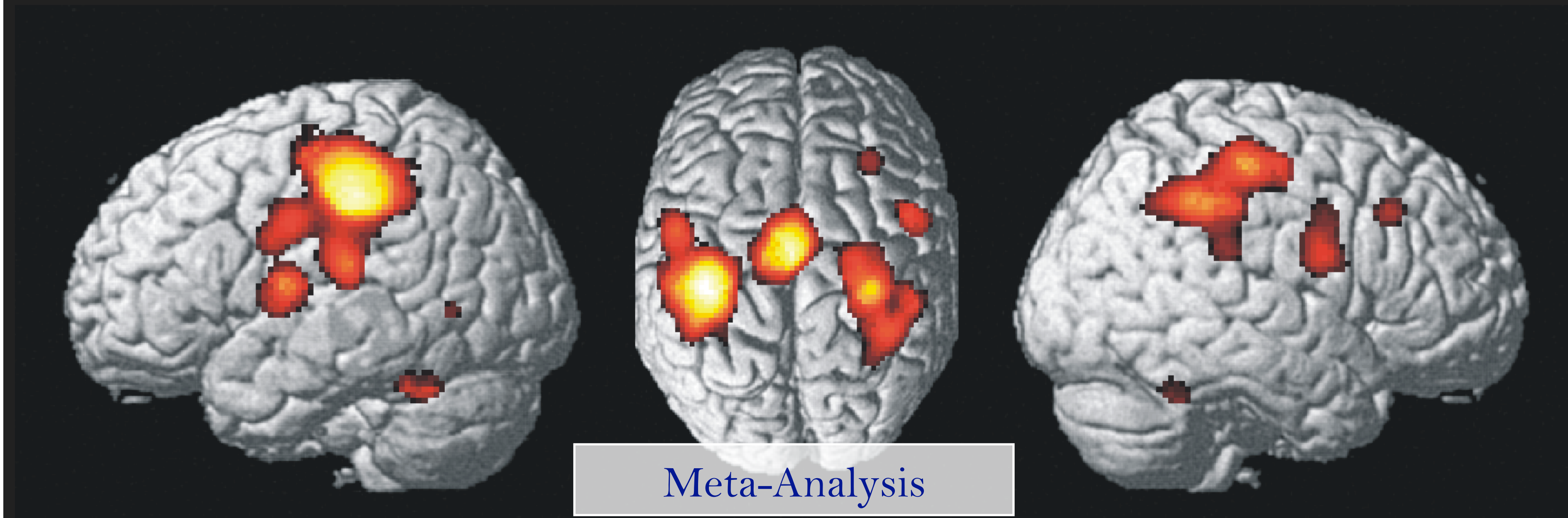
Activation Likelihood Estimates

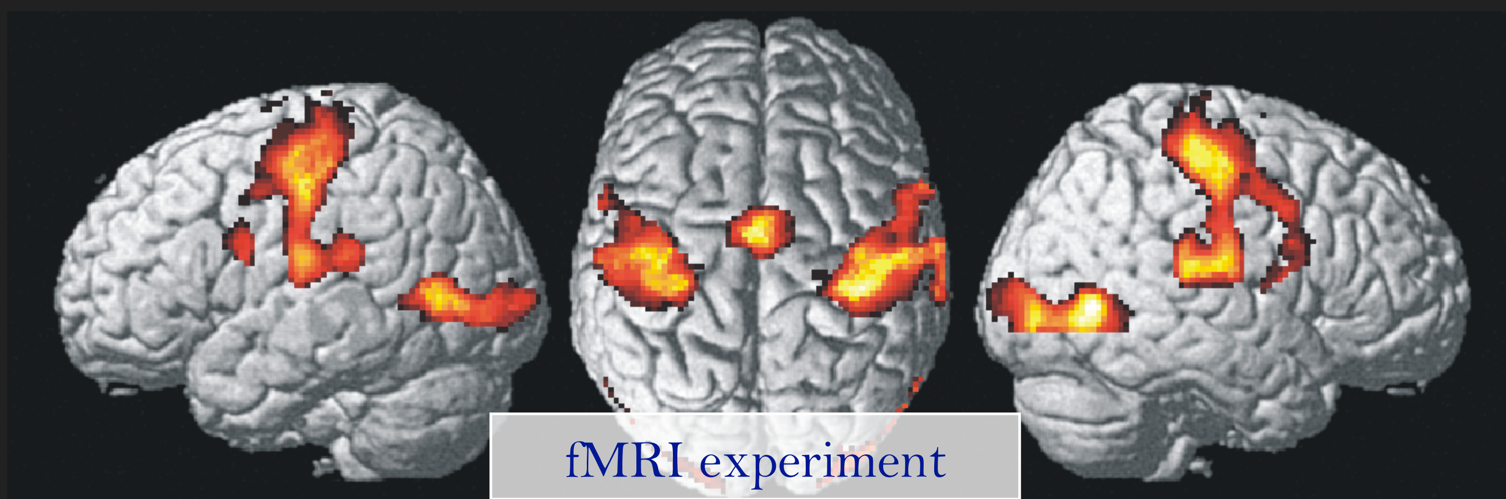
Defined as the union over all experiments



Which of these values are significant?

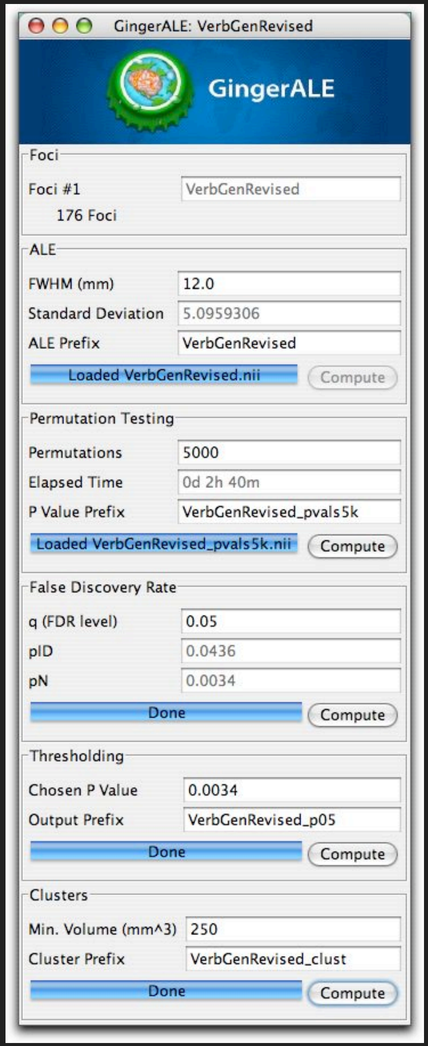
Meta-Analysis on Finger Tapping





Witt et al., In Press; Eickhoff et al., In Review

Modifications to ALE: GingerALE



GUI, image-based, Talairach space

Permutation test corrected for multiple comparisons

Allow for comparisons between two groups of foci

Laird et al., Hum Brain Mapp 25, 155-164, 2005

Somatotopic mapping within the cingulate motor area:

Evidence from an ALE meta-analysis of the Stroop task

Angela Laird[1], Kathryn McMillan[2], Jack Lancaster[1], Peter Kochunov[1], Peter Turkeltaub[3], Jose Pardo[4], Peter Fox[1]

