

# Speech production: Wernicke, Broca and beyond

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## Summary

We investigated the brain systems engaged during propositional speech (PrSp) and two forms of non-propositional speech (NPrSp): counting and reciting overlearned nursery rhymes. Bilateral cerebral and cerebellar regions were involved in the motor act of articulation, irrespective of the type of speech. Three additional, left-lateralized regions, adjacent to the Sylvian sulcus, were activated in common: the most posterior part of the supratemporal plane, the lateral part of the pars opercularis in the posterior inferior frontal gyrus and the anterior insula. Therefore, both NPrSp and PrSp were dependent on the same discrete subregions of the anatomically ill-defined areas of Wernicke and Broca. PrSp was also dependent on a predominantly left-lateralized neural system distributed between multi-modal and amodal regions in posterior

inferior parietal, anterolateral and medial temporal and medial prefrontal cortex. The lateral prefrontal and paracingulate cortical activity observed in previous studies of cued word retrieval was not seen with either NPrSp or PrSp, demonstrating that normal brain-language representations cannot be inferred from explicit metalinguistic tasks. The evidence from this study indicates that normal communicative speech is dependent on a number of left hemisphere regions remote from the classic language areas of Wernicke and Broca. Destruction or disconnection of discrete left extrasylvian and perisylvian cortical regions, rather than the total extent of damage to perisylvian cortex, will account for the qualitative and quantitative differences in the impaired speech production observed in aphasic stroke patients.

**Keywords:** Broca's area; functional neuroimaging; medial prefrontal cortex; propositional speech; Wernicke's area

**Abbreviations:** ASL = American Sign Language; Ct = counting forwards; NG = noun generation; NPrSp = non-propositional speech; PrSp = propositional speech; Rh = nursery rhymes; Rt = rest scan; SMA = supplementary motor area; VG = verb generation; XSp = non-speech condition

## Introduction

Clinical studies of patients with aphasia, usually as the result of a stroke, have been used to infer normal language processes and their location (e.g. McCarthy and Warrington, 1990). Emphasis has been placed on left perisylvian cortex: less interest has been taken in the white matter tract damage that inevitably accompanies strokes except in the instance of conduction aphasia. While the role of 'disconnection' was revived over three decades ago (Geschwind, 1965), imaging tract degeneration (Basser *et al.*, 2000) is technically demanding and is not performed routinely. By default, functions impaired by the stroke are often attributed to local cortical damage and not to disconnection of intact cortical regions remote from the lesion.

This study on normal subjects used functional neuroimaging to identify the distributed brain regions used to

convey novel information through speech. It addressed two issues. The first was to establish the precise location of regions involved in speech production within the ill-defined boundaries of the classic language areas of Wernicke and Broca. The second was to determine the distribution and extent of other regions active during speech that are remote from classic language cortex but vulnerable to disconnection by perisylvian white matter damage.

Propositional speech (PrSp) begins as the formulation of a message, either self-initiated or in response to a question (Levelt, 1989). The product is a novel expression that integrates lexical, semantic and episodic (autobiographical) memories. Non-propositional speech (NPrSp), from counting to the recitation of overlearned rhymes, is also reliant on processes involved with word retrieval and, in the case of

rhymes, long-term memories of lines of verse. It does not, however, require the conceptual processing underlying PrSp, nor does it place the same demands on semantic and episodic memory.

It was predicted, therefore, that PrSp would activate a distributed, high-order neural system for the formulation of a message based on personal and semantic memories. In contrast, the prediction was that both NPrSp and PrSp would show lower-order systems predominantly associated with retrieval of words and phrases, the motor act of speech and the post-articulatory self-monitoring of speech output (Levelt, 1989).

There was the opportunity to address a third issue, namely the value of explicit metalinguistic tasks, widely used in functional neuroimaging, in the study of normal brain-language relationships (for example Buckner *et al.*, 1995; Warburton *et al.*, 1996; Lehericy *et al.*, 2000). Cued word retrieval (verbal fluency), is associated with increased activity in left lateral premotor and prefrontal cortex and paracingulate cortex (Raichle *et al.*, 1994; Herholz *et al.*, 1996; Warburton *et al.*, 1996). However, the task places demands on working memory and executive functions, and it is used by clinical neuropsychologists to study left prefrontal function in the *absence* of aphasia (McCarthy and Warrington, 1990). The implication is, therefore, that cued word retrieval recruits frontal systems not involved in everyday speech. Direct comparison of the results from this study with those from a previously published study of verbal fluency (Warburton *et al.*, 1996) allowed us to compare the distributed neural systems associated with normal speech and verbal fluency.

## Material and methods

### Experiment 1

#### Subjects

Eight right handed, normal volunteers were studied. Each gave informed consent. The studies were approved by the Administration of Radioactive Substances Advisory Committee (Department of Health, UK) and the Hammersmith, Queen Charlotte's and Chelsea and Acton Hospitals Research Ethics Committee.

#### Tasks

As talking about oneself and one's intimates forms the bulk of everyday PrSp, subjects were asked to respond to enquiries about their personal experiences, such as '*describe where you lived as a child*' and '*tell me about your last holiday*', prompts adapted from a previous study by Burgess and Shallice (1996). There was one enquiry per scan, and the subjects continued to reminisce until the scan had been completed. In addition, they were asked to use two forms of NPrSp during separate scanning periods: counting forwards (Ct), an ordered, overlearned list of words with very limited

semantic associations and syntactical structure; and the recitation of overlearned nursery rhymes (Rh), which requires the utterance of inflexibly ordered sequences of words in phrases and sentences. The fourth task was a non-speech condition (XSp), during which the subjects neither heard nor uttered speech: an attempt was made to engage the subjects' auditory attention by instructing them to listen out for occasional, irregularly presented, pre-recorded environmental sounds, which occurred immediately before and after the period of data acquisition. Each subject had four scans per condition, pseudo-randomized to minimize time-dependent effects.

