Functional heterogeneity of the posterior cingulate cortex

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The posterior cingulate including retrosplenial cortex (PCC) has been associated with a number of cognitive functions such as episodic memory (*1*), emotion (*2*), navigation (*3*), "resting" (*4*), and shows early declining metabolism in Alzheimer's disease. Lacking an overview, we aimed at clarifying what functions are most consistently associated with PCC and how they are spatially distributed within PCC, thus challenging the hypothesis that the PCC is a functional homogeneous area.

We applied a semi-automated meta-analytic method, where Entrez-PubMed was queried for abstracts on posterior cingulate and retrosplenium restricting to functional magnetic resonance imaging and positron emission tomography that with a high likelihood would contain stereotactic Talairach coordinates (*5*) from human brain mapping experiments. The retrieved abstracts were converted to a vectorial bag-of-words representation and clustered based on the word features (*6*). Dominant components represented memory (especially episodic memory retrieval) and pain (characterized by words such as "pain", "painful" and "somatosensory"). Further components were interpretable as, e.g., Alzheimer's disease (see supplement). To characterize the distribution of the components in the brain we extracted the Talairach coordinates from articles that had the top-twenty highest loading on the memory and pain components. These articles represent the most typical memory and pain articles with respect to PCC. The memory component showed an affinity toward the caudal aspect of the posterior cingulate area (Fig. 1) in accordance with previous observations of memory retrieval (*7*). The pain component was mostly confined to the rostral part of the posterior cingulate area, and a test yields a significant difference of the center of mass of the two sets of foci ($P = 0.0022$ for Hotelling's T^2).

A major review finds successful episodic memory retrieval to be the most prominent cognitive function associated with PCC (*1*), and our finding adds support to this. However, it is surprising to find pain associated with the posterior part of the cingulate cortex since previous reviews have focused on the anterior cingulate (*8,9*). The rostrocaudal division is orthogonal to the cytoarchitectonic standard ventrodorsal delineation of the posterior cingulate and retrosplenial areas (*10*). This discrepancy between function and cytoarchitectonics has also been found for the anterior cingulate cortex which can be subdivided into cognitive and affective areas (*11*). Our results indicate that PCC should not be considered a homogeneous entity.