[1]University of Texas Health Science Center San Antonio

[2]Vanderbilt University

[3]Georgetown University Medical Center

[4]Minneapolis Veterans Affairs Medical Center

The Stroop Effect

Blue

The Stroop task is universally recognized as a standard in examining attentional control

Correct performance in color naming competes with tendency for word reading

Objective: identify regions of concordance to understand the detection of conflict and response selection

Literature Search

Find studies of interest (Medline, PubMed, BrainMap)

Limit studies to those that report standardized coordinates

Simple contrasts: Incongruent - Control

Filter task variations
Normal subjects only
Group data
No deactivations

→

19 contrasts
205 foci

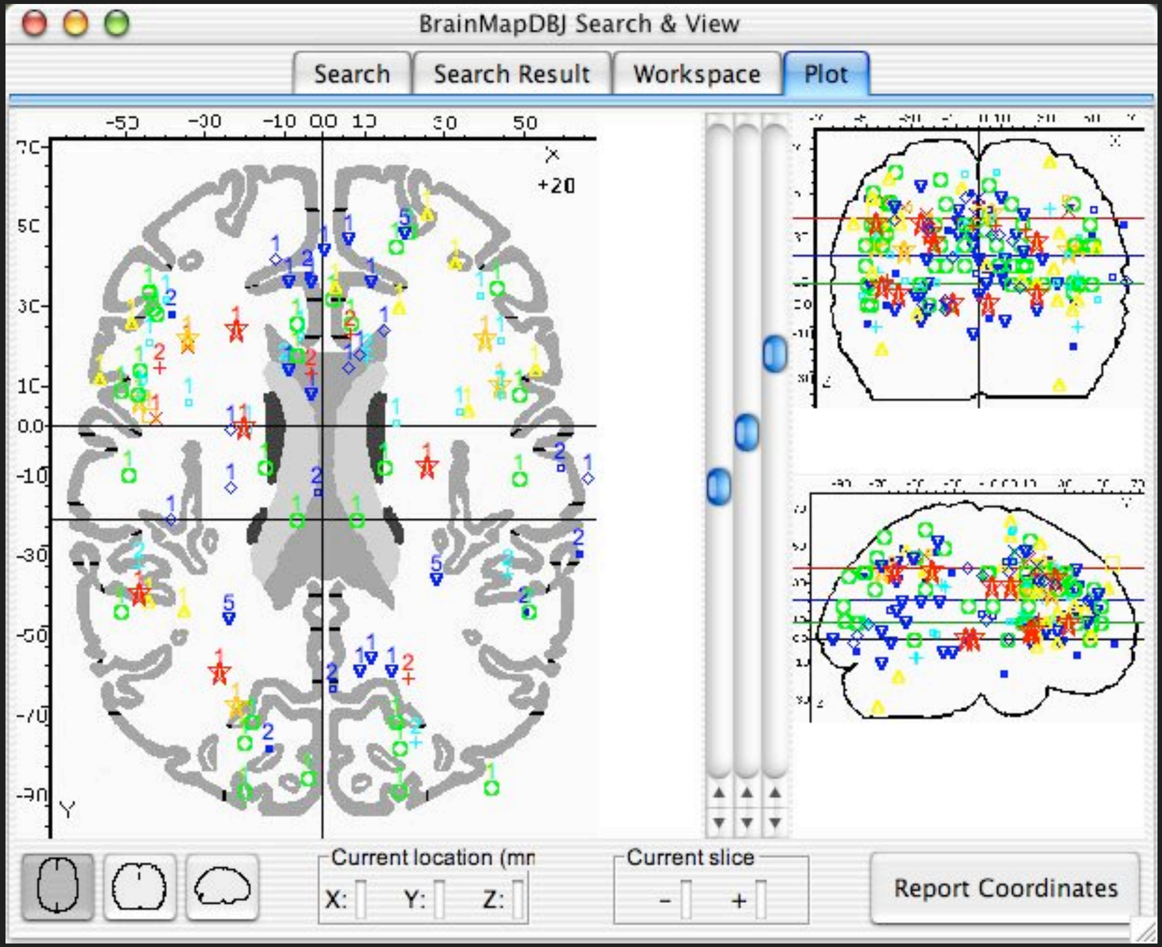
Coordinate Data from Stroop Studies

<u>1. Pooled Stroop</u>
205 foci

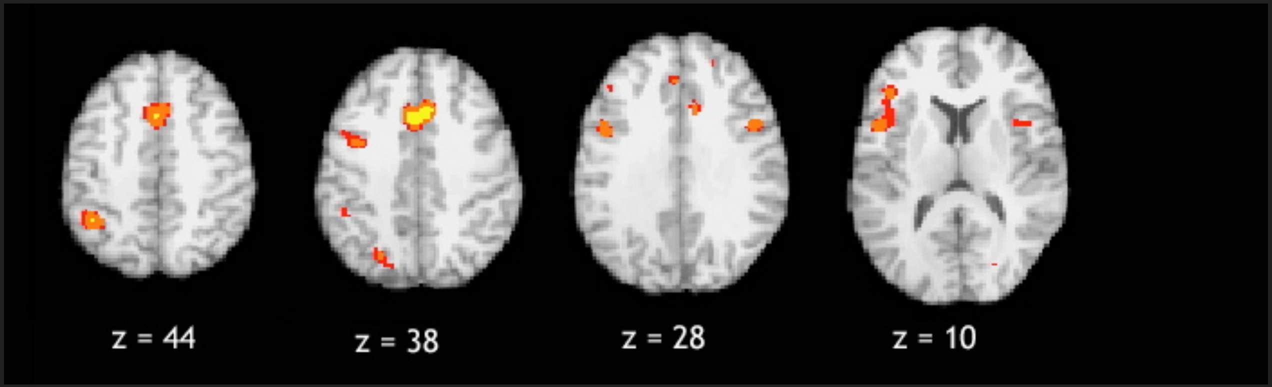
<u>2. Verbal Stroop</u>
152 foci

<u>3. Manual Stroop</u>
53 foci

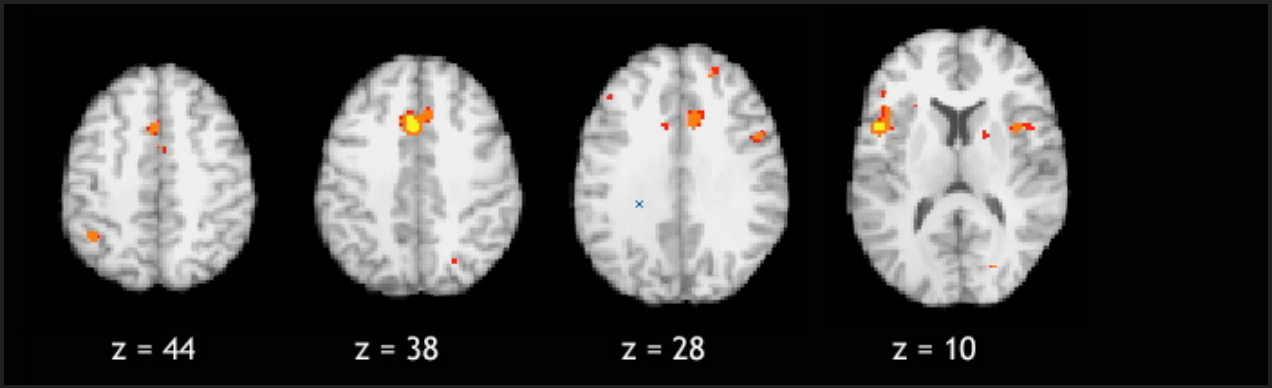
<u>ALE analysis</u>
10 FWHM
5000 permutations



