

The retrosplenial contribution to human navigation: A review of lesion and neuroimaging findings

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The clinical and neuroimaging literatures are surveyed in order to collate for the first time the available data on retrosplenial involvement in human navigation. Several notable features emerge from consideration of the case reports of relatively pure topographical disorientation in the presence of a retrosplenial lesion. The majority of cases follow damage to the right retrosplenial cortex, with Brodmann's area 30 apparently compromised in most cases. All patients displayed impaired learning of new routes, and defective navigation in familiar environments complaining they could not use preserved landmark recognition to aid orientation. The deficit generally resolved within eight weeks of onset. The majority of functional neuroimaging studies involving navigation or orientation in large-scale space also activate the retrosplenial cortex, usually bilaterally, with good concordance in the locations of the voxel of peak activation across studies, again with Brodmann's area 30 featuring prominently. While there is strong evidence for right medial temporal lobe involvement in navigation, it now seems that the inputs the hippocampus and related structures receive from and convey to right retrosplenial cortex have a similar spatial preference, while the left medial temporal and left retrosplenial cortices seem primarily concerned with more general aspects of episodic memory.

Key words: Human, navigation, PET, fMRI, retrosplenial, BA 30

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BACKGROUND: ANATOMY

Often eclipsed by some of its more celebrated neighbours such as the hippocampus, the retrosplenial cortex has nevertheless maintained its standing as one of the key brain regions classically comprising the limbic system. It is part of the cingulate cortex, an anatomically and functionally heterogeneous structure (Vogt *et al.*, 1992). Forming a ring around the corpus callosum, the cingulate is typically subdivided into the anterior and posterior cingulate cortices, the latter being of interest in this review. The posterior cingulate gyrus in turn has two major sub-divisions, the retrosplenial cortex and the cingulate cortex (Morris *et al.*, 2000). In both the human and macaque monkey brain, retrosplenial cortex runs as an arch around the splenium of the corpus callosum. Morris *et al.* (2000) have recently shown that while the dorsal component of the retrosplenial cortex in humans is confined within the callosal fissure as with monkeys, the posteroventral component extends onto the surface of the medial hemisphere to encompass most of the cortical region often referred to as the isthmus of the cingulate gyrus. The cytoarchitecture of parts of the retrosplenial cortex have been amply studied (e.g., Brodmann, 1909; Economo, 1929; Braak, 1979; Vogt *et al.*, 1995; Morris *et al.*, 1999a; Kobayashi & Amaral, 2000; Morris *et al.*, 2000). The focus here is on two areas within the posteroventral retrosplenial region labelled by Brodmann as areas 29 and 30—see Fig. 1. These areas maintain their topographical relationship with one another around the splenium as far as the calcarine fissure. Area 29 is composed of densely packed

granular areas 29a–c, containing small to medium pyramidal neurons below a thick layer I (Vogt, 1976), while 29d includes a layer of loosely packed pyramidal neurons interposed between layers I and III. Area 30 is agranular/dysgranular, the lateral part of area 30 possessing an incipient layer III-IV, whereas its medial aspect is agranular, thus reflecting the transitional nature of cortex in this region (Economo, 1929; Vogt, 1976; Morris *et al.*, 2000).

The connectivity of retrosplenial cortex has been investigated in the monkey brain. The major reciprocal connections are between area 30 and mid-dorsolateral prefrontal

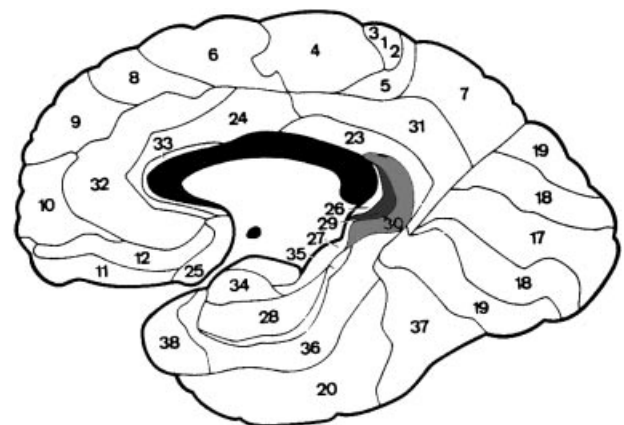


Fig. 1. A schematic representation of Brodmann's cytoarchitectonic areas of the human brain (1909) with the areas of interest—areas 29 and 30—shaded.

cortex (areas 46, 9/46 and 9) (Goldman-Rakic *et al.*, 1984; Morris *et al.*, 1999b; Kobayashi & Amaral, 2000), parahippocampal cortical areas TH and TF (Suzuki & Amaral, 1994), as well as presubiculum and entorhinal cortex. Indeed the second largest source of cortical input into the entorhinal cortex is the retrosplenial cortex, contributing nearly 20% of cortical inputs (Van Hoesen & Pandya, 1975; Insausti *et al.*, 1987). There are further connections with superior temporal sulcus and posterior parietal cortex (Morris *et al.*, 1999b), as well as with lateroposterior, laterodorsal and anterior thalamic nuclei (Amaral & Cowan, 1980). Thus the retrosplenial cortex is exceptionally well-placed to contribute to the medial temporal lobe memory system as well as being a route through which prefrontal regions might interact with limbic areas.

