

Neural resources for processing language and environmental sounds

Evidence from aphasia

Ayşe Pinar Saygin,¹ Frederic Dick,¹ Stephen W. Wilson,² Nina F. Dronkers³ and Elizabeth Bates¹

¹Department of Cognitive Science, University of California, San Diego, ²Neuroscience Interdepartmental Program, University of California, Los Angeles, and ³VA Northern California Health Care System, Martinez, USA

Correspondence to: Ayşe Pinar Saygin, Department of Cognitive Science, University of California, San Diego, 9500 Gilman Drive 0515, La Jolla, CA 92093-0515, USA
E-mail: asaygin@cogsci.ucsd.edu

Summary

Although aphasia is often characterized as a selective impairment in language function, left hemisphere lesions may cause impairments in semantic processing of auditory information, not only in verbal but also in nonverbal domains. We assessed the ‘online’ relationship between verbal and nonverbal auditory processing by examining the ability of 30 left hemisphere-damaged aphasic patients to match environmental sounds and linguistic phrases to corresponding pictures. The verbal and nonverbal task components were matched carefully through a norming study; 21 age-matched controls and five right hemisphere-damaged patients were also tested to provide further reference points. We found that, while the aphasic groups were impaired relative to normal controls, they were impaired to the same extent in both domains, with accuracy and reaction time for verbal and nonverbal trials revealing unusually high correlations ($r = 0.74$ for accuracy, $r = 0.95$ for reaction

time). Severely aphasic patients tended to perform worse in both domains, but lesion size did not correlate with performance. Lesion overlay analysis indicated that damage to posterior regions in the left middle and superior temporal gyri and to the inferior parietal lobe was a predictor of deficits in processing for both speech and environmental sounds. The lesion mapping and further statistical assessments reliably revealed a posterior superior temporal region (Wernicke’s area, traditionally considered a language-specific region) as being differentially more important for processing nonverbal sounds compared with verbal sounds. These results suggest that, in most cases, processing of meaningful verbal and nonverbal auditory information break down together in stroke and that subsequent recovery of function applies to both domains. This suggests that language shares neural resources with those used for processing information in other domains.

Keywords: aphasia; auditory agnosia; environmental sounds; Wernicke’s area; lesion mapping

Abbreviations: AQ = aphasia quotient; ERD = event-related desynchronization; ERP = event-related potentials; fMRI = functional MRI; IPL = inferior parietal lobule; LHD = left hemisphere-damaged; pMTG = posterior middle temporal gyrus; pSTG = posterior superior temporal gyrus; RHD = right hemisphere-damaged; ROI = region of interest; RT = reaction time; VLSM = Voxel-based lesion-symptom mapping; UCSD = University of California San Diego; WAB = Western Aphasia Battery

Introduction

The relationship between language impairments and deficits in other cognitive and sensorimotor domains has been of interest since the early days of neurology. That aphasia itself may be symptomatic of a more general sensorimotor or cognitive disturbance is an idea with ample historical roots (Head, 1926; Goldstein, 1948). Indeed Jackson (1878), who observed a high incidence of nonverbal impairments in aphasic patients, believed that they suffer from a more

general disturbance (sometimes referred to as asymbolia) and may be ‘lame in thinking’.

Many studies have provided evidence for a range of nonverbal impairments in aphasic patients (see for example Gainotti and Lemmo, 1976; Ammon, 1979; Chertkow *et al.*, 1997). It was noted early on (Jackson, 1878; Head, 1926) as well as more recently (De Renzi *et al.*, 1968; Varney, 1978; Duffy and Duffy, 1981; Wang and Goodglass, 1992), that

deficits in comprehension and production of gesture and pantomime are strongly associated with receptive and expressive language disorders. Impairments in nonverbal domains in aphasic patients have been demonstrated in such tasks as associating pictures with corresponding objects (De Renzi *et al.*, 1968), colours with pictures (De Renzi *et al.*, 1972), gestures with objects (De Renzi *et al.*, 1968; Varney, 1978) and sounds with pictures (Spinnler and Vignolo, 1966; Faglioni *et al.*, 1969; Varney, 1980). Unfortunately, only a few studies have attempted to test aphasics systematically on nonverbal tasks that are comparable to those that show deficiencies in the language domain (Spinnler and Vignolo, 1966; Varney, 1980; Bates *et al.*, 2001).

Of particular interest here is auditory agnosia—a rare neurological disorder characterized by a relatively isolated deficit in auditory comprehension despite normal hearing. When the disorder affects only verbal material, it is often called word deafness; when the deficit is in recognizing environmental sounds, it is often termed nonverbal auditory agnosia. Much of the literature on auditory agnosia consists of case studies. The associated lesions are not particularly consistent and have included unilateral right (Spreeen *et al.*, 1965; Haguenaer *et al.*, 1979; Vignolo, 1982; Eustache *et al.*, 1990; Fujii *et al.*, 1990), unilateral left (Vignolo, 1982; Haguenaer *et al.*, 1979; Eustache *et al.*, 1990; Pasquier *et al.*, 1991; Clarke *et al.*, 2000) and bilateral cortical lesions (Albert *et al.*, 1972; Haguenaer *et al.*, 1979; Miceli, 1982; Rosati *et al.*, 1982; Vignolo, 1982; Lechevalier *et al.*, 1984; Motomura *et al.*, 1986; Mendez and Geehan, 1988; Buchtel and Stewart, 1989; Lambert *et al.*, 1989; Engelien *et al.*, 1995; Kaga *et al.*, 2000). Subcortical lesions can also cause this deficit (Kazui *et al.*, 1990). Auditory agnosia restricted to nonverbal material is a rather rare phenomenon, previously associated with bilateral (Spreeen *et al.*, 1965; Albert *et al.*, 1972; Kazui *et al.*, 1990) or right hemisphere (Fujii *et al.*, 1990) lesions.

Based on these studies, two forms of auditory agnosia have been proposed: (i) perceptual-discriminative, with patients failing to identify whether two consecutive sounds are identical; and (ii) associative-semantic, with patients being impaired at audio-visual matching or naming. Bilateral lesions appear to be implicated in severe discriminative disorders (Albert *et al.*, 1972; Rosati *et al.*, 1982; Vignolo, 1982; Lechevalier *et al.*, 1984; Motomura *et al.*, 1986; Mendez and Geehan, 1988; Buchtel and Stewart, 1989; Kazui *et al.*, 1990; Taniwaki *et al.*, 2000). Unilateral right hemisphere lesions can lead to normal association with impaired discrimination (Vignolo, 1982; Eustache *et al.*, 1990), deficient association with normal discrimination (Spreeen *et al.*, 1965) or deficient association and deficient discrimination (Fujii *et al.*, 1990). Unilateral left hemisphere lesions have been reported to cause deficient association and normal discrimination (Vignolo, 1982); however, in many cases discrimination has not been tested. A clear picture does not emerge from these findings, due in part to the heterogeneity of the tests used. Thorough reviews of the relevant case

study literature are provided by Clarke *et al.* (1996, 2000) and Griffiths *et al.* (1999).

Environmental sounds share quite a few perceptual and informational features with language (Gygi, 2001), thus making them useful in exploring possible links between aphasia and (associative) auditory agnosia, and also more broadly between verbal and nonverbal auditory processing. Functional neuroimaging studies of human auditory processing have begun to reveal areas in the temporal lobes that are more activated for certain types of sounds than others. However, it is not yet clear whether these effects reflect divisions based on the type (e.g. music versus speech), semantic content, or spatial and temporal complexity of the sound stimuli used (Belin *et al.*, 2000; Binder *et al.*, 2000; Zatorre and Belin, 2001). Functional activation related to environmental sounds has been reported in only a few studies (Humphries *et al.*, 2001; Lewis *et al.*, 2001; Maeder *et al.*, 2001; Adams and Janata, 2002; Dick *et al.*, 2002b). Although contrasts with linguistic sounds were not always carried out or discussed in these studies, environmental sounds were observed to activate some middle and superior temporal areas in the left hemisphere that have been associated with language-related activation in earlier studies (e.g. Wise *et al.*, 1991; Démonet *et al.*, 1992). These results are consistent with the idea that language shares some neural mechanisms with certain nonverbal processes. In an event-related potentials (ERP) study, Van Petten and Rieffers (1995) explored this hypothesis and found that target words were similarly modulated when preceded by contexts consisting of environmental sounds or sentences, suggesting verbal and nonverbal information may influence a common semantic or associative space. Again using ERP, Cycowicz and Friedman (1998) showed that both types of stimuli elicit brain activity with similar characteristics as a function of familiarity and frequency. Looking at event-related desynchronization (ERD), Lebrun *et al.* (1998, 2001) observed left-lateralization for the semantic, but not perceptual processing of environmental sounds. Identifying differences and similarities in the brain mechanisms for processing these different types of auditory input is likely to be a fruitful line of research.