References and notes

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6. We used the specific query: ("posterior cingulate" OR "posterior cingulum" OR "retrosplenial" OR "retrosplenium") AND ("magnetic resonance imaging" OR "positron emission tomography"). 271 listed abstracts were downloaded. Stop-words with no direct relation to brain functions were removed. The set of abstracts were represented in an abstract-times-words matrix and clustered with non-negative matrix factorization with the least square cost function of D. D. Lee and H. S. Seung, *Nature* **401**, 788 (1999). The number of components was varied from 1 to 12.
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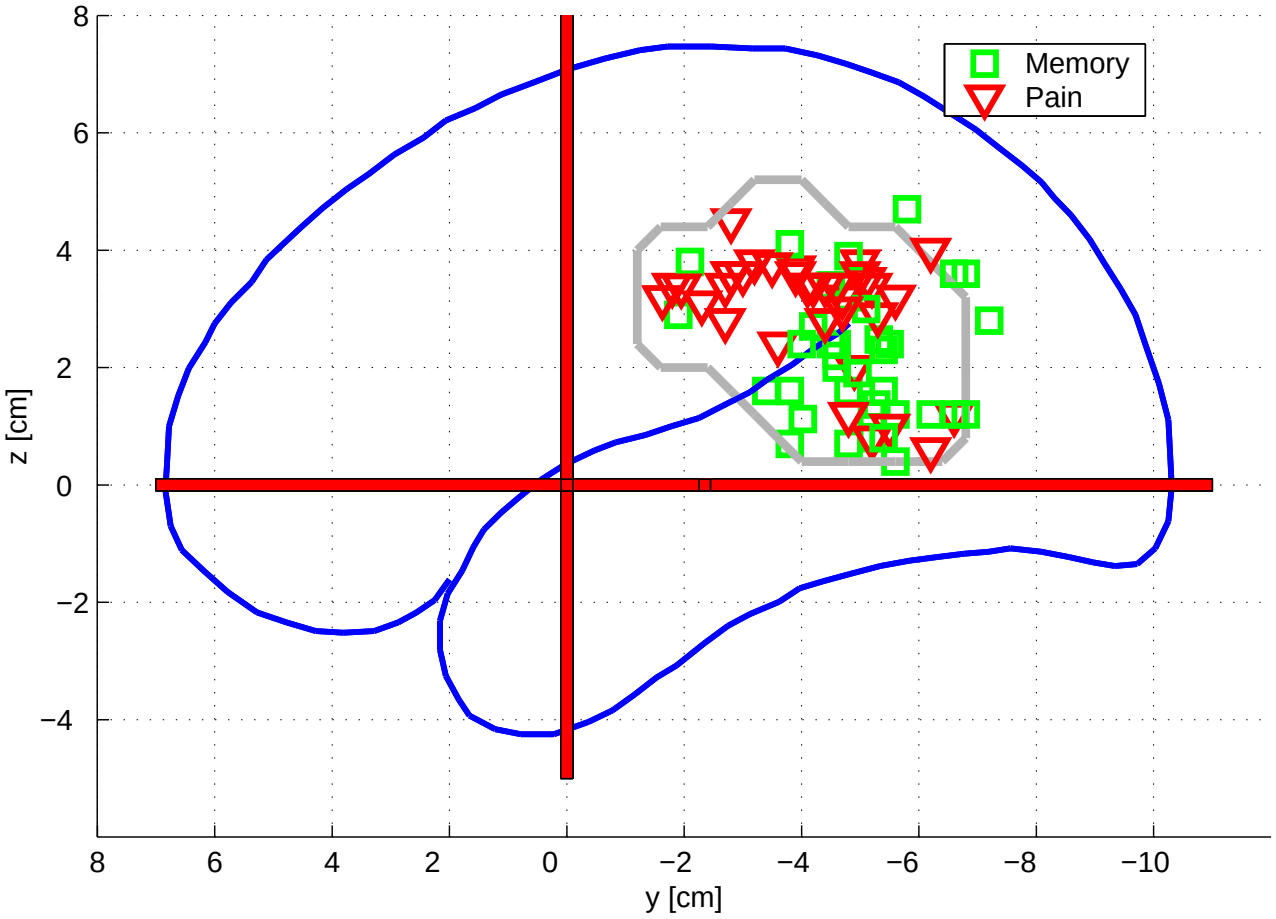

Figure 1: Sagittal view of the focal brain activation distribution of memory (green squares) and pain (red triangles) extracted from the most salient articles of the prominent functional components from the clustering. The gray outline is an isocurvature in a probability volume for posterior cingulate cortex based on modeling of coordinates from the Brede database (http://hendrix.imm.dtu.dk/service/jerne/brede/) labeled either "posterior cingulate" or "retrosplenial".