BACKGROUND: FUNCTION

Despite accumulating knowledge about its cytoarchitecture and connectivity, very little is known about the precise function of the human retrosplenial cortex. Recently it has been proposed that the retrosplenial cortex plays a prominent role in the processing of emotionally salient stimuli (Maddock, 1999). This claim was made on the basis of a meta-analysis of functional neuroimaging studies of emotion where activations were recorded in various parts of the posterior cingulate and retrosplenial cortices. While undoubtedly these areas were active, the nature of neuroimaging data generally does not allow one to conclude the importance of an area for a cognitive process. Simply put, just because an area activates does not mean it is necessary for the performance of that task. In order to address this issue, functional neuroimaging data must be examined in conjunction with neuropsychological or indeed neuroimaging studies of patients (see Price *et al.*, 1999; Price & Friston, 1999). In the case of retrosplenial cortex, it is clear that patients with lesions primarily involving the retrosplenial region are not notable for emotion-related deficits, but rather for significant memory problems (e.g., Valenstein *et al.*, 1987; Bowers *et al.*, 1988; Rudge & Warrington, 1991; Takayama *et al.*, 1991; Katai *et al.*, 1992; Arita *et al.*, 1995; Masuo *et al.*, 1999), a similar point has also been made by Vogt *et al.* (2000). That lesions of the retrosplenial cortex can give rise to memory problems, and in some cases amnesia, highlights its close anatomical links with the medial temporal region and points to a crucial role in memory processing.

Maddock (1999) concedes (p. 313) that other, non-emotional, characteristics of experimental conditions may have contributed to the retrosplenial activations observed in many of the studies he examined in his meta-analysis. Concordant with this and with the patient data alluded to above, the retrosplenial cortex is frequently activated during neuroimaging studies of memory (e.g., Fletcher *et al.*, 1995; Maguire *et al.*, 1999a; Maguire & Mummery, 1999; Wiggs *et*

al., 1999; Maguire *et al.*, 2000; Maguire *et al.* in press). Despite the frequency with which it activates, there is as yet no coherent framework within which to understand the contribution it makes to memory processing.

One potentially significant point (noted also by Kobayashi & Amaral, 2000) in relation to patients with retrosplenial amnesia is that most have either bilateral (e.g., Arita *et al.*, 1995; cases 3–9 Rudge & Warrington, 1991) or unilateral *left* retrosplenial lesions (e.g., Valenstein *et al.*, 1987; cases 1 and 2 Rudge & Warrington, 1991; Takayama *et al.*, 1991; Katai *et al.*, 1992; Von Cramon & Schuri, 1992; Kasahata *et al.*, 1994; Gainotti *et al.*, 1998) (although see Masuo *et al.*, 1999 for amnesia after right-sided lesion). Episodic memory (Tulving, 1983), that is the ability to remember the events of daily life, is typically compromised in these patients. It may be that the left retrosplenial region in particular contributes to aspects of episodic memory. Evidence is emerging that the left human hippocampus may also show a preference for episodic, specifically autobiographical event memory (Maguire in press A). Hippocampal activity, particularly on the left, has been found to increase particularly during retrieval of such memories (Maguire & Mummery, 1999; Maguire *et al.*, 2000; Maguire *et al.* in press), as well as during the retrieval of aspects of personally experienced events in a virtual reality environment (Burgess *et al.* in press). Activation of the left hippocampus has also been noted in neuroimaging studies of navigation (Ghaem *et al.*, 1997; Maguire *et al.*, 1998a; Grön *et al.*, 2000), but this activity was not found to correlate with any navigation measures, unlike right hippocampal activity (see below). Neuropsychological testing of patients has also revealed that patients with lesions in the left medial temporal lobe rather than to the right, were impaired on remembering aspects of personally experienced events (Spiers *et al.* submitted). This suggests that the left hippocampus may be preferentially (but not necessarily exclusively) involved in non-navigation aspects of episodic memory. It may be that the inputs to the medial temporal regions are similarly specialised at the level of the retrosplenial cortex and hence episodic memory deficits are more apparent following left retrosplenial lesions. The nature of the interface between navigation and more general aspects of episodic memory, and the anatomy supporting them remains to be understood (see Maguire, in press A; Maguire in press B; Burgess *et al.* in press; Spiers *et al.* submitted).

