Toolboxes and databases

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Why database?

Bring order to data: Organize data for the individual study or for a whole range of studies.

Make search easy: PubMed and Google are examples on easy search and retrieval on text. They fail to search on specific neuroscience data, e.g., activation in basal ganglia.

Automate analysis: E.g. construct consensus across studies; compare a new study to the existing body of work.

Develop new tools: Neuroscience makes interesting heterogeneous data which enforce development of new tools.

Information increase

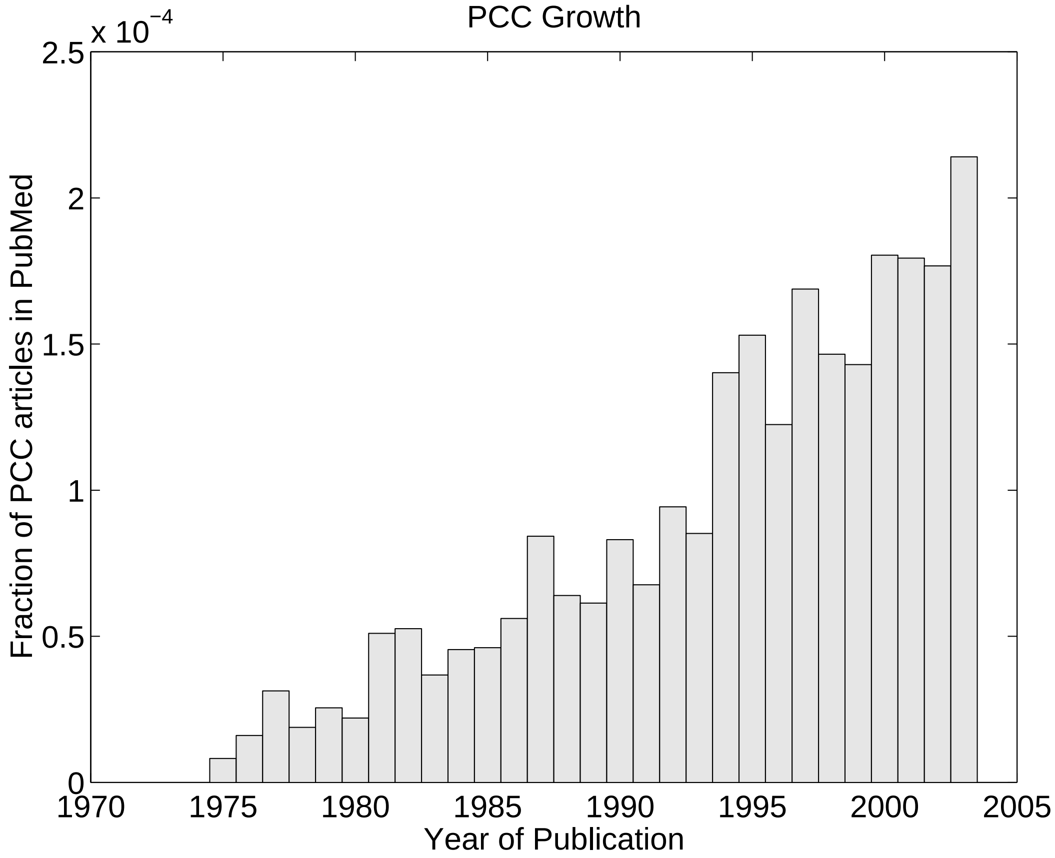


Figure 1: Increase in the number of articles in PubMed which are returned after searching on "Posterior cingulate".

The number of articles increases.

Can databases and computer-based methods help to oganize the large amount of new data?

How should data be represented? How can they be entered into a database? Which data mining methods can be developed? Internet services like bioinformatics?

Functional human brain mapping

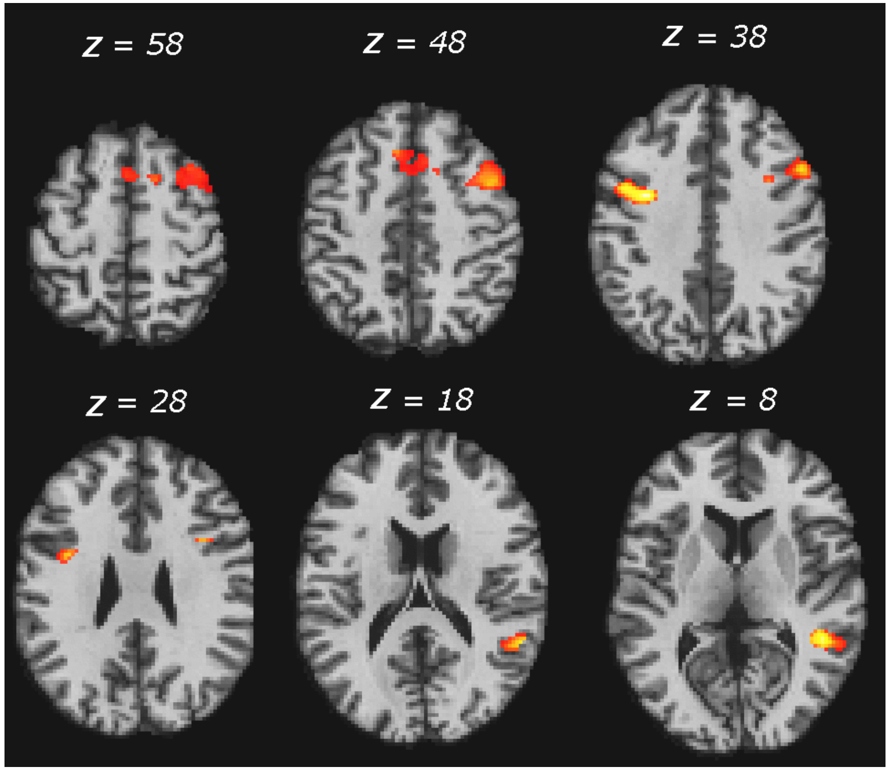


Figure 2: Figure from (Balslev et al., 2005).

"Activation studies" or patient-control comparisons with PET, fMRI or SPECT. Lesionsstudies with MRI.

Results often represented in the literature as 3-dimensional coordinates wrt. a standardized stereotaxic system ("Talairach")

(x, y, z)	z-score
$-38, 0, 40$	4.91
$48, -42, 8$	4.66
$52, 14, 38$	4.07

BrainMap database

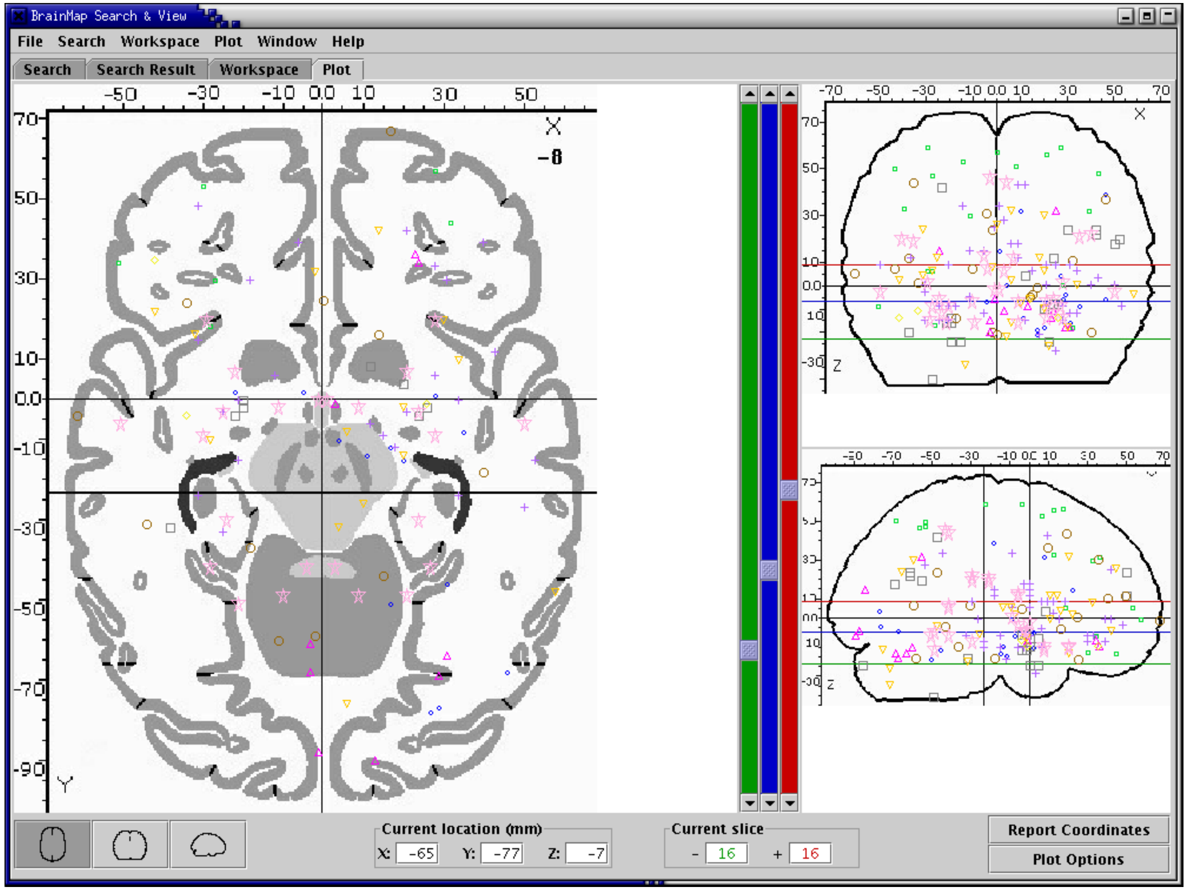


Figure 3: Screen shot of a graphical user interface to the BrainMap database with Talairach coordinates plotted after a search for experiments on olfaction.

One of the first and most comprehensive databases (Fox et al., 1994; Fox and Lancaster, 2002)

Presently 28012 locations from 810 papers

Graphical web-interface with search facilities, e.g., on author, 3D coordinate, . . .