Experimental studies of environmental sound processing in groups of patients with brain lesions have also provided insights. In a series of papers, Vignolo, Spinnler and Faglioni reported disturbances of environmental sound recognition due to unilateral hemispheric damage (Spinnler and Vignolo, 1966; Faglioni *et al.*, 1969; Vignolo, 1982). They observed that right hemisphere-damaged (RHD) patients performed significantly worse than controls on perceptual tests involving environmental sounds while left hemisphere-damaged (LHD) patients performed significantly worse on associative tests. Intrigued by the finding that left hemisphere lesions can cause associative auditory agnosia, Varney (1980) used environmental sounds in order to examine verbal and nonverbal comprehension deficits in aphasic patients, an undertaking similar to the present study. He found that defects in

environmental sound recognition were seen only in subjects with impaired verbal comprehension and that all aphasic patients with intact verbal comprehension performed well on sound recognition. There were, however, aphasic patients who were impaired in verbal comprehension, but not in sound recognition. Verbal comprehension was always as impaired as sound recognition, whereas sound recognition performance could be better than verbal comprehension. Interestingly, a similar relationship has been reported between pantomime recognition and reading comprehension (Varney, 1978). More recently, Schnider *et al.* (1994) observed that both LHD and RHD patients performed significantly worse than a group of normal controls on an environmental sound recognition test. They found no significant differences in the performance of the two patient groups; however, the pattern of errors appeared to differ over groups: LHD patients made more semantically-based errors, while RHD patients and control subjects made almost exclusively acoustic errors. For all patients, accuracy in recognizing environmental sounds correlated with language comprehension as measured by the Western Aphasia Battery (WAB) (Kertesz, 1979). Lesion-behaviour correlations showed that LHD patients with impaired environmental sound recognition tended to have damage to the posterior superior temporal gyrus (pSTG) and the inferior parietal lobe. Clarke *et al.* (1996, 2000) also tested patients with brain damage on different aspects of sound recognition. Here, patients who were deficient in the sound recognition task exhibited much variability. In these studies, however, language comprehension was not tested in relation to sound processing; the purpose of some of the experiments was to contrast sound identification and localization, topics that have recently been the focus of much research (e.g. Belin and Zatorre, 2000; Rauschecker and Tian, 2000).

There are several reasons why the above literature tends to provide fragmentary and incomplete answers when addressing the relationship between verbal and nonverbal auditory processes. Many previous studies of environmental sound processing by aphasics did not attempt to make a direct comparison between verbal and nonverbal auditory processing in the same patients. Those that did compare performance between domains used different tasks or tests in the two domains and did not control for factors such as stimulus frequency and identifiability, or the relationship between the auditory and visual stimuli (Varney, 1980; Schnider *et al.*, 1994). Such factors are known to have effects on performance in verbal and nonverbal tasks. In addition, all previous studies used four or five picture displays in sound to picture matching tasks, entailing a lengthy visual processing component to the task. Thus, in analysing performance in sound processing, these studies were limited to analysing accuracy data only—losing potentially important information about the time course of processing.

The work we report allows us to address directly the relation between verbal and nonverbal auditory comprehension in chronic aphasic patients, using an ‘online’ (timed) recognition paradigm, with verbal and nonverbal stimuli that are matched

for several factors. First, we briefly describe a norming study on a large set of environmental sound recordings. This study allowed us to test the sound stimuli for recognizability as well as to extract linguistic labels to be used in the verbal trials of the main experiment. Then we report on an online task with aphasic patients and age-matched controls in which stimuli in both domains are matched for identifiability, frequency, and semantic relationship to the visual target. In line with earlier studies by Vignolo, Faglioni and Spinnler (Spinnler and Vignolo, 1966; Faglioni *et al.*, 1969), we also address the effect of semantic competition on both domains across our patient groups in order to observe whether processing in the two domains is similarly modulated by higher-level semantic or conceptual constraints.

Methods

Environmental sounds norming study

Participants

Participants were 31 undergraduate and graduate students at University of California San Diego (UCSD), aged 18–31 years with normal vision and hearing. All received class credit for their participation. Prior to the experiment, participants completed a handedness assessment questionnaire and a language history questionnaire. Subjects gave informed consent to participate in the study, which was approved by the UCSD Human Research Protections Program.

Materials

The sound stimuli were taken from digital sound effect libraries including Digifex and BBC®. The sampling rate of the sounds was 44.1 kHz, with 16-bit quantization.

Procedure

Following a procedure used by Ballas (1993), we asked subjects to listen to sounds and to press a button as soon as they believed they had identified the source of each sound. After the sound ended, subjects gave a verbal description, having been instructed to provide both a noun and a verb (e.g. dog barking, engine running). Subjects completed a practice block of eight trials and an experimental block of 236 trials.

Verbal responses were coded by two independent raters. Accuracy was computed using the raters’ codes, and response time was computed only for correct trials. More detail about the procedure and results is available in Saygin (2001) and Saygin *et al.* (2002).

Aphasia study

Participants

Patients were voluntary participants recruited from Veterans’ Administration Medical Centers from San Diego, CA, USA,

Table 1 Characteristics of aphasic and RHD patients

Initials	Age	Patient group	AQ	Site	Lesion site
B.E.	24	Broca's	71.6	SD	Frontal, temporal, parietal, insula, basal ganglia
B.K.	55	Anomic	84.4	M	Basal ganglia, insula
C.H.	66	Anomic	92.2	SD	Basal ganglia
C.W.	72	RHD	–	M	Right hemisphere (not included in group lesion analyses)
D.C.	63	Broca's	74.8	SD	Frontal, insula, basal ganglia
D.D.	56	Broca's	18.9	M	Temporal, parietal, frontal, insula
D.F.	46	Broca's	49.6	M	Temporal, parietal, frontal, insula
E.B.	32	Broca's	68.3	M	Frontal, parietal, insula
E.C.	43	Anomic	91.7	M	Frontal, temporal, parietal, insula
E.R.	81	RHD	–	SD	Right hemisphere (not included in group lesion analyses)
F.N.	58	RHD	–	SD	Right hemisphere parietal (not included in group lesion analysis)
F.Y.	77	Wernicke's	64.1	M	Inferior parietal, small region on superior temporal
G.G.	50	Anomic	90.3	SD	Small, posterior to temporal lobe
H.K.	62	Wernicke's*	47.6	M	Frontal, medial temporal, insula, subcortical
H.M.	72	Broca's	26.7	M	Frontal, temporal, parietal
J.A.	59	Anomic	79.9	M	N/A
J.B.	66	Broca's	13.8	SD	MCA-territory, acute scan shows expanding frontal lesion
J.C.	81	Anomic	91.1	SD	N/A—acute scan shows no lesion boundaries
J.D.	72	Anomic	89.8	M	Frontal, anterior temporal
J.G.	63	Anomic	80.8	M	Basal ganglia
J.H.	62	Anomic	92.4	SD	Frontal, tip of anterior temporal
J.Q.	76	Broca's	11.2	SD	Frontal, temporal, parietal, insula
J.S.	51	Broca's	48.8	SD	Frontal, temporal, parietal
J.W.	72	Anomic	90.9	SD	Temporal, parietal
K.W.	64	Anomic	98.0	SD	Frontal
L.L.	76	Anomic	78.9	M	Excluded from all analyses—possibility of multiple infarcts
L.R.	56	Anomic	79.2	SD	Frontal, temporal, parietal
M.B.	50	Broca's	31.0	SD	Frontal, insular and subcortical extension, parietal
P.B.	75	Anomic	98.0	SD	Medial frontal
P.P.	50	Wernicke's	78.0	SD	Frontal, temporal, parietal, insula
R.K.	52	RHD	–	SD	Right hemisphere (not included in group lesion analyses)
R.S.	74	Wernicke's	33.3	M	Temporal
RS	55	RHD	–	M	Right hemisphere temporal, parietal (not included in group lesion analyses)
V.H.	71	Wernicke's	78.6	SD	Frontal, anterior temporal
W.G.	82	Wernicke's	51.5	M	Temporal, parietal