NAVIGATION

As noted above, in contrast to the left, the right medial temporal region has been strongly implicated in topographical orientation or spatial navigation from functional neuroimaging (e.g., Aguirre *et al.*, 1996; Ghaem *et al.*, 1997; Maguire *et al.*, 1997; Maguire *et al.*, 1998a; Maguire *et al.*, 1999b; Grön *et al.*, 2000), structural neuroimaging (Maguire *et al.*, 2000) and neuropsychological cases (e.g., Habib &

Sirigu, 1987; Bohbot *et al.*, 1998; Luzzi *et al.*, 2000; Spiers *et al.* submitted). Activity in the right hippocampus in particular has been shown to correlate with the accuracy of the path taken to goal destinations in a virtual reality town (Maguire *et al.*, 1998a), while the right parahippocampal gyrus is most active during the memory for landmarks (Maguire *et al.*, 1998b; Mellet *et al.*, 2000). While accepting that the right human hippocampus is not exclusively concerned with navigation, way-finding does seem to be one of its major concerns, paralleling the (bilateral) role of the hippocampus in other animals. It has been suggested that the use of spatial context in episodic recollection might explain how the role of the hippocampus in spatial memory in rats has evolved into a role in more general episodic recall in humans (O'Keefe & Nadel, 1978), and this may be reflected in a divergence of function of the left hippocampus from the right (see also Maguire *et al.*, 1998a; Burgess *et al.*, 1999; Maguire, in press B).

Given the propensity for episodic memory deficits following left temporal and left retrosplenial lesions, and for navigation deficits following right medial temporal lesions, one is led to ask whether damage primarily involving the right retrosplenial cortex results in topographical disorientation. Another question is whether the retrosplenial region is activated during functional neuroimaging studies that involve navigation or orienting in large-scale space, and what kind of concordance is there in the location of such activations across studies. Finally, is there concordance between the location of neuroimaging activations and lesion locations?

REVIEW OF PATIENT CASES

In the context of retrosplenial amnesia, navigation deficits are occasionally reported (Iwasaki *et al.*, 1993; Sato *et al.*, 1998; Yasuda *et al.*, 1997) although it is difficult to discern the prevalence of these deficits in amnesic cases as navigation is often not mentioned and perhaps not tested. In order to probe navigation in particular, I have reviewed the published literature, and Table 1 presents together for the first time all known cases where topographical disorientation is the principal deficit in the context of lesions primarily involving the retrosplenial region (i.e., with intact medial temporal areas). Only cases where the lesion location was verified using modern structural scanning methods (CT or MRI) were included. Thus early cases (e.g., Meyer, 1900; Landis *et al.*, 1986; see also Farrell, 1996; Aguirre *et al.*, 1998a; Barrash, 1998; Aguirre & D'Esposito, 1999 for further details of other cases) may have had a similar deficit but lesions were not verifiable and the broad neuropsychological profile of many of the patients was not reported/tested. Another recent study looking at navigation in patients was not included (Barrash *et al.*, 2000) as retrosplenial cortex lesions were not explicitly mentioned/examined. None of the included patients had

significant and persistent memory problems. In about half of the patients some visual memory deficits were apparent early in the course, but typically these quickly resolved leaving the main outstanding deficit as impaired navigation. In the other cases, patients were noted to retain deficits on one or two visual memory tests. All patients were largely intact on a range of basic neuropsychological tests of language, attention, perception and executive function. Basic patient details and the description of the navigation deficit are also presented on Table 1. I will first highlight some significant features, whose relevance will be considered in the Discussion section.

Ten cases of relatively pure topographical disorientation following retrosplenial lesions were identified in the literature. Several interesting features emerge when they are considered collectively. Firstly, in eight out of the ten cases the lesion was located in the right retrosplenial region. This fits with the pattern outlined above of right lateralisation of navigation. Having detailed the strong evidence for right medial temporal involvement in navigation, it now seems that the inputs the hippocampus and related structures receive from and convey to right retrosplenial cortex are similarly spatial (while the left medial temporal and left retrosplenial cortices seem primarily concerned with episodic memory). Only in the case of Obi *et al.* (1992) and case three of Alsaadi *et al.* (2000) did disorientation follow left retrosplenial lesions. Examination of the reported details of these two cases does not reveal any discernible features to distinguish them from the other eight cases. Takahashi and Kawamura (1995) present cartoons of the lesion locations in four cases of relatively pure topographical disorientation following retrosplenial lesions (details of precisely which of the cases from Table 1 these cartoons refer to could not be clearly discerned from their report). In Fig. 2, I present these lesion locations outlined on a structural MRI scan. The area of overlap in these four representative cases is Brodmann area 30 on the right.