Also possible to submit new studies

Brede Database

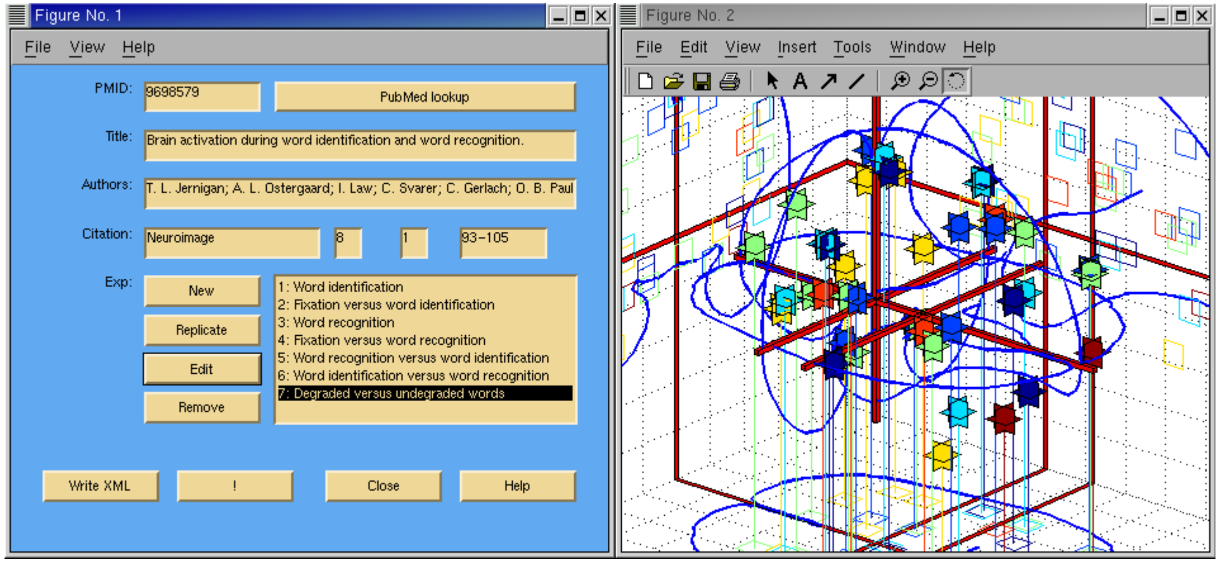


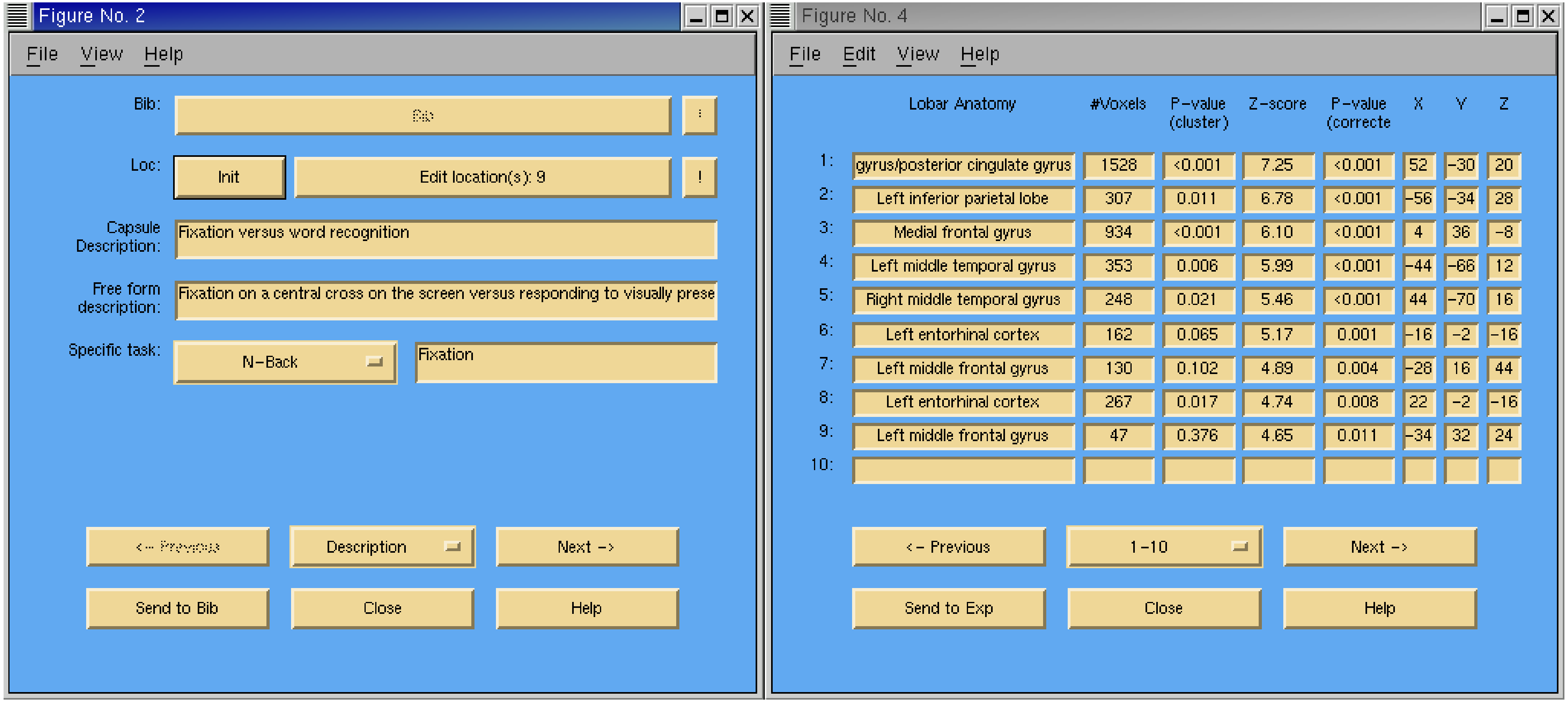
Figure 4: Screenshot of a program for entering data. Here with a study of (Jernigan et al., 1998).

Smaller Brede Database similiar to BrainMap (Nielsen, 2003).

Every studie saves, e.g., author, article title, abstract, scanner, number of subjects, coordinates, anatomical names, topic under study.

Taxonomy for brain regions and topics

Entry of information in the Brede database



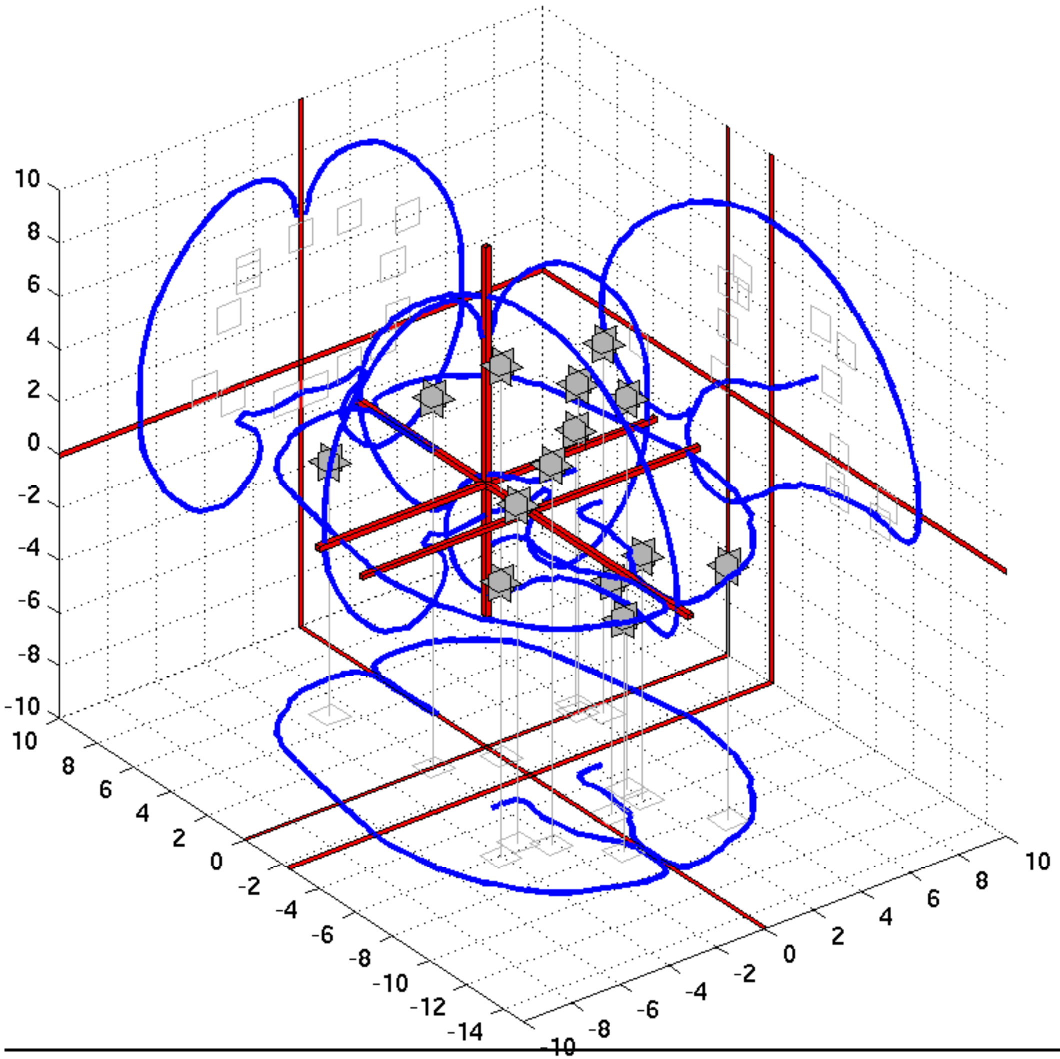
	Lobar Anatomy	#Voxels	P–value (cluster)	Z–score	P–value (correcte	X	Y	Z
1:	gyrus/posterior cingulate gyrus	1528	<0.001	7.25	<0.001	52	−30	20
2:	Left inferior parietal lobe	307	0.011	6.78	<0.001	−56	−34	28
3:	Medial frontal gyrus	934	<0.001	6.10	<0.001	4	36	−8
4:	Left middle temporal gyrus	353	0.006	5.99	<0.001	−44	−66	12
5:	Right middle temporal gyrus	248	0.021	5.46	<0.001	44	−70	16
6:	Left entorhinal cortex	162	0.065	5.17	0.001	−16	−2	−16
7:	Left middle frontal gyrus	130	0.102	4.89	0.004	−28	16	44
8:	Left entorhinal cortex	267	0.017	4.74	0.008	22	−2	−16
9:	Left middle frontal gyrus	47	0.376	4.65	0.011	−34	32	24
10:								

Each location is primarily represented by the 3D-coordinate and a textual field indicating the brain region

XML “Lowtech” storage

```
...
<brainTemplate>SPM95</brainTemplate>
<behavioralDomain>Motion,Execution - Saccades</behavioralDomain>
<woext>57</woext>
<analysisSoftware>SPM95</analysisSoftware>
<analysisSoftware>AIR</analysisSoftware>
<analysisSoftware>AMIR</analysisSoftware>
<Loc>
  <type>loc</type>
  <functionalArea>Left frontal eye field</functionalArea>
  <brodmann></brodmann>
  <zScore>4.82</zScore>
  <coordReported>-0.050000 -0.002000 0.036000</coordReported>
...
```

Read coordinates from a spreadsheet



Coordinate information may also be read from a spreadsheet via a "comma separated values" file with columns "x", "y" and "z".

Matlab commands

Matlab commands to read a spreadsheet and display them in a 3D plot:

```
L = brede_read_csv2loc('LawI1997Activation_1.csv');
figure, brede_ta3_frame, brede_ta3_loc(L)
print -depsc /home/fnielsen/fnielsen/eps/Nielsen2006Toolboxes_law3d.eps
```

Searching on Talairach coordinate

14 14 9 | Location search | e.g., 14 -9 -15

#	Distance	x	y	z	WOBIB	Description
1	0.5	13	14	8	76	Right caudate nucleus - Correlated with pain ratings in hot pain on right hand in rest, mental imagery and hypnosis (WOEXP: 238)
2	3.5	15	11	6	92	Caudate nucleus - Mildly depressed cancer patients (WOEXP: 293)
3	4.9	15	12	13	180	Right caudate nucleus - Intelligence and gray matter volume negative correlation (WOEXP: 564)
4	7.0	12	8	12	178	Right caudate - Semantic versus case (WOEXP: 550)
5	7.5	10	8	11	178	Right caudate - Semantic versus syllable counting via case judgment (WOEXP: 558)
6	8.1	5	14	8	76	Right caudate nucleus - Hot pain on right hand during hypnosis (WOEXP: 235)
7	8.3	13	7	3	171	Right striatum - Rhyme judgement and nonlinear ('convex') response in rapid auditory processing (WOEXP: 526)
8	8.3	13	7	3	171	Right striatum - Rhyme judgement and linear increase response in rapid auditory processing (WOEXP: 527)

Result after search for nearest coordinates to (14, 14, 9). Similar searches possible in xBrain and Antonia Hamilton's AMAT programs.

Searching on experiments

+1: 1.00000 **Mentalizing versus rule solving**. *Playing a computer-based version of "stone, paper, scissor" while believing the opponent was an other human versus playing while believing the opponent was a computer with a fixed rule-based algorithm.* WOEXP: 218.
Helen L. Gallagher; Anthony I. Jack; Andreas Roepstorff; Christopher D. Frith. *Imaging the intentional stance in a competitive game.* *NeuroImage* **16**(3 Pt 1):814-21, 2002. PMID: 12169265. WOBIB: 70.

+2: 0.68676 **Posttraumatic stress disorder**. *Benzodiazepine binding in posttraumatic stress disorder versus binding in normal subjects.* WOEXP: 206.
J. D. Bremner; R. B. Innis; S. M. Southwick; L. Staib; S. Zoghbi; D. S. Charney. *Decreased benzodiazepine receptor binding in prefrontal cortex in combat-related posttraumatic stress disorder.* *American Journal of Psychiatry* **157**(7):1120-1126, 2000. PMID: 10873921. WOBIB: 67.