*Criteria for classification for Wernicke's aphasia based on WAB subscores are as follows: fluency = 5–10; comprehension = 0–6.9; repetition = 0–7.9; naming = 0–9. Criteria for transcortical sensory aphasia are identical except for repetition (8–10). Since repetition is not a component of the task here, we found it appropriate to analyse this subject's data in the Wernicke's aphasia group. M = Martinez, CA, USA; SD = San Diego, CA, USA. Lesion summaries are based on CT or MRI scans or medical records.

or Martinez, CA, USA, and were paid \$25.00 for their participation. Thirty LHD patients with varying types and severity of aphasia and five RHD patients with no measurable aphasia participated in the experiment. CT or MRI scans and the medical records of all patients were evaluated by a neurologist; only patients with unilateral lesions due to a single cerebrovascular accident were included. Exclusionary criteria included diagnosed or suspected hearing difficulties, dementia, head trauma, tumours or multiple infarcts. Aphasic patients were classified using the WAB (Kertesz, 1979) as anomic ($n = 14$), Broca's ($n = 10$) or Wernicke's aphasics ($n = 6$). Details are provided in Table 1.

Age-matched controls were 21 adults aged 53–78 years, with no history of audiological, neurological or psychiatric disorders; all had normal or corrected-to-normal vision, and were tested for hearing impairment with a standard question-

naire and/or with an audiometer. All were paid \$25.00 for their participation. Informed consent was obtained from all subjects in accordance with guidelines of the UCSD Human Research Protections Program.

Data from two control subjects were excluded (one talked to the experimenter throughout the testing session and one reported low-frequency hearing loss afterwards). Data from one patient (L.L., anomic) were excluded due to a possibility of multiple infarcts.

Experimental design and materials

A 2-within- \times 1-between-subjects design was used, with domain (verbal versus nonverbal) and semantic competition (visual target related to distracter versus visual target unrelated to distracter) as within-subject factors, and patient

group (control, RHD, Broca's, Wernicke's, anomic in the main analysis; LHD, RHD, control in a supplementary analysis) as the between-subjects factor.

Stimuli were black-and-white line drawings, nonverbal sounds and speech sounds. Visual stimuli were 10.6 cm × 10.6 cm digitized drawings culled from extensively normed picture databases. Naming norms for these pictures have been reported elsewhere (Bates *et al.*, 2003). Forty-five nonverbal sound stimuli were selected from the set normed in the preliminary study explained above. Selection criteria included identifiability (moderate to high), inter-rater reliability for identifiability, imageability (identifiability/availability of picture) and recognition time. Selected sounds included animal cries ($n = 10$; e.g. cow mooing, bird chirping), human sounds ($n = 6$; e.g. sneezing, laughing), vehicle noises ($n = 5$; e.g. train, car, tractor noises), tool/machinery sounds ($n = 4$; e.g. drill, lawnmower noises), alarms/bells ($n = 5$; e.g. telephone ringing, bells tolling), water sounds ($n = 6$; e.g. dripping, pouring), sports ($n = 4$; e.g. bowling, golf) and music ($n = 5$; e.g. piano, violin). A full list of sounds used, as well as norming results on these sounds, are reported in Saygin *et al.* (2002). Speech stimuli were phrases based on the most common labels provided by the subjects in the preliminary experiment. Grammatical complexity was kept constant by putting together commonly reported nouns and verbs in 'noun phrase + verb-ing (+ object)' constructions. Examples of phrases used were 'cow mooing', 'water boiling' and 'someone eating an apple'. All phrases were read by a 38-year-old male speaker of American English and were digitally recorded at a sampling rate of 44.1 kHz with 16-bit quantization.

Three line drawings were matched to each sound pair: a target, a related distracter and an unrelated distracter. For example, for the sound of a cow 'mooing' or its verbal description, the target drawing was 'cow', the semantically related distracter was 'sheep', and the unrelated distracter was 'violin' (see Fig. 1). In order to ensure that the semantically related and unrelated distracters were appropriately assigned, we made use of the semantic relatedness measure latent semantic analysis (Landauer *et al.*, 1998). The average latent semantic analysis index for semantically related pairs was 0.36; for unrelated pairs it was 0.04.

Over the course of the experiment, each picture appeared eight times in a fully counterbalanced fashion: picture type (target/distracter) × domain (verbal/nonverbal) × distracter type (related/unrelated to the target). Each of the 45 sound 'types' (e.g. 'cow') was also crossed with domain (verbal/nonverbal) and distracter type (related/unrelated). A full list of items used is reported in Saygin *et al.* (2002).

Procedure

The experiment was run on Apple Macintosh PowerBook 3400c computers using the PsyScope experimental driver (Cohen *et al.*, 1993). Participants sat in front of a VGA monitor, Yamaha YST-M7 speakers were placed on each side, and a standard PsyScope button box was used to collect

responses. The experimenter read a set of instructions to each participant and asked him or her to complete a practice session of six trials.

The experimental block consisted of 180 experimenter-advanced trials. In each trial, subjects were presented with a two-picture display on the screen. After 1000 ms, the sound stimulus (either verbal or nonverbal) was presented through the speakers. This delay allowed subjects enough time to process the visual stimuli, thus mitigating visual processing contributions to reaction time data. Subjects pushed the button under the picture they believed matched the sound. Reaction time and accuracy were recorded for each trial. Subjects were continuously monitored for attention to the task, and were asked at intervals whether they needed a break. The nature of errors was noted, as were any comments made during or after the experiment. Special care was taken to note whether or not the subject was immediately aware of the error (as indicated by an overt verbal or physical response). Motivational feedback (e.g. 'you are doing great so far') was provided as often as considered necessary to keep participants engaged in the task (for aphasic patients, this was approximately once every 20 trials); however, this feedback did not relate any information about the subject's accuracy in a particular trial.

Lesion analysis

As noted above, head CT or MRI images were obtained for all of the patients. For 20 of our LHD patients, computerized lesion reconstructions to be used in lesion overlay analyses were available. For another six patients, we had MRI or CT scans showing lesion boundaries, which were used in some analyses but not for the lesion overlays. Only acute scans were available for the remaining three LHD subjects; chronic scans showing distinct lesion boundaries could not be obtained. Lesion reconstructions were available only for two of the RHD patients who participated in this study, so we did not include this group in our lesion analyses.

Lesion reconstructions were based on CT or MRI scans at least 3 weeks post-onset and were hand-drawn onto 11 axial slice templates based on the atlas of DeArmond *et al.* (1976). They were then entered into a Macintosh computer via electronic bitpad using software developed at the VA Medical Center in Martinez, California (Frey *et al.*, 1987). All reconstructions were completed by a board-certified neurologist, experienced in neuroradiology, but blind to the behavioural deficits of the patients. Individual variations in gyral patterns and any differences in imaging angles were compensated for by using subcortical structures as landmarks.

To determine common areas of infarction in patients who exhibit similar behavioural profiles, we overlapped their lesions using the voxel-based lesion symptom mapping (VLSM) software developed by our group (Wilson *et al.*, 2002).