#### PET scanning

Water labelled with a positron-emitting isotope of oxygen ( $\text{H}_2^{15}\text{O}$ ) was used as tracer to demonstrate changes in regional cerebral blood flow (rCBF). Each subject's study required 16 estimations of rCBF encompassing the whole brain, made with a Siemens/CPS ECAT Exact HR++ (966) PET camera at 6-min intervals. For each scan, 5–6 mCi of  $\text{H}_2^{15}\text{O}$  was administered as a slow intravenous bolus, and the total counts per voxel during the build-up phase of radioactivity served as an estimate of CBF. Measured attenuation correction was used to correct the emission scans.

#### Analyses

The data were analysed using statistical parametric mapping (SPM), version SPM99 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). Each individual's data were realigned to remove head movements between scans, normalized into a standard stereotactic space, and smoothed using an isotropic 10 mm, full width half-maximum Gaussian kernel to account for individual variation in gyral anatomy and to improve the signal-to-noise ratio (Friston *et al.*, 1995a). Specific effects were investigated using appropriate contrasts to create statistical parametric maps of the *t*-statistic (Friston *et al.*, 1995b). An analysis of covariance with global counts as confound was used to remove the effect of global changes in perfusion across each individual's scans (Friston *et al.*, 1990). The threshold for significance was  $P < 0.05$ , corrected for analysis across the whole brain, except where stated otherwise.

Three analyses were performed. The first identified those voxels activated by all three forms of speech, PrSp and both forms of NPrSp, compared with XSp. The second analysis contrasted the two forms of NPrSp (Rh – Ct) to identify brain regions more active during the retrieval of overlearned meaningful sentences (Rh), compared with NPrSp with limited semantic content and grammatical structure (Ct). The third analysis, (PrSp – NPrSp), i.e. [PrSp – (Ct + Rh)], demonstrated regions activated by PrSp but not by either form of NPrSp.

## Experiment 2

### Subjects and tasks

Data from a previous study of verbal fluency was taken from archive and reanalysed. Six of the nine subjects, scanned on a Siemens CTI 985B PET scanner with a field-of-view limited to 11 cm in the  $z$ -plane, included planes that covered the entire frontal lobes, and the data from these subjects were used. Image manipulation was carried out as outlined above, smoothing with an isotropic 10 mm, full width half-maximum Gaussian kernel. Scans were performed during three conditions, with four scans per condition (Warburton *et al.*, 1996). In the first condition they were asked to 'empty your mind', a so-called rest scan (Rt). The second involved verb generation (VG), when the subjects had to think of as many verbs as they could, in response to a basic level, concrete noun (e.g. shirt . . . wash, iron, mend, etc.). The third condition was noun generation (NG), when the subjects had to think of basic level nouns in response to a superordinate noun (e.g. fish . . . cod, salmon, perch, etc.). The subjects did not articulate their responses in either VG or NG.

### Analyses

All scans from the two studies were entered into the SPM99 design matrix as a two-group analysis. The regional activations in the contrast of [(VG + NG) – Rt] were displayed at a threshold of  $P < 0.05$ , corrected. The resulting statistical parametric map was masked with the following contrasts from the present study: (PrSp – XSp), (XSp – PrSp), (PrSp – NPrSp) and (NPrSp – PrSp), at a threshold of  $P < 0.05$ , uncorrected ( $Z$ -score  $> 1.9$ ), excluding all voxels present in the contrast of [(VG + NG) – Rt] that lay within any of these masks. This revealed regional activations associated with verbal fluency contrasted with Rt, at a conservative threshold, that were not associated with increases or decreases in activity, even at a low threshold, between PrSp and either NPrSp or XSp. Failure to observe an activation within a region even at a low statistical threshold does not mean that this region was not involved in the particular task, albeit at a low level (in terms of net synaptic activity). However, the purpose was to determine the strong likelihood that verbal fluency, even in the absence of articulation, engages left frontal systems not required for PrSp, in accordance with the dissociation observed in some patients with frontal lesions, namely normal speech but impaired verbal fluency.

## Results

### Experiment 1

#### Behavioural data

Speech samples were recorded during all PET scans on each subject for off-line analysis. Mean syllable production rates per minute across subjects were as follows: Ct, 193.3 (SD

40.9); Rh, 202.5 (SD 27.6); PrSp, 225.1 (SD 36.8). Independent  $t$ -tests showed no significant difference between syllable production rate for Ct and Rh, but PrSp production was faster than both Ct and Rh ( $P < 0.01$ ). However this represented only a 10–15% difference in the rates of speaking between PrSp and NPrSp.

