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Mining the posterior cingulate: Segregation between memory and pain components

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We present a general method for automatic meta-analyses in neuroscience and apply it on text data from published functional imaging studies to extract main functions associated with a brain area—the posterior cingulate cortex (PCC). Abstracts from PubMed are downloaded, words extracted and converted to a bag-of-words matrix representation. The combined data are analyzed with hierarchical non-negative matrix factorization. We find that the prominent themes in the PCC corpus are episodic memory retrieval and pain. We further characterize the distribution in PCC of the Talairach coordinates available in some of the articles. This shows a tendency to functional segregation between memory and pain components where memory activations are predominantly in the caudal part and pain in the rostral part of PCC.

Keywords: Meta-analysis; PubMed; Positron emission tomography; Magnetic resonance imaging; Cingulate gyrus; Brain mapping; Memory; Pain; Alzheimer's disease; Automatic data processing; Bibliometrics

Introduction

Functional neuroimaging methods such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) map function to brain anatomy by manipulating behavior and measuring a change in regional activity. The resulting maps are used to infer the principles of brain function. The interpretability and value of these functional maps however depend critically on the specificity of the behavioral paradigm and on the sensitivity of the analytical tools for detecting the interesting signal. In any individual study, it is very difficult, if not impossible, to avoid the particular subject's in part irreproducible behavior, and it is not possible a priori to describe the spatiotemporal characteristics of the signal necessary for accurate modeling and detection. Investigating the consensus among results from a large number of brain imaging studies can overcome the problem of false positive and false negative results. Furthermore, neuroimaging studies may discover unexpected changes in activity in areas that so far have not been associated with a given behavior, thus generate new hypotheses. Unexpected activations may be genuine, showing a novel and interesting association between brain and behavior, or spurious, for instance, a false positive activation from some uninteresting behavior that the paradigm did not control for. If such changes are repeatedly encountered over a large number of different paradigms that addressed the same behavioral function, then it is probable that they are of significance and deserve further investigation.

The potential for data mining across neuroimaging studies has already been recognized and exploited to investigate the consistency of activation patterns associated with a given brain function (Cabeza and Nyberg, 2000) or to generate new hypotheses about the function of a given brain area (Bush et al., 2000; Maddock, 1999; Maguire, 2001). In these papers, the authors manually generate tables and figures that summarize results across a large number of studies in order to inspect for consensus. The expanding number of published studies, however, makes it increasingly time-consuming for the individual researcher to generate exhaustive result summaries. Here, we propose an automatic method which can extract from the neuroimaging literature the consensus about the functions of a given brain area. This method is thought to assist researchers by providing a quick summary of a large number of scientific publications. To illustrate the approach, we apply this method to extract functions that are consistently associated with the posterior cingulate cortex (PCC). The studies we include are not restricted to examine any particular behavioral function: we simultaneously examine multiple functions. To this end, we have used article abstracts indexed by PubMed under the keywords that relate to both PCC and functional imaging methods.

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Despite the increasing attention that the PCC has attracted over the years (see Fig. 1), there is no "textbook" consensus about the functions undertaken by this area. Different reviews associate this area with a variety of brain functions, e.g., evaluative functions (for spatial orientation and memory) (Vogt et al., 1992), successful episodic memory retrieval (Cabeza and Nyberg, 2000), emotion (Maddock, 1999), navigation (Maguire, 2001), visuospatial attention (Mesulam et al., 2001; Small et al., 2003), pain (Bromm, 2001), and "resting state" (Binder et al., 1999; Mazoyer et al., 2001; Raichle et al., 2001; Shulman et al., 1997).

Our method is two-stage: in the first stage, we will make unsupervised text mining in the form of clustering based on the words in abstracts of PubMed that mention our specific target area (the PCC), and we compare these results with the results reported by previous manual reviews to assess the validity of this automatic analysis. In the second stage, we use the Talairach coordinates (Talairach and Tournoux, 1988) within the clustered articles and describe the spatial distribution in terms of the cluster labels from the first stage. This is in order to test whether the functional clusters are anatomically segregated within the posterior cingulate cortex.

That is, in terms of PCC, we ask whether our machine-based methodology is able to capture themes in alignment with major reviews and whether there is functional segregation within the PCC.

Method

We download abstracts from the PubMed Web service by restricting the search to posterior cingulate area and functional neuroimaging with the following query: ("posterior cingulate" OR "posterior cingulum" OR "retrosplenial" OR "retrosplenium") AND ("magnetic resonance imaging" OR "positron emission tomography").

This query will return functional neuroimaging as well as other types of neuroimaging studies. With the present capabilities of PubMed, this is unavoidable. However, other restrictions are possible, e.g., only inclusion of human studies and exclusion of the "review" publication type.

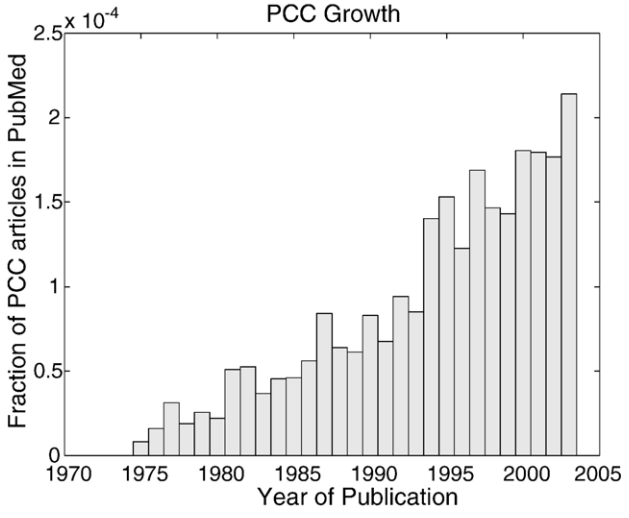

Fig. 1. Number of posterior cingulate entries in the PubMed database as a function of the year of publication. The query was "("posterior cingulate" OR "posterior cingulum" OR "retrosplenial" OR "retrosplenium")". It is normalized with the total number of entries of each year in the PubMed database.

The abstracts are converted into matrix form: $\mathbf{X}(N \times Q)$ where N corresponds to the number of abstracts and Q corresponds to the number of words. This is the so-called "vector space model" or bag-of-words representation (Salton et al., 1975). Ignoring case, we count the words in each abstract and set the element x_{nq} to the number of times the qth word occurs in the nth abstract. When the matrix contains the raw frequency, it means that abstracts which contain many occurrences of the same word will affect the subsequent analysis more than an abstract where the word occurs just once. This scheme is not necessarily optimal, but it is simple, and it is likely that, if a word is mentioned many times in an abstract, it is because the word is important. Words that only occur in a single abstract are discarded from the matrix, and certain stop words are eliminated, resulting in a matrix with fewer columns. The stop words are a compound list consisting of ordinary English words such as "the", "of" augmented with medical stop words used in MEDLINE/PubMed (http://www.ncbi.nlm.nih.gov/entrez/query/static/help/pmhelp.html#Stopwords) and by a large manually constructed list for elimination of words that does not directly describe cognitive functions, e.g., words for brain anatomy are eliminated.

A number of methods for discovering latent classes ("clusters" or "components") in texts have been described, e.g., spherical K-means and singular value decomposition (SVD) (Dhillon and Modha, 2001), simple counting (Goldman et al., 1999), Probabilistic Latent Semantic Analysis (PLSA) (Hofmann, 1999), hierarchical clustering (Gaussier et al., 2002), non-negative matrix factorization (NMF) (Lee and Seung, 1999), Generalizable Gaussian Mixture (GGM) model (Hansen et al., 2000), and independent component analysis (ICA) (Isbell and Viola, 1999; Kolenda et al., 2000). Some of these have been applied for data mining medical literature (Dobrokhotov et al., 2003; Goldman et al., 1999), and, for example, the XplorMed Internet-based tool enables interactive exploration of noun relatedness in PubMed abstracts producing simple two-word classes (Perez-Iratxeta et al., 2001). In our case, we will use the NMF with an optimization algorithm for the Euclidean distance cost function (Lee and Seung, 2001), where a matrix $\mathbf{X}(N \times Q)$ is factorized into two non-negative matrices $\mathbf{W}(N \times K)$ and $\mathbf{H}(K \times P)$.

$$\mathbf{X} = \mathbf{WH} + \mathbf{E}, \tag{1}$$

and the cost function (reconstruction error) E is defined as

$$E = \mathrm{trace}\left(\mathbf{EE}^{\mathrm{T}}\right) = \mathrm{trace}\left(\mathbf{E}^{\mathrm{T}}\mathbf{E}\right) = \|\mathbf{E}\|_F^2, \tag{2}$$

This cost function is minimized for a fixed number of latent classes K. Each of the column vectors in $\mathbf{W}$ corresponds to a latent class with loadings for each abstract, and each of the rows in $\mathbf{H}$ contains a latent class with loadings over words. The algorithm is dependent on the initialization of $\mathbf{W}$ and $\mathbf{H}$. To avoid unfavorable local minima, we run the algorithm multiple times and choose the result with the lowest cost function value. In practice, we run the algorithm 3 times. To be reasonably sure that the global minima is found, many more runs would be needed and that will be time-consuming. NMF has the advantage that each vector (in either $\mathbf{W}$ or $\mathbf{H}$) corresponds to one latent class. In SVD and (ordinary) ICA, there might be two classes in each vector since the algorithms implicitly assume a symmetric distribution around zero, for an

example, see Kleinberg (1999). SVD further requires that the relevant loading vectors are orthogonal. ICA requires either loadings over abstracts or loadings over words to be statistically independent. Furthermore, NMF produces sparse components that are intuitively more suitable for text than the holistic components from SVD analysis (Lee and Seung, 1999). The mathematical uniqueness of NMF is a topic of current research see, e.g., Donoho and Stodden, 2004. In hard assigning clustering algorithms such as K-means, we only get an indicator for membership. In NMF, we get a continuous value for "more or less membership" to the latent class which means that we are able to sort both the elements of $\mathbf{W}$ and $\mathbf{H}$ and report the top most representative abstract and words associated with each class.

The number of latent classes K in NMF is the only parameter that needs to be set. In cluster analysis, we have previously determined an optimal number of classes by information criteria or cross-validation (Balslev et al., 2002; Goutte et al., 1999, 2001). Here, we will instead run the algorithm over different numbers of classes and use a visualization technique to get an overview of the structures in the data: We plot the classes as nodes in a 2-dimensional plot with K on the y axis and the individual classes $k = 1 \ldots K$ on the x axis. Thus, each row represents one run of NMF with a specific number of classes, for example, the 5th row is for $K = 5$. On each node, we print the words with the highest load in the classes of $\mathbf{H}$. These words represents the most typical words for the class. Nodes in adjacent layers (between K and $K + 1$) are connected with lines, and the thickness of these lines is determined from the similarity between the classes. The similarity between the kth class in a K class NMF and the kth class in a $(K + 1)$ class NMF is computed as the inner product between the corresponding latent class vectors.

$$s_{k,k'} = \left(\mathbf{w}_k^K\right)^T \mathbf{w}_{k'}^{K+1}. \tag{3}$$

Only the lines where the similarity is high are shown. A threshold c was found as

$$s_{k,k'} \;/\; \max_{k,k'} s_{k,k'} > c, \tag{4}$$

where a useful value for c was found in the range 0.05–0.15.