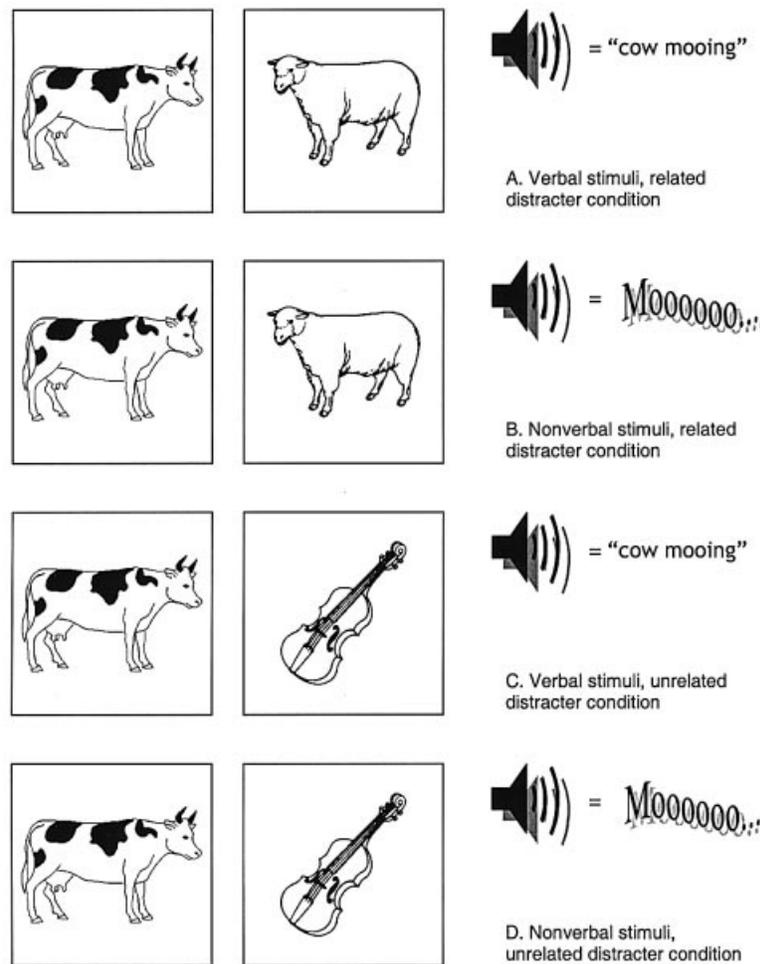


Fig. 1 Summary of the experimental design. Domain (verbal/nonverbal) and distracter type (related to target/unrelated to target) were within-subject factors, and subject group was the between-subjects factor. The target ‘cow’ appeared four times, twice with verbal sound stimuli (the phrase ‘cow mooing’), twice with non-verbal stimuli (the sound of a cow mooing), twice with ‘sheep’ as the distracter (related condition), and twice with ‘violin’ as the distracter (unrelated condition). All these trial types with the target ‘cow’ are depicted in the pictures. Forty-five pictures and sounds were used as targets and related and unrelated foils, giving rise to 45 triplets such as ‘cow–sheep–violin’. A total of 180 trials was administered. Twenty quasi-random orders of the list were rotated among the subjects.

Statistical analysis

Performance across groups was compared using repeated measures analysis of variance (ANOVA). Regression and correlation analyses were performed to examine the relationships between performance in the two domains. We also conducted outlier analyses to identify any dissociations in performance. All analyses were performed using JMP and StatView statistical packages (Sall *et al.*, 2001).

Results

Here we examine differences in accuracy and reaction time between patient and control groups, the correlation in performance across verbal and nonverbal domains and the relationship between lesion site and processing deficits.

Is nonverbal processing spared in aphasic patients?

We examined accuracy and reaction time (RT) for the aphasic (LHD) and RHD subjects, and their age-matched controls. LHD subjects were grouped according to aphasia subtype (as determined by the WAB) into Broca’s, Wernicke’s and anomic groups. RTs were analysed only for correct responses. We analysed RT data in several different ways (e.g. patients’ RT measured as the difference from the normal controls’ RT, or converted into standardized scores) with no change in the pattern of results. Therefore, we report results for the simple case of RTs measured from the onset of sound.

As depicted in Fig. 2, groups differed in their overall accuracy [$F(4,48) = 8.533, P < 0.0001$]; planned comparisons showed that control, anomic and RHD groups did not differ significantly from each other (all making very few errors),

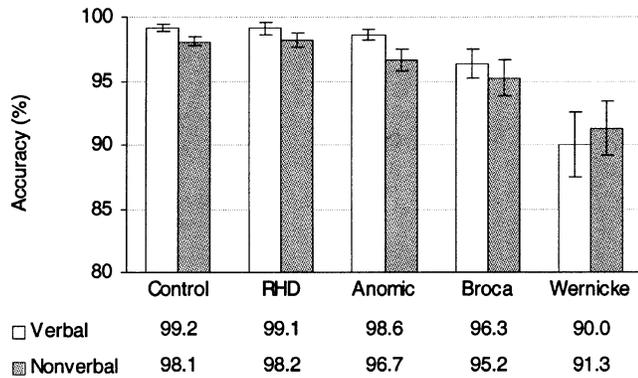


Fig. 2 Accuracy depicted across verbal and nonverbal domains for all subject groups. Groups differed in their overall accuracy ($P < 0.0001$) with control = RHD = anomic > Broca's > Wernicke's (all comparisons corrected $P < 0.01$).

whereas Broca's aphasics and Wernicke's aphasics were less accurate than all other groups and, furthermore, differed significantly from each other, with Broca's more accurate than Wernicke's ($P < 0.01$ for all significant differences, with correction for multiple comparisons).

Distracter type had an effect on accuracy, such that subjects were less accurate when the distracter picture was semantically related to the target picture [$F(1,48) = 62.920$, $P < 0.0001$]. The effect of distracter type was also modulated by group [$F(4,48) = 5.612$, $P = 0.0009$]. Patient groups were more adversely affected when the distracter was related to the target (see Fig. 3). This interaction appears to be driven mainly by the Broca's and Wernicke's aphasics. When both of these severely affected groups were excluded from the analyses, the distracter type by group interaction was no longer significant [$F(2,34) = 1.458$, $P = 0.25$]; conversely, ANOVA comparisons between either Broca's or Wernicke's patients and normal controls revealed significant distracter type by group interactions [$F(1,27) = 10.730$, $P = 0.0029$ and $F(1,23) = 57.816$, $P < 0.0001$, respectively].

There was no main effect of domain; accuracy in verbal and nonverbal conditions did not differ significantly [$F(1,48) = 2.895$, $P = 0.095$]. Domain did not interact with distracter type [$F < 1$], nor was there an interaction of group by domain [$F(4,48) = 1.333$, $P = 0.27$] or a three-way interaction of group, domain and distracter type [$F(4,48) = 1.397$, $P = 0.25$].

The fact that the group by domain interaction did not reach significance is especially notable, as we might expect aphasic groups to commit more errors in verbal trials compared both with normals and with patients with RHD. In fact, the (non-significant) numerical results were in the opposite direction (verbal accuracy > nonverbal) for all groups except for Wernicke's aphasics, the most impaired group. To determine whether the anticipated interaction would hold if we restricted our attention only to these patients, the ANOVA was repeated for Wernicke's and controls only. In this case, the group by domain interaction reached significance [$F(1,23) = 4.442$, $P = 0.046$]. Comparable re-analysis

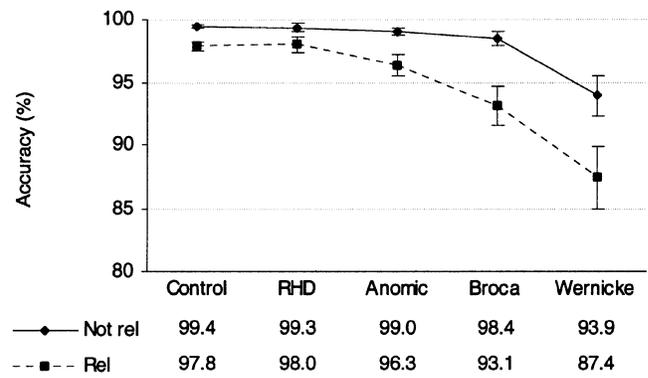


Fig. 3 Accuracy depicted across related and unrelated distracter conditions for all subject groups. There was a main effect of distracter type ($P < 0.0001$). There was also an interaction of distracter type with group ($P < 0.01$), driven mainly by the Broca's and Wernicke's aphasics.

comparing each of the other patient groups with normals did not reveal any evidence for a group by domain interaction (see Fig. 2).

RT was analysed for the accurate trials only. We found significant differences in RT over patient group, as plotted in Fig. 4 [$F(4,48) = 9.891$, $P < 0.0001$]. Pairwise comparisons showed the following ordering of RT (from slowest to fastest, $P < 0.0001$ for all differences): Wernicke's = Broca's > anomic = RHD > control patients. As with accuracy, there were significant effects of distracter type on RT [$F(1,48) = 254.849$, $P < 0.0001$], where RTs to semantically related target and distracter pairs were higher than those to unrelated ones. The distracter type interaction with patient group just reached significance [$F(4,48) = 2.605$, $P = 0.047$]. Here, control subjects were slightly less affected in their response latencies by the distracters compared with all groups except RHD ($P < 0.05$); none of the other groups differed from one another.