### PET data

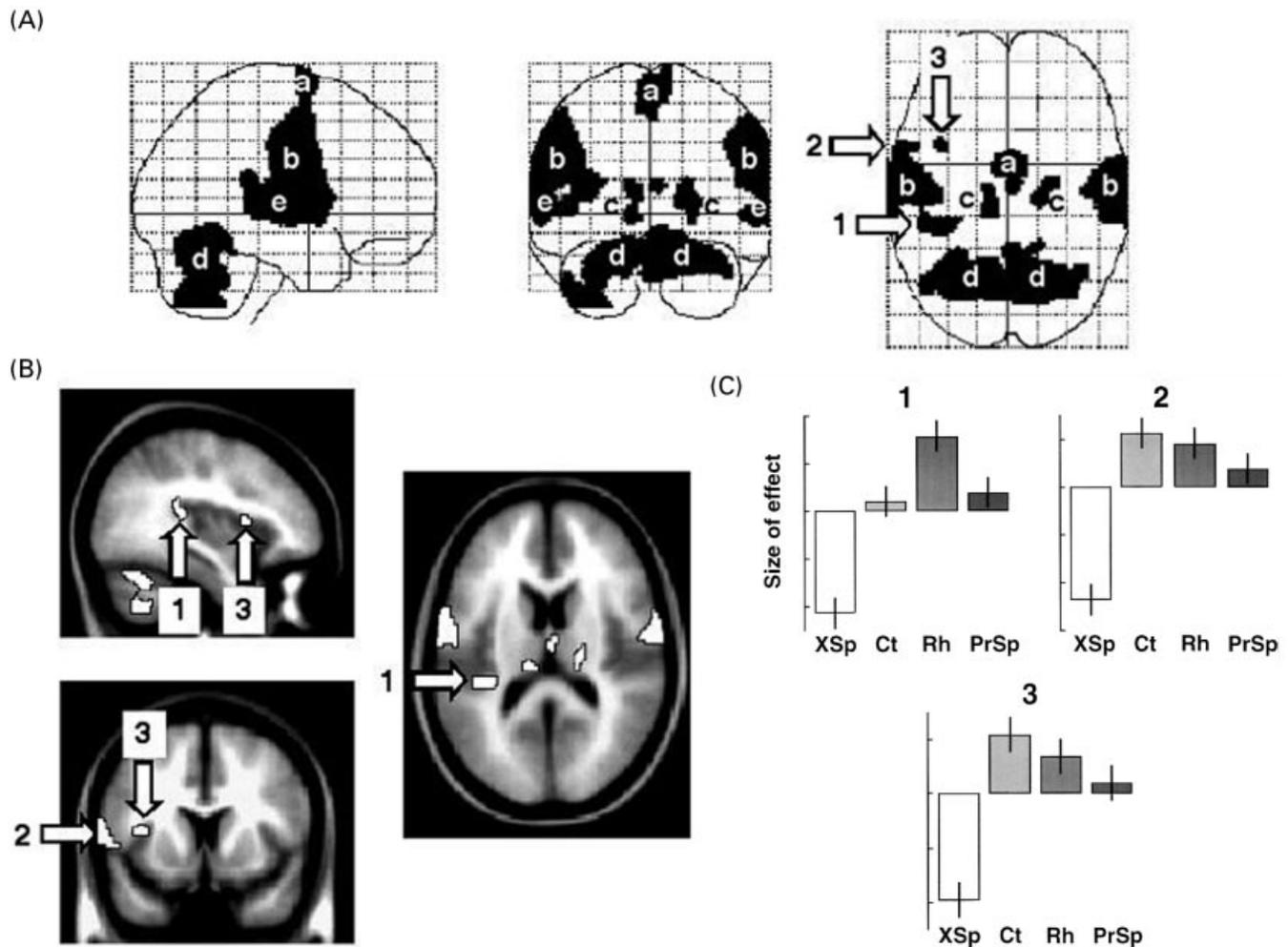
*Regions common to NPrSp (Ct and Rh) and PrSp, contrasted with XSp.* Much of this extensive neural system (Fig. 1A) was symmetrically distributed between the two sides of the brain: primary motor cortex, the lateral parts of the superior temporal sulci, the thalami and predominantly paravermal cerebellum. The supplementary motor area (SMA) (which approximates to that part of medial premotor cortex lying posterior to the coronal plane of the anterior commissure) was also activated, although the resolution of the scanning technique meant it was not possible to determine whether this medial activation was lateralized. There were, in addition, three left-lateralized activations (Fig. 1B): in the posterior part of the supratemporal plane in the depth of the Sylvian sulcus; in the left anterior insula; and in the inferior frontal gyrus (the lateral part of the pars opercularis).

*Regions activated by Rh contrasted with Ct.* No region was activated at the threshold of  $P < 0.05$ , corrected. At a threshold of  $P < 0.0001$ , uncorrected ( $Z$ -score  $> 3.7$ ) three regions were identified (Fig. 2): in the pre-SMA (which approximates to that part of medial premotor cortex lying anterior to the coronal plane of the anterior commissure); in the left inferior frontal gyrus, within the pars opercularis (Tomaiuolo *et al.*, 1999); and at the junction of the pars opercularis with the left anterior insula.

*Regions specific to PrSp when contrasted with both forms of NPrSp.* Figure 3 demonstrates a widely distributed neural network, the majority lying in cortex of the left cerebral hemisphere: the dorsal two-thirds of the left superior frontal gyrus, with the main peaks in the pre-SMA and at the frontal pole; an extensive part of the left anterolateral temporal lobe (temporal pole, middle and inferior temporal gyri), the fusiform gyrus, left and right angular gyri, posterior cingulate cortex; and two regions in right cerebellar hemisphere (both peaks within Crus I) (Schmahmann *et al.*, 1999). In all of these regions, except those in the right cerebellum, activity during XSp was greater than during both the Ct and Rh conditions (see Fig. 3).