The text mining described above allows us to identify sub-categories in connection with PCC.

In our second step, we use spatial modeling to further characterize each of these sub-categories in terms of distribution in Talairach space (Fox et al., 2001). For each class k, the loadings on abstracts in $\tilde{\mathbf{w}}_k$ are sorted, and the Talairach coordinates from the top twenty abstracts are plotted. We only take the coordinates from abstracts that are "winners" of each class by applying a "winner-takes-all" function $\tilde{\mathbf{W}} = \mathrm{wta}(\mathbf{W})$ with the elements determined as

$$\tilde{\mathbf{w}}_{nk} = \begin{cases} \mathbf{w}_{nk} & \text{if } \forall_{k'} : \mathbf{w}_{nk} \geq \mathbf{w}_{nk'}, \\ 0 & \text{otherwise.} \end{cases} \tag{5}$$

A specific row n in $\mathbf{W}$, corresponding to a specific article, might contain two or more non-zero elements, that is, it is not exclusively assigned to a specific component k. The winner-takes-all function will force an article to be exclusively assigned to only one component: The component where the article has the highest loading—the winner. This reductionism allows us to ascribe one specific behavioral function to each coordinate in the articles.

To summarize the extraction of abstracts: first, the winner-takes-all function is applied, then the elements of $\tilde{\mathbf{w}}_k$ are sorted, and finally the top twenty abstracts with the highest loading are identified. The top twenty will be the most representative abstracts for the component. Another kind of threshold could be based on the loading.

The coordinates are extracted from the Brede database (Nielsen, 2003) or, if not available in this database, typed in manually. During entry, the coordinates in the Brede database are converted from the MNI space to the original Talairach space where appropriate (Brett et al., 2001). The coordinates not found in the Brede database are not converted. At the level of PCC, there is up to 4 mm discrepancy between the MNI and Talairach spaces, and this will cause extra variance in the distribution of the coordinates, making a statistical test less powerful.

We compare the distributions of Talairach coordinates from two classes by statistical tests (Berman et al., 1999; Christoff and Grabrieli, 2000; Duncan and Owen, 2000). The coordinates from the two classes are represented in two data matrices $\mathbf{Z}_1(M_1 \times 3)$ and $\mathbf{Z}_2(M_2 \times 3)$, and the two-sample Hotelling T^2 statistical test is applied where a scaled sample Mahalanobis distance follows an F distribution if independent multivariate Gaussian distributions are assumed (Mardia et al., 1979, p. 77).

$$\frac{M_1 M_2 (M - P - 1)}{M(M-2)P} D^2 \sim F_{P,M-P-1}. \tag{6}$$

The Mahalanobis distance is computed as

$$D^2 = (\bar{\mathbf{z}}_1 - \bar{\mathbf{z}}_2)^{\mathrm{T}} \mathbf{S}_u^{-1} (\bar{\mathbf{z}}_1 - \bar{\mathbf{z}}_2), \tag{7}$$

with the covariance $\mathbf{S}_u$ found as

$$\mathbf{S}_u = (M_1 \mathbf{S}_1 + M_2 \mathbf{S}_2)/(M-2), \tag{8}$$

where $M = M_1 + M_2$, $\bar{\mathbf{z}}_1$ and $\bar{\mathbf{z}}_2$ are the means for the two sets of Talairach coordinates and $\mathbf{S}_1$ and $\mathbf{S}_2$ are the biased covariance maximum likelihood estimates, e.g., $\mathbf{S}_1 = \mathbf{Z}_1^{\mathrm{T}}\mathbf{Z}_1 / M_1 - \bar{\mathbf{z}}_1^{\mathrm{T}}\bar{\mathbf{z}}_1$. P is the dimension of the space, i.e., $P = 3$ if the test is applied in the full 3-dimensional Talairach space. Taking a pluralistic approach to modeling (Lange et al., 1999) and since the distributions seem mildly non-Gaussian, we also consider a permutation test on the Euclidean, median, and Mahalanobis distances between the two sets of coordinates (Arnold et al., 1997; Edgington, 1986; Mardia, 1970). Permutation on the Mahalanobis distance will correspond to a permutation test on the Hotelling T^2 statistics since there is only a scaling difference between the Mahalanobis distance and the Hotelling T^2, cf. Eq. (6). The median test is only applied in one dimension. It is infeasible to perform all permutations, and we only make approximate permutation tests by subsampling among all permutations, leading to approximate P values (Dwass, 1957; Nichols and Holmes, 2001). Hotelling's T^2 test has large statistical power and is a faster test than a permutation test. It will, however, not be valid if the distribution of the coordinates are not Gaussian. If a test is applied in full 3-dimensional space, it will not be able to tell if the separation between groups of coordinates is in a specific direction. This is possible with the one-dimensional tests.

The stop word lists and the tools for the analysis are available in the Brede neuroinformatics toolbox (Nielsen and Hansen, 2000) presently available from http://hendrix.imm.dtu.dk/software/brede/.

Results

PubMed returned 271 items matching the query on PCC and imaging on the date 2003-08-14. After the abstracts had been

converted to vectorial form and single occurrence words and stop words were eliminated, 549 words remained from originally 4792, resulting in the data matrix $\mathbf{X}(271 \times 549)$. "Memory", "alzheimer", "visual", "metabolic", "retrieval", and "pain" showed up as the most frequent occurring words. "Memory" occurred twice as often compared to the second most frequent word.

Fig. 2 shows the automatically generated "NMF tree" where each of the yellow nodes indicates an NMF component. These are labeled with the words with the highest score in **H**. The tree with the root in (1, 1) shows that memory is a dominant theme throughout the hierarchy ($K = 1 \ldots 12$). The words showing the highest association with the component are "memory", "retrieval", and "episodic". An automatically generated list of articles scoring high on the "memory" component $\tilde{\mathbf{w}}_{k\,=\,\mathrm{memory}}$ is available in Table 1.

Other important themes are Alzheimer's disease with mild cognitive impairment (represented by words such as "alzheimer", "metabolic", "mci", "dementia") and pain ("painful", "non-painful", "somatosensory", "sensation", "heat"). Table 2 lists the abstracts associated with the pain component. Furthermore, a "sensorimotor" component is associated with words such as "hand", "motor", "visual", and "reaching", but only a few functional studies support this theme (Inoue et al., 1998; Kertzman et al., 1997).

A component associated with Posttraumatic Stress Syndrome (PTSD) is dominated by a few abstracts by J.D. Bremner (Bremner, 2002; Bremner et al., 1999a,b, 2003). Other components also showed to be dominated by a single author. This is the case for the visual motion component (Cornette et al., 1998) and the associative learning component (Hunkin et al., 2002). A final component contains emotion, familiarity, and facial expression perception. We will refer to this as the "emotion" component, even though only about half the abstracts were genuine emotion studies. The associated abstracts are listed in Table 3. This list is generated through the NMF with 12 components ($K = 12$), thus there might be overlap in the items of the lists in Tables 1 and 2 which are generated with $K = 4$.

Although the particular configuration of the NMF tree changes when the algorithm is restarted, the major themes are invariant over runs, for example, the dominant component (memory) with $K = 4$ will usually have a 19–20 articles overlap between runs among the top twenty articles, while the pain component has a lower overlap: 14–20.

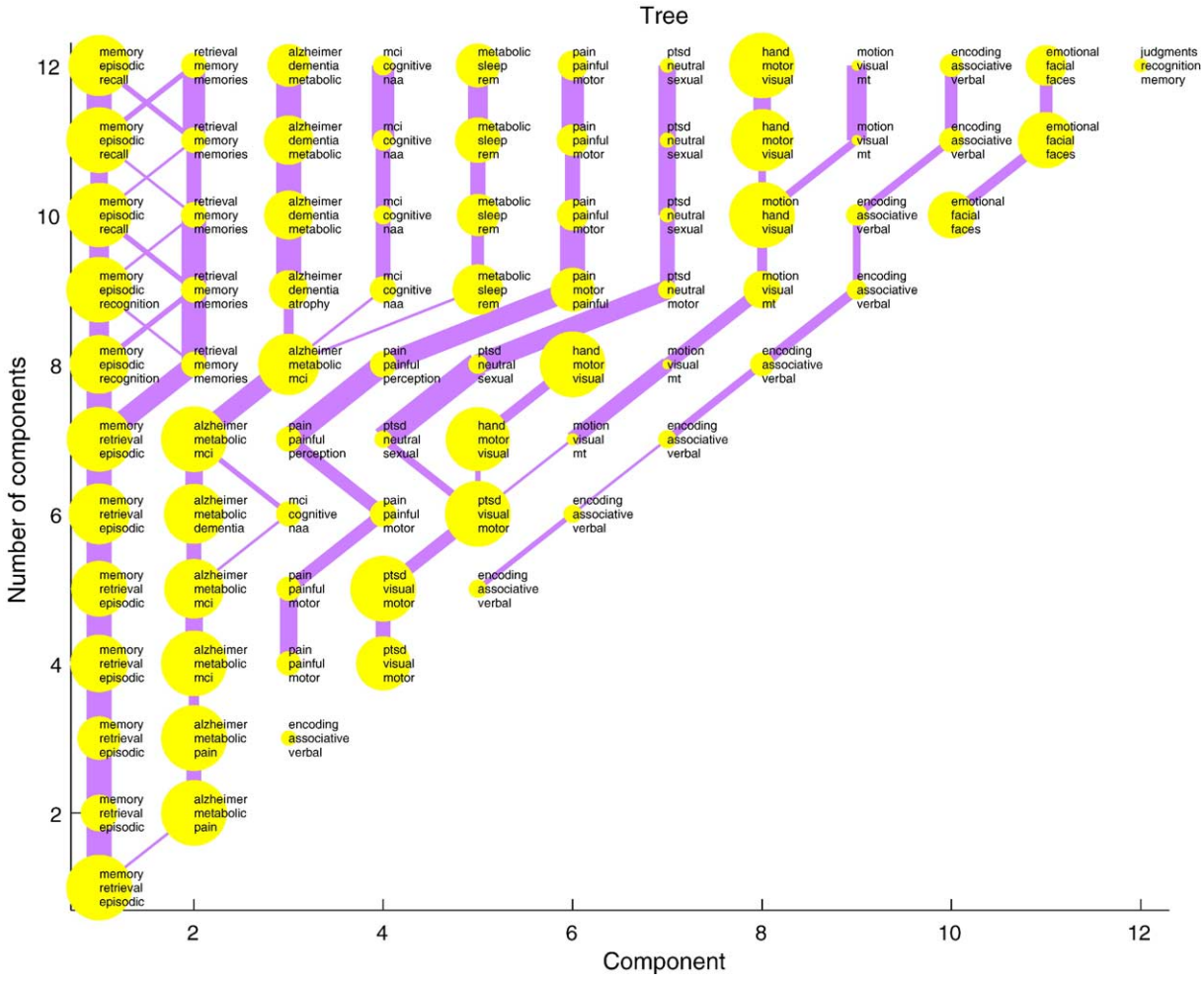

Fig. 2. NMF tree with components from non-negative matrix factorization of the bag-of-words converted posterior cingulate abstracts. The nodes indicated by yellow dots represent each a specific component $k \in \{1 \ldots K\}$ for a specific K. The y axis is indicating a specific number of classes K. The size of the dots indicates the fraction of documents assigned to the component, for example, for $K = 4$, the numbers of abstracts assigned to the components are (from left to right) 79, 92, 26, and 74. The lines indicate the similarity between components, see Eqs. (3) and (4) in the text.