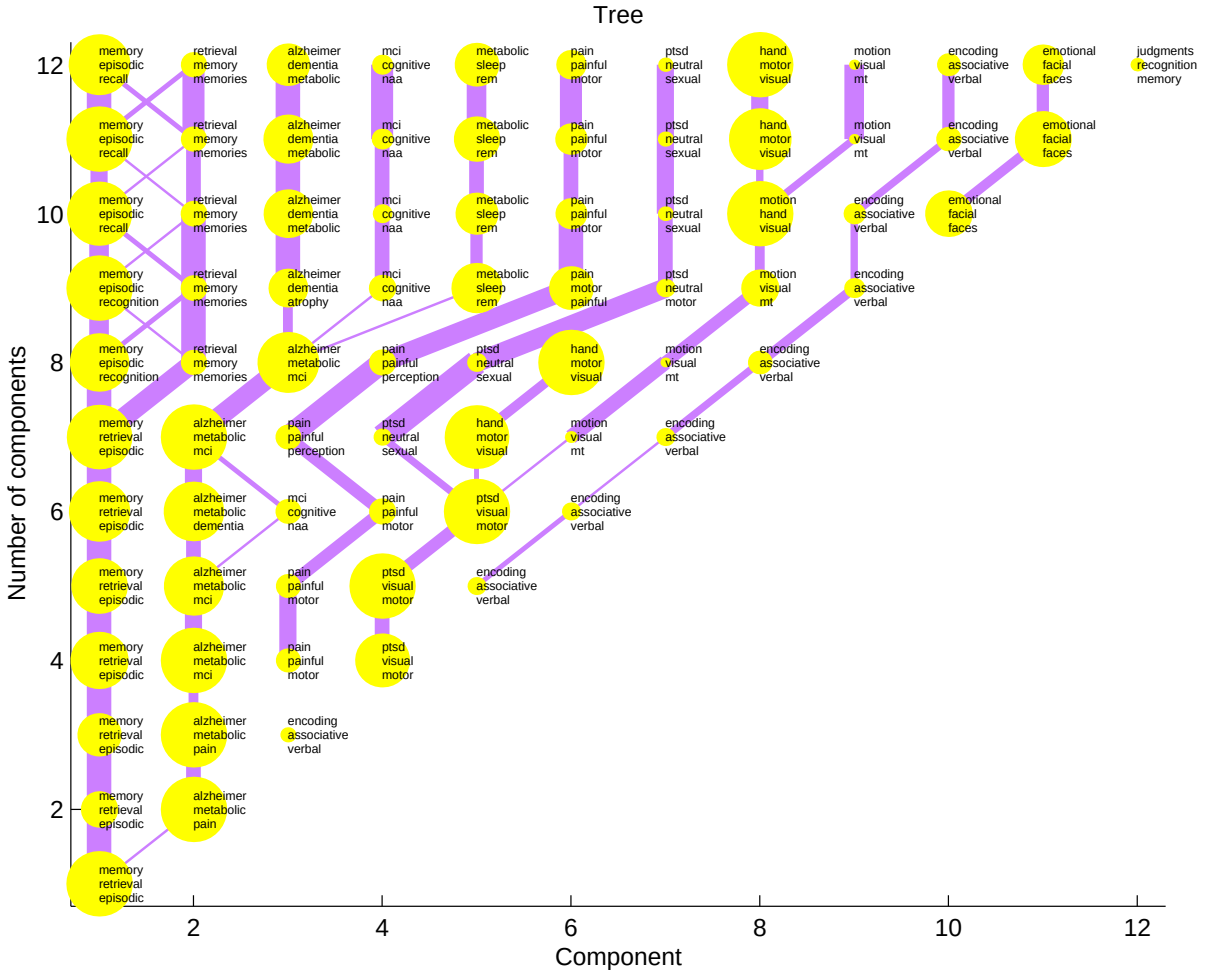

Figure 2: Components from non-negative matrix factorization (NMF) $\mathbf{WH} = \text{nmf}(\mathbf{X})$ of the $\mathbf{X}$(abstracts $\times$ words) matrix into the $\mathbf{W}$(abstracts $\times K$) and $\mathbf{H}(K \times$ words) matrices, where K is the number of components. Each row represents one run of NMF with a specific number of components (e.g., the 5th row is for $K = 5$). The nodes indicated by yellow dots represent each a specific component for a specific K. The words at the nodes are the highest scoring words on the components of $\mathbf{H}$ representing the most typical words for this component. The thickness of the lines between the nodes corresponds to the similarity between the components. Only the lines where the similarity is high are shown. The size of the dots indicates the fraction of documents assigned to the component. The tree with the root in $(1, 1)$ shows that memory from one cluster ($K = 1$) to 12 clusters ($K = 12$) is a dominant theme, and as more components are added it is modeled by several components. The words showing the highest association with the component are "retrieval", "episodic" and "memory".