#### Effects of different rates of speech during PrSp and NPrSp.

The three speech conditions were entered into a separate design matrix, using syllable rate as a covariate of interest. This analysis established that the observed differences in cerebral activity in the contrast of PrSp with NPrSp were not



**Fig. 1** Motor contrast. (A) Statistical parametric map of the contrast [(PrSp + Rh + Ct) – XSp]. The threshold was set at  $P < 0.05$ , corrected, excluding clusters with spatial extent of  $< 20$  voxels. The co-ordinates of the peak voxels are displayed in the stereotactic space of the Montreal Neurological Institute, implemented in SPM99. Bilateral or mid-line activations include: a, SMA [Brodmann area (BA) 6] (2, 2, 66), ( $z > 10$ ); b, precentral gyrus (BA 4), left (–52, –14, 34) ( $z > 10$ ) and right (52, –12, 36) ( $z > 10$ ); c, posterior thalamus, left (–8, –22, 10) ( $z = 7.4$ ) and right (20, –18, 14) ( $z = 7.4$ ); d, paravermal cerebellum left (–18, –62, –22) ( $z > 10$ ) and right (10, –66, –18) ( $z > 10$ ); e, superior temporal sulcus (BA 22), left (–68, –24, 4) ( $z = 7.6$ ) and right (56, –28, 0) ( $z = 6.7$ ). There were three left lateralized activations: (1) posterior part of the supra-temporal plane (Tpt) (–34, –32, 14) ( $z = 6.0$ ); (2) pars opercularis (BA 44) (–60, 10, 8) ( $z = 6.68$ ); and (3) anterior insula (–36, 10, 8) ( $z = 5.9$ ). (B) The left lateralized activations illustrated in A are mapped on to sagittal (upper left), coronal (lower left) and transverse (right) slices of the T<sub>1</sub>-weighted MRI template. (C) Plots for each of the peak voxels 1, 2 and 3 are shown. Each contrast was centred around zero, and the ordinate of each plot is the mean size of the effect for each condition  $\pm$  standard error of mean, within the peak voxel.

the result of the small (10–15%) difference in the rates of speech production between the two conditions.

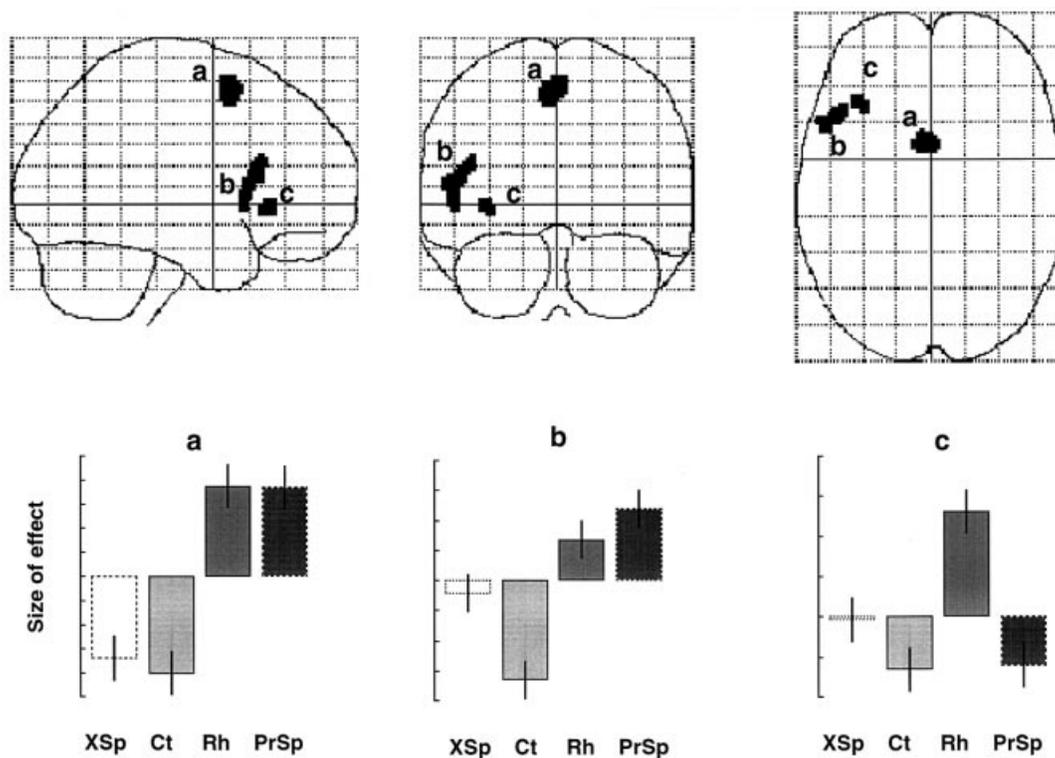
## Experiment 2

### *The comparison of covert verbal fluency with NPrSp and PrSp*

Figure 4 demonstrates that activity in the left lateral premotor and prefrontal and paracingulate cortex associated with covert verbal fluency was not observed with either NPrSp or PrSp, either in relation to each other or to XSp.