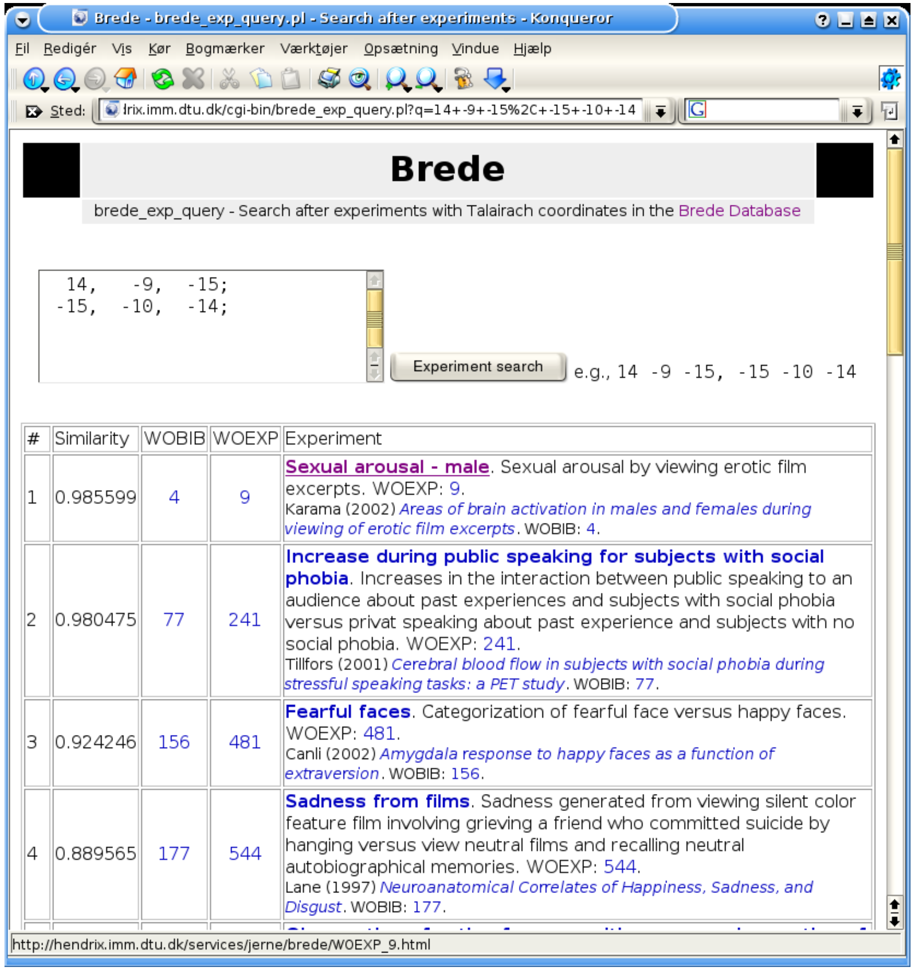
+3: 0.67565 **Forgiveness judgements**. *Judgements of visually displayed sentences about forgiveness situations with button press versus judgement involving social reasoning.* WOEXP: 451.
T. F. Farrow; Y. Zheng; I. D. Wilkinson; S. A. Spence; J. F. Deakin; N. Tarrier; P. D. Griffiths; P. W. Woodruff. *Investigating the functional anatomy of empathy and forgiveness.* *NeuroReport* **12**(11):2433-2438, 2001. PMID: 11496124. FMRIDCID: . WOBIB: 147.

+4: 0.64805 **Case judgment versus syllable counting**. *Case judgment of letters from visually presented words with button press versus counting the number of syllables in a visually presented word.* WOEXP: 553.
Russell A. Poldrack; Anthony D. Wagner; Matthew W. Prull; John E. Desmond; Gary H. Glover; John D. E. Gabrieli. *Functional Specialization for Sematic and Phonological Processing in the Left Inferior Prefrontal Cortex.* *NeuroImage* **10**(1):15-35, 1999. PMID: 10385578. DOI: 10.10061/nimg.1999.0441. FMRIDCID: . WOBIB: 178.

+5: 0.60237 **Subject 3: Answering self-reflective questions versus answering semantic questions**. *Self-reflective and semantic yes/no questions posed through headphones were answered with button press.* WOEXP: 56.
Sterling C. Johnson; Leslie C. Baxter; Lana S. Wilder; James G. Pipe; Joseph E. Heiserman; George P. Prigatano. *Neural correlates of self-reflection.* *Brain* **125**(Pt 8):1808-14, 2002. PMID: 12135971. WOBIB: 20.

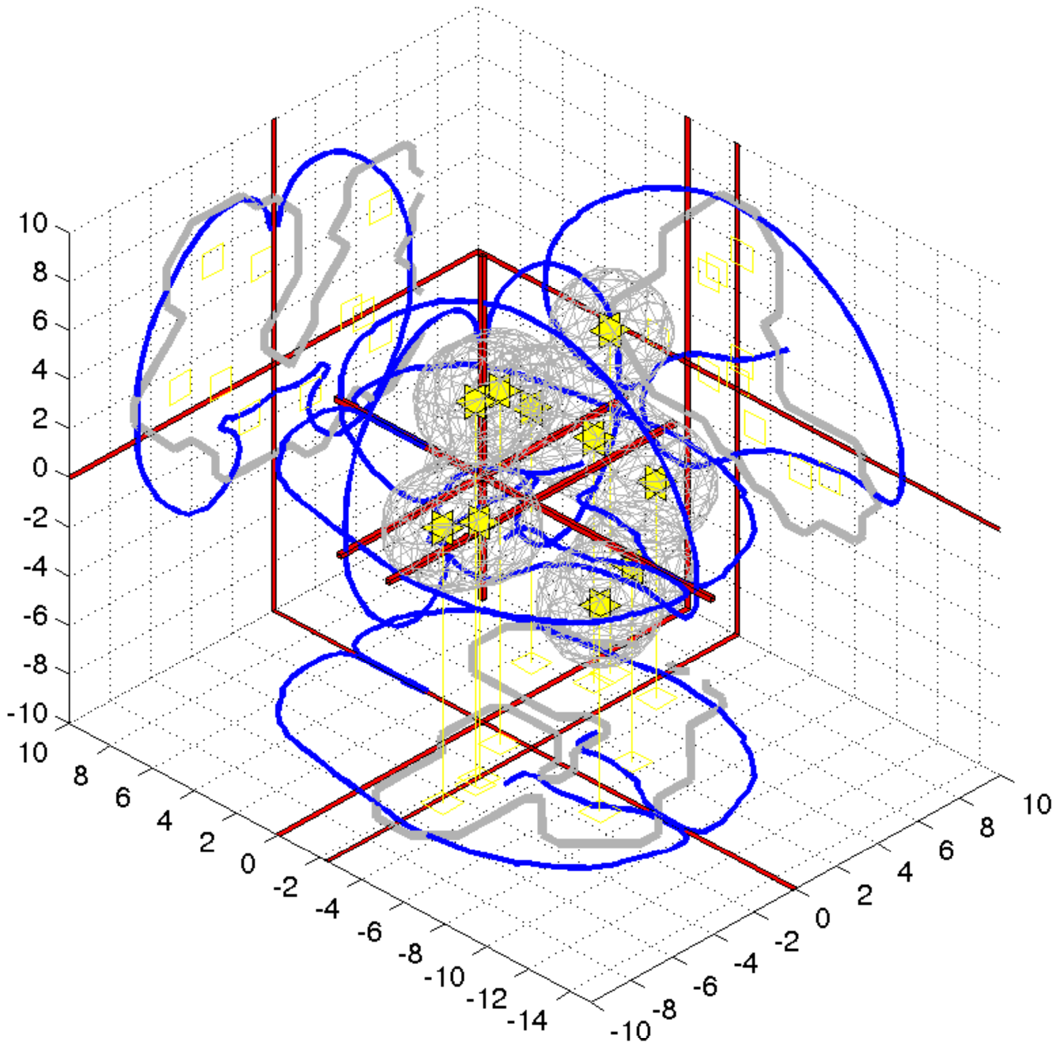
List with results after searching experiments that report similar activations as a "mentalizing" experiment of (Gallagher et al., 2002).

Online experiment search



Online search on two coordinates in left and right amygdala in the experiments recorded in the Brede Database.

Coordinates-to-volume transformation

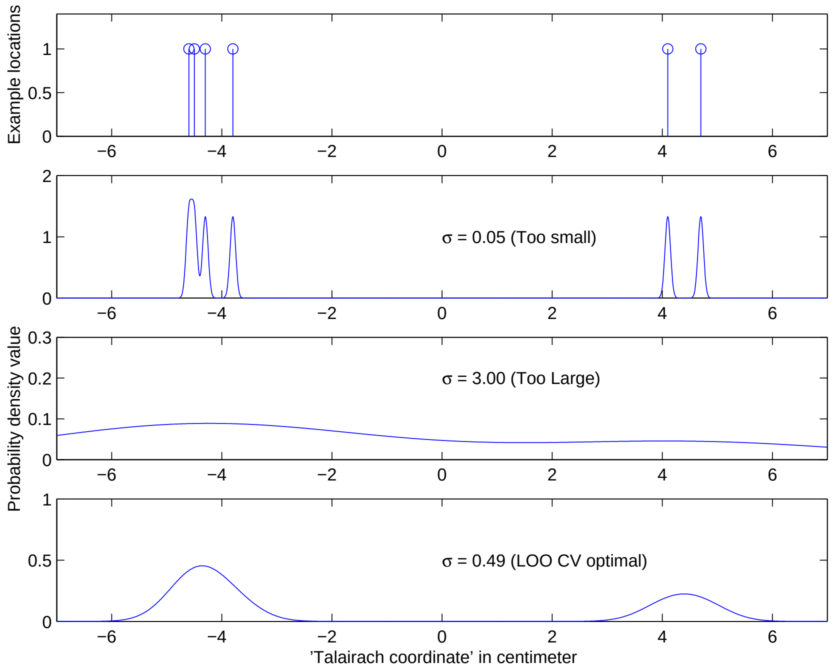


Coordinates in an article converted to volume-data by filtering each point (kernel density estimation) (Nielsen and Hansen, 2002; Turkeltaub et al., 2002)

One volume for each article

Yellow coordinates from a study by (Blinkenberg et al., 1996), with grey wireframe indicating the isosurface in the generated volume

Kernel density estimators for locations



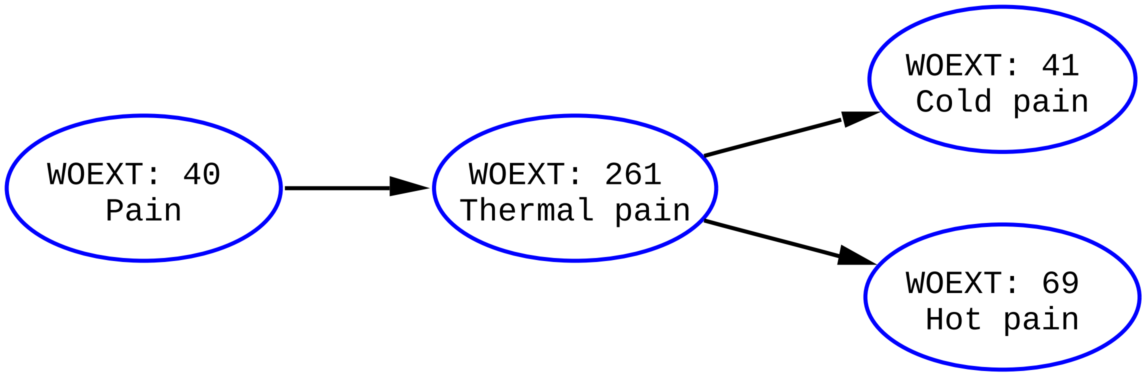
Regard the "locations" as being generated from a distribution $p(\mathbf{x})$, where $\mathbf{x}$ is in 3D Talairach space (Fox et al., 1997).

Kernel methods (N kernels centered on each location: $\boldsymbol{\mu}_n$) with homogeneous Gaussian kernel in 3D Talairach space $\mathbf{x}$

$$\hat{p}(\mathbf{x}) = \frac{(2\pi\sigma^2)^{-3/2}}{N} \sum_n^N e^{-\frac{1}{2\sigma^2}(\mathbf{x}-\boldsymbol{\mu}_n)^2}$$

σ^2 fixed ($\sigma = 1$cm) or optimized with leave-one-out cross-validation (Nielsen and Hansen, 2002).

Taxonomy for cognitive components, . . .