Another striking feature of the ten cases is the similarity in the characterisation of the navigation deficit. In every case, the patient was able to recognise the landmarks in their neighbourhoods and retained a sense of familiarity. In several cases it is noted that they were even able to describe specific places in detail and the activities that occur there. Despite this, none of the patients was able to find his/her way in familiar environments, and all but one was unable to learn new routes. One patient was able to learn a simple route in hospital (Cammalleri *et al.*, 1996), although they do not report if this was possible outside of the hospital. Most could not draw maps nor describe routes in detail. The typical description of the problem was that the patients could not use the preserved recognition of landmarks in order to proceed, they could not orient, they did not know which direction to take. This was in the context of intact general memory and visuo-spatial perception.

Table 1. Cases where topographical disorientation is the principal deficit following damage limited primarily to retrosplenial cortex

Study	Patient details	Aetiology	Lesion location	Nature of topographical deficit	Duration	Other deficits
Bottini <i>et al.</i> (1990)	72 years, RH, male, former clergyman	glioblastoma	CT confirmed bilateral median and R paramedian hypodense lesion centred on the splenium of the corpus callosum	Not able to draw or describe well-known routes, able to recognise photographs of buildings from the city. Not able to find his way in hospital, not able to indicate direction from his room to exam room.	death one month after admission	verbal recall, supraspan spatial learning, constructional apraxia, geographical knowledge, mental rotation
Obi <i>et al.</i> (1992)	59 years, RH, male	infarction	MRI confirmed abnormal intensity in left medial parieto-occipital region and left splenium of the corpus callosum	Not able to recall relative positions of landmarks, but could recognise them, and name places and describe the area. Could not describe routes in his own house, nor draw maps of its layout. Not able to find his way in hospital.	still there at 60 days when testing finished	all resolved quickly except topographical deficit
Cammalleri <i>et al.</i> (1996)	53 years, RH, male, town clerk	angioma	MRI confirmed area of increased signal in the right cingulate gyrus with compression of the corpus callosum. Lesion at border of areas 24/23 and retrosplenial areas 29/30	Several transient attacks (5–10 mins) where his village was familiar to him but he could not orient. Then a similar episode of longer duration. Able to find way in hospital. Able to draw streets of village.	short-lived episodes	supraspan spatial learning
Takahashi <i>et al.</i> (1997) 3 cases; see also Takahashi & Kawamura (1995)	54 years, RH, male food industry worker	focal haemorrhage	MRI confirmed high signal in R retrosplenial region, extending into inferior precuneus	Home town buildings familiar but not able to orient. In hospital not able to find his way. Could not draw map of his town, nor place landmarks on a map. Could not recall routes.	3 weeks	Benton Visual Retention Test
	55, RH, male taxi driver (reported also in Shiota & Kawamura, 1995)	focal haemorrhage	MRI confirmed high signal in R retrosplenial region, extending into inferior precuneus	Able to recognise buildings and landscapes of home city but not able to determine the direction to proceed. Could not place landmarks on a map. Not able to recall routes.	one month	Benton Visual Retention Test, Rey figure immediate and delayed recall

61 years, RH, male, general store worker	focal haemorrhage	CT confirmed high density area in sub-cortical white matter extending into R retrosplenial region and medial parietal area	Lost the ability to know what direction to travel in. In hospital could not find his way. Able to place landmarks on a map. Could not recall routes. Not able to draw map of the hospital interior.	two months	none reported
Suzuki <i>et al.</i> (1998)	70 years, RH, female, retired teacher	haemorrhage	MRI confirmed lesion in right medial parietal lobe mainly in precuneus, and impinging on cuneus, and (from visual inspection of figures) anteriorly into retrosplenial region. Lacunae in deep white matter bilaterally	two months	none lasting
Katayama <i>et al.</i> (1999)	82 years, RH, female	infarction	MRI confirmed lesion of isthms of the R posterior cingulum and R lateral thalamus	ongoing?	constructional apraxia, Benton Visual Memory Test, Rey figure immediate and delayed recall, table-top object location, maze, mental rotation
Alsaadi <i>et al.</i> (2000)	75 years, RH, male practising lawyer (case 1)	infarct	CT confirmed small infarct affecting R splenium and cuneus	several months, then carcinoma developed and global disorientation followed	none reported
	62 years, RH, male (case 3)	infarct	MRI confirmed infarction of the L splenium	resolved by two months later	none reported