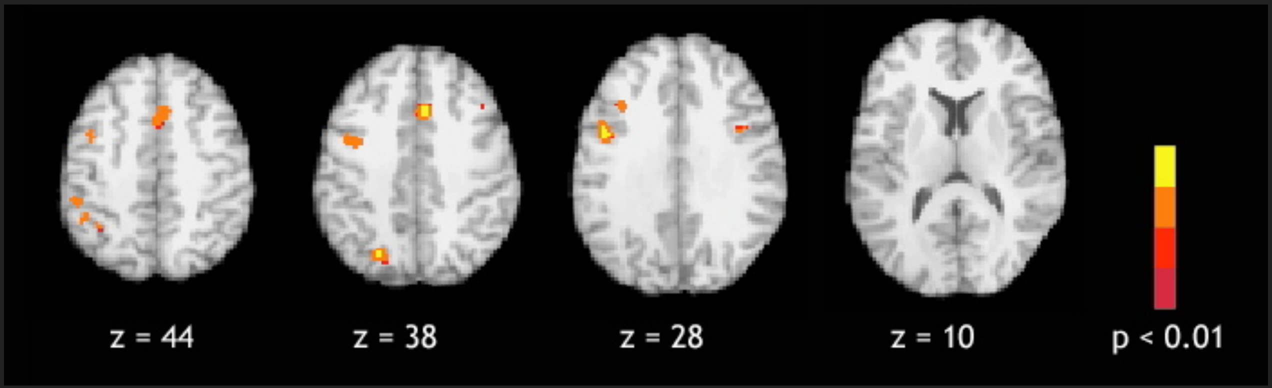
Pooled Stroop
ACG, bi frontal,
L IPL,
L precuneus,
Bilateral insula



Verbal Stroop
Bilateral insula,
L IFG, BA 44,
ACG



Manual Stroop
ACG,
L IPL,
L MiFG,
L precuneus

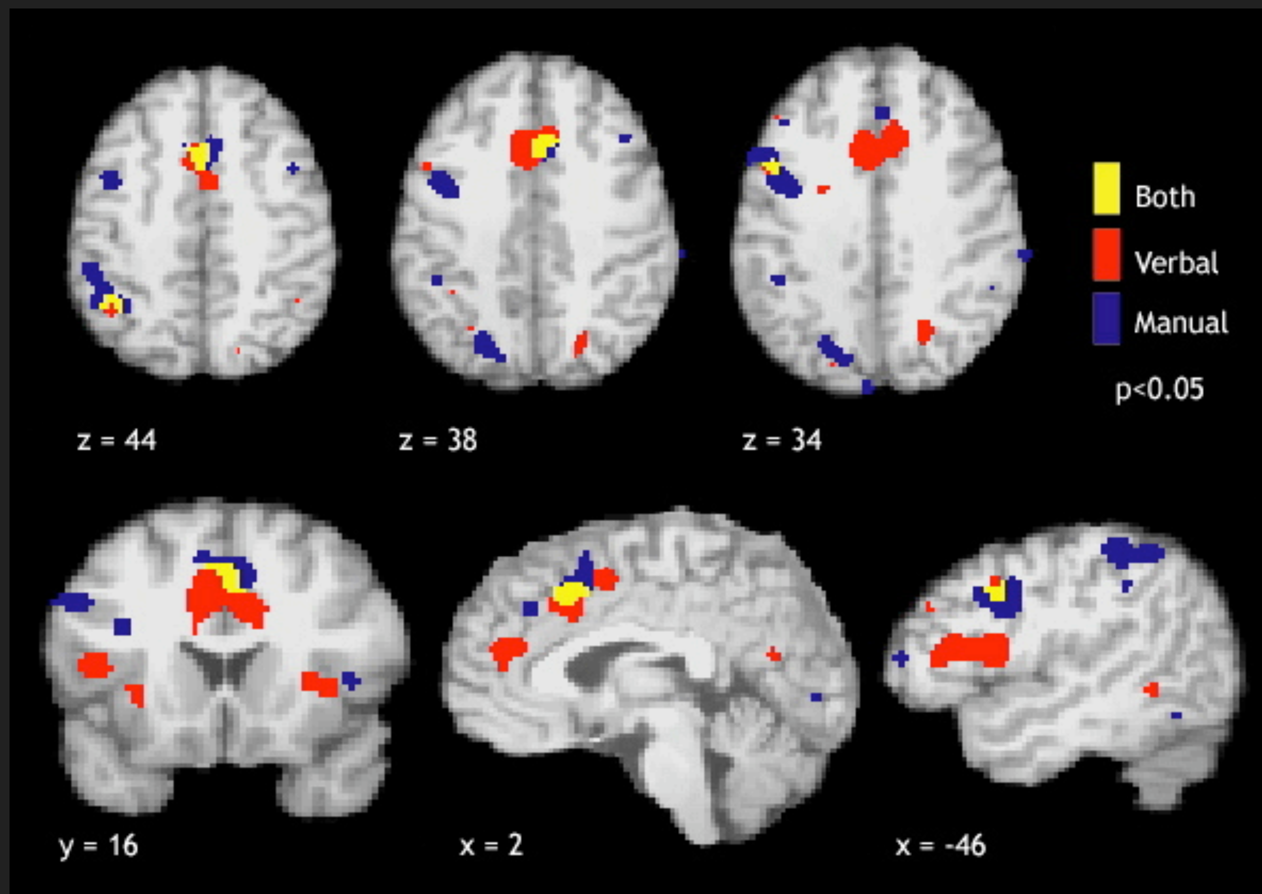


Overlap of Verbal vs. Manual

ACG
(2, 16, 41)

L IFJ (between precentral and inf frontal gyri)
(-44, 6, 34)

L IPL
(-36, -52, 44)



Overlap of Verbal vs. Manual

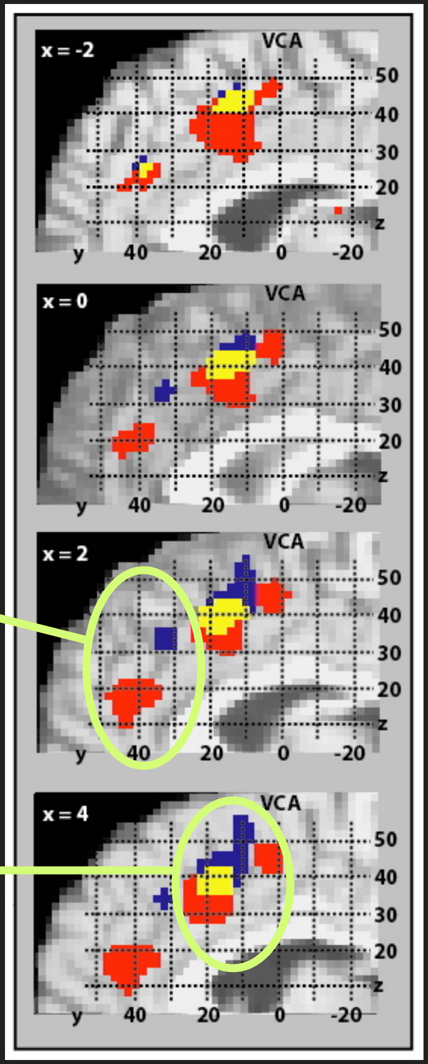
Viewed composite map ($P<0.05$)