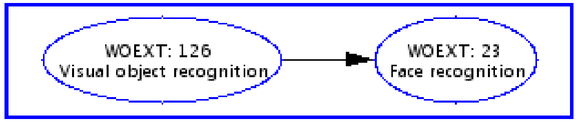
Memory, episodic memory, episodic memory retrieval, empathy, disgust, 5-HT2A receptor, . . .

Organized in a hierarchy — a directed acyclic graph.

Supervised labeling

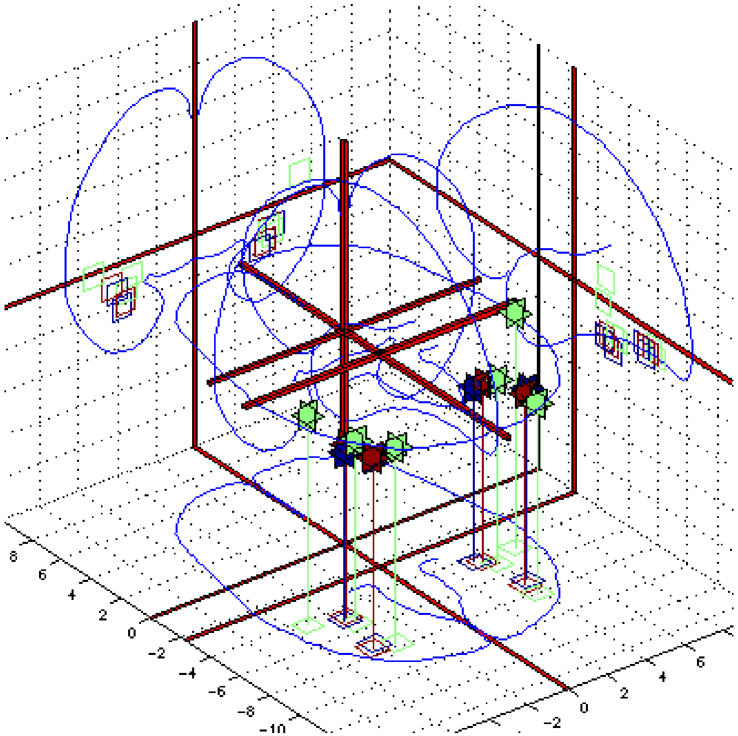
WOEXT: 23. **Face recognition.**
Processing of face images.

Parents	Siblings	Children
Visual object recognition		



Experiments:

1. **Face visual object.** *Visual objects: Faces versus building*. WOEXP: 11.
   I Levy; U Hasson; G Avidan; T Hendler; R Malach. *Center–periphery organization of human object areas.*. *Nat Neurosci* **4**(5):533–9, 2001.
   PMID: 11319563. WOBIB: 5.
2. **Photographs of faces versus houses and chairs.** *Conjunction between passive viewing and delayed match–to sample of gray–scale photographs versus scrambled pictures and faces versus houses and chairs, with matching choice indicated by pressing a button with the right of left thumb*. WOEXP: 91.
   A. Ishai; L. G. Ungerleider; A. Martin; J. V. Haxby. *The representation of objects in the human occipital and temporal cortex.*. *J Cogn Neurosci* **12 Suppl 2**:35–51, 2000.
   PMID: 11506646. FMRIDCID: 2–2000–1113D.
   WOBIB: 28.
3. **Front–face.** *Line drawings of front face versus line drawings of tumblers*. WOEXP: 123.
   U. Hasson; T. Hendler; D. Ben Bashat; R. Malach. *Vase or face? A neural correlate of shape–selective grouping processes in the human brain.*. *J Cogn Neurosci* **13**(6):744–53, 2001.
   PMID: 11564319. FMRIDCID: 2–2001–111P8.
   WOBIB: 36.

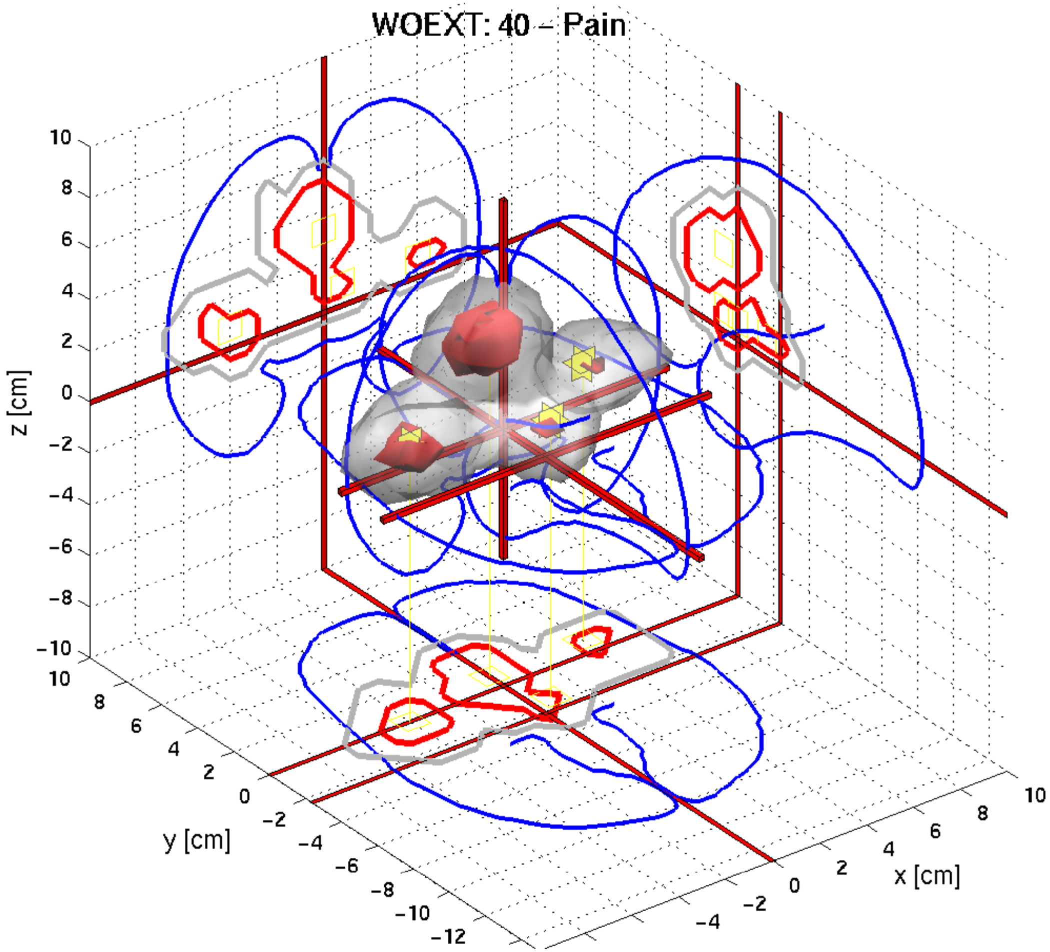


Example with "Face recognition" studies in a "corner cube" visualization.

The "expert" label added during database entry can provide the grouping structure.

Statistical tests can be constructed to measure whether the spatial distribution is "clustered" (Turkeltaub et al., 2002; Nielsen, 2005).

Supervised datamining



Volume for a specific taxonomic component: "Pain"

Volume threshold at statistical values determined by resampling statistics (Nielsen, 2005).

Red areas are the most significant areas: Anterior cingulate, anterior insula, thalamus. In agreement with "human" reviewer (Ingvar, 1999).

Two sets of coordinates: Compare these!

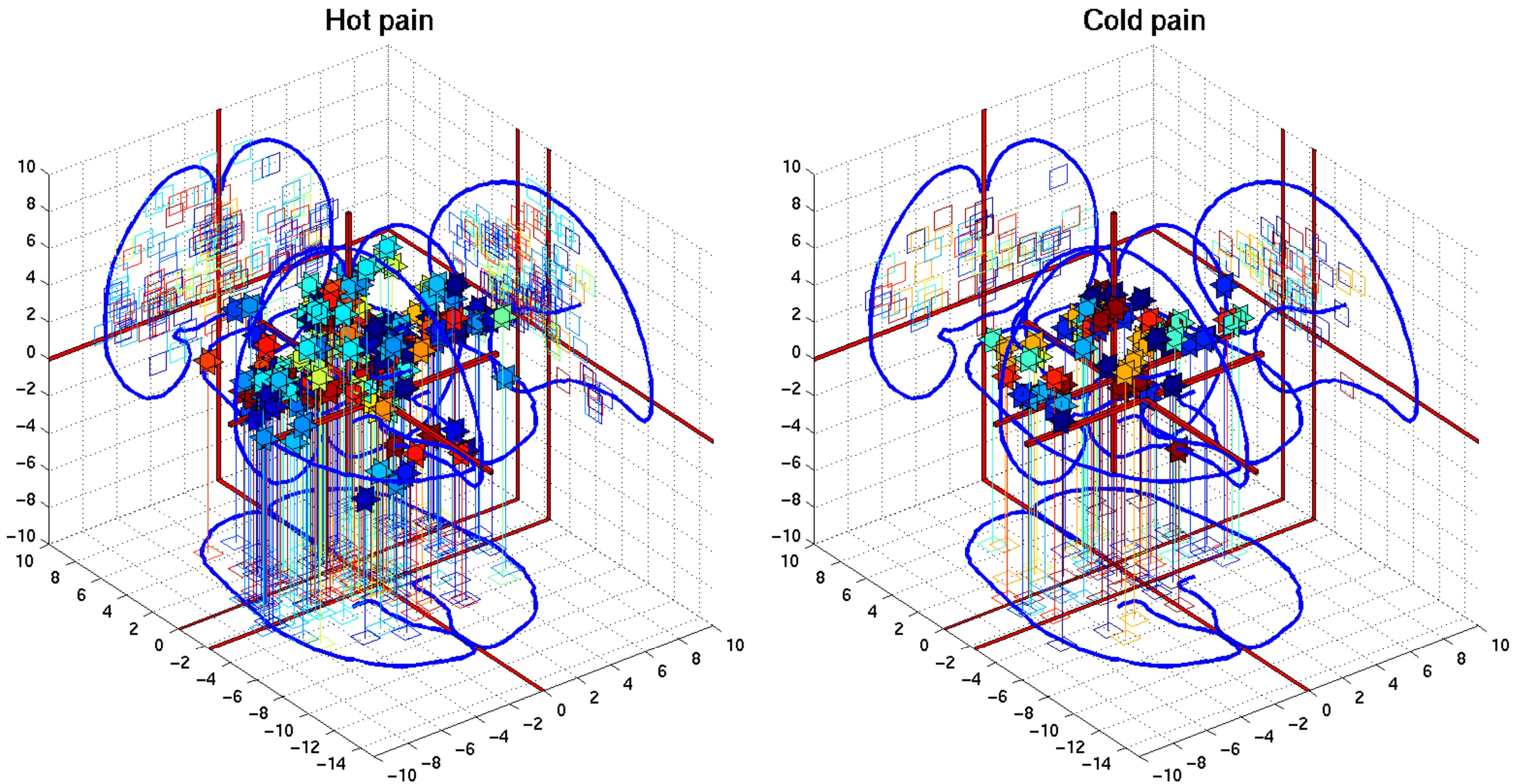


Figure 6: Visualization of the Talairach coordinates from hot pain and cold pain studies

Testing for difference

Two groups are compared by looking at the subtraction volume image

$$\mathbf{t} = \mathbf{v}_1 - \mathbf{v}_2. \tag{1}$$

The statistic is the maximum in the subtraction image

$$t = \max_i(t_i) \tag{2}$$

A null distribution is established by resampling the labels between the two sets of Talairach coordinates and computing the resampled maximum statistic t_n^* for all N resamplings.