RH = right-handed

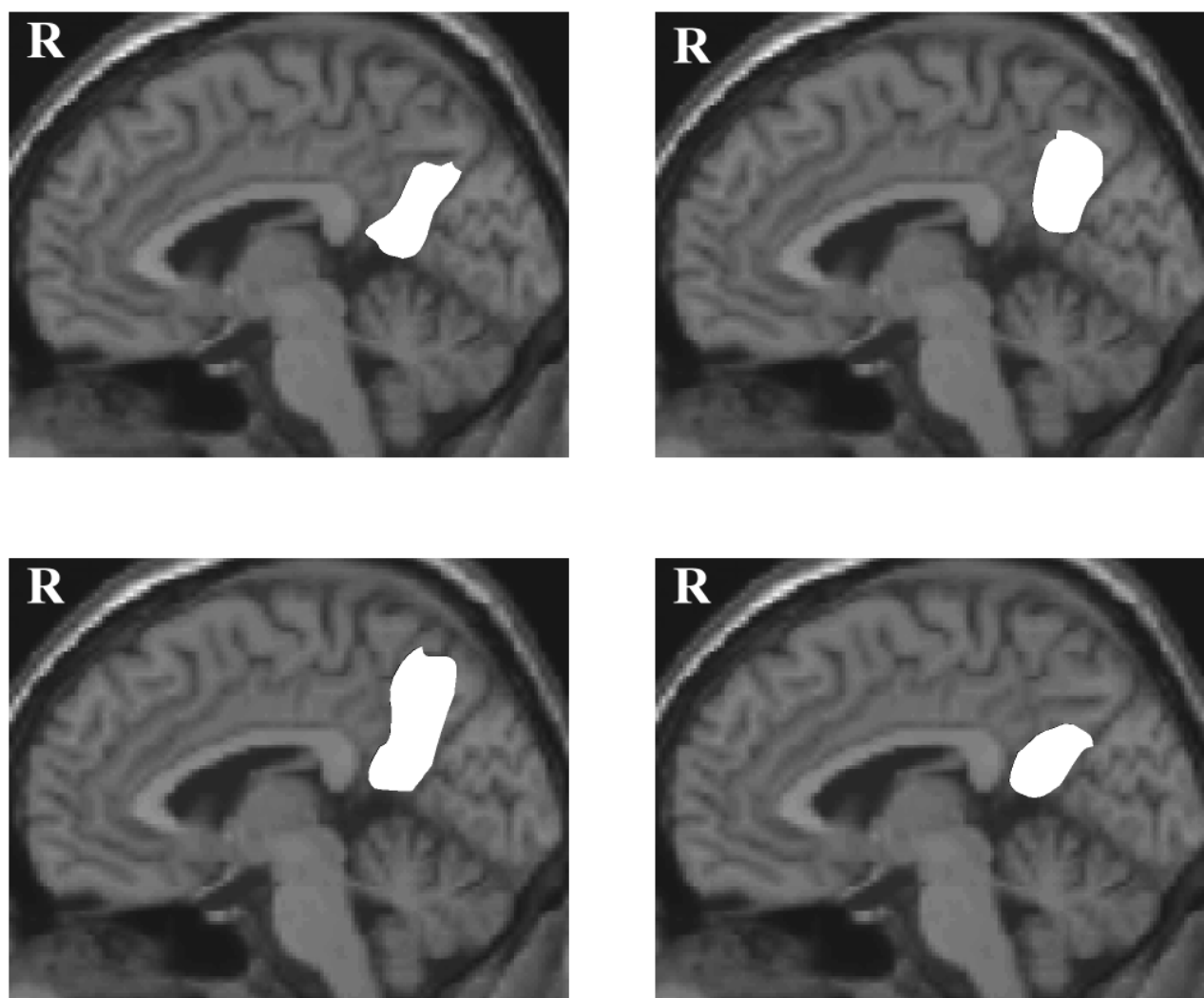


Fig. 2. Outline of the lesions of four patients with topographical disorientation shown here on a structural MRI scan (presented originally in Fig. 4 of Takahashi & Kawamura, 1995 in cartoon fashion).

The final feature of these cases that will be highlighted here is the duration of the deficit. In contrast to many cases of topographical disorientation following medial temporal lesions (see Farrell, 1996; Aguirre & D'Esposito, 1999), in six of the eight cases where this is relevant (i.e., where the patient did not die or deteriorate medically) the disorientation had resolved itself by 3–8 weeks following initial onset (in the other two relevant cases the duration could not be discerned from the reports). Thus, the impaired navigation of patients following damage to the right retrosplenial region was not a permanent deficit and could apparently be overcome.

REVIEW OF FUNCTIONAL NEUROIMAGING STUDIES

Having examined the cases of topographical disorientation following lesions to the retrosplenial cortex, I present

together for the first time all of the functional neuroimaging studies currently identified in the literature and known to the author where navigation or orienting in large-scale space has been involved—see Table 2. The use of film footage, virtual reality paradigms and the like (see descriptions on Table 2) has facilitated the examination of the dynamic process of navigation within the constrained environment of brain scanners, typically PET (positron emission tomography) and fMRI (functional magnetic resonance imaging). I only include those studies where large-scale space is involved—not table-top spatial tasks of the kind reported by Charlot *et al.* (1992), Owen *et al.* (1996), Flitman *et al.* (1997), Aguirre *et al.* (1998b) and Johnsrude *et al.* (1999). I also report the voxel of peak activation while accepting that in many cases the activations were bilateral. It is also important to note that this is not a formal meta-analysis, but rather a descriptive survey. Thus, while all of the coordinates given are in terms of Talairach and Tournoux (1988)