Table 1
Memory class: abstracts associated with the memory class sorted according to loading, i.e., values in $\tilde{\mathbf{w}}_{k\ =\ \text{memory}}$

#	Load	Title	Reference
1	7.81	Remembering the past: two facets of episodic memory explored with positron emission tomography	(Andreasen et al., 1995b)
2	7.56	Differential remoteness and emotional tone modulate the neural correlates of autobiographical memory	(Piefke et al., 2003)
3	5.74	Differential modulation of a common memory retrieval network revealed by positron emission tomography	(Maguire and Mummery, 1999)
4	5.11	Remembering familiar people: the posterior cingulate cortex and autobiographical memory retrieval	(Maddock et al., 2001)
5	5.06	Neuroanatomical correlates of episodic encoding and retrieval in young and elderly subjects	(Daselaar et al., 2003)
6	4.89	Verbal encoding deficits in a patient with a left retrosplenial lesion	(McDonald et al., 2001)
7	4.73	The functional neuroanatomy of episodic memory: the role of the frontal lobes, the hippocampal formation, and other areas	(Desgranges et al., 1998)
8	4.57	Parietal and hippocampal contribution to topokinetic and topographic memory	(Berthoz, 1997)
9	4.43	The effects of bilateral hippocampal damage on fMRI regional activations and interactions during memory retrieval	(Maguire et al., 2001)
10	4.33	Network analysis in episodic encoding and retrieval of word-pair associates: a PET study	(Krause et al., 1999)
11	4.21	Cerebral representation of one's own past: neural networks involved in autobiographical memory	(Fink et al., 1996)
12	3.98	Brain regions associated with acquisition and retrieval of verbal episodic memory	(Shallice et al., 1994)
13	3.86	The role of the basal forebrain in episodic memory retrieval: a positron emission tomography study	(Fujii et al., 2002)
14	3.49	A combined neuropsychological and neuroimaging study of topographical and non-verbal memory in semantic dementia	(Cipolotti and Maguire, 2003)
15	3.00	Changing patterns of brain activation during maze learning	(Van Horn et al., 1998)
16	2.82	Neural correlates of semantic and episodic memory retrieval	(Wiggs et al., 1999)
17	2.75	Network analysis of positron emission tomography regional cerebral blood flow data: ensemble inhibition during episodic memory retrieval	(Nyberg et al., 1996)
18	2.71	Task-related and item-related brain processes of memory retrieval	(Düzel et al., 1999)
19	2.66	Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task	(Maddock et al., 2003)
20	2.49	Neocortical system abnormalities in autism: an fMRI study of spatial working memory	(Luna et al., 2002)

For this specific list, the (1, 4) node from Fig. 2 was selected.

In the following, we will only consider the components that had a large amount of abstracts with high load on the respective components.

Most of the articles displayed in the Tables 1–3 listed Talairach coordinates: for the memory component, 15 of the top 20 studies, for pain 14, and for emotion 12. We extracted PCC coordinates from these articles, even though some of the entries were not strictly associated with the main theme of the component, for example, a taste study (Gautier et al., 1999) appears in the pain component. A coordinate marked "Left posterior cingulate/

Table 2
Pain class: abstracts associated with the pain class sorted according to loading, i.e., values in $\tilde{\mathbf{w}}_{k\ =\ \text{pain}}$

#	Load	Title	Reference
1	9.87	Central representation of chronic ongoing neuropathic pain studied by positron emission tomography	(Hsieh et al., 1995)
2	8.14	Regional brain activity changes associated with fentanyl analgesia elucidated by positron emission tomography	(Adler et al., 1996)
3	7.97	Region-specific encoding of sensory and affective components of pain in the human brain: a positron emission tomography correlation analysis	(Tölle et al., 1999)
4	7.66	Central processing of rectal pain: a functional MR imaging study	(Baciu et al., 1999)
5	6.60	Phantom limb pain in the human brain: unraveling neural circuitries of phantom limb sensations using positron emission tomography	(Willoch et al., 2000)
6	5.70	A PET activation study of dynamic mechanical allodynia in patients with mononeuropathy	(Petrovic et al., 1999)
7	5.38	A comparative fMRI study of cortical representations for thermal painful, vibrotactile, and motor performance tasks	(Gelnar et al., 1999)
8	4.71	Spatial summation of pain processing in the human brain as assessed by cerebral event related potentials	(Chen et al., 2002)
9	4.56	Pain processing in four regions of human cingulate cortex localized with co-registered PET and MR imaging	(Vogt et al., 1996)
10	4.45	Functional MR imaging analysis of pain-related brain activation after acute mechanical stimulation	(Creac'h et al., 2000)
11	4.27	Central nervous pathways mediating angina pectoris	(Rosen et al., 1994)
12	2.15	Cerebral mechanisms of hypnotic induction and suggestion	(Rainville et al., 1999)
13	1.88	Neuroimmune relations in patients with fibromyalgia: a positron emission tomography study	(Lekander et al., 2000)
14	1.44	Human brain activation under controlled thermal stimulation and habituation to noxious heat: an fMRI study	(Becerra et al., 1999)
15	1.01	Central representation of visceral and cutaneous hypersensitivity in the irritable bowel syndrome	(Verne et al., 2003)
16	0.97	Anatomical localization and intra-subject reproducibility of laser evoked potential source in cingulate cortex, using a realistic head model	(Bentley et al., 2002)
17	0.88	Brain images of pain	(Bromm, 2001)
18	0.39	Regions of the human brain affected during a liquid-meal taste perception in the fasting state: a positron emission tomography study	(Gautier et al., 1999)
19	0.37	fMRI of the responses to vibratory stimulation of digit tips	(Francis et al., 2000)
20	0.36	Cerebral activation in patients with irritable bowel syndrome and control subjects during rectosigmoid stimulation	(Naliboff et al., 2001)

For this specific list, the (3, 4) node from Fig. 2 was selected.

Table 3
Emotion class: abstracts associated with the emotion class sorted according to loading, i.e., values in $\tilde{\mathbf{w}}_{k\ =\ \text{emotion}}$

#	Load	Title	Reference
1	14.15	Investigation of facial recognition memory and happy and sad facial expression perception: an fMRI study	(Phillips et al., 1998)
2	11.60	Ketamine alters neural processing of facial emotion recognition in healthy men: an fMRI study	(Abel et al., 2003)
3	7.60	Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task	(Maddock et al., 2003)
4	4.79	The neural correlates of person familiarity. A functional magnetic resonance imaging study with clinical implications	(Shah et al., 2001)
5	4.76	Dissociable prefrontal brain systems for attention and emotion	(Yamasaki et al., 2002)
6	2.66	Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study	(Tillfors et al., 2001)
7	2.56	Functional neuroanatomy of visually elicited simple phobic fear: additional data and theoretical analysis	(Fredrikson et al., 1995)
8	2.39	Activation of left posterior cingulate gyrus by the auditory presentation of threat-related words: an fMRI study	(Maddock and Buonocore, 1997)
9	2.20	Cerebral blood flow during anxiety provocation	(Fredrikson et al., 1997)
10	1.82	A functional cerebral response to frightening visual stimulation	(Wik et al., 1993)
11	1.29	Cortical networks recruited for time perception: a monkey positron emission tomography (PET) study	(Onoe et al., 2001)
12	1.22	Investigating the functional anatomy of empathy and forgiveness	(Farrow et al., 2001)
13	1.17	Neural substrates for the perception of acutely induced dyspnea	(Peiffer et al., 2001)
14	1.05	Brain abnormalities in early-onset schizophrenia spectrum disorder observed with statistical parametric mapping of structural magnetic resonance images	(Sowell et al., 2000)
15	1.02	The neural basis of romantic love	(Bartels and Zeki, 2000)
16	0.97	The posterior cingulate and medial prefrontal cortex mediate the anticipatory allocation of spatial attention	(Small et al., 2003)
17	0.84	Focal gray matter density changes in schizophrenia	(Hulshoff Pol et al., 2001)
18	0.77	Neural basis of the Stroop interference task: response competition or selective attention?	(Mead et al., 2002)
19	0.73	Functional magnetic resonance imaging of human visual cortex during face matching: a comparison with positron emission tomography	(Clark et al., 1996)
20	0.53	6-(18)F-DOPA PET study in patients with schizophrenia. Positron emission tomography	(Elkashef et al., 2000)

For this specific list, the (11, 12) node from Fig. 2 was selected.

precuneus" (Boxer et al., 2003) was left out since it was too posterior ($y = -96$) to be in PCC. Another outlier left out was "right postcentral gyrus/posterior cingulate gyrus" with $x = 52$ (Jernigan et al., 1998). Single subjects activations in PCC from a third study (Maddock and Buonocore, 1997) were averaged to one single coordinate. All included studies except one event-related potential (ERP) study (Chen et al., 2002) were either PET or fMRI studies. The ERP study combined EEG measurements with structural magnetic resonance imaging, and "Magnetic Resonance Imaging" was indexed by PubMed as an MeSH term. It contained Talairach coordinates, and these were included in the further analysis. Based on the label given by the authors, we extract all coordinates for all experiments (contrasts) in the articles. These include activations, deactivations, focal points of hypo- or hyper-metabolism between groups of persons, as well as centers of lesions (if any). Thus, we will not be able say that a specific area is "activated" or "deactivated"—only that it is "associated", "involved", or "changed" with respect to a brain function.

Fig. 3 displays a sagittal view of the focal brain activation distribution of memory (green squares) and pain (red triangles) extracted from the most salient articles of the two most prominent components from the NMF analysis, i.e., the articles listed in Tables 1 and 2. A clear difference is seen between the two with memory brain activations primarily in the caudal part of PCC, while the pain brain activations are mostly confined to the rostral or superior part of PCC. Two of the pain activations in the caudal part are actually from the taste study (Gautier et al., 1999).