The P-value for the ith voxel is the proportion of resampled maximum statistics above the statistic t_i (Nielsen et al., 2004a)

$$P_i = 1/N \sum_n^N |t_i < t_n^*| \,. \tag{3}$$

Resampling distribution

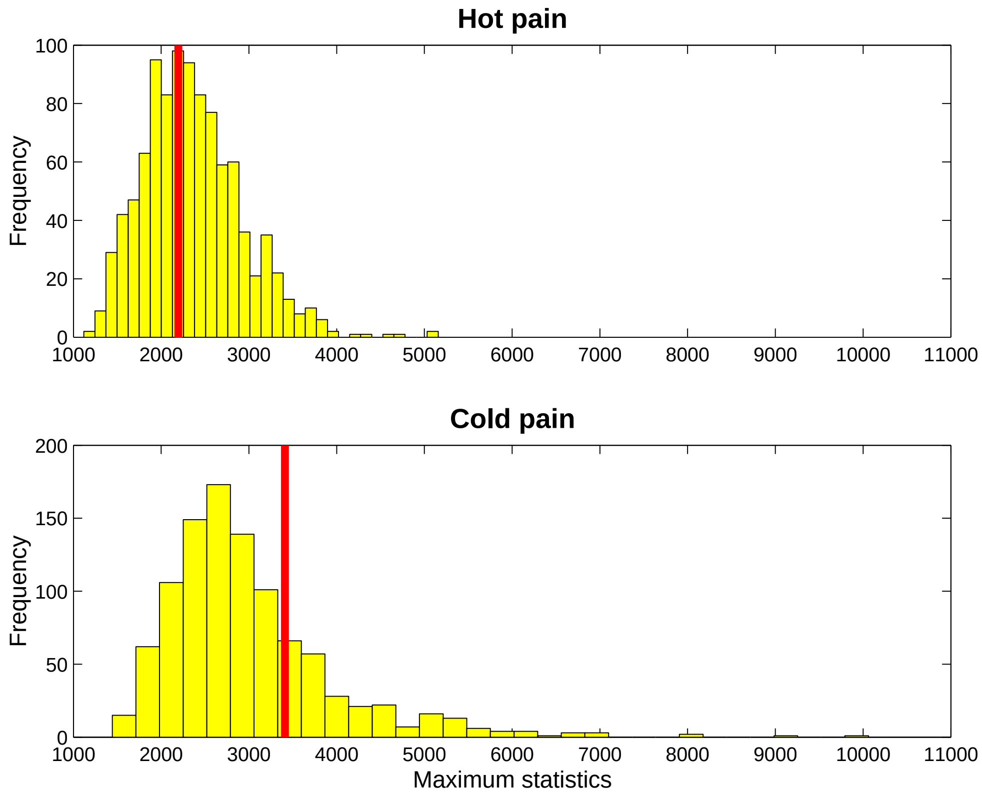


Figure 7: Empirical histograms of the maximum statistics t^* after 1000 permutations. The thick red lines indicate the maxima for the hot and cold pain statistics t_{hot} and t_{cold}.

Histogram of resampled maximum statistics with 1000 resamplings.

Two plot: Different numbers of experiments in hot (24) and cold (8) pain:

$$
\begin{aligned}
t_{\mathrm{hot}} &= \max(\mathbf{v}_{\mathrm{hot}} - \mathbf{v}_{\mathrm{cold}}) \\
t_{\mathrm{cold}} &= \max(\mathbf{v}_{\mathrm{cold}} - \mathbf{v}_{\mathrm{hot}}).
\end{aligned}
$$

No difference between hot and cold pain detected.

Testing between pain and object vision

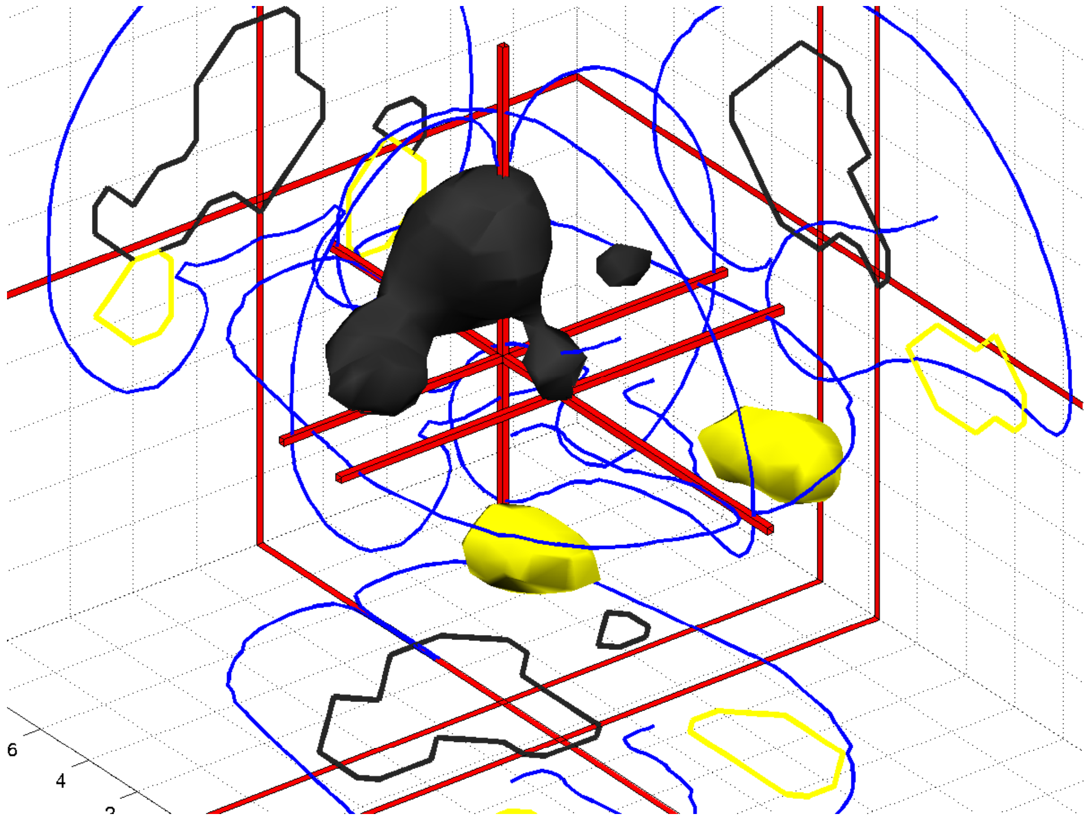


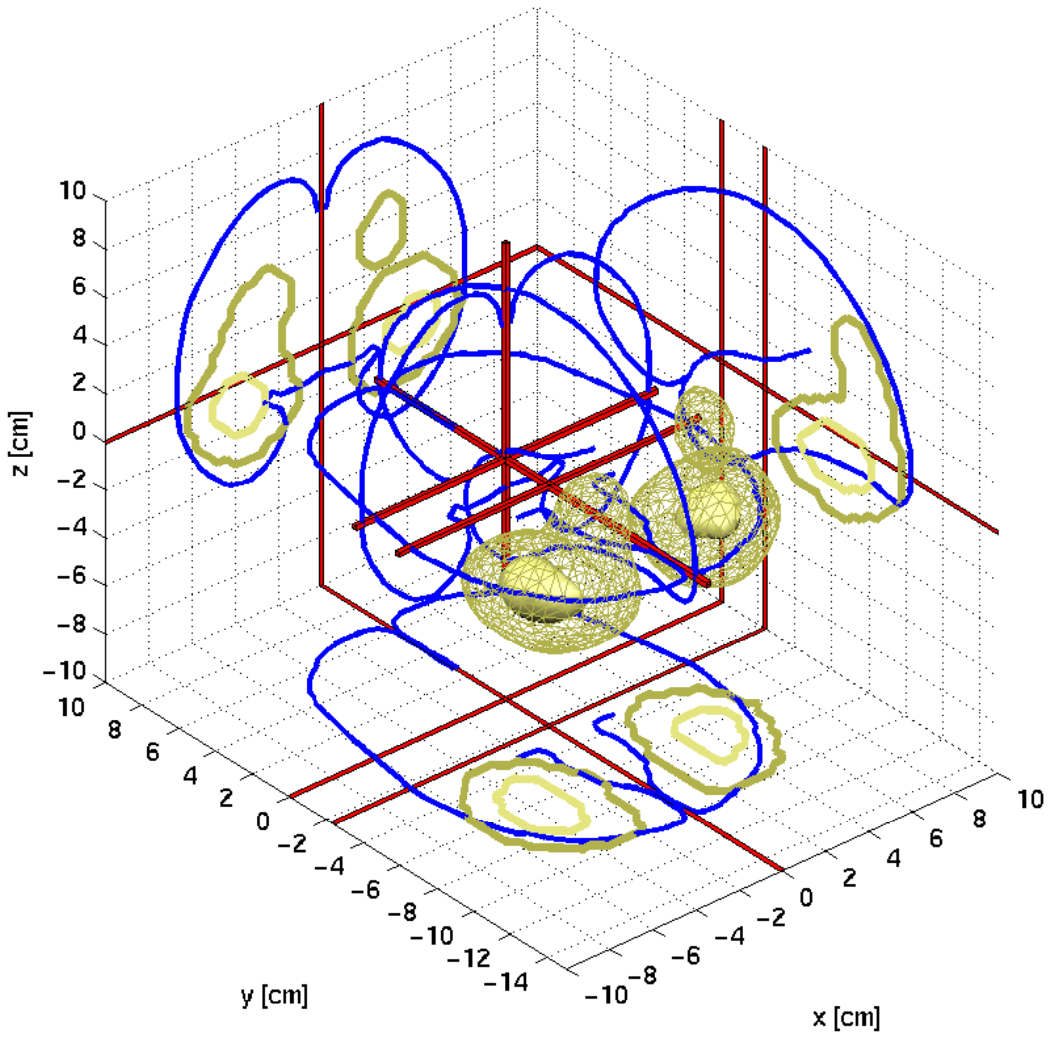
Figure 8: Statistical image. Black is thermal pain and yellow is visual object recognition.

Isosurfaces at thresholds in t_{pain} and t_{object}.

Thresholds are at the usual 0.05-level.

Expected areas appear above threshold. For pain: Anterior cingulate, insula, thalamus. For visual object recognition: fusiform gyrus.

Unsupervised datamining



Construction of a matrix $\mathbf{X}$(papers $\times$ voxels)

Decomposition of this matrix by multivariate analysis, e.g., principal component analysis, clustering, independent component analysis

Left image: non-negative matrix factorization with components weighting for (perhaps) face recognition (Nielsen et al., 2004b)

Other technique: Replicator dynamics (Neumann et al., 2005).

Non-negative matrix factorization

Non-negative matrix factorization (NMF) decomposes a non-negative data matrix $\mathbf{X}(N \times P)$ (Lee and Seung, 1999)

$$\mathbf{X} = \mathbf{W}\mathbf{H} + \mathrm{U}, \tag{4}$$

where $\mathbf{W}(N \times K)$ and $\mathbf{H}(K \times P)$ are also non-negative matrices.

"Euclidean" cost function for

$$E_{\text{“eucl”}} = ||\mathbf{X} - \mathbf{W}\mathbf{H}||_F^2 \tag{5}$$

Iterative algorithm (Lee and Seung, 2001)

$$\mathbf{H}_{kp} \leftarrow \mathbf{H}_{kp} \frac{\left(\mathbf{W}^{\mathsf{T}}\mathbf{X}\right)_{kp}}{\left(\mathbf{W}^{\mathsf{T}}\mathbf{W}\mathbf{H}\right)_{kp}} \tag{6}$$

$$\mathbf{W}_{nk} \leftarrow \mathbf{W}_{nk} \frac{\left(\mathbf{X}\mathbf{H}^{\mathsf{T}}\right)_{nk}}{\left(\mathbf{W}\mathbf{H}\mathbf{H}^{\mathsf{T}}\right)_{nk}}. \tag{7}$$

Text representation: a “bag-of-words”

	‘memory’	‘visual’	‘motor’	‘time’	‘retrieval’	...
Fujii	6	0	1	0	4	...
Maddock	5	0	0	0	0	...
Tsukiura	0	0	4	0	0	...
Belin	0	0	0	0	0	...
Ellerman	0	0	0	5	0	...
⋮	⋮	⋮	⋮	⋮	⋮	⋱

Representation of the abstract of the articles in “bag-of-word”. Table counts how often a word occurs

Exclusion of “stop words”: common words (the, a, of, ...), words for brain anatomy, and a large number of common words that appear in abstracts. Mostly words for brain function are left.