Table 2. Functional neuroimaging experiments involving navigating/orienting in large-scale space: voxels of peak activation in retrosplenial cortex

Study	Modality	Experimental context	Contrast	Peak coordinates	Encoding/context *
Roland & Friberg (1985)	PET	Imagine walking out your front door, walk alternatively left and right around the corners you encounter. Focus on surroundings and not on street names.	route vs: rest/jingle thinking/subtraction	none given, medial aspect not mentioned	ret
Roland <i>et al.</i> (1987)	PET	as above	as above	none given, mentions superior-parietal-posterior-medial area	ret
Aguirre <i>et al.</i> (1996) **	fMRI	VR simple maze, first person 3D five objects present, active navigation	free exploration vs. repetitive traversal of simple corridor (effects of learning and retrieval similar)	-15, -55, 9 ^L -15, -67, 12	both
Maguire <i>et al.</i> (1996)	PET	Passive viewing of film footage showing navigation along two routes, shown one after another, actively encode so could find way. Post-scan scene recognition testing.	More activity the less good the post-scan test performance	-12, -52, 20 ^L	enc
Aguirre & D'Esposito (1997)	fMRI	VR town, 16 places, exploration prior to scanning, place names highlighted by experimenter. Pictures shown during scanning, name-place association task and cardinal direction of target task. Scrambled stimuli as control.	association vs control direction vs control	none given but posterior cingulate described in the text and shown in their Fig. 4B	ret
Ghaem <i>et al.</i> (1997)	PET	Physical navigation of route one day prior to scanning, 7 landmarks pointed out to subjects. During scanning, mentally traverse the route, or visualisation of the landmarks.	route recall vs rest landmark recall vs rest	-14, -54, 8 ^L 14, -56, 8 ^R 18, -54, 16	ret

(continued)

Table 2 Continued

Study	Modality	Experimental context	Contrast	Peak coordinates	Encoding/ context *
Maguire <i>et al.</i> (1997)	PET	Licensed London taxi drivers recalled out loud complex routes around the city, eyes closed. Also recalled and described famous landmarks. Memory and sequencing control was the recall of film plots, and static memory control was film scenes. Baseline task was number repetition.	routes vs control landmarks vs control topographical (routes + landmarks) vs non-top (film plots + scenes) interaction: more for sequencing in topographical memory	-14, -60, 26 ^L 14, -52, 20 ^R 18, -60, 18 ^R 16, -58, 18 ^R	ret
Maguire <i>et al.</i> (1998b)	PET	VR 5 arm maze-like environment with an object in each arm. Active navigation, instruction to explore and memorise.	more active during "free" exploration vs. systematic "left/right" strategy of exploration	18, -26, 28 ^R	enc
Maguire <i>et al.</i> (1998a)	PET	VR complex town explored prior to scanning. Navigation during scanning to places in the town as learned, or with introduced barriers forcing detours, or non-memory follow a route of arrows, or static feature detection in scenes from the town.	all conditions with movement vs static control (sub-threshold) navigation (as learned + detours) vs follow arrows	2, -54, 22 ^R -4, -52, 22 ^L	ret
Epstein <i>et al.</i> (1999)	fMRI	Experiment 3. Viewing of photograph sequences taken with a moving camera through an environment, reportedly giving a vivid sense of forward motion. Other task was viewing a series of unrelated photographs.	movie vs unrelated	region of interest analysis, only parahippocampal region studied	enc

Grön <i>et al.</i> (2000)	fMRI	VR simple maze, active navigation, 6 wall elements of different colour/textures served as landmarks. Male and female subjects. Static control-attention task.	group: navigation vs control males: navigation vs control females: navigation vs control	-16, -54, 18 ^{6L} 18, -52, 16 ^{7R} -8, -48, 10 20, -56, 18 -18, -52, 18 18, -48, 14	enc
Mellet <i>et al.</i> (2000)	PET	Re-analysis of Ghaem data (see above). Also new data where subjects learned an environment from a map presented via slides.	routes vs rest	-12, -46, 28 ^{8L} -30, -64, 6 24, -68, 24 16, -56, 12 ^{8R} -12, -46, 28 ^{8L}	ret
Pine <i>et al.</i> (submitted)	fMRI	VR complex town adapted from that employed by Maguire <i>et al.</i> (1998b) for use with adults and adolescents. Navigation success scored during scanning, and allocentric ability measured post-scanning with landmark location on a map.	routes vs map the effect of a combination of adolescence and poorer allocentric ability on the navigation vs arrows contrast	-4, -42, 42 ^{9L}	ret
Burgess <i>et al.</i> (in press)	e-fMRI	VR complex town adapted from Maguire <i>et al.</i> (1998b). The town is used as the real-world context where events are experienced by subjects prior to scanning—certain people giving them objects in certain places, and a visual control task. Subjects were scanned during retrieval of aspects of the events.	place vs control person vs control place vs person place vs object object vs control	-15, -60, 18 ^{10L} 18, -69, 24 ^{9R} 15, 68, 27 ^{10R} -15, -60, 18 ^{11L} -12, -54, 9 ^{12R} 32, -54, 6 ^{11R} -9, -45, 6 ^{13L} 12, -48, 6 ^{12R} -15, -66, 21 -15, -57, 15 ^{14L} 15, -54, 12 ^{13R} 18, -63, 24	ret

* The primary process being examined is noted, although in real-world tasks such as these, encoding and retrieval probably have an ongoing dynamic interaction.