There was no main effect of domain on reaction times [$F < 1$], but contrasts were carried out to examine whether there was a differential effect of domain across patient groups. Comparing each patient group with controls revealed that anomic patients [$F(1,30) = 4.485$, $P = 0.042$] and, to a lesser extent, the RHD patients [$F(1,22) = 4.118$, $P = 0.055$] tended to respond slower relative to controls on the nonverbal material. For anomics, this is the opposite to what might be predicted in a traditional account of aphasia. There were no significant interactions between controls and Broca's [$F(1,27) = 0.242$, $P = 0.63$] or Wernicke's [$F(1,23) = 2.771$, $P = 0.11$] patients.

In summary, our analyses did not reveal a sparing of nonverbal processing in aphasic patients; in particular, LHD patients performed poorly in the nonverbal domain at levels comparable to their performance in the verbal domain.

Analyses over hemisphere of lesion

Although the analyses reported above examine the effects of lesion side on performance in the experiment, we also report

results of analyses in which aphasic subjects were considered as a single LHD group. This is mainly to enable comparison with previous studies that used side of lesion as the grouping variable across subjects and did not form groups based on aphasia type.

For accuracy, there were main effects of group (LHD, RHD, controls) [$F(2,50) = 4.625, P < 0.014$] and of distracter type [$F(1,50) = 18.864, P < 0.0001$]. Controls and RHD patients performed better than LHD patients. The group by distracter type interaction reached significance, with the LHD group making more errors when related distracters were presented [$F(2,50) = 5.872, P = 0.0051$]. Once again, the group by domain interaction was not significant [$F < 1$]. The RT data closely parallel the accuracy data and previous analyses: The main effects of group [$F(2,50) = 12.563,$

$P < 0.0001$] and distracter type [$F(1,50) = 160.925, P < 0.0001$] are significant. The LHD group was the slowest; the RHD group was faster than the LHD group, but slower than the control subjects. The group by distracter type interaction reached significance, with the LHD group more adversely affected by related distracters [$F(2,50) = 5.307, P = 0.0081$]. The group by domain interaction was again not significant [$F(2,50) = 1.311, P = 0.28$].

To summarize, hemisphere of lesion did not significantly affect the relative impairment on the verbal and nonverbal conditions in this experiment. There was, however, a reliable effect of semantically related distracters: LHD patients found them harder to process than RHD and control subjects.

Associations between task performance across domains and outlier analyses

Within the LHD group, accuracy in verbal and nonverbal domains was very tightly correlated ($r = 0.74, P < 0.0001$), with reaction time data demonstrating an even closer relationship, approaching an identity function ($r = 0.95, P < 0.0001$). Impairments in verbal and nonverbal domains go hand in hand in our data. Fig. 5A and B show correlation scatter plots and linear fits for accuracy and RT in LHD subjects over the two domains.

We also assessed the relationship between patients' WAB-derived aphasia quotient (AQ), a measure of overall aphasia severity, and performance in our task. Note that AQ is a task-external measure of language impairment. Overall, accuracy was correlated with AQ ($r = 0.526, P = 0.0033$); when split by domain, both verbal and nonverbal performance were correlated with severity of aphasia (verbal: $r = 0.539,$

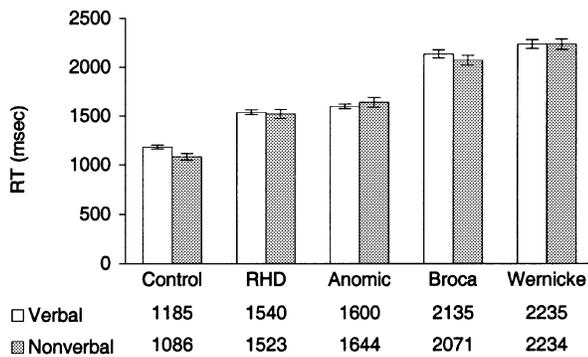


Fig. 4 Reaction time for correct responses depicted across verbal and nonverbal domains for all subject groups. Groups differed in their response latencies ($P < 0.0001$) with control < RHD = anomic < Broca's = Wernicke's (all comparisons corrected $P < 0.01$)

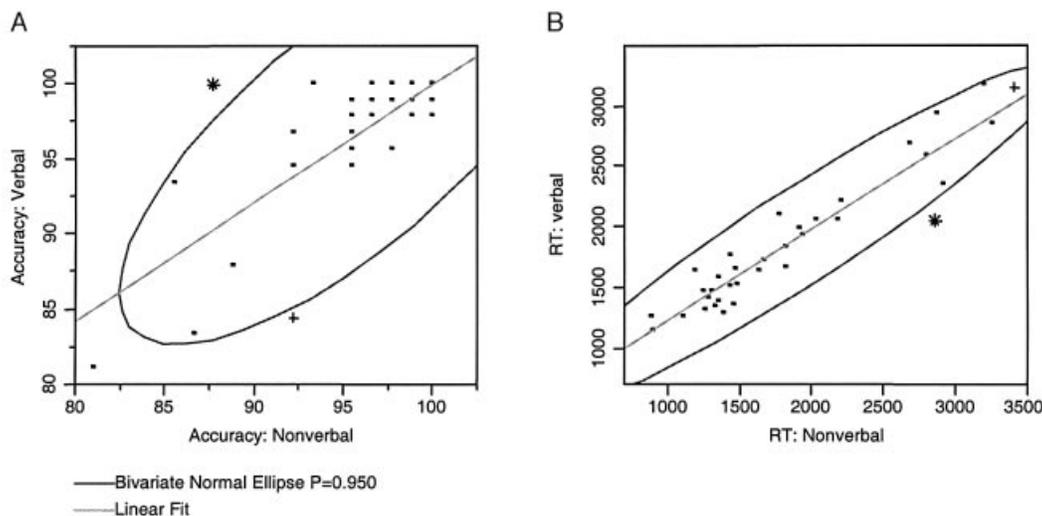


Fig. 5 Correlation of performance in the verbal and nonverbal domains within the aphasic group for (A) accuracy and (B) reaction time. Linear fits and density ellipses using a confidence interval of 95% are shown. Correlations are significant ($P < 0.0001$ for both) and high ($r = 0.74$ and 0.95 , respectively). Data points outside the ellipses are outliers based in Mahalanobis distances. + denotes patient R.S. and * denotes patient J.W; the two patients who show signs of possible dissociations between the two domains.

$P = 0.0025$; nonverbal: $r = 0.440$, $P = 0.017$). RT measures also correlated with AQ ($r = 0.619$, $P = 0.0003$); when split by domain, both the verbal performance ($r = 0.689$, $P < 0.0001$) and the nonverbal performance ($r = 0.546$, $P = 0.0022$) showed significant relationships to aphasia severity. Very similar results have been reported by Schnider *et al.* (1994).

In order to explore the outliers in the dataset, we calculated density ellipses using a confidence interval of 95% using the outlier analysis tool of the JMP statistical software package. These ellipses are based on Mahalanobis distances and, assuming a bivariate normal distribution, show where a given percentage of the data is expected to lie. The Mahalanobis distance takes into account the correlation structure of the data as well as the individual scales (Appelbaum *et al.*, 1999; Sall *et al.*, 2001). We used a 95% confidence ellipse for both of our measures. These outlier analyses report only the aphasic (LHD) population; we also carried out the analysis including RHD subjects and found very similar results.

For accuracy, three subjects remained outside the ellipse and were identified as outliers, (as shown in Fig. 5A). For RT, we identified only one outlier—as can be seen in Fig. 5B. In order to compare these results with what would be expected by chance, we carried out a small-scale randomization test. The verbal and nonverbal accuracy scores were shuffled 50 times and outlier analysis was performed each time. The mean number of outliers obtained was 2.9 (range 2–4). This demonstrates that the procedure identifies roughly the same number of outliers regardless of the correlation structure of the data; thus, no special significance should be attached to the number of patients identified. Rather, the advantage of outlier analysis is that it provides a quantitative method of identifying patients who may potentially exhibit dissociations.

The actual process of identifying genuine dissociations is more qualitative. Based on Fig. 5A, we saw that patient J.W. (*) showed a striking dissociation with 100% accuracy on verbal (better than healthy controls) and 87.7% accuracy on nonverbal trials. Patient R.S. (+) showed some dissociation with 92.2% accuracy on nonverbal and 84.4% accuracy on verbal trials. Patient W.G. was an outlier by virtue of the fact that he was severely impaired with 81% accuracy in both domains. RT analyses pinpointed J.W. as the sole outlier, shown in Fig. 5B.