## Discussion

The most basic contrast was that of PrSp, Rh and Ct with XSp (Fig. 1). Common to all speech conditions was the phonological encoding of the correct sequence of appropriately stressed syllables, phonetic encoding and articulation. The muscles of speech, those controlling voluntary respiration, the larynx and pharynx, are bilaterally innervated (Barr and Kiernan, 1983), and so the symmetrical activation of both left and right primary motor cortex during NPrSp and PrSp was expected. This is in accord with the clinical observation that pure motor stroke, resulting in a contralateral hemiplegia, is



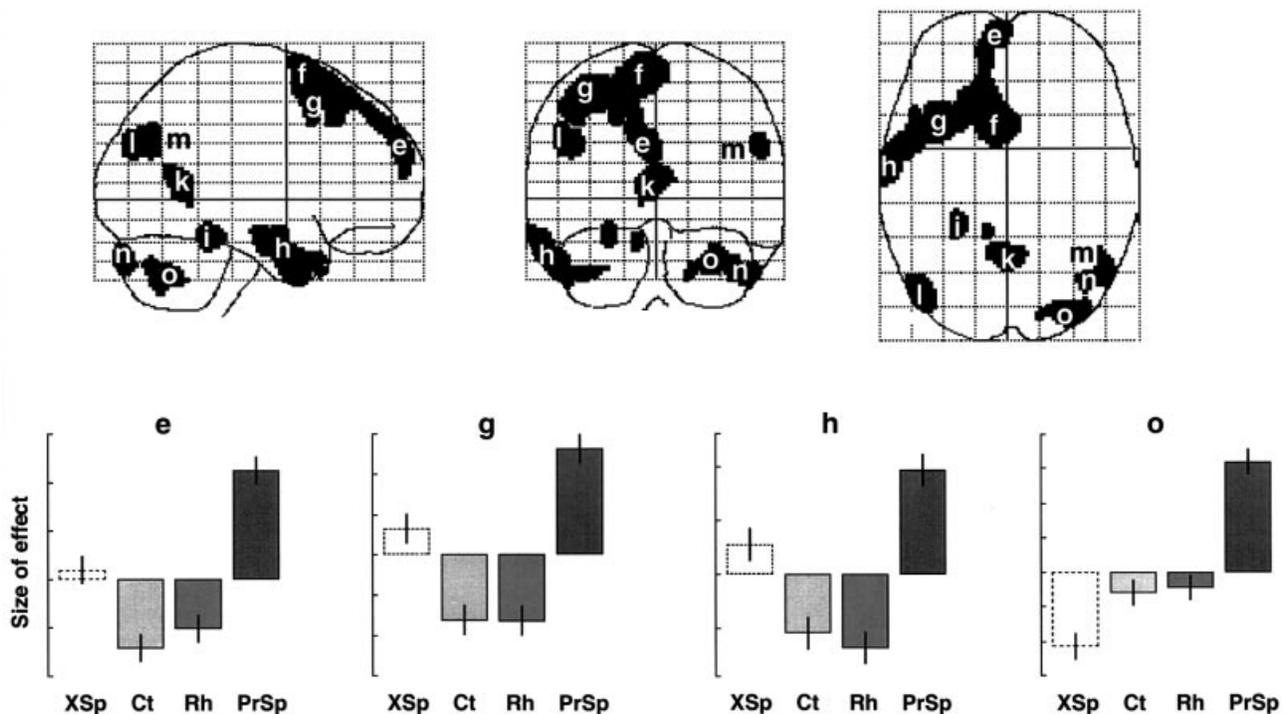
**Fig. 2** Statistical parametric map of the contrast (Rh - Ct). The threshold was set at  $P < 0.0001$ , uncorrected, excluding clusters with spatial extent of  $< 20$  voxels. The co-ordinates of the peak voxels are: a, pre-SMA (BA 6) (-4, 8, 54) ( $z = 5.0$ ); b, pars opercularis (BA 44) (-52, 18, 10) ( $z = 4.4$ ); c, junction of the frontal operculum and the anterior insula (-36, 28, 0) ( $z = 4.2$ ). Each contrast was centred around zero, and the ordinate of each plot is the mean size of the effect for each condition  $\pm$  standard error of the mean, within the peak voxel.

not associated with anything more than a minor impairment of articulation, whereas bilateral motor strokes result in severe dysarthria (Warlow, 1991). Other activations observed in this contrast fit well with the notion that they are associated with articulatory processes. Superior cerebellar infarction, especially when close to the vermis (midline) results in dysarthria (Ackermann *et al.*, 1992; Barth *et al.*, 1993), and thalamic nuclei are involved in the 'motor loops' between premotor and motor cortex and the cerebellum (Thach, 1987). Lesions of the SMA result in temporary mutism (Masdeu *et al.*, 1978; Damasio and Van Hosen, 1980; Ziegler *et al.*, 1997) and functional imaging studies have implicated the SMA in both the voluntary control of respiration independent of speech production (Ramsay *et al.*, 1993), and breathing control during speech (Murphy *et al.*, 1997).

The response of pre-SMA was different from that of SMA. PrSp and the recitation of nursery rhymes involves the generation of utterances with more complex and variable phonetic structure than the repetitive utterances associated with counting (e.g. *twenty-one*, *twenty-two*, etc.). The observation that pre-SMA was more active during Rh and PrSp is in keeping with the reciprocal relationship between pre-SMA and SMA proper in motor planning: pre-SMA is more active in tasks that require response selection and SMA is more active during repetitive movements (for a comprehensive review see Picard and Strick, 1996).