High ALE values found along cingulate sulcus, rostral to vertical plane passing through AC

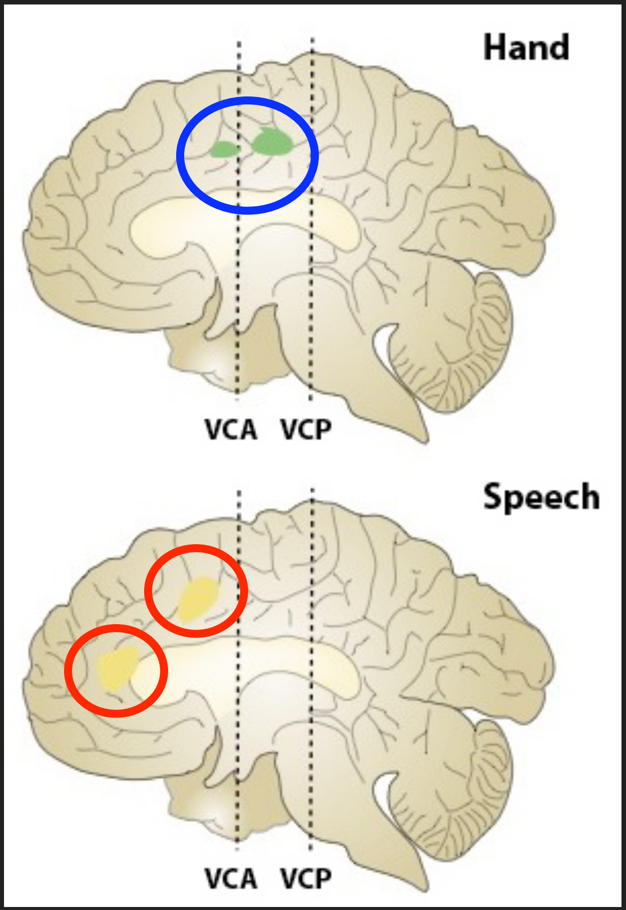
Observed multiple distinct regions for verbal and manual responses

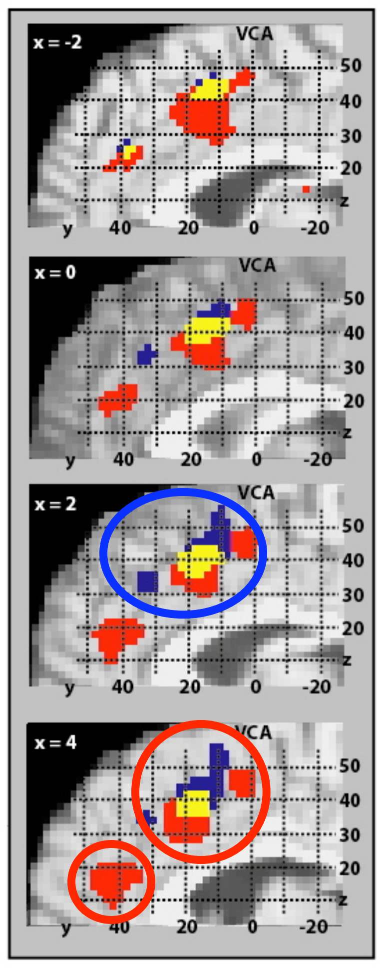
2 regions in rCZa

2 regions in rCZp



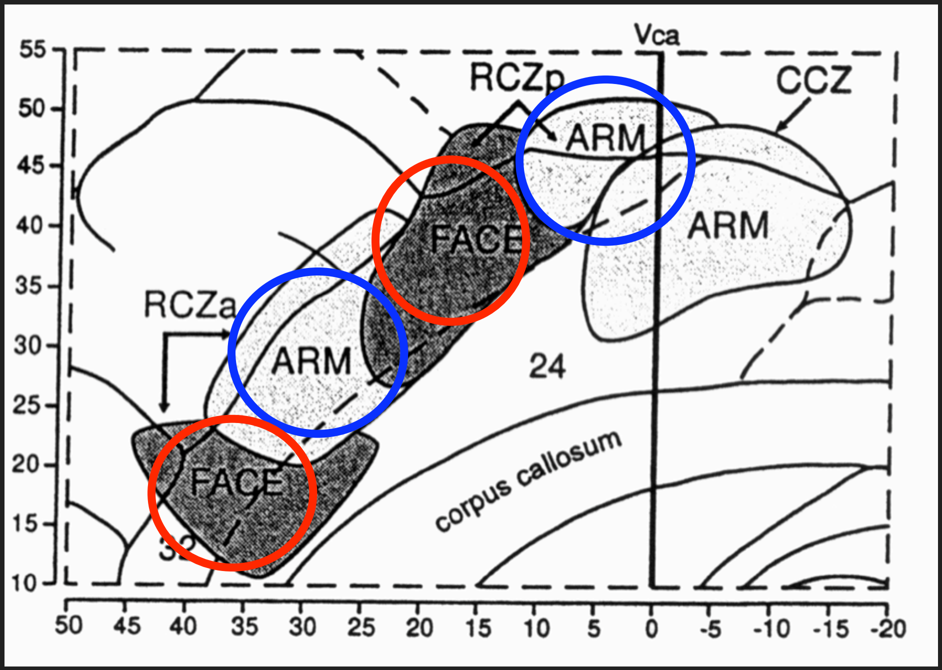
Somatotopy in the ACG

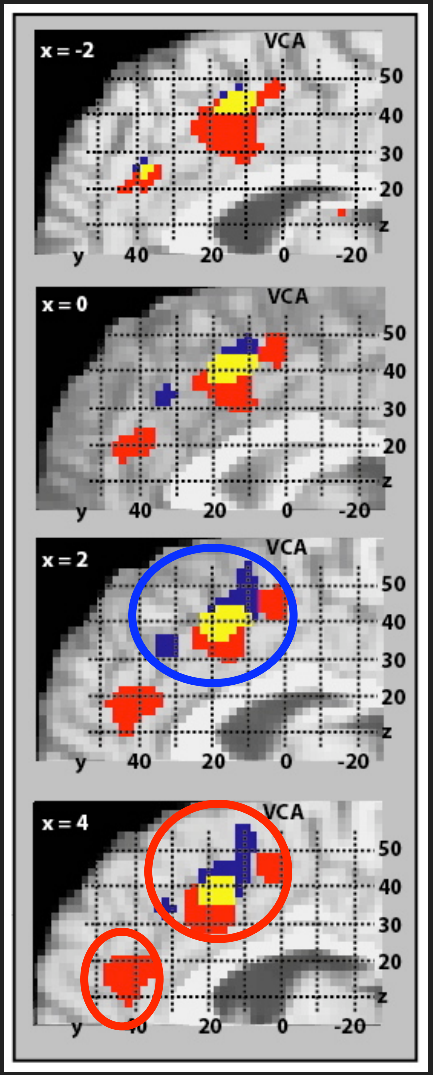




Paus et al., J Neurophys 70: 453-69 (1993)