R.S. and W.G. are both severe Wernicke's aphasics, with large lesions involving temporal and parietal regions. In order to further investigate R.S. as a patient exhibiting a potential dissociation, we re-tested him on the same task after a six-month delay. His performance was better, with 95% accuracy on nonverbal and 90.2% accuracy on verbal trials. At the time of re-testing, he had made more gains in the nonverbal domain and, with these scores, he would no longer be an outlier with respect to the rest of the sample. However, a relatively low score in the verbal domain remains in his profile; we conclude that his dissociation should be noted but interpreted with care.

For J.W. on the other hand, who showed a striking dissociation in a rather unexpected direction (worse nonverbal processing in an aphasic patient) which was also reflected in his RT scores, follow-up testing revealed that the dissociation was persistent and reliable. J.W. has an unusual neurological profile: despite a large temporoparietal lesion, he presents with a very mild aphasia (anomic) with almost completely intact verbal auditory comprehension. We carried out several additional tests on this patient after a nine-month delay and verified that he has severe auditory agnosia for nonverbal sounds (Saygin and Moineau, 2002).

Lesion location analyses

We performed a lesion analysis to investigate further the neural correlates of auditory comprehension. First, we overlapped the computer-reconstructed lesions of the patients who exhibited behavioural profiles of interest (e.g. poor performance in nonverbal sounds) to determine if they shared a common area of infarction. Next, we used these shared areas of injury as regions of interest (ROIs) to determine statistical differences between groups of patients whose lesions either spared or involved these particular areas.

For the lesion overlays, the 20 LHD patients for whom we had lesion reconstructions were grouped together based on their performance in the task, regardless of aphasia classification. We used accuracy and RT values, respectively; both converted into z -scores with respect to normal controls as a measure of patients' degree of impairment. The VLSM software (Wilson *et al.*, 2002) was used to assess the degree of spatial overlap in lesions shared by patients with similar behavioural deficits. Patients who performed ≥ 2 SDs below the normal controls were considered deficient and their lesions overlapped to determine if a common area of infarction could be found.

For accuracy, overlays are provided in the top panel of Fig. 6, broken down by stimulus domain. Here, we show the results on three axial slices that pass through the middle temporal (slice 1), superior temporal (slice 2) and inferior parietal regions (slice 3). Based on the criteria used here, eight patients were deficient in nonverbal sounds and 10 were deficient in verbal sounds. As can be seen, the overlays are very similar across these two domains. Consistent with Schnider *et al.* (1994) and recent neuroimaging studies of environmental sound processing (e.g. Adams and Janata, 2002), the areas of maximal overlap for patients impaired in the nonverbal domain are centred in the posterior superior temporal gyrus (pSTG, in slice 2) extending into some middle temporal (in slice 1) and inferior parietal (in slice 3) regions. The implicated areas for verbal sound processing are strikingly similar, though a slightly smaller fraction of patients overlap on these regions, i.e. not all patients with poor verbal comprehension have damage to the areas of maximal overlap.

For reaction time, overlays for patients who were identified as deficient based on slow response latencies appear to be

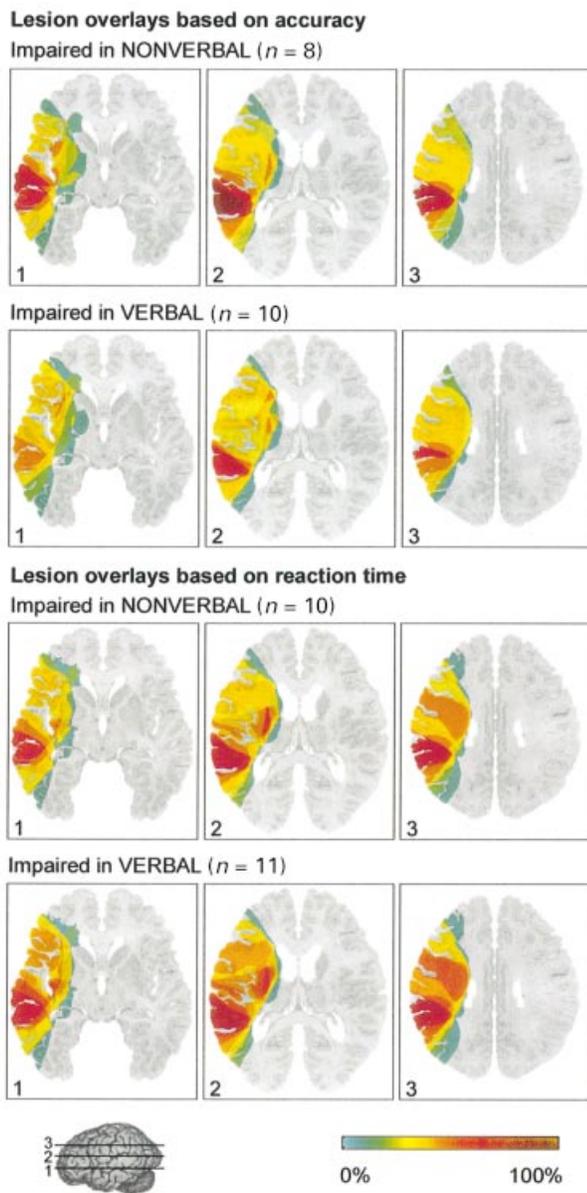


Fig. 6 Lesion overlays for LHD patients who performed poorly in the nonverbal and verbal domains based on accuracy and reaction time. The overlays consist of lesions from patients who performed ≥ 2 SDs below the age-matched controls in the corresponding measure in each condition. Lesions are depicted on three axial slices that go through middle temporal, superior temporal and inferior parietal lobes. The colour maps indicate the percentage of patients whose lesions involve that particular region.

almost identical for the two domains (verbal versus nonverbal). The lower panel of Fig. 6 shows that the same pSTG region identified for accuracy is once again the focal point for patients with slow RT (Fig. 6). The pattern of results looks very similar to that revealed by the overlays based on accuracy, although for RT, there seems to be a stronger overlap in the insula.

The analyses above selected patients based on behavioural deficits and identified the common areas of infarction.

Another possible method is to examine the behavioural profiles associated with the ROIs previously discussed. This type of analysis enables us to see how general the localization results are and allows us to assess quantitatively which areas are differentially implicated in verbal versus nonverbal processing. For the analyses below, we identified as ROIs the maximal areas of infarction for each slice in the lesion overlays. Then we divided the patients into groups consisting of those who had a lesion in that ROI and those whose lesions spared that area. This permitted us to compare and contrast performance in relation to the ROIs and the two domains quantitatively. Only patients whose lesion reconstructions (or scans, for the six patients for whom we did not have digital reconstructions) clearly involved or spared the ROIs were included in the groups.

Patients were first divided into two groups consisting of those who had a lesion in the region with the darkest colour in Fig. 6, slice 2 (pSTG) and those whose lesions did not involve this region [$n(\text{lesioned}) = 11$, $n(\text{intact}) = 14$]. For accuracy, there was a significant main effect of pSTG lesion [$F(1,23) = 5.714$, $P = 0.025$]; patients who had lesions in this location had significantly lower accuracy scores than patients who did not have a lesion here [mean(lesioned) = 92.8%, mean(intact) = 97.2%]. There was also an interaction of pSTG lesion with domain [$F(1,23) = 4.349$, $P = 0.048$], mainly driven by the nonverbal errors (see Fig. 7). The difference between patients with pSTG lesions versus those without was larger in the nonverbal domain than in the verbal domain. Furthermore, the difference between verbal and nonverbal domains was larger in the pSTG-lesioned patients than the difference between domains in those without lesions to this area. Additionally, pSTG-lesioned patients were significantly slower than the patients whose lesions spared this region [mean(lesioned) = 2223 ms, mean(intact) = 1649 ms, $F(1,23) = 5.338$, $P = 0.030$]. However, there was no interaction of domain and pSTG lesion for RT [$F(1,23) = 1.529$, $P = 0.23$], consistent with the great similarity of the overlays for the two domains in Fig. 6.