In addition to bilateral or midline regions, this study is the first to demonstrate that speech production involves the co-activation of three distinct areas of limited spatial extent in the left perisylvian cortex. A number of recent functional neuroimaging studies have drawn attention to the role of the left frontal operculum and the anterior insula in speech production (Paulesu *et al.*, 1993; Fiez and Petersen, 1998; Wise *et al.*, 1999; Fox *et al.*, 2000). Mohr's careful clinical and *post mortem* observations in the 1970s established that infarction largely confined to the left anterior insula and pars opercularis rendered patients transiently mute or severely dysarthric without accompanying aphasia (Mohr *et al.*, 1978). The clinical study by Dronkers further confirmed a role for the left anterior insula in speech production (Dronkers, 1996). One recent functional imaging study has drawn attention to the role of the most posterior part of the left supratemporal plane in speech production (Wise *et al.*, 2001). Importantly, the study excluded the possibility that this region is involved in the perception of own utterances. Therefore, phonological and phonetic encoding during speech can be attributed to very discrete regions within the ill-defined boundaries of the areas of Wernicke and Broca.

The activations observed in left and right superior temporal sulci, also observed when subjects listen to the speech of another (Binder *et al.*, 1997; Mummery *et al.*, 1999; Belin *et al.*, 2000), can be attributed to self-monitoring or percep-