The statistical tests for difference in distributions between memory and pain coordinates showed a large segregation with P values around $P \approx 0.002$ for both Hotelling's T^2 test and the Mahalanobis permutation test, while the permutation test on the Euclidean distance was somewhat lower ($P \approx 0.0004$). If the test was restricted to the sagittal coordinates (y and z), the P values were lower, for example, Hotelling T^2 test P value for the coordinates from articles listed in Tables 1 and 2 was $P = 0.000658$ and $P \approx 0.0003$ for the mean permutation test. Statistical tests also gave evidence for a separation between memory and Alzheimer with $P \approx 0.01$ ($P_{T^2,\text{3D}} = 0.0172$, $P_{T^2,\text{Sagittal}} = 0.0098$, $P_{\text{Maha. Perm., Sagittal}} \approx 0.008$). The ordinary tests show very little difference between pain and Alzheimer $P > 0.5$, although this might be due to outliers in the Alzheimer set: many Alzheimer coordinates lay inferior to pain coordinates, while only a few are positioned superior. A permutation test on the median on the Talairach z coordinate showed a clear separation ($P \approx 0.001$). Statistical testing between memory and emotion showed a very high P value $P > 0.5$. There were not much difference between the Hotelling T^2 and permutation test for any of the tests. The above P values were all calculated with data from the top twenty articles. If the data are restricted to the top 5, 10, or 15 articles, P values for Hotelling's T^2 and Mahalanobis permutation tests for a difference between memory and pain coordinates are $P \approx 0.3$, $P \approx 0.3$, and $P < 0.00003$, respectively: with only ten articles or less, there is insufficient power to detect a difference between these two components. The heterogeneity of PCC with respect to memory and pain is further examined in the Appendix A.

There were few abstracts assigned to the PTSD components. Only 8 coordinates were contained in this components and furthermore were genuine PTSD articles (Bremner et al., 1999a,b, 2003; Pissiota et al., 2002). These showed to be mostly distributed in the rostral part of PCC and with the two most caudal brain activations actually being deactivations in relation to PTSD provocation (Pissiota et al., 2002). This could give evidence for PTSD activation to be confined to the rostral part. To investigate this further, we augmented the set with additional coordinates mentioned in a recent review (Bremner, 2002; Lanius et al., 2001; Shin et al., 1997, 1999), and we divided them into "positive" and

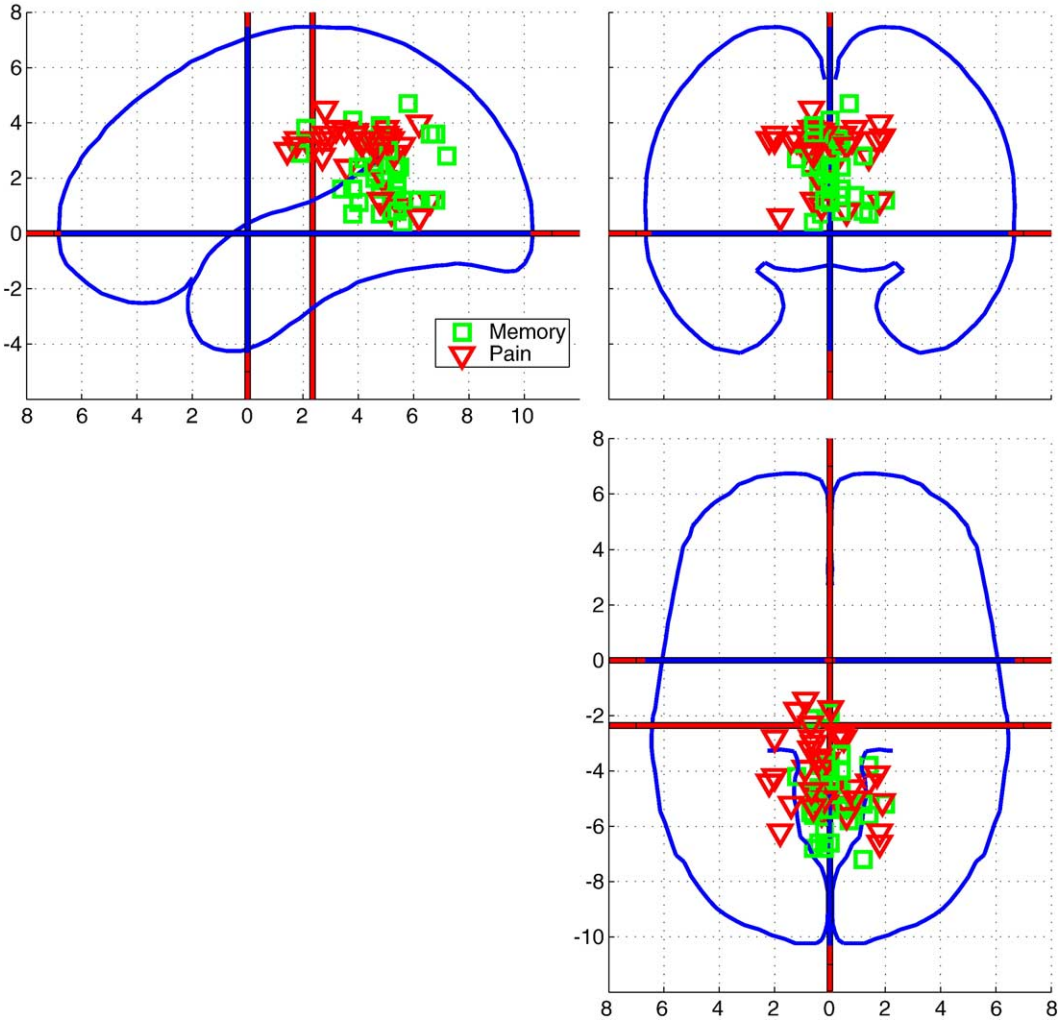

Fig. 3. Distribution of memory and pain brain activations in the posterior cingulate cortex shown on a sagittal plot: *y* is the AP axis with posterior as negative. The blue outline follows that of the Talairach atlas. The gray outline is an isocurvature in a probability volume for posterior cingulate cortex based on modeling of coordinates from the Brede database. Green squares are associated with "memory" articles and red triangles with "pain" articles.

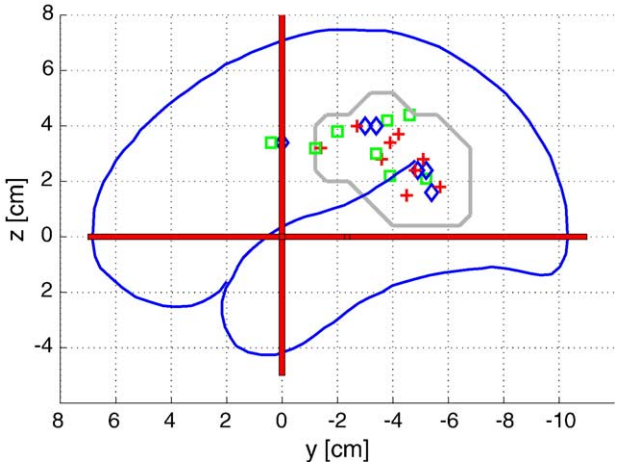

Fig. 4. Distribution of PTSD brain activations. Green squares are from our initial set, while red pluses and blue diamonds are "positive" and "negative" PTSD activations from an extra set of articles. The gray outline is an isocurvature in a probability volume for PCC based on modeling of all coordinates from the Brede database labeled either "posterior cingulate" or "retrosplenial" (Nielsen and Hansen, 2002a).

"negative" PTSD activations, see Fig. 4. These new coordinates did not support the hypothesis since they were distributed across the entire PCC.

Discussion

We find the most prominent component to be associated with words such as "memory", "retrieval", and "episodic". This is in alignment with a major review that associates PCC with successful episodic memory retrieval (Cabeza and Nyberg, 2000). The important role of the caudal posterior cingulate cortex in successful autobiographical memory retrieval has previously been noted (Maddock et al., 2001), and this is also in very well alignment with our finding of the spatial distribution of memory activations, although our results do not emphasize the success and autobiographical content, but rather general episodic memory retrieval.

Our finding of Alzheimer's Disease and Mild Cognitive Impairment as an important theme is also in agreement with

findings of the neuroimaging literature where PCC hypometabolism is prevalent, see, e.g., (Minoshima et al., 1994; Nybäck et al., 1991; Volkow et al., 2002).

The large contribution from pain in PCC studies is surprising: pain activation has especially been associated with the anterior or middle part of cingulate cortex (Brodmann areas 24/32) (Ingvar, 1999; Peyron et al., 2000; Vogt et al., 1992), seldom posterior to Talairach coordinate $y = -2$ cm. Magneto- and encephalography results have suggested involvement of the posterior cingulate area (Bromm, 2001), for example, a study estimated a laser evoked potential dipole source to be at the border between the anterior and posterior cingulate cortex in the left hemisphere (Bentley et al., 2002). Our results suggest that a larger part of cingulate cortex than just anterior cortex is associated with pain. Furthermore, this pain component has a focus that is shifted compared to the focus of the memory component: all statistical tests identify a differentiation between the memory and pain components, and simple visual inspection of Fig. 3 also testifies to this. Our analysis does not enable us to say whether specific sub-components of pain (such as affective, sensory, or cognitive) are especially pronounced in PCC and if the PCC contribution to pain might be a part of the stronger activation in the anterior cingulate cortex. Our differentiation between the pain and the memory components appears along a rostrocaudal axis, while standard cytoarchitectonic areas have a "ventrodorsal" order with Brodmann areas 29, 30, 23, and 31 (Vogt et al., 2001). Cytoarchitectonic rostrocaudal differentiation has been made in *Macaca fascicularis* with the definition of 23e, 23i, and 23v, where 23v is the most caudal (Kobayashi and Amaral, 2000), and differences in thalamic connection have been found between the posteroventral (caudal) and dorsal regions of area 23b in *Macaca fuscata* (Shibata and Yukie, 2003). However, it is not clear whether these differences relate to the functional differentiation we find.

Emotion has been associated with PCC, and a review concludes that "the retrosplenial cortex is the cortical region that is most consistently activated by the emotional salience of experimental stimuli" (Maddock, 1999), where "retrosplenial" here means the most caudal part of PCC (Vogt et al., 2000, 2001). Apart from articles mentioned by the review (Maddock, 1999), PCC has been associated with emotion in, e.g., facial anger viewing (Sprengelmeyer et al., 1998), facial happiness viewing (Kilts et al., 1996; Phillips et al., 1998), visual elicited phobic fear (Fredrikson et al., 1995), and romantic love (Bartels and Zeki, 2000). A single component contains a number of these emotion studies, but the component is not very "clean" in the sense that it does not exclusively contain emotion studies, so we can only leniently conclude that there is a tendency for overlap between the emotion and the memory in the spatial distribution in Talairach space and it appears in caudal PCC.

Measurements in several species indicate that PCC is implicated in eye movements (Olson et al., 1996; Vogt et al., 1992), and functional neuroimaging in humans identify PCC activation in saccades and pursuit tracking (Berman et al., 1999). One could expect to find a component corresponding to eye movement, but this did not appear as a major theme in our analysis of functional neuroimaging studies.