For the posterior middle temple gyrus (pMTG) region that is identified as possibly important for sound processing in slice 1, a similar analysis with eight lesioned patients and 16 non-lesioned patients revealed a main effect of pMTG on accuracy [$F(1,22) = 7.582$, $P = 0.012$]. Patients with lesions here were significantly less accurate than patients whose lesions spared this region [mean(lesioned) = 91.6%, mean(intact) = 96.9%]. However, this region did not make a differential contribution to the two domains: the interaction of pMTG lesion and domain was not significant [$F < 1$]. In a separate analysis on reaction times, patients with pMTG lesions were significantly slower than those without lesions here [mean(lesioned) = 2450 ms, mean(intact) = 1613 ms, $F(1,22) = 11.767$, $P = 0.0024$], but again the pMTG lesion and domain interaction did not reach significance [$F(1,23) = 2.214$, $P = 0.15$], as was also the case for RT for the pSTG.

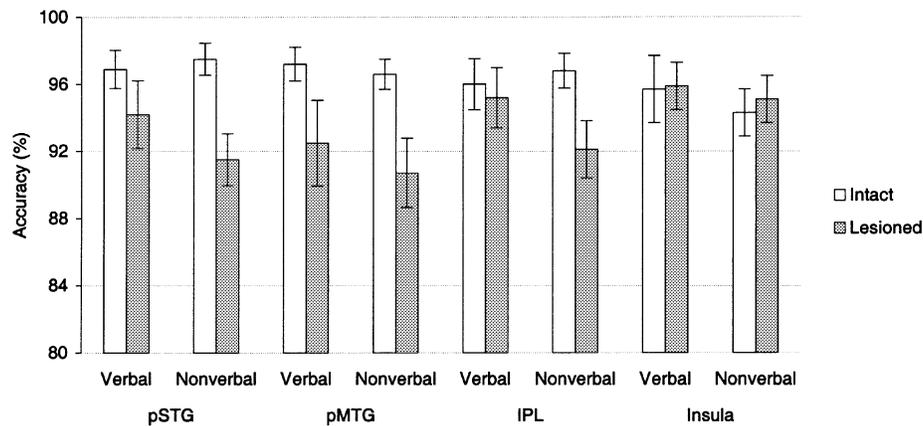


Fig. 7 Summary of statistics on the regions of interest based on Fig. 6: pSTG, pMTG, IPL and insula. There is a significant main effect of pSTG and pMTG on accuracy. We also found significant interactions indicating the involvement of the pSTG and IPL in nonverbal deficits above and beyond verbal deficits. As can be seen, there is no clear implication to the portion of the insula that we examined on accuracy in either of the domains.

For the inferior parietal lobule (IPL) region in slice 3, we carried out the analogous analyses [$n(\text{lesioned}) = 11$, $n(\text{intact}) = 13$]. Here, although there was no main effect of group on accuracy [$F(1,22) = 1.827$, $P = 0.19$] or RT [$F(1,22) = 2.680$, $P = 0.12$], the IPL lesion by domain interaction was significant for accuracy [$F(1,22) = 6.695$, $P = 0.017$], largely due to the fact that those patients whose lesions included this region were significantly less accurate for the nonverbal trials [mean(lesioned, verbal) = 95.2%, mean(lesioned, nonverbal) = 92.1%]. These latter findings suggest that the IPL region may be especially important for processing nonverbal sounds; however, the absence of a main effect demands caution in drawing strong conclusions.

Recall that on slice 2, there was some evidence from the RT data for insula involvement. However when we examined all the LHD patients [$n(\text{lesioned}) = 14$, $n(\text{intact}) = 7$], damage involving this portion of the insula was not significantly associated with accuracy or RT in either domain [all $F_s < 1$].

Although we observed extremely high correlations between performance in the two domains, for exploratory purposes we also performed lesion overlay analysis for patients who performed relatively better in one domain compared with the other (Fig. 8). First, we identified patients whose accuracy in one domain was ≥ 1 SD different from their performance in the other domain. We then constructed an overlay of lesions for those patients who performed more poorly in the nonverbal domain ($n = 10$) and those who performed more poorly in the verbal domain ($n = 5$). As can be seen, the patients who were relatively more impaired in the nonverbal domain have lesions along the middle and posterior portions of the superior temporal gyrus and in the IPL. Notice that these are the same areas already identified as being important in Fig. 6 and showed some significant quantitative effects after lesion-location-based group analy-

ses. We see now that these regions (especially the pSTG) are implicated even when the patients whose deficits are comparable in the verbal and nonverbal domains are excluded from this highly correlated dataset. This lends further support to the importance of these regions for environmental sound processing. On the other hand, once the patients whose deficits also equally involve the nonverbal domain are excluded, the lesion overlay for the patients with verbal deficits becomes less focal and has a visibly more anterior and medial focus moving towards the anterior insula, basal ganglia and caudate nucleus.

Turning to results for reaction time, we regrouped the patients into those whose performance was slower in the nonverbal than the verbal domain ($n = 10$) and compared them with those whose verbal performance was slower in the verbal compared with the nonverbal domain ($n = 11$). Here a similar anterior focus for relatively slow response times in the verbal domain can be seen, whereas the focus for relatively slow response times in the nonverbal domain does not change.

However, unlike the posterior foci analysed above, this anterior area which is implicated in patients who perform relatively poorly in the verbal domain is not significantly associated with our behavioural measures. When analogous statistics are computed between groups of patients with ($n = 10$) and without ($n = 11$) lesions to the region of maximal overlap for worse performance in the verbal domain in Fig. 8, no differences can be found between these patients in accuracy or RT. Nor are there any interactions or tendencies towards selective involvement in one domain versus the other [all $F_s < 1$]. Note that this common lesion location in patients with poorer performance in the verbal domain may reflect the participation of aphasic patients with haemorrhagic stroke who tend to have more subcortical involvement.

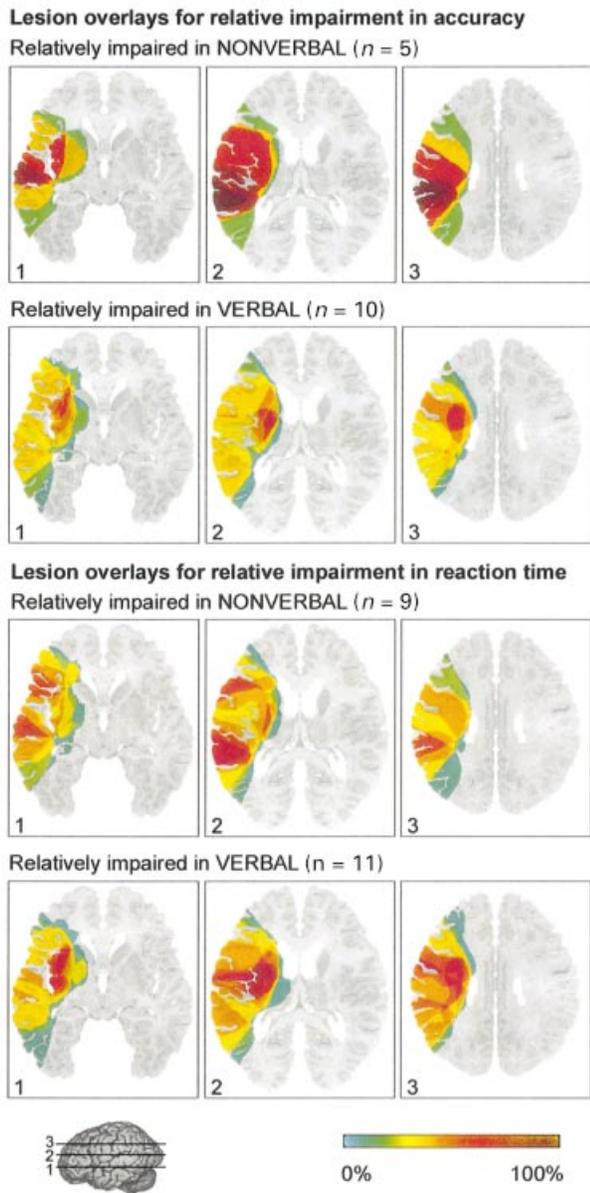


Fig. 8 Lesion overlays for patients whose performance in one domain was worse compared with the other domain. For accuracy, the overlays consist of lesions from patients whose accuracy z-scores were ≥ 1 SD apart between the two domains. For reaction time, the scores were too tightly correlated and very few patients had scores that were 1 SD apart. The overlays for this measure were thus computed based on positive or negative z-score differences. Patients whose lesions are overlapped in the top panel for the RT overlays were thus relatively slower in responding to nonverbal trials than they were to verbal trials. Conversely, lesion overlays in the bottom panel depicts patients who were slower in responding to the verbal trials.