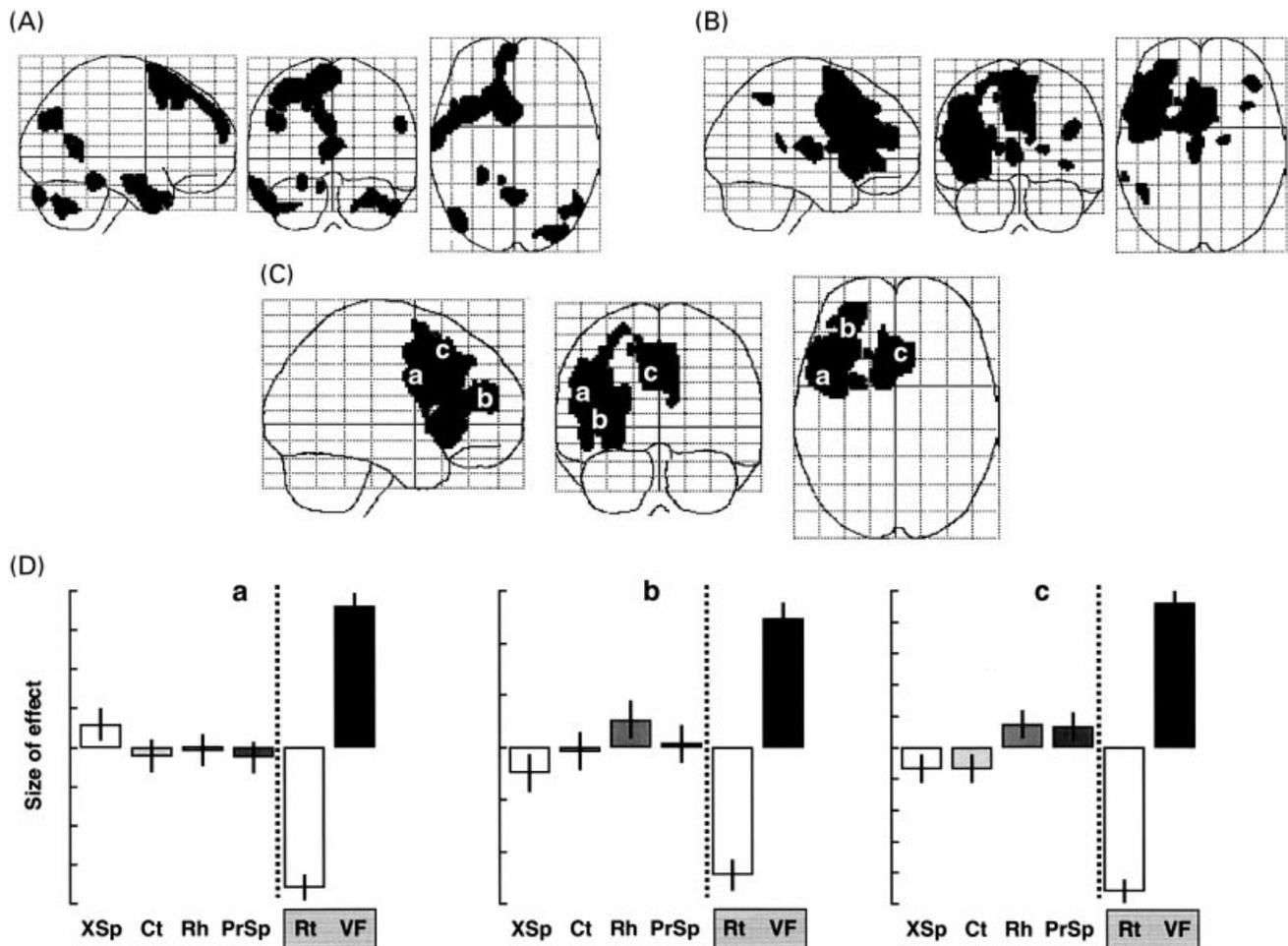


**Fig. 3** Statistical parametric map of the contrast [PrSp - (Ct + Rh)]. The threshold is set at  $P < 0.05$ , corrected, excluding clusters with spatial extent of  $< 20$  voxels. The co-ordinates of the peak voxels are: e, rostral superior frontal gyrus (BA 10) (-4, 62, 28) ( $z = 7.7$ ); f, pre-SMA (BA 6) (-2, 11, 68) ( $z = 7.3$ ); g, middle frontal gyrus (BA 6) (-36, 12, 58) ( $z = 7.3$ ); h, left middle temporal gyrus (MTG) (BA 21) (-64, -41, -20) ( $z = 6.8$ ); i, fusiform gyrus (BA 37) (-24, -38, -18) ( $z = 6.7$ ); k, posterior cingulate gyrus (0, -56, 12) ( $z = 6.7$ ); l, left angular gyrus (BA 39) (-46, -74, 30) ( $z = 7.0$ ); m, right angular gyrus (BA 39) (54, -70, 30) ( $z = 6.0$ ); n and o, Crus I (30, -86, -32) ( $z = 6.7$ ) and (52, -66, -40) ( $z = 6.5$ ). Plots for the superior frontal gyrus (e), the middle frontal gyrus (g), the left MTG (h) and Crus I (o) are shown. Each contrast was centred around zero, and the ordinate of each plot is the mean size of the effect for each condition  $\pm$  standard error of the mean, within the peak voxel.

tion of own voice. This is compatible with the notion that the same neural systems are used for the perception of own and other voice (Levelt, 1989). The baseline task, XSp, required the subjects to listen out for very occasional environmental sounds, and this auditory attention task may account for an apparent absence of activity in response to own voice in the supratemporal plane within and adjacent to primary auditory cortex (Jancke *et al.*, 1999). However, in a previous study, hearing and repeating lists of single words contrasted with auditory 'anticipation' was associated with activation in primary auditory cortex (Wise *et al.*, 1999). Thus, the effects of the chosen baseline on the distribution of activity in superior temporal cortex observed in response to the perception of self-generated utterances would appear to be a complex issue that will benefit from further systematic study.

The production of PrSp involves many levels of processing not present in the other conditions, beginning with an initial intention to speak (in this instance, prompted by a question or instruction from the experimenter). The formulation of linked concepts ('messages') to answer a relatively open-ended question such as 'describe where you lived as a child' requires the selection of relevant memories followed by the selection of words of appropriate meaning and grammaticality (lemmas) to incorporate into sentence frames that

adequately express those memories. Although these many levels of processing have been discerned from behavioural studies (Levelt *et al.*, 1999), inevitably they are confounded in a functional imaging study of PrSp. Some of the observed activations may be attributable specifically to episodic memory retrieval during PrSp such as the one in posterior cingulate cortex that has been associated with episodic memory retrieval in both neuroimaging (Maguire and Mummery, 1999) and clinical studies (Rudge and Warrington, 1991). Other activated regions are more likely to be directly related to speech production, such as the right cerebellar hemisphere (Crus I). Reciprocal connections exist between the posterior lobe of the cerebellum and association cortex, including prefrontal and anterior temporal cortex (Schmahmann, 1996). Impairments in conversational speech including agrammatism have been described in association with cerebellar hemispheric damage (Silveri *et al.*, 1994; Schmahmann and Sherman, 1998), suggesting a role for the cerebellum in the cognitive aspects of speech production (Schmahmann, 1996). Left anterior cerebral artery territory infarcts have been associated with the syndrome of transcortical motor aphasia (TCMA) (Alexander and Schmitt, 1980; Freedman *et al.*, 1984), characterized by a sparse spontaneous speech output with sparing of automatic



**Fig. 4** Statistical parametric maps with a threshold of  $P < 0.05$ , corrected, excluding clusters with spatial extent of  $< 20$  voxels. (A) The contrast [PrSp - (Ct + Rh)] is shown as in Fig. 2B. (B) The contrast of verbal fluency to rest (VF - Rt) from archived data is shown (Warburton, 1996), revealing extensive dorsolateral prefrontal and anterior cingulate activations. (C) The statistical parametric map of the contrast (VF - Rt), displayed at a threshold of  $P < 0.05$ , corrected for all voxels, was masked with the following contrasts, (PrSp - XSp), (XSp - PrSp), (PrSp - NPrSp) and (NPrSp - PrSp), at a threshold of  $P < 0.05$ , uncorrected ( $Z$ -score  $> 1.9$ ). This excluded all voxels in the contrast of (VF - Rt) that lay within one of these masks. This descriptive analysis reveals regional activations associated with VF contrasted with Rt, at a conservative threshold, that were not associated with significant differences, even at a low threshold, between PrSp and either NPrSp or XSp, either relative increases or decreases. The following brain regions were activated strongly by VF, but showed no differences in activity between any of the conditions in this study: a, inferior frontal gyrus (BA 8) (-44, 6, 26) ( $z > 10$ ); b, middle frontal gyrus (BA 46/9 junction) (-26, 46, 20) ( $z = 7.7$ ); c, paracingulate gyrus (BA 32) (-6, 10, 46) ( $z > 10$ ). (D) Plots for each of the peak voxels a, b and c as in C are shown. Each contrast was centred around zero, and the ordinate of each plot is the mean size of the effect for each condition  $\pm$  standard error of the mean, within the peak voxel.

phrases, counting and repetition. Although behavioural deficits in TCMA have been attributed to damage to the SMA or cingulate cortex (Berthier, 1999), lesions typically are extensive and involve multiple regions within the superior frontal gyrus (Freedman *et al.*, 1984). Our results argue that it is damage to or disconnection of the superior frontal gyrus rostral to the SMA that is the critical lesion in TCMA.