** In this study, two other activations are noted as being in posterior cingulate cortex, however, they were judged here as cuneus (-3, -70, 9; 4, -70, 9).

1-14L The main peaks of activation in left retrosplenial cortex are plotted on a structural MRI scan in Talairach & Tournoux (1988) coordinates on Fig. 1.

1-13R The main peaks of activation in right retrosplenial cortex are plotted on a structural MRI scan in Talairach & Tournoux (1988) coordinates on Fig. 1.

VR = virtual reality; e-fMRI = event-related fMRI.

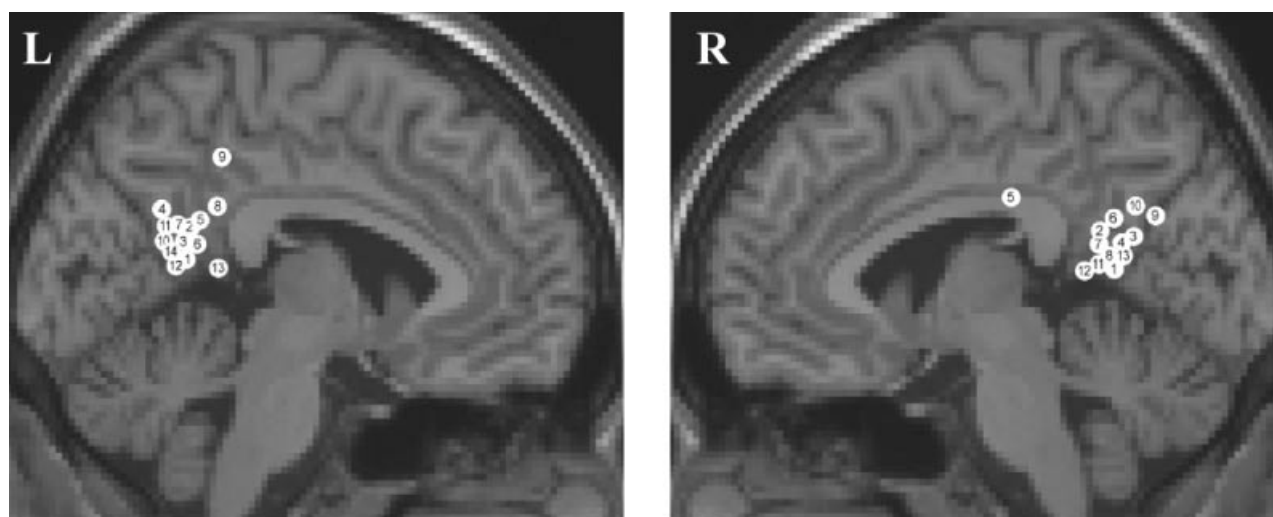


Fig. 3. The approximate locations of the main peak activations from the studies listed on Table 2 (see superscripts attached to coordinates for key), shown on a structural MRI scan in stereotactic space (see caveats in the text). While the Talairach and Tournoux (1988) coordinate system is used, their atlas was not, as labelling of the retrosplenial area is not correct (see Vogt *et al.*, 2000). The locations were labelled with reference to Brodmann (1909) and Duvernoy (1999).

stereotactic space, and many studies used Statistical Parametric Mapping (SPM—Wellcome Department of Cognitive Neurology, London, UK) for data analysis, some did not and additionally the brain templates used in normalisation differed across studies. The amount of smoothing applied also differed, with the average smoothing across studies being 13 mm. Notwithstanding these differences, it was still felt worthwhile to examine the relevant studies in a descriptive manner. Fig. 3 presents the approximate locations of many of the peak activations on a structural MRI scan in stereotactic space, shown for clarity on a medial view (i.e., this does not reflect any variations medio-laterally). Once again, given the constraints outlined above, this is an approximation. As before, salient features will be highlighted and then considered in the Discussion section.