A missing theme in our analysis is navigation and spatial orientation: the involvement of PCC in navigation is supported by ten case studies with patients showing topographical disorientation as the primary deficit (Maguire, 2001). Furthermore, a number of animal lesion and electrophysiological studies have shown that PCC contributes to "spatial orientation" (Vogt et al., 1992). Human retrosplenial activation has also been reported in an allocentric environment-based task which required no real or virtual locomotion (Committeri et al., 2003). The reason why a navigation component does not show up is probably due to that some of the fMRI and PET navigation studies do not mention PCC (including retrosplenial cortex) in the title or abstract even when changes in this area are in fact reported: 8 of the 11 PET or fMRI studies listed in a review of retrosplenial cortex in navigation (Maguire, 2001) do not mention PCC. Another study is excluded from our analysis because "magnetic resonance imaging" is neither mentioned in the abstract nor indexed in the MeSH terms by PubMed (only "MRI" is mentioned in the abstract) (Grön et al., 2000). Two studies included in our analysis (Burgess et al., 2001; Ghaem et al., 1997) show high loading on the "memory" component which might be a suitable categorization since these "navigation" studies investigated *retrieval* of the spatial context and "memorized routes". The few navigation studies are not able to generate their own component. The same problem applies for the few studies contrasting "resting state" (where the subjects have been instructed to close their eyes) with a number of diverse activation states finding posterior cingulate or nearby precuneus activation (Andreasen et al., 1995a; Binder et al., 1999; Mazoyer et al., 2001; Raichle et al., 2001; Shulman et al., 1997). Of these, only two are included (Andreasen et al., 1995a; Mazoyer et al., 2001), both primarily classified as "memory", the major theme of the former. The NMF algorithm cannot identify all themes. Only if the theme is supported by a sufficient number of studies will the algorithm detect it as a component. Furthermore, the NMF algorithm will at some point – given enough number of components – find components that are dominated by few or single studies. Thus, only the major components will give full credence for their theme.

The bag-of-words approach, although a crude representation of written narrative, has proved to be able to identify themes that appear meaningful and aligned with "human powered" meta-analysis. The simple representation is however not able to identify in which local context the words appear. We used a large stop word list to discard frequent words with little reference to cognitive function. More advanced feature extraction algorithms would invoked more advanced phrase structure and natural language processing which has proven to give superior results in question/answering information retrieval tasks (Pasca and Harabagiu, 2001). One example of a problem with the bag-of-words scheme is negative context, e.g., that a memory task did not associate with a change in PCC. In practice, such cases seem to be rare. The NMF algorithm views the abstracts as stochastic, where each abstract is generated from a theme (a component) and contaminanted with noise, i.e., the varying usage of words. Even if this underlying model is correct, the NMF will, for a given data set, not be able to recover the themes exactly. However, as the number of abstracts increases, the topics will be more precisely identified and individual spurious abstract will have vanishing influence.

We did not intend to find all articles that are relevant for PCC. Many articles that report PCC activation do not mention the area in the abstract, and furthermore, our specific query with search on a limited number of words does not capture all relevant articles. Yet, our presently available database does yield sensible results and serves as proof of concept for future extensive data mining investigations. As databases such as BrainMap DBJ (Fox and Lancaster, 2002) and Brede (Nielsen, 2003) increase in scope, this will further the successful retrieval of relevant articles, and indeed

our method can be implemented as an integrated part of services offered in connection with these databases, as it is the case with "related volumes" services already in operation (Nielsen and Hansen, 2004). Increasing availability of electronic full text articles on the Internet will also assist the identification of relevant research. In our present analysis, the words in the abstract might describe several disparate experiments (contrasts), e.g., one where PCC was involved, others were it was not. The NMF algorithm would associate all words in the abstract with PCC. An advantage with the dedicated neuroscience databases is that they have annotation on the level of the experiments. An analysis on this level would avoid mixing multiple experiments. Our approach is only fully automatic in the first stage—the stage with NMF clustering of abstracts. The second stage with extraction of coordinates from articles is labor-intensive. Only if the coordinates can be found in neuroscience databases can our approach be fully automated. Thus, future studies will benefit by the increasing the scope of these databases.

Comparison with the permutation test on the Mahalanobis distance showed that the parametric Hotelling T^2 two-sample test is not very much affected by mild non-Gaussianity. However, the two tests are probably not unbiased: the tests assume independent distributed or "exchangeable" activations, and this is probably not true since there might be "intra-author" and "intra-study" effects that violate the independence assumption and activations within an article are not independent. These effects are hard to model or access. However, our investigation of memory and pain brain activation is based on a large number of mostly independent studies, so the overall conclusion should not be affected.

Another bias arises since the individual abstracts can probably not be regarded as fully independent and identically distributed: dominant authors or laboratories might tend to use a stereotypical vocabulary. We have inspected the tables to explore for this effect but did not find obvious examples.

Our present method uses the frequency of words as the features. A number of other weighting schemes have been suggested in the information retrieval literature, see, e.g., Salton and Buckley (1988), and these have an effect on the NMF components. We choose to use the frequency of words because of the simplicity and the emphasis it will put on the high frequency themes. However, some components can be dominated by single abstracts. In most cases, this effect is unwanted, and future work will be devoted to develop weighting schemes where these effects can be controlled.

It should be possible to apply the first stage of our method with NMF analysis of abstracts to a single behavioral function and examine its association across all brain regions. This would require a change in the query to PubMed and a different stop word list. The test in the second stage will typically not be appropriate since a behavioral function could have multiple modes, i.e., far from a Gaussian distribution, but other kinds of tests could be applied (Nielsen et al., 2004).

The limited resolution of functional neuroimaging along with differences in brain templates and image registration procedures as well as spatial filtering during analysis and variation in the way the Talairach coordinates are found will probably make it difficult to localize the precise area, e.g., in terms of cytoarchitecture. Our analysis shows that the Talairach coordinates have an advantage over lobar anatomy: Talairach coordinates allow for more precise delineation of an area than the lobar anatomy terminology typically employed.

It should be noted that the "anterior cingulate" and "posterior cingulate" are not well defined areas anatomically, for example, PCC can be taken to mean only the Brodmann areas 23 and 31. A mid-cingulate area can be defined (Tzourio-Mazoyer et al., 2002), which means that the area referred to as posterior cingulate will be confined to the caudal region. In this work, we have used the ostensive definition in articles and simply taken PCC to mean what is referred to as posterior cingulate and retrosplenial. Our analysis is not affected by this difference unless a part of the functional neuroimaging community, e.g., those involved in "memory", tend to use "mid-cingulate" for the rostral part of posterior cingulate, while others, e.g., pain researchers, tend to use "posterior cingulate".

Conclusion

We have presented a method for discovering major themes for a specific brain area. Apart from the manual entering of Talairach coordinates, our method can be completely automatized.

Our method is not confined to the analysis of the posterior cingulate but can be applied to other brain regions or other words and phrases, and their relation to brain anatomy can be identified.

We have found functional heterogeneity in posterior cingulate cortex, and the finding of the association between pain and the rostral part of the PCC shows the essence of data mining and knowledge discovery where previously overlooked small correlations become evident when information is aggregated and analyzed.

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Appendix A. Further investigation of memory and pain via the PubMed and Brede databases

Using a query for "memory" with the following format: Memory AND ("posterior cingulate" OR "posterior cingulum" OR "retrosplenial" OR "retrosplenium) AND ("magnetic resonance imaging" OR "positron emission tomography"), we downloaded memory abstracts from PubMed on 2004-11-25. This resulted in 126 abstracts. A similar query for "pain" was performed and resulted in 25 abstracts. Using the PubMed identifier as key, we found corresponding items in the Brede database. Only 15 (for memory) and 6 (for pain) corresponding articles were available in the Brede database. Building a probability density model using all of the PCC coordinates in the Brede database (Nielsen and Hansen, 2002a,b), we extracted the coordinates from the memory and pain articles that with a high probability would be in this area. This resulted in two sets of coordinates with 53 and 11 members, and tests for the difference in 3-dimensional location gave $P < 0.001$. This result is somewhat affected by the idiosyncrasies of the Brede database (for example, there are many thermal pain studies). Furthermore, there is a large overlap between studies found via the NMF algorithm and the studies found by searching PubMed with the "memory" and "pain" queries, so the results in this Appendix are not independent

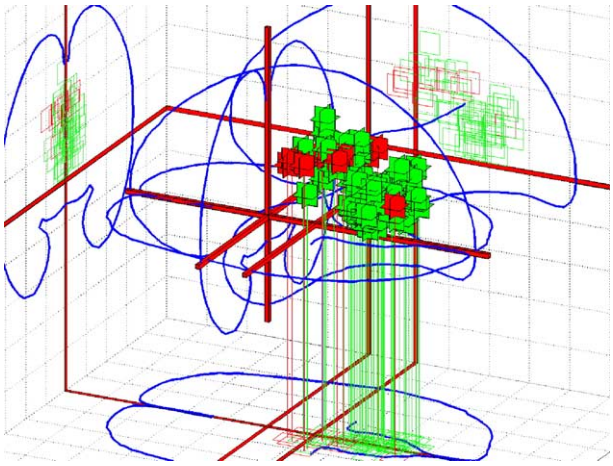

Fig. 5. Corner cube visualization of the memory (green) and pain (red) Talairach coordinates in the PCC with data from the Brede database and clustered based on the PubMed query: apart from a single outlier, the pain Talairach coordinates are confined to the rostral part of PCC.

from the main results. A corner cube visualization (Rehm et al., 1998) is shown in Fig. 5.

References

Abel, K.M., Allin, M.P.G., Kucharska-Pietura, K., David, A., Andrew, C., Williams, S., Brammer, M.J., Phillips, M.L., 2003. Ketamine alters neural processing of facial emotion recognition in healthy men: an fMRI study. NeuroReport 14 (3), 387–391.

Adler, L.J., Gyulai, F.E., Diehl, D.J., Mintun, M.A., Winter, P.M., Firestone, L.L., 1996. Regional brain activity changes associated with fentanyl analgesia elucidated by positron emission tomography. Anesth. Analg. 84 (1), 120–126.

Andreasen, N.C., O'Leary, D.S., Cizadlo, T., Arndt, S., Rezai, K., Watkins, G.L., Ponto, L.L., Hichwa, R.D., 1995a. II. PET studies of memory: novel versus practiced free recall of word lists. NeuroImage 2 (4), 296–305.

Andreasen, N.C., O'Leary, D.S., Cizadlo, T., Arndt, S., Rezai, K., Watkins, G.L., Ponto, L.L.B., Hichwa, R.D., 1995b. Remembering the past: two facets of episodic memory explored with positron emission tomography. Am. J. Psychiatry 152 (11), 1576–1585.