Grouping of words from articles

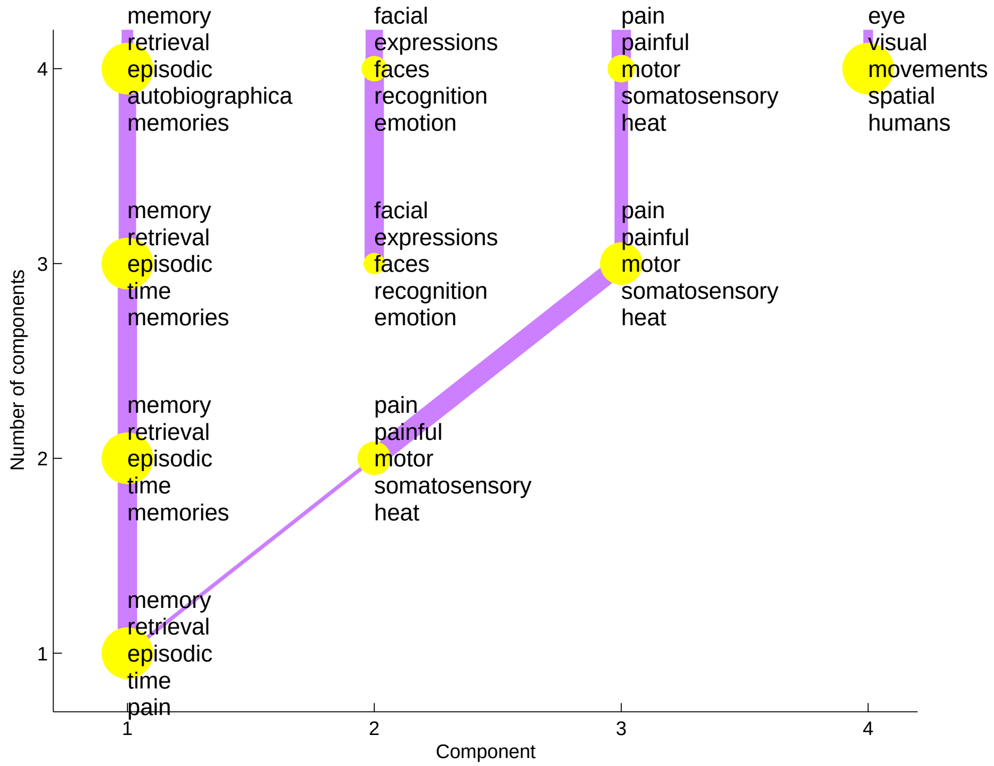


Figure 9: Grouped words.

Multivariate analysis (NMF) of the text in *posterior cingulate* articles to find "themes", which can be represented with weights over words and articles (Nielsen et al., 2005).

Most dominating words: memory, retrieval, episodic

pain, painful, motor, somatosensory

facial, expressions, faces,

eye, visual, movements

Matlab commands

```
% B = brede_read_xml(f, 'output', 'collapsesecond');
load wobibs.mat

M = brede_bib_bib2mat(B, 'type', 'abstract');
M = brede_mat_elimsingle(M)
M = brede_mat_elimstop(M, 'filename', 'stop_english1.txt')
M = brede_mat_elimstop(M, 'filename', 'stop_medline.txt')
M = brede_mat_elimstop(M, 'filename', 'stop_lobaranatomy.txt')
M = brede_mat_elimstop(M, 'filename', 'stop_meshcommon.txt')
M = brede_mat_elimstop(M, 'filename', 'stop_pubmed_neg1.txt')
[W, H] = brede_mat_nmf(M, 'Info', 5)
```

Text and volume: Functional atlas

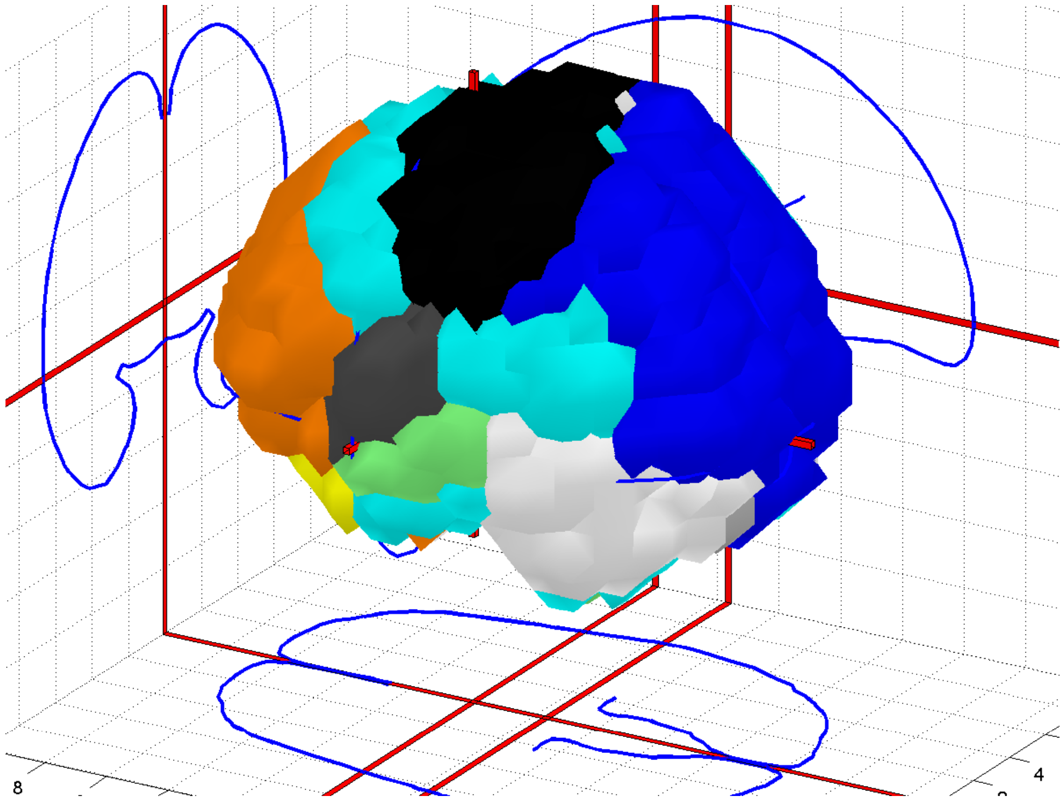


Figure 10: Functional atlas in 3D visualization.

Automatic construction of functional atlas, where words for function become associated with brain areas

Blue area: visual, eye, time

Black: motor, movements, hand

White: faces, perceptual, face

Green: auditory, spatial, neglect, awareness, langauge

Orange: semantiv, phonological, cognitive, decision

Functional atlas — medial view

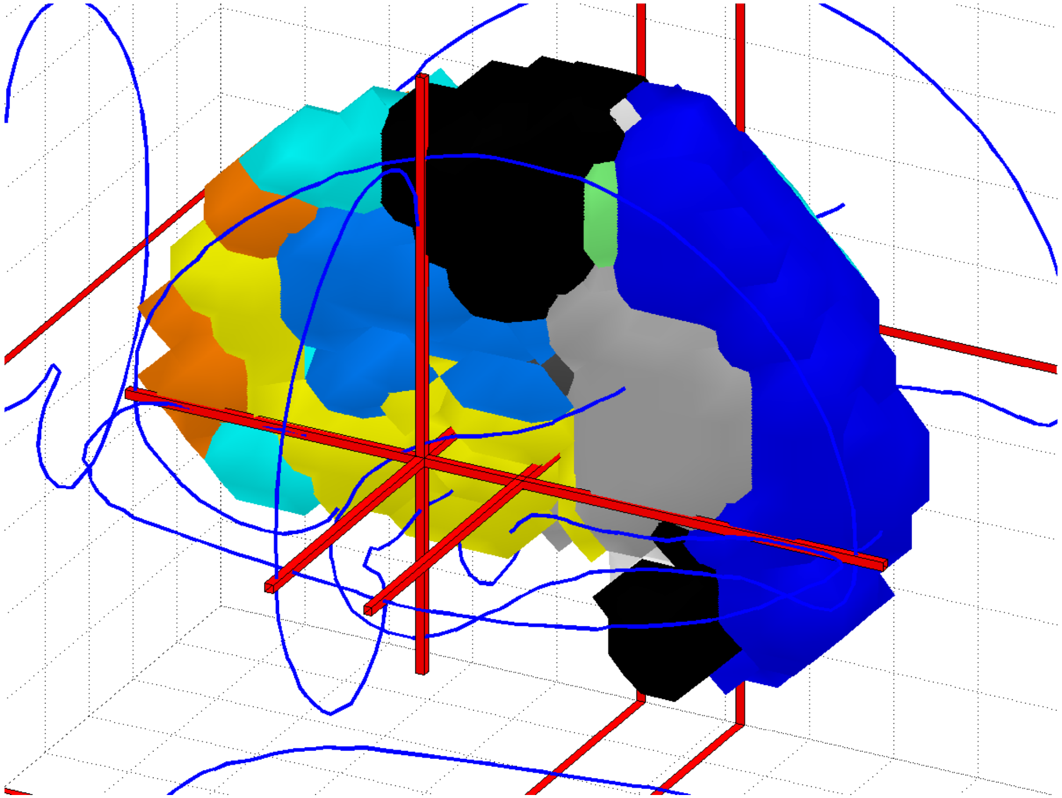


Figure 11: Visualization of the medial area.

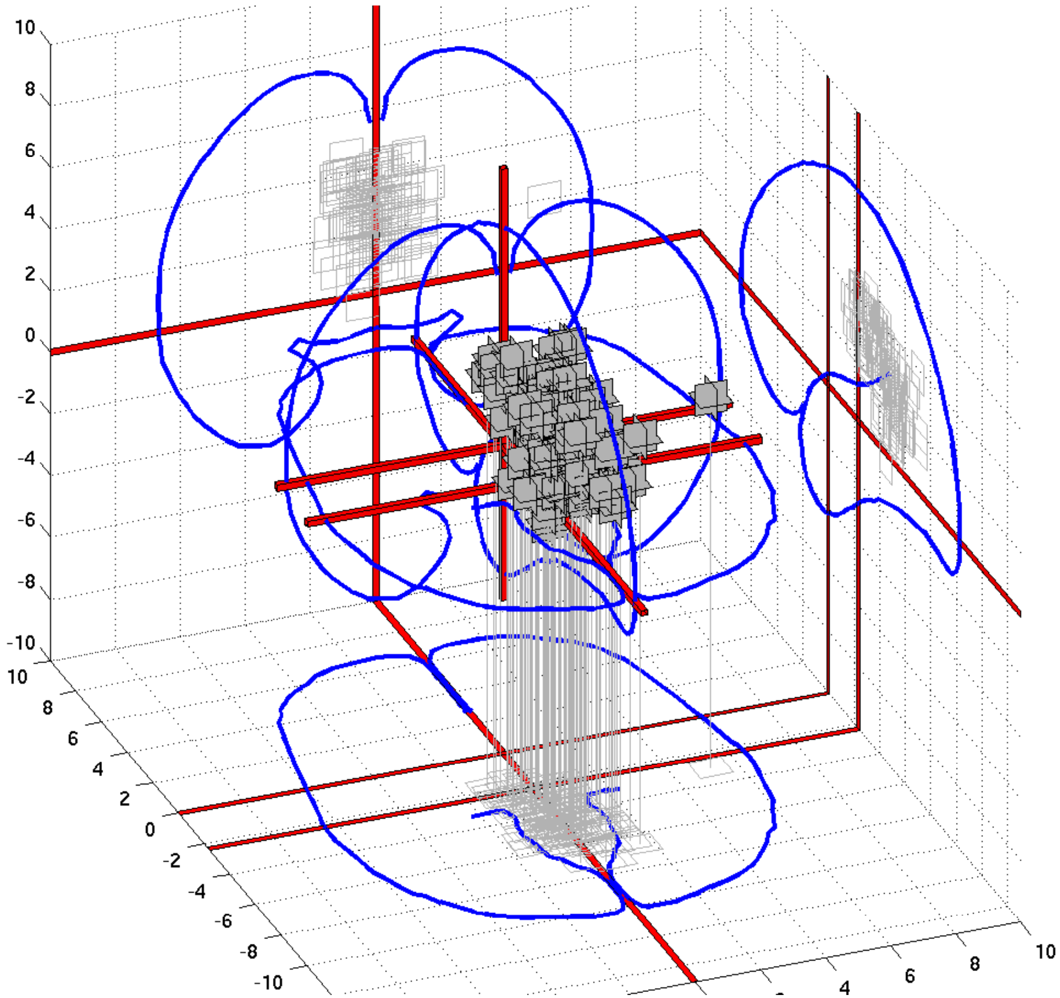
Grey area: retrieval, neutral, words, encoding.