Fourteen functional neuroimaging studies involving navigation or orientation in large-scale space were identified in the literature or are known to the author. In Table 2 the general experimental context and the specific contrasts where retrosplenial activations were observed are described, and in most of the recent studies coordinates are given. Excepting the two early studies from the 1980's where it is not clear from the reports (Roland & Friberg, 1985; Roland *et al.*, 1987), in all of the studies where the whole brain was scanned, the retrosplenial cortex was activated, in most cases bilaterally. Examination of the coordinates on Table 2 and the approximate plots on Fig. 3 reveals a striking concordance in the locations of peak activation across studies. The activations, in so far as they can be compared in this descriptive way, seem to lie largely in Brodmann's area 30. The two outliers, 9L and 5R, may, from the contrast descriptions, represent processes slightly different to those tapped in the other studies. In all other cases, the

retrosplenial activations were noted when active navigation was compared with a control condition. This control condition was sometimes but not always static. For example, in the case of Aguirre *et al.* (1996—1L) and Maguire *et al.* (1998a—5L) control conditions also involved movement through an environment. Neither is it the case that the retrosplenial activations are merely an index of memory *per se*. In several of the studies the topographical memory conditions were compared with non-navigation/non-spatial memory conditions, and enhanced activity in retrosplenial cortex was apparent for navigation/space (Mellet *et al.*, 2000—8L; Burgess *et al.* in press—12L, 11 R).

DISCUSSION

This is the first attempt to survey the clinical and neuroimaging literature in order to better understand the relationship between the retrosplenial cortex and navigation in humans. The nature of lesion data and the spatial resolution of neuroimaging techniques preclude the fine-grained anatomical distinctions noted at the outset. However, in this survey an impressive concordance emerged across techniques suggesting that Brodmann's area 30 on the right is significantly involved in navigation in humans. The complimentary use of both neuroimaging data *and* patients with the relevant deficits strengthens conclusions that can be drawn about the role of a region in a particular cognitive process beyond either technique in isolation (cf. Maddock, 1999). In this regard, the neuroimaging data alone suggest bilateral retrosplenial contributions to navigation, however, the patient data suggest that only those activations on the right are necessary. It might be that the left retrosplenium is contributing constructively to navigation (via some general

episodic memory input?), but perhaps this is not absolutely crucial. Given, however, that in most cases of right-sided damage the disorientation resolved within eight weeks, it is clear that while this region is involved in the normal scheme of things, its loss can be circumvented. It is possible that its duties are assumed by the left retrosplenial cortex, given that it also seems to have a significant role in memory, albeit not a specifically spatial one.

What is occurring in the right retrosplenial cortex during navigation? The contrasts where the retrosplenial cortex activation increases in neuroimaging studies are as yet too general to permit strong conclusions. However, the nature of the deficit in the patients may give a clue. As observed by Aguirre & D'Esposito (1999), patients seem to have lost their "heading" within the environment. Head direction cells—cells that fire when rats are maintaining a certain heading or orientation within an environment (Ranck, 1984; Taube, 1998)—are numerous in structures such as the anterior dorsal nucleus of the thalamus and presubiculum. However, Chen *et al.* (1994) have identified a small population (about 8%) of head direction cells in rodent retrosplenial cortex. It may be that the retrosplenial cortex represents the transition zone between egocentric/vestibular inputs from areas such as posterior parietal cortex, and head direction and ultimately allocentric processes in the medial temporal region, given its strong anatomical links with both (Vogt *et al.*, 1992; Aguirre & D'Esposito, 1999).

While a number of studies found lesions which included the retrosplenial cortex to impair spatial navigation in rats (Sutherland *et al.*, 1988; Markowska *et al.*, 1989; Sutherland & Hoising, 1993; Cooper & Mizumori, 1999), other studies have failed to find similar impairments in rats (Neave *et al.*, 1994; Aggleton *et al.*, 1995; Warburton *et al.*, 1998) and monkeys (Murray *et al.*, 1989; Parker & Gaffan, 1997). However, as Aggleton *et al.* (2000) note, the rat retrosplenial cortex is very extensive and in all published cases the most caudal portion was spared. Perhaps it is this area that is homologous to area 30 in humans. Aggleton *et al.* (2000) report some unpublished data (from Vann) where lesions were made to include the caudal region. Spatial navigation deficits now emerged, although they note that these were milder than those observed following hippocampal lesions. Perhaps this might have some parallel with the finding in humans of navigation deficits resolving after several weeks. More work is needed to explore this possibility in rodents and non-human primates.

The intention of this brief review was to collate and present for the first time the available data on retrosplenial involvement in human navigation. Several notable features have emerged, as has a good concordance both between patients, between neuroimaging studies, and across the two techniques. The conclusions about the precise contribution of the retrosplenial cortex to navigation that can be drawn are as yet limited. However, future neuroimaging work will hopefully refine navigation tasks to specifically target

possible functions of this region, e.g., in terms of heading direction, etc. It might also be useful to consider the contrasts where retrosplenial activation did *not* emerge for further clues. More detailed testing of patients, once the main topographical deficit has resolved, might also reveal subtle deficits not circumvented by newly-recruited regions (paralleling the residual extinction observed in neglect patients following recovery). Finally, it would be very interesting to scan patients using functional neuroimaging during the course of their deficit and recovery to note any plasticity in the anatomy underlying navigation.

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