Arnold, J.T., Daw, N.C., Stenberg, P.E., Jayawardene, D., Srivastava, D.K., Jackson, C.W., 1997. A single injection of pegylated murine megakaryocyte growth and development factor (MGDF) into mice is sufficient to produce a profound stimulation of megakaryocyte frequency, size, and ploidization. Blood 89 (3), 823–833.

Baciu, M.V., Bonaz, B.L., Papillon, E., Bost, R.A., Bas, J.-F.L., Fournet, J., Segebarth, C.M., 1999. Central processing of rectal pain: a functional MR imaging study. Am. J. Neuroradiol. 20 (10), 1920–1924.

Balslev, D., Nielsen, F.Å., Frutiger, S.A., Sidtis, J.J., Christiansen, T.B., Svarer, C., Strother, S.C., Rottenberg, D.A., Hansen, L.K., Paulson, O.B., Law, I., 2002. Cluster analysis of activity–time series in motor learning. Hum. Brain Mapp. 15 (3), 135–145.

Bartels, A., Zeki, S., 2000. The neural basis of romantic love. NeuroReport 11 (17), 3829–3834.

Becerra, L.R., Breiter, H.C., Stojanovic, M., Fishman, S., Edwards, A., Comite, A.R., Gonzalez, R.G., Borsook, D., 1999. Human brain activation under controlled thermal stimulation and habituation to noxious heat: an fMRI study. Magn. Reson. Med. 41 (5), 1044–1057.

Bentley, D.E., Youell, P.D., Jones, A.K.P., 2002. Anatomical localization and intrasubject reproducibility of laser evoked potential source in cingulate cortex, using a realistic head model. Clin. Neurophysiol. 113 (8), 1351–1356.

Berman, R.A., Colby, C.L., Genovese, C.R., Voyvodic, J.T., Luna, B., Thulborn, K.R., Sweeney, J.A., 1999. Cortical networks subserving pursuit and saccadic eye movements in humans: an fMRI study. Hum. Brain Mapp. 8 (4), 209–225.

Berthoz, A., 1997. Parietal and hippocampal contribution to topokinetic and topographic memory. Philos. Trans. R. Soc. London, Ser. B Biol. Sci. 352 (1360), 1437–1448.

Binder, J.R., Frost, J.A., Hammeke, T.A., Bellgowan, P.S., Rao, S.M., Cox, R.W., 1999. Conceptual processing during the conscious resting state. A functional MRI study. J. Cogn. Neurosci. 11 (1), 80–95.

Boxer, A.L., Rankin, K.P., Miller, B.L., Schuff, N., Weiner, M., Gorno-Tempini, M.-L., Rosen, H.J., 2003. Cinguloparietal atrophy distinguishes Alzheimer disease from semantic dementia. Arch. Neurol. 60 (7), 949–956.

Bremner, J.D., 2002. Neuroimaging studies in post-traumatic stress disorder. Curr. Psychiatry Rep. 4 (4), 254–263.

Bremner, J.D., Narayan, M., Staib, L.H., Southwick, S.M., McGalshan, T., Charney, D.S., 1999a. Neural correlates of memories of childhood sexual abuse in women with and without posttraumatic stress disorder. Am. J. Psychiatry 156 (11), 1787–1795.

Bremner, J.D., Staib, L.H., Kaloupek, d., Southwick, S.M., Soufer, R., Charney, D.S., 1999b. Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without posttraumatic stress disorder: a positron emission tomography study. Biol. Psychiatry 45 (7), 806–816.

Bremner, J.D., Vythilingam, M., Vermetten, E., Southwick, S.M., McGlashan, T., Staib, L.H., Soufer, R., Charney, D.S., 2003. Neural correlates of declarative memory for emotionally valenced words in women with posttraumatic stress disorder related to early childhood sexual abuse. Biol. Psychiatry 53 (10), 879–889.

Brett, M., Christoff, K., Cusack, R., Lancaster, J.L., 2001. Using the Talairach atlas with the MNI template. NeuroImage 13 (6), S85.

Bromm, B., 2001. Brain images of pain. News Physiol. Sci. 16 (5), 244–249.

Burgess, N., Maguire, E.A., Spiers, H.J., O'Keefe, J., 2001. A temporoparietal and prefrontal network for retrieving the spatial context of lifelike events. NeuroImage 14 (2), 439–453.

Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn. Sci. 4 (6), 215–222.

Cabeza, R., Nyberg, L., 2000. Imaging cognition II: an empirical review of 275 PET and fMRI studies. J. Cogn. Neurosci. 12 (1), 1–47.

Chen, A.C.N., Niddam, D.M., Crawford, H.J., Oostenveld, R., Arendt-Nielsen, L., 2002. Spatial summation of pain processing in the human brain as assessed by cerebral event related potentials. Neuroscience Letters 328 (2), 190–194.

Christoff, K., Grabrieli, J.D.E., 2000. The frontopolar cortex and human cognition: evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. Psychobiology 28 (2), 168–186.

Cipolotti, L., Maguire, E.A., 2003. A combined neuropsychological and neuroimaging study of topographical and non-verbal memory in semantic dementia. Neuropsychologia 41 (9), 1148–1159.

Clark, V.P., Keil, K., Maisog, J.M., Courtney, S., Ungerleider, L.G., Haxby, J.V., 1996. Functional magnetic resonance imaging of human visual cortex during face matching: a comparison with positron emission tomography. NeuroImage 4 (1), 1–15.

Committeri, G., Galati, G., Paradis, A.-L., Pizzamiglio, L., Berthoz, A., LeBihan, D., 2003. Egocentric and allocentric spatial coding in a 3D environment. Presented at the 9th International Conference on Functional Mapping of the Human Brain, June 19–22, 2003, New York, NY, NeuroImage, 19 (2), Elsevier. Available on CD-Rom.

Cornette, L., Dupont, P., Spileers, W., Sunaert, S., Hecke, P.V., Mortelsmans, L., Orban, G.A., 1998. Human cerebral activity evoked by motion reversal and motion onset. Brain 121 (1), 143–157.

Creac'h, C., Henry, P., Caillé, J.M., Allard, M., 2000. Functional MR imaging analysis of pain-related brain activation after acute mechanical stimulation. AJNR Am. J. Neuroradiol. 21 (8), 1402–1406.