Broca's area has long been associated with grammatical speech production, and the agrammatism of patients with the syndrome of Broca's aphasia has been attributed to destruction of the left inferior frontal gyrus and adjacent cortex (for review, see Caplan, 1987). Therefore, it was unexpected that speech rich in syntax only resulted in a small, spatially

limited activation in anterior Broca's area (Fig. 2). This was true for both the overlearned Rh condition and for PrSp: PrSp contrasted with both NPrSp conditions did not reveal any additional activation in the left inferior frontal gyrus. One consideration is that the production of grammatical speech in both the recitation of nursery rhymes and during everyday PrSp is so automatic that it results in little change in net synaptic activity in Broca's area. Certainly, it has been shown that rehearsal and learning by subjects prior to scanning, at least when motor and explicit metalinguistic tasks are involved, reduce lateral cortical signal in functional imaging studies (Jenkins *et al.*, 1994; Raichle *et al.*, 1994). A number of functional imaging studies investigating the perception of

grammatical structure have shown left inferior frontal activation (e.g. Stromswold *et al.*, 1996; Meyer *et al.*, 2000). We are aware of only one study that has specifically investigated syntactic encoding in speech production (Indefrey *et al.*, 2001). The authors demonstrated activation of the left posterior pars opercularis during speech with normal syntactic structure, at a site indistinguishable in location from the region that was activated by all three speech conditions in this study (Fig. 1). The study used production of single words or noun phrases as control tasks. However, the activation was within a region of ventral premotor cortex, and intuitively it seems implausible that premotor cortex is the site of grammatical encoding of utterances. An alternative interpretation is that it could be a final common pre-articulatory region (a 'convergence' zone), where relative activity is weighted by input from regions responsible for grammatical encoding, with signal from the latter too subtle and distributed to be detected as separate peaks in a functional imaging study. A counter argument is that it is known that verbal numerals have a syntactic structure based around rules of concatenation and overwriting (Power and Longuet-Higgins, 1978), and that there is thus some syntactic structure in each of the speech conditions in the current study. However, a recent functional imaging study of discourse production, using both spoken English and American Sign Language (ASL) (Braun *et al.*, 2001), failed to demonstrate any additional activation in the left inferior frontal gyrus with either speech or ASL contrasted with complex motor control tasks involving the production of phonemes (articulated or signed), but not words. Certainly activation in the pars opercularis is not confined to syntactical processing: many other studies that did not include anything remotely grammatical in their construction have demonstrated activation in Broca's area. Indeed, this region is also activated by non-verbally cued finger movements (Krams *et al.*, 1998; Iacoboni *et al.*, 1999), and at the present time it is not possible to assign specific modular functions to the lateral frontal cortex based on an overview of functional neuroimaging studies (Duncan and Owen, 2000).

A striking feature from this study was that PrSp, in contrast to both forms of NPrSp, was associated with activation of the rostral left ventrolateral temporal cortex. Atrophy of the anterior temporal lobe (as opposed to posterior temporal cortex) has been implicated in semantic dementia (Chan *et al.*, 2001), with correlation between severity of semantic deficit and the degree of ventrolateral cortical loss (Mummery *et al.*, 2000). This region is anatomically connected to the rostral superior frontal gyrus by the uncinate fasciculus, a major white matter tract that courses under the left inferior frontal gyrus (Gloor, 1997). We propose that the formulation of PrSp is dependent on interactions between the rostral left temporal cortex, the left pars opercularis and the left superior frontal gyrus. Furthermore, in light of the contribution of white matter tract damage to the syndrome of Broca's aphasia (Mohr, 1976), we infer that disconnection of the rostral left temporal lobe from the left superior frontal gyrus, even if both

cortical regions remained intact, would be associated with a major impairment in PrSp. Associated damage to the left pars opercularis and anterior insula would impair the production of all forms of speech.

It is evident from this study and that of Braun *et al.* (2001), that grammatical speech production is not dependent on the left dorsolateral prefrontal and premotor cortex separate from the pars opercularis. A meta-analysis of silent verbal fluency versus rest from 12 European PET centres, including some of the subjects reported in Experiment 2, has demonstrated that verbal fluency reliably activates both the left inferior and middle frontal gyri (Poline *et al.*, 1996). Although this extensive region of left dorsolateral prefrontal cortex is often infarcted in patients with Broca's aphasia, neither PrSp nor Rh induced activity that was different from either speech with very limited syntax (Ct) or from a non-speech condition (XSp). We propose that most of the dorsolateral prefrontal cortex is, therefore, a region damaged only by association following a major cerebral artery occlusion resulting in aphasia. Thus, executive and working memory processes account for most of the activation in left dorsolateral prefrontal cortex activation observed with metalinguistic tasks, and language processes appear to be restricted to the caudal left inferior frontal gyrus. This perhaps limits the usefulness of word generation tasks in the study of recovery from aphasia.

In summary, we have identified three left lateralized regions, within the traditional areas of Broca and Wernicke, engaged in both NPrSp and PrSp. Furthermore we have identified a widely distributed, extrasylvian, predominantly left-lateralized neural system engaged in the processes involved in PrSp prior to articulation. These regions are strikingly similar to those reported by Braun *et al.* (2001), using speech and ASL. Finally, we have demonstrated that the left dorsolateral frontal cortex activated by metalinguistic tasks is, at most, only minimally involved in normal speech.

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