Somatotopy in the ACG





Picard and Strick, Cereb Cortex 6: *342-53* (1996)

Conclusions

Verbal and manual Stroop meta-analysis ALE identified 3 regions crucial to task performance

Examined cingulate motor areas and provided evidence for somatotopy based on response modality

Determined verbal and manual region in both the rCZa and the rCZp (rostral cingulate motor zone)

Laird et al., Hum Brain Mapp 25, 6-21, 2005

Completed Meta-Analyses Grouped By Paradigm

Primary Systems

Action, Perception (Audition, Vision, Gustation, Olfaction, Somatosensation (including Pain), Interoception

Higher Cognition

Calculation, Emotion, Language Comprehension and Production, Mental Rotation, Stroop, n-back, Steinberg, Simon, Paired Associate Recall, Picture Naming, Music Production, Word Generation

Comparison of Subject Groups

Viewing of Sad Images in Depressed vs. Normals, Executive Function in Schizophrenics vs. Normals, Reading in Chinese vs. English, Stuttered vs. Normal Speech, Executive Function in OCD vs. Normals

Meta-Analysis of Structural Neuroimaging Studies

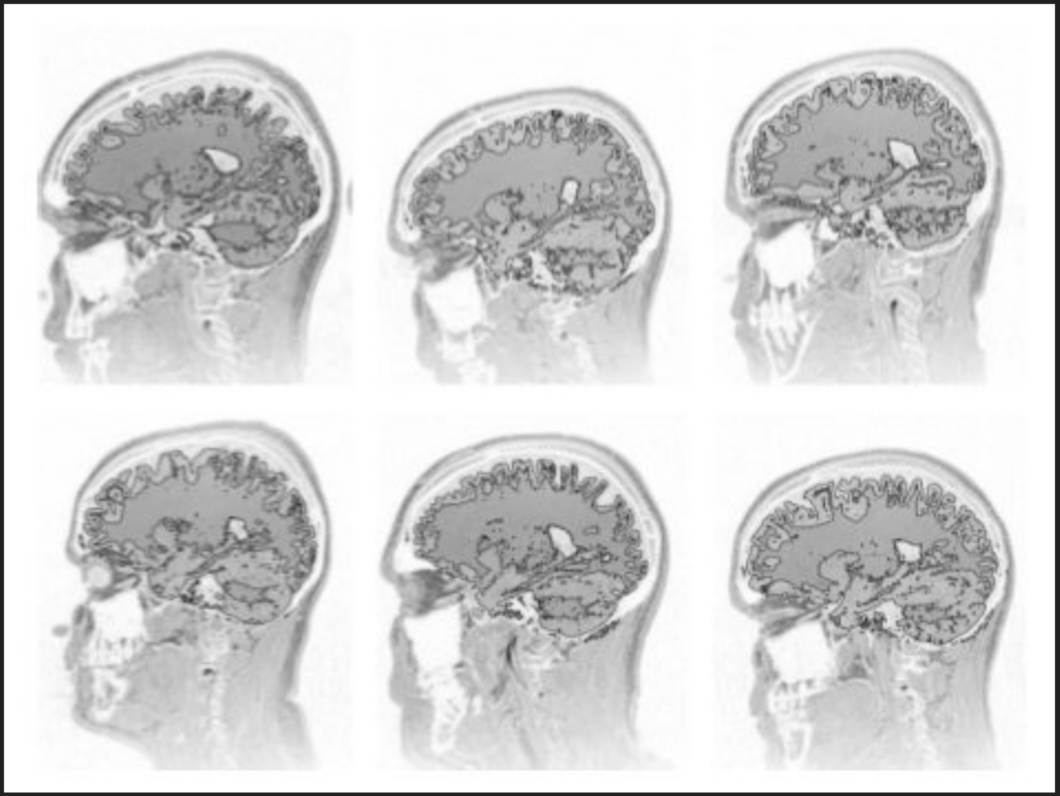
Brain morphology studies - ROI approaches

- Manually or automatically delineated ROIs
- Procedures differ between labs (difficult to compare)
- Compounded by different labels
- Choice of regions introduces bias, other regions ignored

→ Traditional review methods are less than optimal

Voxel-Based Morphometry

"voxel-wise comparison of the local concentration of gray matter (or WM or CSF) between two groups of subjects"



Contours of extracted GM and WM on high-res T1 images

Ashburner and Friston, 2000

Voxel-Based Morphometry

1. High resolution neuroimages from two populations (e.g., diseased and controls)
2. Spatial normalization; segmentation into GM, WM and CSF; smoothing
3. Analyze the group-level differences between aligned voxels
4. Output images of maps that identify significant differences between groups

→ *x,y,z* coordinates in stereotactic space

An Expansion of BrainMap?

Meta-Analysis of VBM in Schizophrenia

- Inclusion Criteria
  - Reported whole brain results in x,y,z format
  - Included SCZ and healthy comparisons
  - Followed VBM protocols (Ashburner and Friston, 2000)

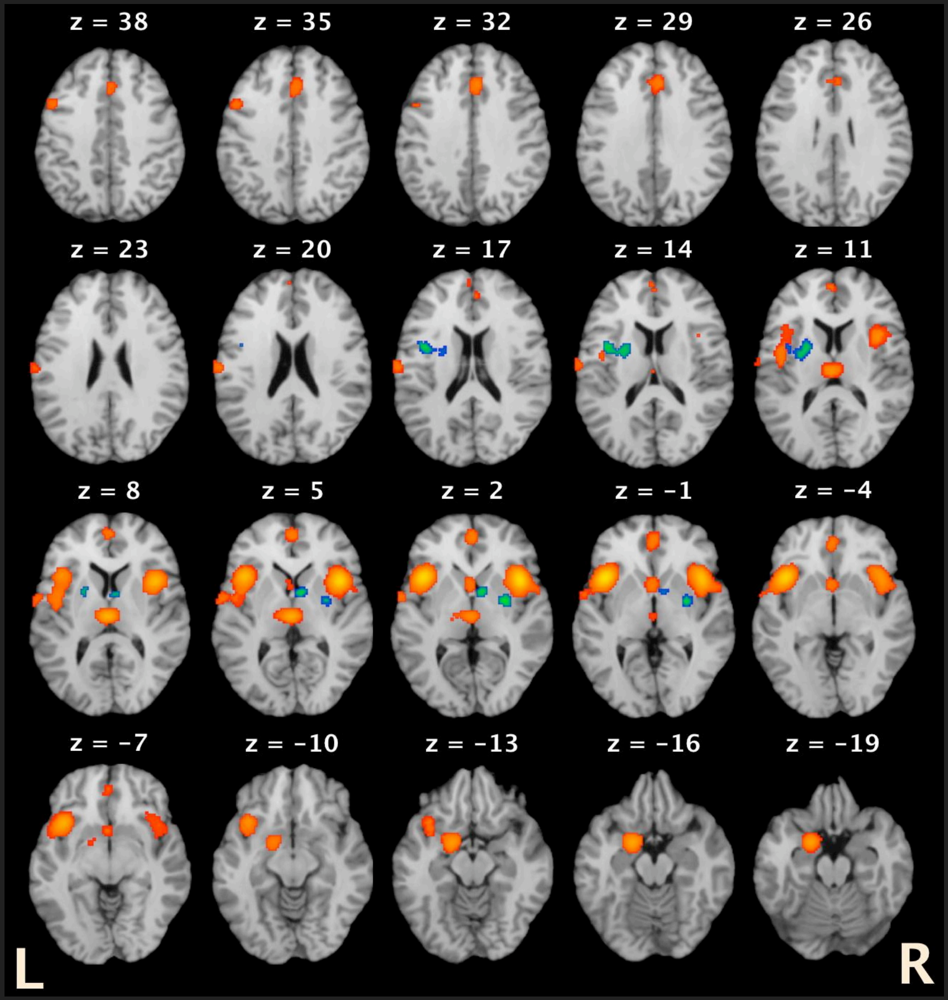
- Exclusion Criteria
  - Reported changes over time
  - Included individuals at risk for SCZ
  - Treatment effects, substance use effects