Daselaar, S.M., Veltman, D.J., Rombouts, S.A.R.B., Raaijmakers, J.G.W.,

Jonker, C., 2003. Neuroanatomical correlates of episodic encoding and retrieval in young and elderly subjects. Brain 126 (Pt. 1), 43–56.
Desgranges, B., Baron, J.C., Eustache, F., 1998. The functional neuroanatomy of episodic memory: the role of the frontal lobes, the hippocampal formation, and other areas. NeuroImage 8 (2), 198–213.
Dhillon, I., Modha, D., 2001. Concept decompositions for large sparse text data using clustering. Mach. Learn. 42 (1), 143–175.
Dobrokhotov, P., Goutte, C., Veuthey, A.-L., Gaussier, E., 2003. A probabilistic information retrieval approach to medical annotation in SWISS-PROT. In: Baud, R., Fieschi, M., Beux, P.L., Ruch, P. (Eds.), The New Navigators: From Professionals to Patients. Proceedings of MIE2003, Volume 95 of Studies in Health Technology and Informatics. IOS Press, Amsterdam, The Netherlands.
Donoho, D., Stodden, V., 2004. When does non-negative matrix factorization give a correct decomposition into parts? In: Thrun, S., Saul, L., Schölkopf, B. (Eds.), Advances in Neural Information Processing Systems, 16. MIT Press, Cambridge, MA.
Duncan, J., Owen, A.M., 2000. Common regions of the human frontal lobe recruited by diverse cognitive demands. Trends Neurosci. 23 (10), 475–483.
Düzel, E., Cabeza, R., Picton, T.W., Yonelinas, A.P., Scheich, H., Heinze, J.-J., Tulving, E., 1999. Task-related and item-related brain process of memory retrieval. Proc. Natl. Acad. Sci. U. S. A. 96 (4), 1794–1799.
Dwass, M., 1957. Modified randomization tests for nonparametric hypotheses. Ann. Math. Stat. 28, 181–187.
Edgington, E.S., 1986. Randomization Tests, volume 77 of Statistics: Textbooks and Monographs, Second ed. Marcel Dekker, New York.
Elkashef, A.M., Doudet, D., Bryant, T., Cohen, R.M., Li, S.-H., Wyatt, R.J., 2000. 6-^{18}F-DOPA PET study in patients with schizophrenia. Positron emission tomography. Psychiatry Res. 100 (1), 1–11.
Farrow, T.F., Zheng, Y., Wilkinson, I.D., Spence, S.A., Deakin, J.F., Tarrier, N., Griffiths, P.D., Woodruff, P.W., 2001. Investigating the functional anatomy of empathy and forgiveness. NeuroReport 12 (11), 2433–2438.
Fink, G.R., Markowitsch, H.J., Reinkemeier, M., Bruckbauer, T., Kessler, J., Heiss, W.D., 1996. Cerebral representation of one's own past: neural networks involved in autobiographical memory. J. Neurosci. 16 (13), 4275–4282.
Fox, P.T., Lancaster, J.L., 2002. Mapping context and content: the BrainMap model. Nat. Rev., Neurosci. 3 (4), 319–321.
Fox, P.T., Huang, A., Parsons, L.M., Xiong, J.-H., Zamarippa, F., Rainey, L., Lancaster, J.L., 2001. Location–probability profiles for the mouth region of human primary motor-sensory cortex: model validation. NeuroImage 13 (1), 196–209.
Francis, S.T., Kelly, E.F., Bowtell, R., Dunseath, W.J., Folger, S.E., McGlone, F., 2000. fMRI of the responses to vibratory stimulation of digit tips. NeuroImage 11 (3), 188–202.
Fredrikson, M., Wik, G., Annas, P., Ericson, K., Stone-Elander, S., 1995. Functional neuroanatomy of visually elicited simple phobic fear: additional data and theoretical analysis. Psychophysiology 32 (1), 43–48.
Fredrikson, M., Fischer, H., Wik, G., 1997. Cerebral blood flow during anxiety provocation. J. Clin. Psychiatry 58 (16), 16–21.
Fujii, T., Okuda, J., Tsukiura, T., Ohtake, H., Miura, R., Fukatsu, R., Suzuki, K., Kawashima, R., Itoh, M., Fukuda, H., Yamadori, A., 2002. The role of the basal forebrain in episodic memory retrieval: a positron emission tomography study. NeuroImage 15 (3), 501–508.
Gaussier, E., Goutte, C., Popat, K., Chen, F., 2002. A hierarchical model for clustering and categorising documents. In: Crestani, F., Girolami, M., can Rijsbergen, C.J. (Eds.), Advances in Information Retrieval. 24th BCS-IRSG European Colloquium on IR Research Glasgow, UK, March 25–27, 2002 Proceedings, Volume 2291 of Lecture Notes in Computer Science. Springer, Berlin, Germany, pp. 229–247.
Gautier, J.F., Chen, K., Uecker, A., Bandy, D., Frost, J., Salbe, A.D., Pratley, R.E., Lawson, M., Ravussin, E., Reiman, E.M., Tataranni, P.A., 1999. Regions of the human brain affected during a liquid-meal taste perception in the fasting state: a positron emission tomography study. Am. J. Clin. Nutr. 70 (5), 806–810.
Gelnar, P.A., Krauss, B.R., Sheehe, P.R., Szeverenyi, N.M., Apkarian, A.V., 1999. A comparative fMRI study of cortical representations for thermal painful, vibrotactile, and motor performance tasks. NeuroImage 10 (4), 460–482.
Ghaem, O., Mellet, E., Crivello, F., Tzourio, N., Mazoyer, B., Berthoz, A., Denis, M., 1997. Mental navigation along memorized routes activates the hippocampus, precuneus, and insula. NeuroReport 8 (3), 739–744.
Goldman, J.A., Chu, W.W., Parker, D.S., Goldman, R.M., 1999. Term domain distribution analysis: a data mining tool for text databases. Methods Inform. Med. 38 (2), 96–101.
Goutte, C., Toft, P., Rostrup, E., Nielsen, F.Å., Hansen, L.K., 1999. On clustering fMRI time series. NeuroImage 9 (3), 298–310.
Goutte, C., Hansen, L.K., Liptrot, M.G., Rostrup, E., 2001. Feature–space clustering for fMRI meta-analysis. Hum. Brain Mapp. 13 (3), 165–183.
Grön, G., Wunderlich, A.P., Spitzer, M., Tomczak, R., Riepe, M.W., 2000. Brain activation during human navigation: gender-different neural networks as substrate of performance. Nat. Neurosci. 3 (4), 404–408.
Hansen, L.K., Sigurðsson, S., Kolenda, T., Nielsen, F.Å., Kjems, U., Larsen, J., 2000. Modeling text with generalizable Gaussian mixtures. Proceedings of ICASSP'2000 (Turkey), IEEE, Piscataway, New Jersey.
Hofmann, T., 1999. Probabilistic latent semantic analysis. Proceedings of the 15th Conference on Uncertainty in AI. Morgan Kaufmann, pp. 289–296.
Hsieh, J.-C., Belfrage, M., Stone-Elander, S., Hansson, P., Ingvar, M., 1995. Central representation of chronic ongoing neuropathic pain studied by positron emission tomography. Pain 63 (3), 225–236.
Hulshoff Pol, H.E., Schnack, H.G., Mandl, R.C., van Haren, N.E.M., Koning, H., Collins, D.L., Evans, A.C., Kahn, R.S., 2001. Focal gray matter density changes in schizophrenia. Arch. Gen. Psychiatry 58 (12), 1118–1125.
Hunkin, N.M., Mayes, A.R., Gregory, L.J., Nicholas, A.K., Nunn, J.A., Brammer, M.J., Bullmore, E.T., Williams, S.C.R., 2002. Novelty-related activation within the medial temporal lobes. Neuropsychologia 40 (8), 1456–1464.
Ingvar, M., 1999. Pain and functional imaging. Philos. Trans. R. Soc. London, Ser. B Biol. Sci. 354 (1387), 1347–1358.
Inoue, K., Kawashima, R., Satoh, K., Kinomura, S., Goto, R., Koyama, M., Sugiura, M., Ito, M., Fukuda, H., 1998. PET study of pointing with visual feedback of moving hands. J. Neurophysiol. 79 (1), 117–125.
Isbell Jr., C.L., Viola, P., 1999. Restructuring sparse high dimensional data for effective retrieval. In: Kearns, M.S., Solla, S.A., Cohen, D. (Eds.), Advances in Neural Information Processing Systems 11: Proceedings of the 1998 Conference. MIT Press, Cambridge, MA, pp. 480–486.
Jernigan, T.L., Ostergaard, A.L., Law, I., Svarer, C., Gerlach, C., Paulson, O.B., 1998. Brain activation during word identification and word recognition. NeuroImage 8 (1), 93–105.
Kertzman, C., Schwarz, U., Zeffiro, T.A., Hallett, M., 1997. The role of posterior parietal cortex in visually guided reaching movements in humans. Exp. Brain Res. 114 (1), 170–183.
Kilts, C.D., Egan, G.J., Gideon, D.A., Faber, T., Hoffman, J.M., 1996. The functional organization of the human brain for face emotion perception: a PET neuroactivation analysis. NeuroImage 3 (5 Part. 2), S227.
Kleinberg, J.M., 1999. Authoritative sources in a hyperlinked environment. JACM 46 (5), 604–632.
Kobayashi, Y., Amaral, D.G., 2000. Macaque monkey retrosplenial cortex: I. three-dimensional and cytoarchitectonic organization. J. Comp. Neurol. 426 (3), 339–365.
Kolenda, T., Hansen, L.K., Sigursson, S., 2000. Independent components in text. In: Girolami, M. (Ed.), Advances in Independent Component Analysis, Perspectives on Neural Computing. Springer Verlag, Berlin, Germany (Chap. 13).
Krause, B.J., Horwitz, B., Taylor, J.G., Schmidt, D., Mottaghy, F.M., Herzog, H., Halsband, U., Muller-Gartner, H., 1999. Network analysis in episodic encoding and retrieval of word-pair associates: a PET study. Eur. J. Neurosci. 11 (9), 3293–3301.

Lange, N., Strother, S.C., Anderson, J.R., Nielsen, F.Å., Holmes, A.P., Kolenda, T., Savoy, R., Hansen, L.K., 1999. Plurality and resemblance in fMRI data analysis. NeuroImage 10 (3), 282–303.

Lanius, R.A., Williamson, P.C., Densmore, M., Boksman, K., Gupta, M.A., Neufeld, R.W., Gati, J.S., Menon, R.S., 2001. Neural correlates of traumatic memories in posttraumatic stress disorder: a functional MRI investigation. Am. J. Psychiatry 158 (11), 1920–1922.

Lee, D.D., Seung, H.S., 1999. Learning the parts of objects by non-negative matrix factorization. Nature 401 (6755), 788–791.

Lee, D.D., Seung, H.S., 2001. Algorithms for non-negative matrix factorization. In: Leen, T.K., Dietterich, T.G., Tresp, V. (Eds.), Advances in Neural Information Processing Systems 13: Proceedings of the 2000 Conference. MIT Press, Cambridge, MA, pp. 556–562.

Lekander, M., Fredrikson, M., Wik, G., 2000. Neuroimmune relations in patients with fibromyalgia: a positron emission tomography study. Neurosci. Lett. 282 (3), 193–196.

Luna, B., Minshew, N.J., Garver, K.E., Lazar, N.A., Thulborn, K.R., Eddy, W.F., Sweeney, J.A., 2002. Neocortical system abnormalities in autism: an fMRI study of spatial working memory. Neurology 59 (6), 834–840.

Maddock, R.J., 1999. The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. Trends Neurosci. 22 (7), 310–316.

Maddock, R.J., Buonocore, M.H., 1997. Activation of left posterior cingulate gyrus by the auditory presentation of threat-related words: an fMRI study. Psychiatry Res. 75 (1), 1–14.

Maddock, R.J., Garrett, A.S., Buonocore, M.H., 2001. Remembering familiar people: the posterior cingulate cortex and autobiographical memory retrieval. Neuroscience 104 (3), 667–676.

Maddock, R.J., Garrett, A.S., Buonocore, M.H., 2003. Posterior cingulate cortex activation by emotional words: fMRI evidence from a valence decision task. Hum. Brain Mapp. 18 (1), 30–41.

Maguire, E.A., 2001. The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. Scand. J. Psychol. 42, 225–238.

Maguire, E.A., Mummery, C.J., 1999. Differential modulation of a common memory retrieval network revealed by positron emission tomography. Hippocampus 9 (1), 54–61.

Maguire, E.A., Vargha-Khadem, F., Mishkin, M., 2001. The effects of bilateral hippocampal damage on fMRI regional activations and interactions during memory retrieval. Brain 124 (6), 1156–1170.

Mardia, K.V., 1970. Measures of multivariate skewness and kurtosis with applications. Biometrika 36, 519–530.

Mardia, K.V., Kent, J.T., Bibby, J.M., 1979. Multivariate analysis. Probability and Mathematical StatisticsAcademic Press, London.

Mazoyer, B., Zago, L., Mellet, E., Bricogne, S., Etard, O., Houde, O., Crivello, F., Joliot, M., Petit, L., Tzourio-Mazoyer, N., 2001. Cortical networks for working memory and executive functions sustain the conscious resting state in man. Brain Res. Bull. 54 (3), 287–298.

McDonald, C.R., Crosson, B., Valenstein, E., Bowers, D., 2001. Verbal encoding deficits in a patient with a left retrosplenial lesion. Neurocase 7 (5), 405–417.

Mead, L.A., Mayer, A.R., Bobholz, J.A., Woodley, S.J., Cunningham, J.M., Hammeke, T.A., Rao, S.M., 2002. Neural basis of the Stroop interference task: response competition or selective attention? J. Int. Neuropsychol. Soc. 8 (6), 735–742.

Mesulam, M.-M., Nobre, A.C., Kim, Y.-H., Parrish, T.B., Gitelman, D.R., 2001. Heterogeneity of cingulate contributions to spatial attention. NeuroImage 13 (6), 1065–1072.

Minoshima, S., Foster, N.L., Kuhl, D.E., 1994. Posterior cingulate cortex in Alzheimer's disease. Lancet 344, 895.

Naliboff, B.D., Derbyshire, S.W., Munakata, J., Berman, S., Mandelkern, M., Chang, L., Mayer, E.A., 2001. Cerebral activation in patients with irritable bowel syndrome and control subjects during rectosigmoid stimulation. Psychosom. Med. 63 (3), 365–375.

Nichols, T.E., Holmes, A.P., 2001. Nonparametric permutation tests for PET functional neuroimaging experiments: a primer with examples. Hum. Brain Mapp. 15 (1), 1–25.

Nielsen, F.Å., 2003. The Brede database: a small database for functional neuroimaging. Presented at the 9th International Conference on Functional Mapping of the Human Brain, June 19–22, 2003, New York, NY, NeuroImage, 19 (2), Elsevier. Available on CD-Rom.

Nielsen, F.Å., Hansen, L.K., 2000. Experiences with Matlab and VRML in functional neuroimaging visualizations. In: Klasky, S., Thorpe, S. (Eds.), VDE2000—Visualization Development Environments, Workshop Proceedings, Princeton, New Jersey, USA, April 27–28, 2000. Princeton Plasma Physics Laboratory, Princeton, NJ, pp. 76–81.

Nielsen, F.Å., Hansen, L.K., 2002a. Automatic anatomical labeling of Talairach coordinates and generation of volumes of interest via the BrainMap database. Presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan, NeuroImage, 16 (2), Elsevier. Available on CD-Rom.