Yellow: emotion, emotions, disgust, sadness, happiness

Light blue: pain, noxious, verbal, unpleasantness, hot

Constructed with a text matrix and a matrix with volumes and NMF.

Searching on a specific area

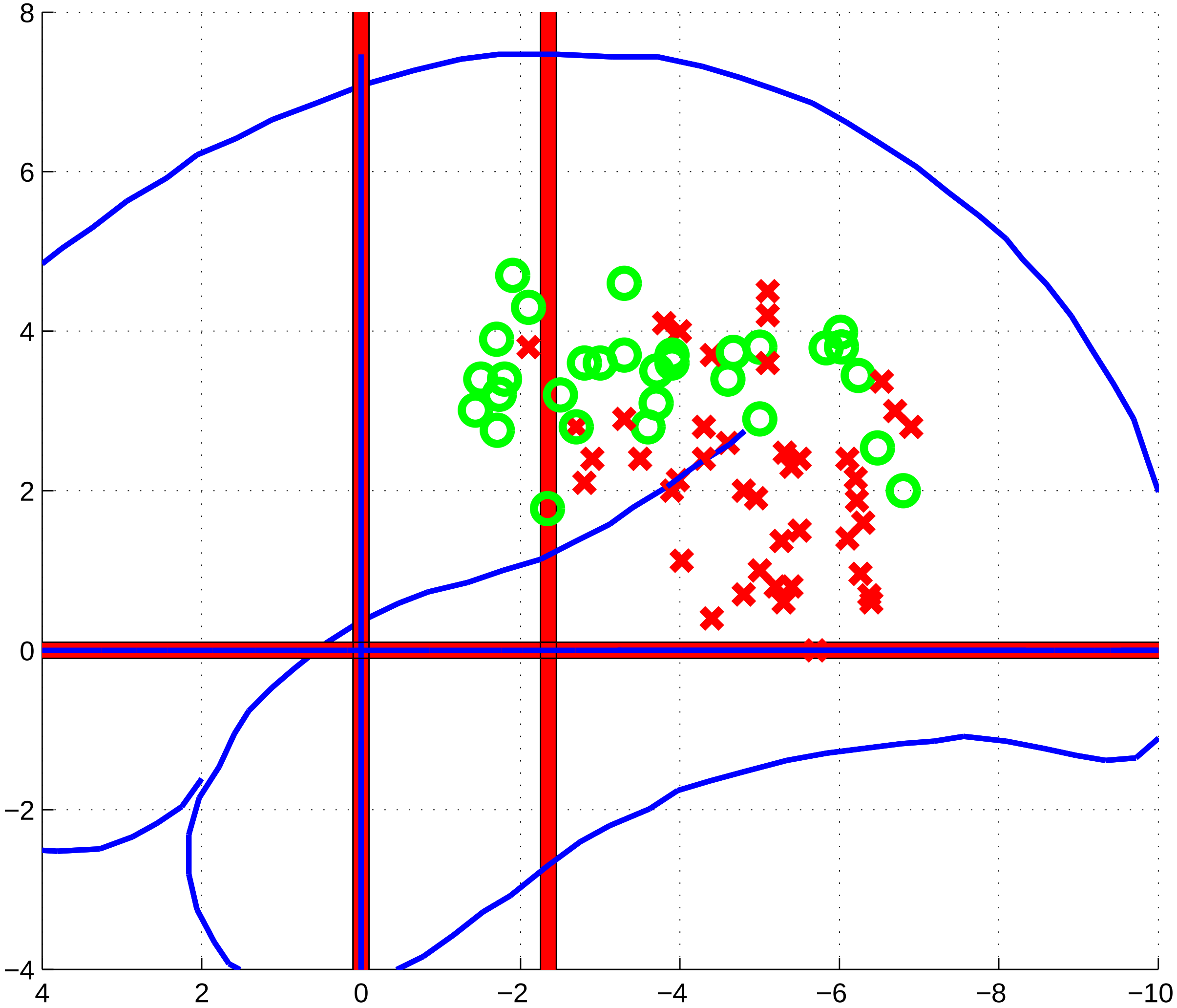


Searching for all coordinates labeled as "posterior cingulate": Here 116 "posterior cingulate" coordinates.

One outlier: "Right postcentral gyrus/posterior cingulate gyrus" from (Jernigan et al., 1998).

Possible to find the corresponding articles for the coordinates — and cluster these articles

Memory and pain



Is there a different between how memory and pain coordinates distribute in posterior cingulate?

Sagittal plot of memory (red x) and pain (green circles).

Apparently the memory coordinates have a tendency to lie in the posterior/inferior part for posterior cingulate.

Imaging databases

fMRIDC: fMRI Data Center stores scanning data from fMRI studies. With Internet-based search.

Neurogenerator: Storing, information retrieval and visualization of imaging data.

SumsDB: Cortex surface-based database.

Rodent databases: NeSys (projections), Mouse brain library: Nissl-stained

BrainInfo (NeuroNames): Database of brain structures.

Connectivity databases: CoCoMac, CoCoDat, BAMS, XANAT, . . .

CoCoMac connectivity database

Connectivity output list, PrimaryProjections
SearchString: ('CD') [KEYWORDS]

34 Items, page 1/2 select page: 1 2

details — user comments — display

output type: HTML -> Brow — items per page: 20 — order by: SourceMap, ascending

display all results | edit search | show url | back to search | start new search

Item	SourceSite	PDC	Hemisph.	Density	PDC	Course	TargetSite	PDC	Hemisph.	Laminae
1.	B09-19	D	?	X	-	I	BD77-Cd	A	?	Laminae LS
2.	B09-19	D	?	X	-	I	BD77-Cd	A	?	Laminae LS
3.	B09-18	D	?	X	-	I	BD77-Cd	A	?	Laminae LS
4.	B09-18	D	?	X	-	I	BD77-Cd	A	?	Laminae LS
5.	B09-18	D	?	X	-	I	BD77-Cd	A	?	Laminae LS
6.	B09-18	D	?	X	-	?	BD77-Cd	F	?	Laminae LS
7.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdr	C	L	Laminae LS
8.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdr	C	L	Laminae LS
9.	RTMB99-Cd	L	L	0	-	I	RTMB99-46sup	C	L	Laminae LS
10.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdc	C	L	Laminae LS
11.	RTMB99-Cd	L	L	0	-	I	RTMB99-46inf	C	L	Laminae LS
12.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMvc	C	L	Laminae LS
13.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMv	C	L	Laminae LS
14.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdc	C	L	Laminae LS
15.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdc	C	L	Laminae LS
16.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMdc	C	L	Laminae LS
17.	RTMB99-Cd	L	L	0	-	I	RTMB99-SMA	C	L	Laminae LS
18.	RTMB99-Cd	L	L	0	-	I	RTMB99-PMvr	C	L	Laminae LS
19.	RTMB99-Cd	L	L	0	-	I	RTMB99-SMA	C	L	Laminae LS
20.	RTMB99-Cd	L	L	0	-	I	RTMB99-M1	C	L	Laminae LS

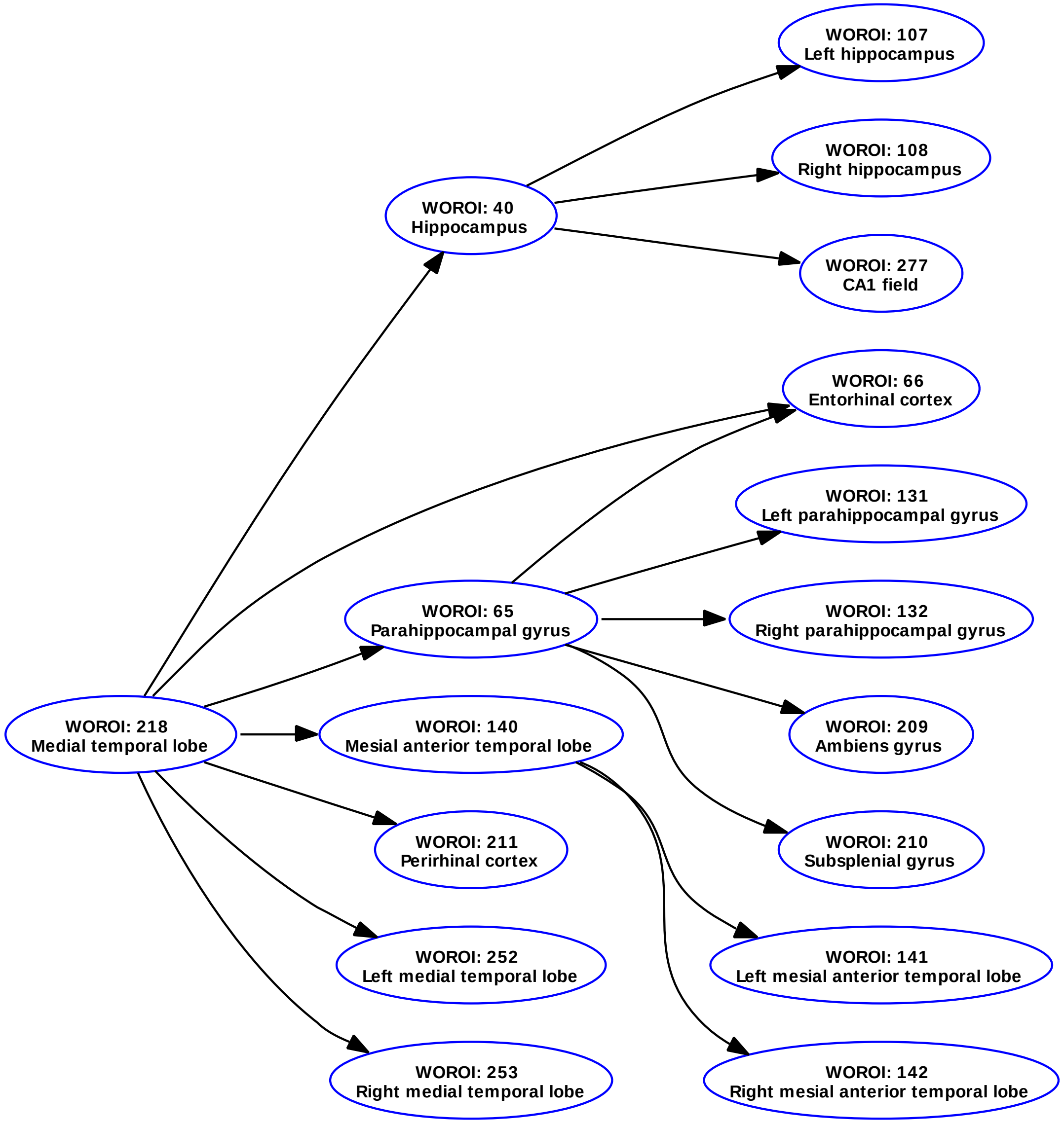
CoCoMac records anatomical connectivity in the Macaque brain with data from presently 395 papers.

Brain region ontology (Stephan et al., 2000).

Stores "from", "to" and how strong the link is, what tracer, etc.

Visualization of connectivity, analysis of, e.g., small-worldness (Sporns et al., 2004)

Brede brain region taxonomy



Taxonomy of neuroanatomical areas.

Items linked in a hierarchy with "Brain" in the top root and smaller areas in the leafs.

Based on another neuroanatomical database "BrainInfo/NeuroNames" (Bowden and Martin, 1995) and atlases, e.g. "Mai atlas" (Mai et al., 1997).

Fields recorded: Canonical name, variation in names, abbreviations, links to NeuroNames and other databases.