→ 31 papers with 1,195 patients and 1,262 healthy controls

Anatomic Likelihood Estimation (ALE)

- CT > SCZ (315 foci)
- SCZ > CT (64 foci)
- icbm2tal; or Brett's tal2min, then icbm2tal
- GingerALE environment
- FWHM = 12mm
- 5000 permutations; P<0.01, corrected

VBM ALE Meta-Analysis:
Gray Matter Anomalies in Schizophrenia



Increases in Controls
(CT > SCZ)
Bilat insula, L parahipp, dACC, vACC, subgenual ACC, thalamic, L mid front gyrus

Increases in Patients
(SCZ > CT)
Bilat putamen, R head of caudate

Glahn et al., Biol Psych, In Press;
Ellison-Wright et al., Am J Psych, In Press

Why Meta-Analysis?

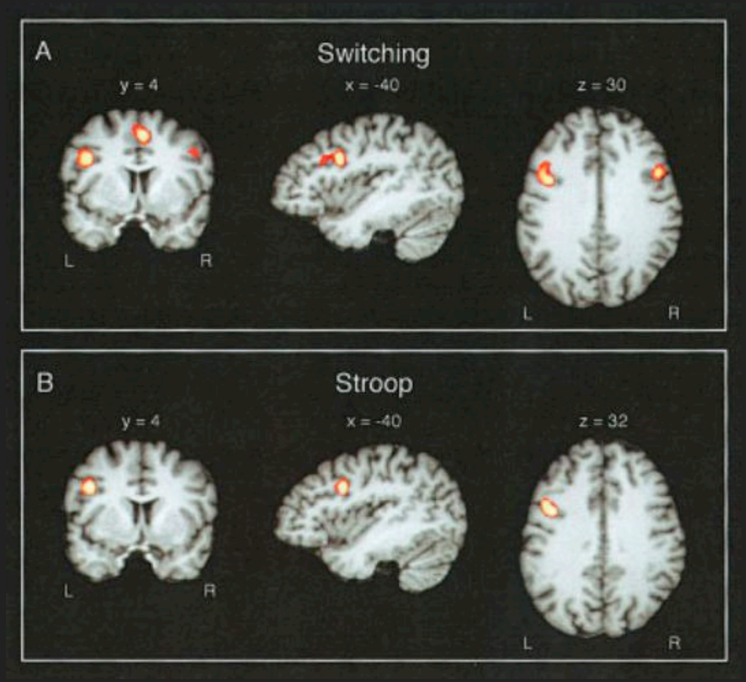
1. Resolve conflict between existing studies

   Example: Somatotopy of ACC in Stroop meta-analysis

2. Generate new hypotheses

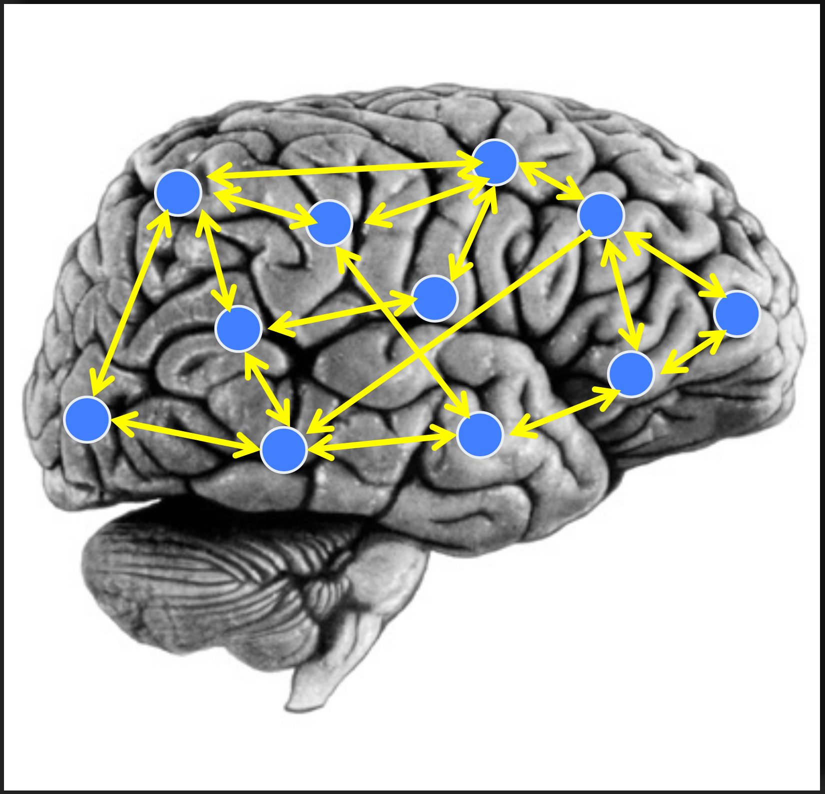
   Example: Importance of IFJ in conflict resolution

   (Derrfuss et al., 2005)



Why Meta-Analysis?