Nielsen, F.Å., Hansen, L.K., 2002b. Modeling of activation data in the BrainMap ™ database: detection of outliers. Hum. Brain Mapp. 15 (3), 146–156.

Nielsen, F.Å., Hansen, L.K., 2004. Finding related functional neuroimaging volumes. Artif. Intell. Med. 30 (2), 141–151.

Nielsen, F.Å., Chen, A.C.N., Hansen, L.K. 2004. Testing for difference between two groups of functional neuroimaging experiments. In Olsen, S.I. (Ed.), Proceedings fra den 13. Danske Konference i Mønstergenkendelse og Billedanalyse, number 2004/10 in DIKU Technical Reports, Copenhagen, Denmark. Dansk Selskab for Automatisk Genkendelse af Mønstre, Datalogisk Institut, University of Copenhagen, pp. 121–129.

Nybäck, H., Nyman, H., Blomqvist, G., Sjögren, I., Stone-Elander, S., 1991. Brain metabolism in Alzheimer's dementia: studies of ^{11}C-deoxyglucose accumulation, CSF monoamine metabolites and neuropsychological test performance in patients and healthy subjects. J. Neurol., Neurosurg. Psychiatry 54 (8), 673–678.

Nyberg, L., McIntosh, A.R., Cabeza, R., Nilsson, L.-G., Houle, S., Habib, R., Tulving, E., 1996. Network analysis of positron emission tomography regional cerebral blood flow data: ensemble inhibition during episodic memory retrieval. J. Neurosci. 16 (11), 3753–3759.

Olson, C.R., Musil, S.Y., Goldberg, M.E., 1996. Single neurons in posterior cingulate cortex of behaving macaque: eye movement signals. J. Neurophysiol. 76 (5), 3285–3300.

Onoe, H., Komori, M., Onoe, K., Takechi, H., Tsukada, H., Watanabe, Y., 2001. Cortical networks recruited for time perception: a monkey positron emission tomography (PET) study. NeuroImage 13 (1), 37–45.

Pasca, M., Harabagiu, S., 2001. High-performance question/answering. In: Croft, W.B., Harper, D.J., Kraft, D.H., Zobel, J. (Eds.), SIGIR 2001: Proceedings of the 24th Annual International ACM SIGIR Conference on Research and Development in Information Retrieval, September 9–13, 2001, New Orleans, Louisiana, USA. ACM, New York, pp. 366–374.

Peiffer, C., Poline, J.-B., Thivard, L., Aubier, M., Samson, Y., 2001. Neural substrates for the perception of acutely induced dyspnea. Am. J. Respir. Crit. Care Med. 163 (4), 951–957.

Perez-Iratxeta, C., Bork, P., Andrade, M.A., 2001. XplorMed: a tool for exploring MEDLINE abstracts. Trends Biochem. Sci. 26 (9), 573–575.

Petrovic, P., Ingvar, M., Stone-Elander, S., Petersson, K.M., Hansson, P., 1999. A PET activation study of dynamic mechanical allodynia in patients with mononeuropathy. Pain 83 (3), 459–470.

Peyron, R., Laurent, B., Garcia-Larrea, L., 2000. Functional imaging of brain responses to pain. a review and meta-analysis. Neurophysiol. Clin./Clin. Neurophysiol. 30 (5), 263–288.

Phillips, M.L., Bullmore, E.T., Howard, R., Woodruff, P.W., Wright, I.C., Williams, S.C., Simmons, A., Andrew, C., Brammer, M., David, A.S., 1998. Investigation of facial recognition memory and happy and sad facial expression perception: an fMRI study. Psychiatry Research 83 (3), 127–138.

Piefke, M., Weiss, P.H., Zilles, K., Markowitsch, H.J., Fink, G.R., 2003. Differential remoteness and emotional tone modulate the neural correlates of autobiographical memory. Brain 126 (Part 3), 650–668.

Pissiota, A., Frans, O., Fernandez, M., von Knorring, L., Fischer, H.,

Fredrikson, M., 2002. Neurofunctional correlates of posttraumatic stress disorder: a PET symptom provocation study. Eur. Arch. Psychiatry Clin. Neurosci. 252 (2), 68–75.

Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. Proc. Natl. Acad. Sci. U. S. A. 98 (2), 676–682.

Rainville, P., Hofbauer, R.K., Paus, T., Duncan, G.H., Bushnell, M.C., Price, D.D., 1999. Cerebral mechanisms of hypnotic induction and suggestion. J. Cogn. Neurosci. 11 (1), 110–125.

Rehm, K., Lakshminarayan, K., Frutiger, S.A., Schaper, K.A., Sumners, D.L., Strother, S.C., Anderson, J.R., Rottenberg, D.A., 1998. A symbolic environment for visualizing activated foci in functional neuroimaging datasets. Med. Image Anal. 2 (3), 215–226.

Rosen, S.D., Paulesu, E., Frith, C.D., Frackowiak, R.S.J., Davies, G.J., Jones, T., Camici, P.G., 1994. Central nervous pathways mediating angina pectoris. Lancet 344 (8916), 147–150.

Salton, G., Buckley, C., 1988. Term-weighting approaches in automatic text retrieval. Inf. Process. Manag. 24 (5), 513–523.

Salton, G., Wong, A., Yang, C.S., 1975. A vector space model for automatic indexing. Commun. ACM 18, 613–620.

Shah, N.J., Marshall, J.C., Zafiris, O., Schwab, A., Zilles, K., Markowitsch, H.J., Fink, G.R., 2001. The neural correlates of person familiarity. a functional magnetic resonance imaging study with clinical implications. Brain 124 (4), 804–815.

Shallice, T., Fletcher, P., Frith, C.D., Grasby, P., Frackowiak, R.S.J., Dolan, R.J., 1994. Brain regions associated with acquisition and retrieval of verbal episodic memory. Nature 368 (6472), 633–635.

Shibata, H., Yukie, M., 2003. Differential thalamic connections of the posteroventral and dorsal posterior cingulate gyrus in the monkey. Eur. J. Neurosci. 18 (6), 1516–1626.

Shin, L.M., Kosslyn, S.M., McNally, R.J., Alpert, N.M., Thompson, W.L., Rauch, S.L., Macklin, M.L., Pitman, R.K., 1997. Visual imagery and perception in posttraumatic stress disorder. Arch. Gen. Psychiatry 54 (3), 233–241.

Shin, L.M., McNally, R.J., Kosslyn, S.M., Thompson, W.L., Rauch, S.L., Alpert, N.M., Metzger, L.J., Lasko, N.B., Orr, S.P., Pitman, R.K., 1999. Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD: a PET investigation. Am. J. Psychiatry 156 (4), 575–584.

Shulman, G.L., Fiez, J.A., Corbetta, M., Buckner, R.L., Miezin, F.M., Raichle, M.E., Petersen, S.E., 1997. Common blood flow changes across visual tasks: II. decreases in cerebral cortex. J. Cogn. Neurosci. 9 (5), 648–656.

Small, D.M., Gitelman, D.R., Gregory, M.D., Nobre, A.C., Parrish, T.B., Mesulam, M.-M., 2003. The posterior cingulate and medial prefrontal cortex mediate the anticipatory allocation of spatial attention. NeuroImage 18 (3), 633–641.

Sowell, E.R., Levitt, J., Thompson, P.M., Holmes, C.J., Blanton, R.E., Kornsand, D.S., Caplan, R., McCracken, J., Asarnow, R., Toga, A.W., 2000. Brain abnormalities in early-onset schizophrenia spectrum disorder observed with statistical parametric mapping of structural magnetic resonance images. Am. J. Psychiatry 157 (9), 1475–1484.

Sprengelmeyer, R., Rausch, M., Eysel, U.T., Przuntek, H., 1998. Neural structures associated with recognition of facial expressions of basic emotions. Proc. R. Soc. London, Ser. B Biol. Sci. 265 (1409), 1927–1931.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme Medical Publisher Inc, New York.

Tillfors, M., Furmark, T., Marteinsdottir, I., Fischer, H., Pissiota, A., Langstrom, B., Fredrikson, M., 2001. Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study. Am. J. Psychiatry 158 (8), 1220–1226.

Tölle, T.R., Kaufmann, T., Siessmeier, T., Lautenbacher, S., Berthele, A., Munz, F., Zieglgans-berger, W., Willoch, F., Schwaiger, M., Conrad, B., Bartenstein, P., 1999. Region-specific encoding of sensory and affective components of pain in the human brain: a positron emission tomography correlation analysis. Ann. Neurol. 45 (1), 40–47.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 15 (1), 273–289.

Van Horn, J.D., Gold, J.M., Esposito, G., Ostrem, J.L., Mattay, V., Weinberger, D.R., Berman, K.F., 1998. Changing patterns of brain activation during maze learning. Brain Res. 793 (1–2), 29–38.

Verne, G.N., Himes, N.C., Robinson, M.E., Gopinath, K.S., Briggs, R.W., Crosson, B., Price, D.D., 2003. Central representation of visceral and cutaneous hypersensitivity in the irritable bowel syndrome. Pain 103 (1–2), 99–110.

Vogt, B.A., Finch, D.M., Olson, C.R., 1992. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. Cereb. Cortex 2, 435–443.

Vogt, B.A., Derbyshire, S., Jones, A.K.P., 1996. Pain processing in four regions of human cingulate cortex localized with co-registered PET and MR imaging. Eur. J. Neurosci. 8 (7), 1461–1473.

Vogt, B.A., Absher, J.R., Bush, G., 2000. Human retrosplenial cortex: where is it and is it involved in emotion? Trends Neurosci. 23 (5), 195–197.

Vogt, B.A., Vogt, L.J., Perl, D.P., Hof, P.R., 2001. Cytology of human caudomedial cingulate, retrosplenial, and caudal parahippocampal cortices. J. Comp. Neurol. 438 (3), 353–376.

Volkow, N.D., Zhu, W., Felder, C.A., Mueller, K., Welsh, T.F., Wang, G.J., de Leon, M.J., 2002. Changes in brain functional homogeneity in subjects with Alzheimer's disease. Psychiatry Res. 114 (1), 39–50.

Wiggs, C.L., Weisberg, J., Martin, A., 1999. Neural correlates of semantic and episodic memory retrieval. Neuropsychologia 37 (1), 103–118.

Wik, G., Fredrikson, M., Ericson, K., Eriksson, L., Stone-Elander, S., Greitz, T., 1993. A functional cerebral response to frightening visual stimulation. Psychiatry Res.: Neuroimaging 50 (1), 15–24.

Willoch, F., Rosen, G., Tolle, T.R., Oye, I., Wester, H.J., Berner, N., Schwaiger, M., Bartenstein, P., 2000. Phantom limb pain in the human brain: unraveling neural circuitries of phantom limb sensations using positron emission tomography. Ann. Neurol. 48 (6), 842–849.

Yamasaki, H., LaBar, K.S., McCarthy, G., 2002. Dissociable prefrontal brain systems for attention and emotion. Proc. Natl. Acad. Sci. U. S. A. 99 (17), 11447–11451.