Example on connectivity matrix

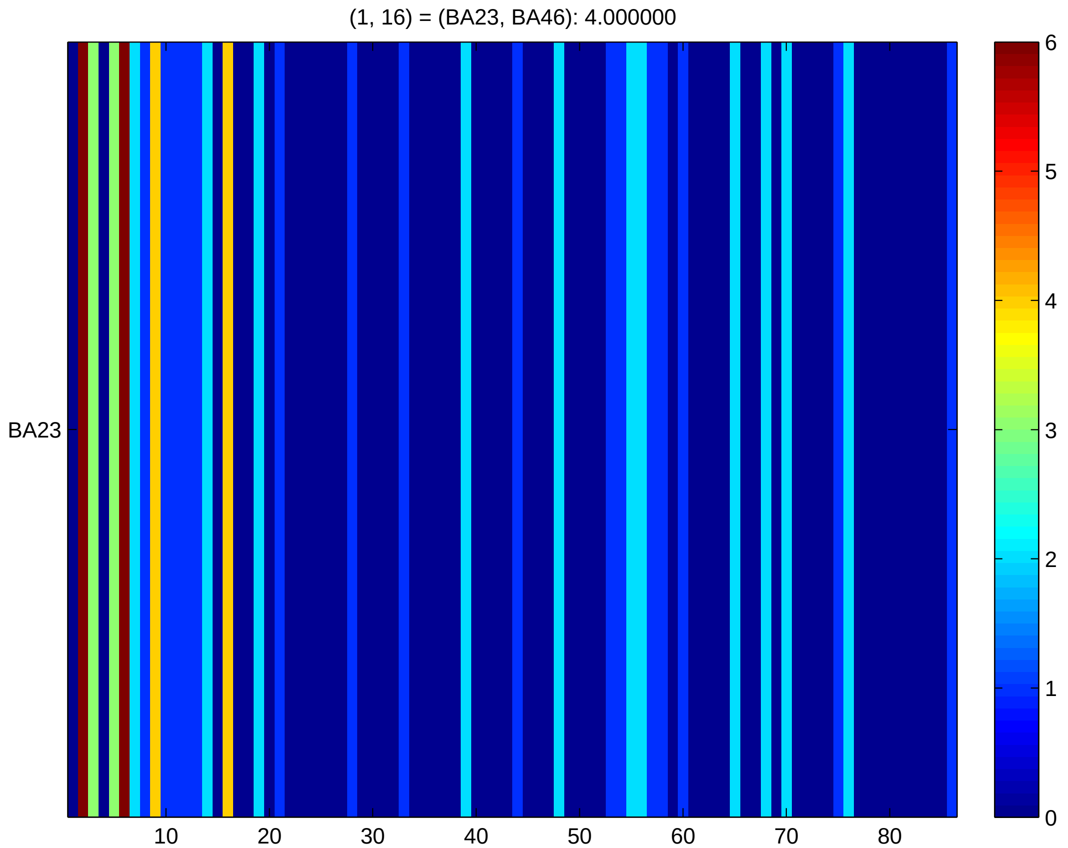


Figure 12: Connection-"matrix" from BA23. Row as source brain site, columns as target brain site.

Download XML-file with 308 entries for area 23 (i.e., BA23) as "source" "brain site" when querying CoCoMac.

Matching CoCoMac brain sites to Brede brain region taxonomy.

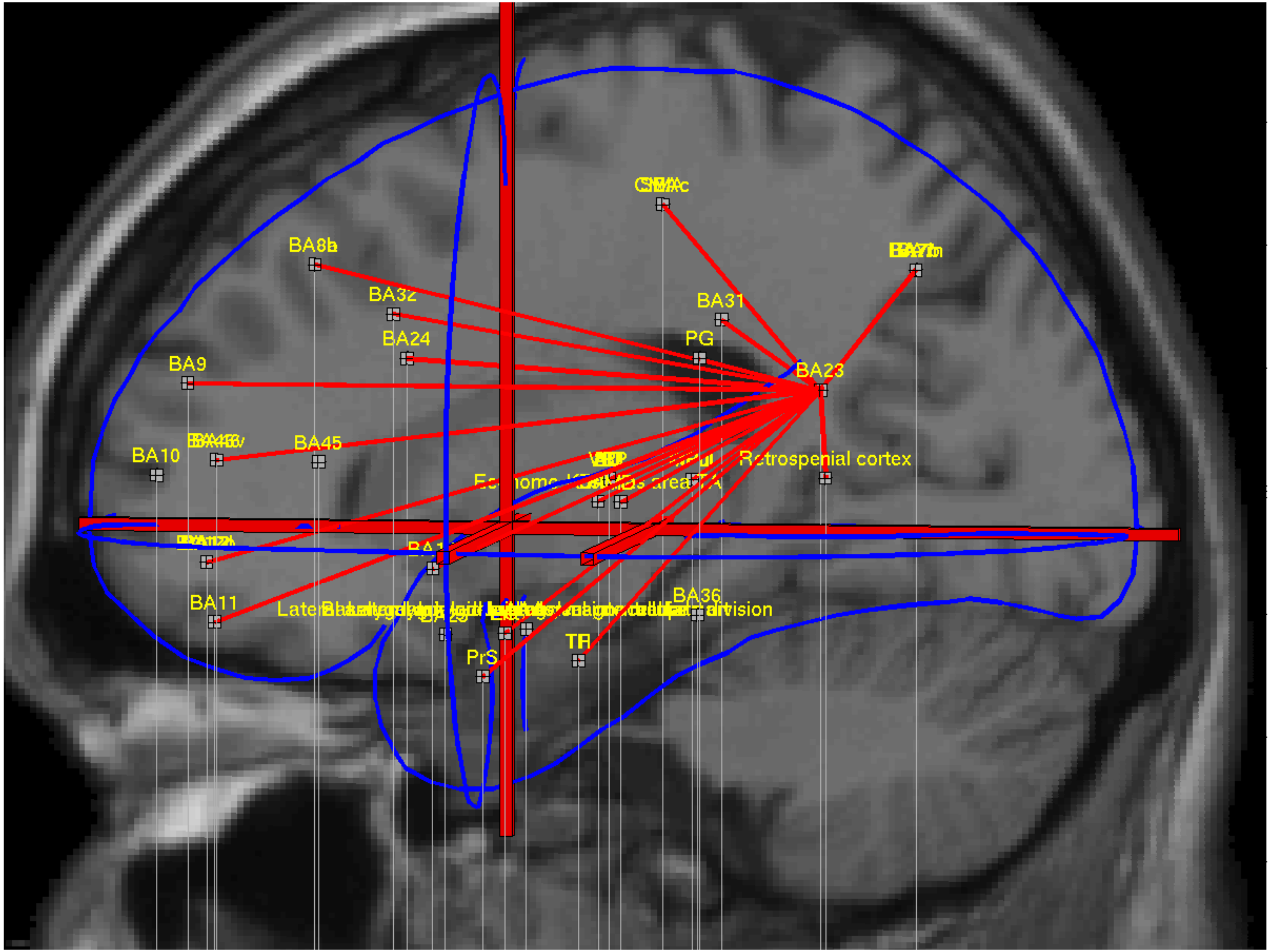
86 brain areas matched with 33 brain areas with non-zero (anatomical) connections.

These can be plotted in 3D stereotaxic space.

Matlab commands

Four matlab commands to readin, convert, display and print the CoCoMac data with the Brede Toolbox:

```
S23 = brede_read_xml_cocomac('cocomac_connectivity_23.xml');
M23 = brede_cocomac_connectivity2mat(S23);
brede_ui_mat(M23)
print -depsc /home/fnielsen/fnielsen/eps/Nielsen2006Linking_ba23.eps
```


BA32
BA24
BA9
BA31
PG
BA23
BA10
BA45
BA11
BA36
PrS

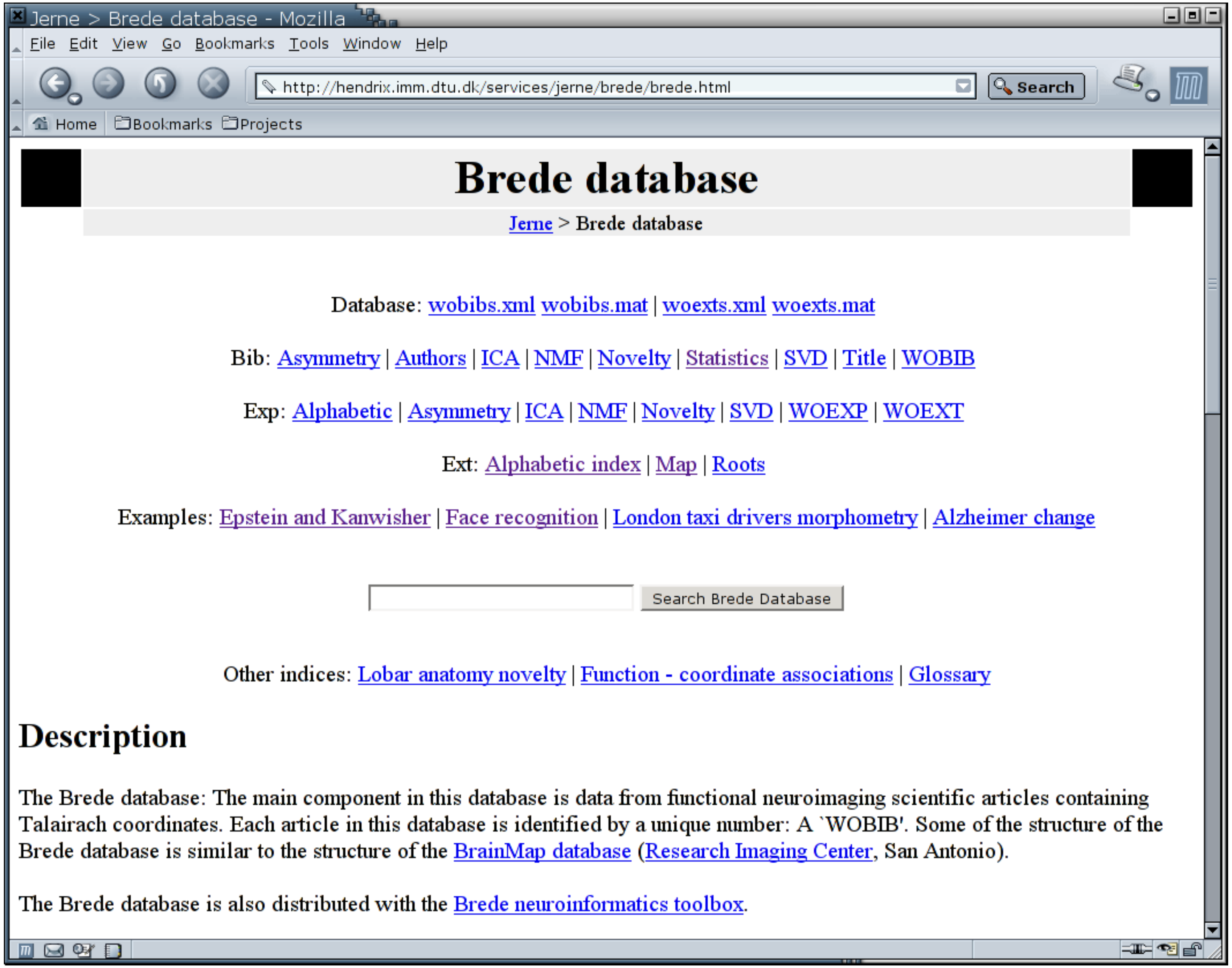
More information

Bibliography on Neuroinformatics:

http://www.imm.dtu.dk/~fn/bib/Nielsen2001Bib/

Article: “fMRI Neuroinformatics” (Nielsen et al., 2006)

Brede database on the web



Jerne > Brede database - Mozilla

File Edit View Go Bookmarks Tools Window Help

http://hendrix.imm.dtu.dk/services/jerne/brede/brede.html

Search

Home Bookmarks Projects

Brede database

Jerne > Brede database

Database: wobibs.xml wobibs.mat | woexts.xml woexts.mat

Bib: Asymmetry | Authors | ICA | NMF | Novelty | Statistics | SVD | Title | WOBIB

Exp: Alphabetic | Asymmetry | ICA | NMF | Novelty | SVD | WOEXP | WOEXT

Ext: Alphabetic index | Map | Roots

Examples: Epstein and Kanwisher | Face recognition | London taxi drivers morphometry | Alzheimer change

Search Brede Database

Other indices: Lobar anatomy novelty | Function - coordinate associations | Glossary

Description

The Brede database: The main component in this database is data from functional neuroimaging scientific articles containing Talairach coordinates. Each article in this database is identified by a unique number: A `WOBIB'. Some of the structure of the Brede database is similar to the structure of the BrainMap database (Research Imaging Center, San Antonio).

The Brede database is also distributed with the Brede neuroinformatics toolbox.

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