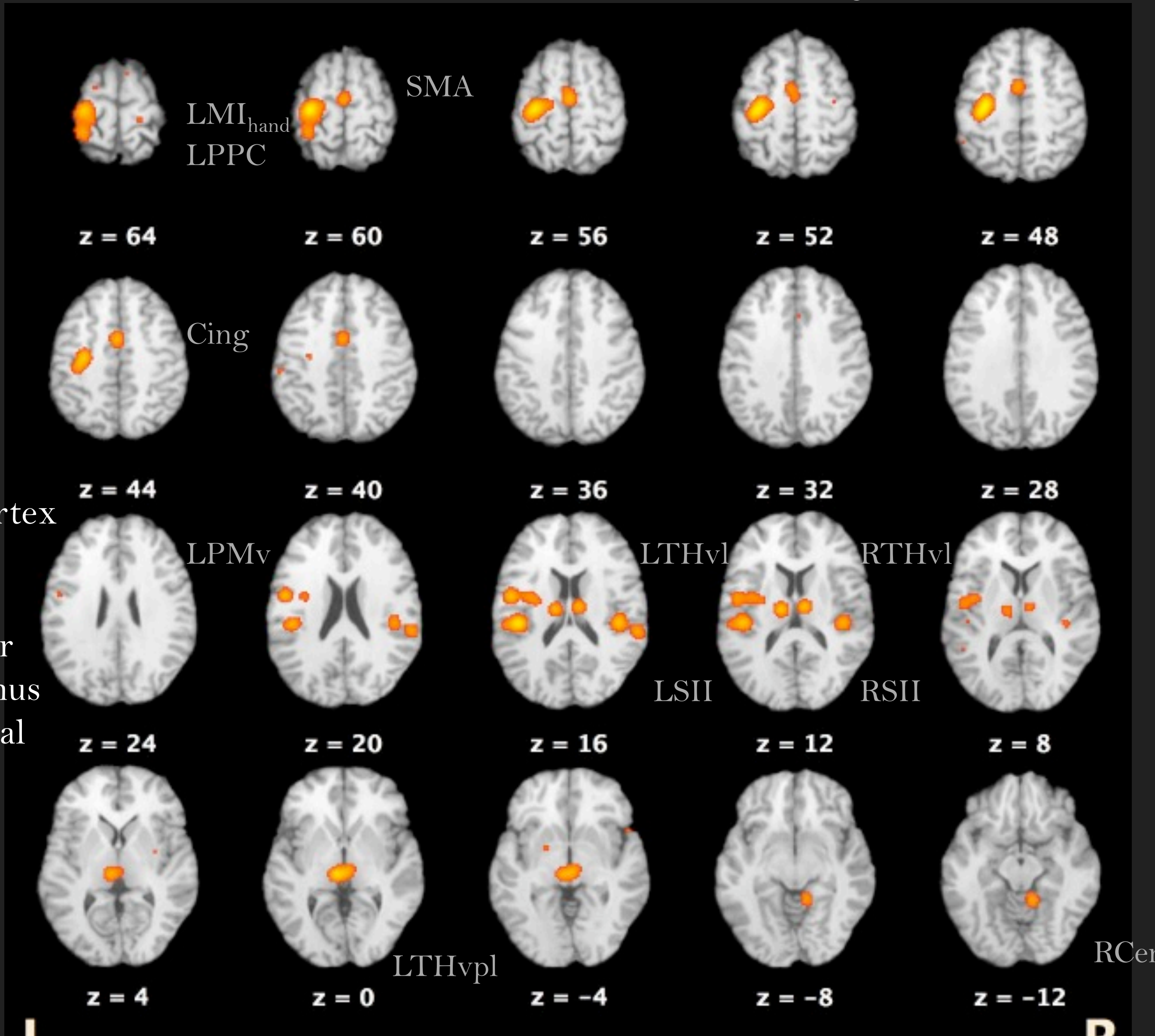
3. Spatial pattern matching to identify ICA/PCA components
4. Isolate ROIs for studies of effective connectivity



LM1 TMS ALE Meta-Analysis

9 papers
11 experiments
102 foci

LMI = left motor cortex
LPPC = posterior parietal cortex
SMA = supp. motor area
Cing = ant. cingulate
LPMv = left ventral premotor
THvl = ventral lateral thalamus
THvpl = ventral posterolateral
RCer = right cerebellum



P<0.05, FDR-corrected

Results

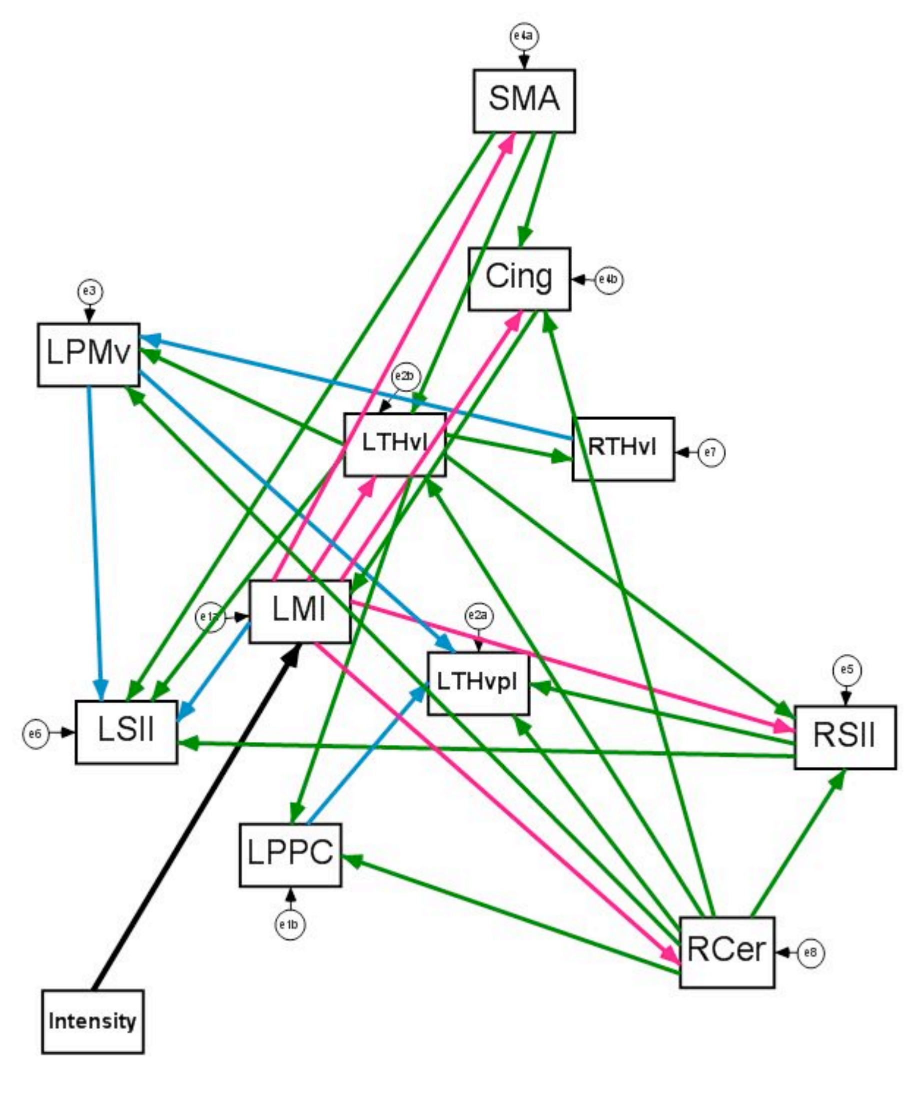
Red = 1st level paths

Green = 2nd level paths

Blue = 3rd level paths

Final model fit was outstanding

– $X^2(38) = 22.150$, $P = 0.981$
– CFI = 1.0
– TLI = 1.0
– RMSEA = 0.000
– 90% CI_{RMSEA} = 0.00-0.00



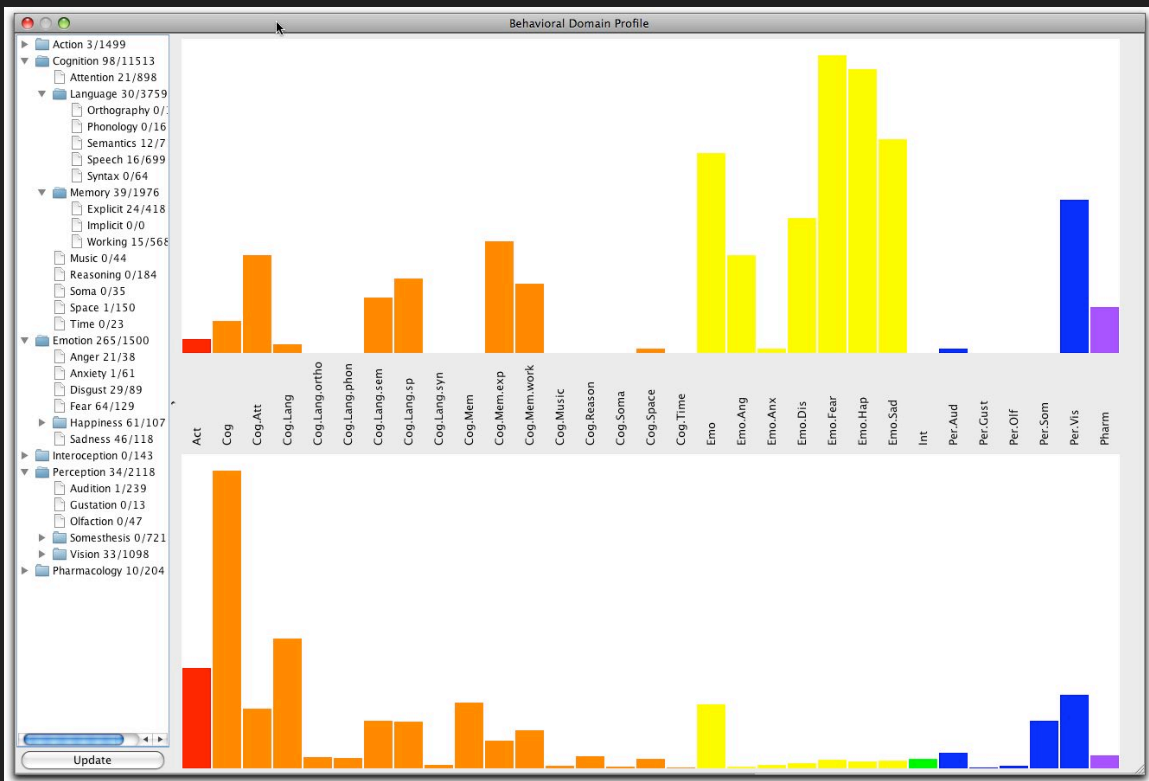
Plausibility of Results

Excellent agreement

- TMS ALE & TMS/PET data
- TMS ALE & Finger Tapping ALE
- Path connections in human and primate literature (FI_{arm}) e.g., direct paths from LMI_{hand} to SMA, Cingulate, SII, Thalamus, Cerebellum

May provide closer approximation to animal models

Future Meta-Analytic Work



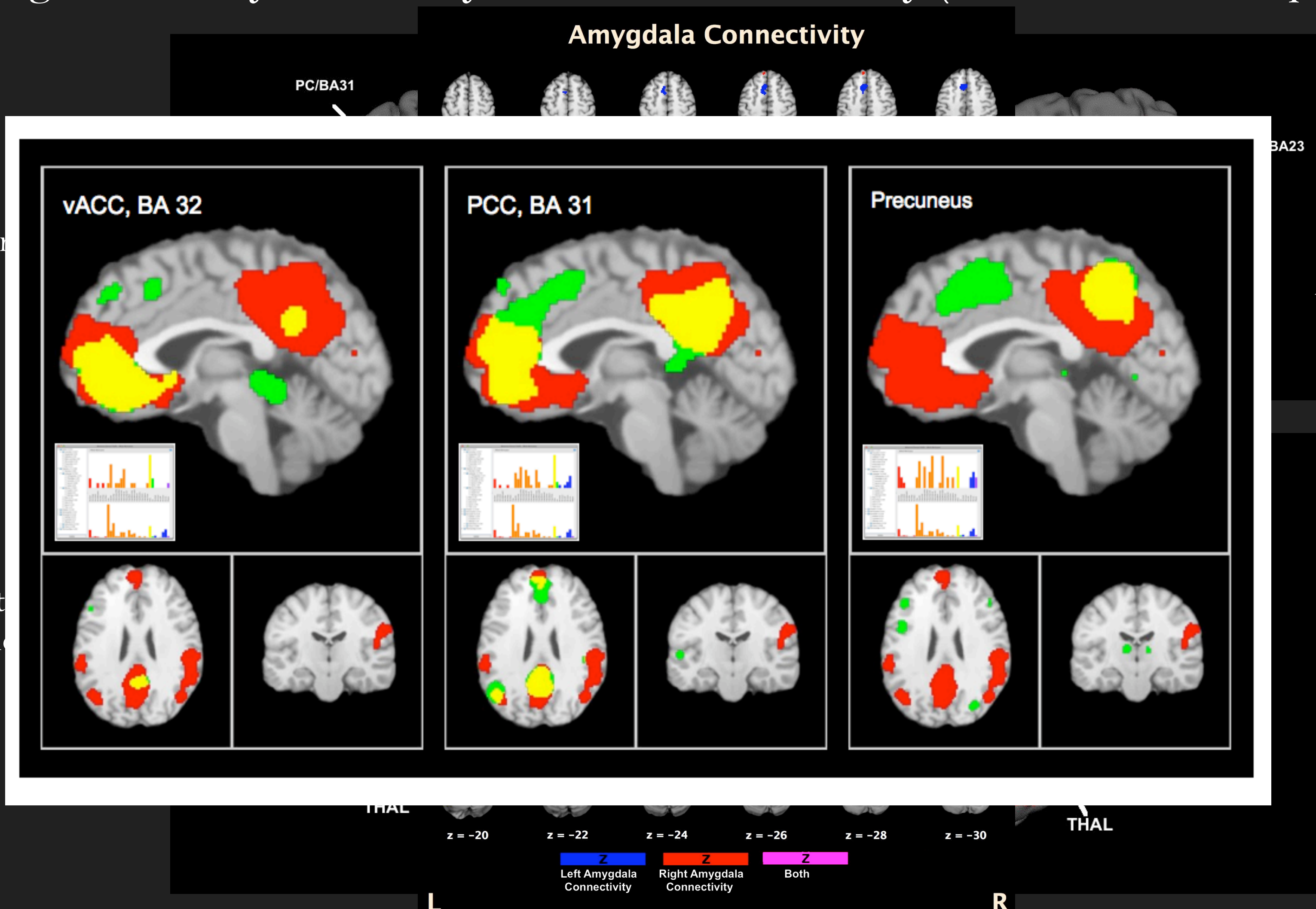
- Working towards an atlas of brain function
- Action, language, memory, attention, perception

Future Meta-Analytic Work

Using meta-analysis to study functional connectivity (via co-occurrence patterns)

left

right



Deactivations

ROI-Based Coactivations

Conjunction

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