Thus, the results for the relative impairment overlays corroborate prior results that point to the pSTG as a critical region for nonverbal sound processing. This area is also important for verbal comprehension. However, despite obtaining a different pattern of lesions for patients who are more deficient in the verbal domain, based on the present

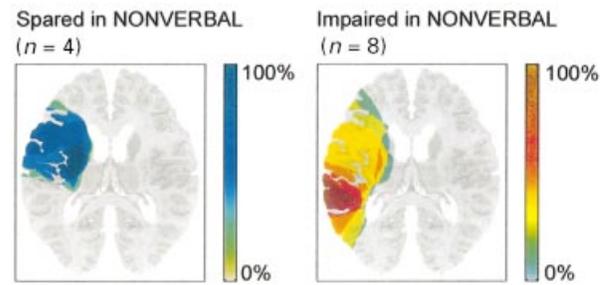


Fig. 9 Lesion overlay on slice 2 depicting patients who are ‘spared’ in the nonverbal domain along with an overlay depicting patients who are impaired. Note that the latter overlay is the same as slice 2 of the top panel in Fig. 6, replicated for easy contrast.

data, we cannot identify a specific region that is differentially and specifically implicated for verbal processing.

We performed one more lesion overlay to determine whether the pSTG region that is significantly implicated in nonverbal processing in prior analyses is essential for performing well in this domain. Four patients in our sample were 100% accurate on nonverbal trials, thus performing better than normal controls. Fig. 9 depicts the lesion overlays on slice 2 for these patients (on a blue colour scale to emphasize that this is a map of sparing) along with an overlay for patients who were deficient in the nonverbal domain (2 SDs below the controls; same as the overlay in Fig. 6). As can be seen, all of the patients who performed well in the nonverbal domain have lesions that spare the pSTG region (as well as the pMTG region, data not shown). Thus, based on our sample, it appears that the pSTG region may be crucial for normal nonverbal auditory processing.

Discussion

Aphasic patients do not have spared nonverbal processing

The data revealed no clear evidence of an advantage for nonverbal auditory processing in these aphasic patients. We did not find a consistent interaction of stimulus domain (verbal versus nonverbal) by patient group in the direction of spared performance on the nonverbal domain by the clinically language-impaired subjects. We did find differences between patient groups that were reliable and systematic: Broca’s and Wernicke’s aphasics performed similarly in the task, with the latter group faring slightly worse, while anomic and RHD patients performed similarly to each other. All patient groups were impaired relative to normal control subjects. However, impairment in the verbal condition tended to go hand-in-hand with impairment in the nonverbal condition for all patient groups. In the single instance where processing of language stimuli was less accurate than nonverbal stimuli (in latter patients), the result was not mirrored in the RT data. In fact, the latter measure showed that anomic and RHD patients had longer reaction times for nonverbal than verbal stimuli,

thus implying that our nonverbal stimuli were even more challenging for these groups than were the verbal stimuli. In short, there was little evidence for a specific deficit in language processing in our group of patients.

Impairments in the two domains go hand-in-hand

That our aphasic patients are not selectively deficient in linguistic processes is an interesting result, but the lack of a statistically significant difference between verbal and nonverbal processing does not necessarily imply a similarity or contiguity in processing. However, additional results and analyses strengthen our contention that these two domains may draw on some of the same processing resources. Similar to findings by Schnider *et al.* (1994) and Varney (1980), but unlike findings of Clarke *et al.* (1996), we observed correlated patterns between behavioural deficits of our patients across the two domains. First, aphasia severity was correlated strongly not only with performance on the verbal condition of our task, but almost equally as well with performance on the nonverbal condition. This is consistent with results reported by Schnider *et al.* (1994). That a significant amount of the variance in our nonverbal task was predicted by a separate measure of aphasic patients' language competence is suggestive of an association between processing of verbal and nonverbal auditory information. Secondly, within the LHD group, high cross-domain correlations over both RT and accuracy (Fig. 5) demonstrate that the severity of language deficit goes hand-in-hand with the severity of the deficit in environmental sound recognition.

A potential alternative explanation for the associations we show here may be that subjects are engaging in verbal/sub-vocal mediation in the processing of environmental sounds. However, there is some evidence against this explanation. First, both younger controls (Saygin, 2001) and the elderly control subjects reported here were significantly faster in processing the environmental sounds stimuli than the verbal stimuli (see Fig. 4). If subjects were using verbal mediation for both tasks, then we could expect reaction times for environmental sounds to be at least equal to, if not longer than, those for verbal material. Secondly, we made an explicit test of this sub-vocal rehearsal hypothesis (Dick *et al.*, 2002a). We asked subjects to perform the nonverbal portion of the task with and without sub-vocal naming of the sounds. The results were clear; while using the verbal mediation strategy, subjects responded an average of 20% more slowly than when using no linguistic mediation. Given the pattern of reaction times we have obtained in these experiments, it seems unlikely that sub-vocalization or naming is the root of the close relationships observed here.

Another hypothesis to entertain is that the behavioural correlations we see in the patients are not due to a systematic neural relationship between the processing of nonverbal and verbal sounds, but are simply due to lesion size. It could be

that patients with larger lesions perform poorly in both domains because they are likely to have damage to both verbal and nonverbal processing systems that may actually have separate neural substrates. Similarly, patients with smaller lesions would be less likely to have damage to either system and hence have relatively spared processing in both domains.

To explore this possibility, we examined the effect of lesion size on performance in the verbal and non-verbal domains. For the 20 patients with reconstructed lesions, we computed lesion volume (in cm³) on standardized space. While we had a range of lesion volumes in this group (ranging from 6.4 cm³ to 162.6 cm³ with mean volume of 66.7 cm³), the correlation of lesion size with overall accuracy ($r = 0.04$) or RT ($r = 0.21$) did not approach significance ($F_s < 1$), nor were there any significant correlations of lesion size within the verbal or the nonverbal domains ($F_s < 1$). This suggests that it is unlikely that lesion size alone could suffice to explain the high degree of correlation we observed on performance across the two domains.

Furthermore, if lesion size were a crucial factor, it might be expected that similarly high correlations would be observed between any two behavioural measures. To investigate this possibility, we examined correlations between different WAB subscale scores in a larger set of 97 LHD patients (including most of the LHD patients included in this study). Significant correlations with effect sizes comparable to the verbal/nonverbal correlations reported above ($r = 0.75$ for accuracy, $r = 0.95$ for RT) are only found within the respective verbal and nonverbal domains on the WAB. Table 2 summarizes some examples of within- and across-domain correlations for three verbal subscales and three nonverbal subscales. The three verbal scales reported here are 'auditory word comprehension' (AudComp; a word-to-picture matching task), 'object naming' (ObjName; a cued picture-naming task) and 'fluency' (a performance rating of speech output, incorporating factors such as phrase length, word-finding, and grammatical complexity). The nonverbal subscales are 'Raven's coloured progressive matrices' (Raven; assesses visuospatial perception and processing), 'block design' (Block; is a subtest derived from a performance IQ test), and 'calculation' (Calc.; tests arithmetical ability utilizing one or two digit numbers controlling for any comprehension or reading deficits). While correlations between pairs of verbal measures are generally high, as are correlations between pairs of nonverbal measures, correlations between verbal and nonverbal measures tend to be low—sometimes even non-significant. In other words, the correlation between performance on environmental sounds and their matched linguistic descriptors 'looks like' a correlation between two closely related language tasks on the WAB.

In summary, these analyses indicate that higher correlations in patient datasets are not merely due to covariates such as lesion size, but are likely caused by further perceptual, neural and cognitive commonalities between behaviourally

Table 2 Within- and between-domain correlations among aphasic patients' WAB subscale scores

WAB subscale	Verbal			Nonverbal		
	AudComp	ObjName	Fluency	Raven	Block	Calc.
AudComp	1	0.87**	0.63**	0.32**	0.22*	0.37**
ObjName		1	0.77**	0.26**	0.17 (n.s.)	0.29**
Fluency			1	0.21 (n.s.)	0.19 (n.s.)	0.27*
Raven				1	0.77**	0.78**
Block					1	0.81**
Calc.						1

Verbal measures depicted here are auditory word comprehension (AudComp), object naming (ObjName) and fluency of speech production. The nonverbal measures are Raven's progressive matrices (Raven), block design (Block) and calculation (Calc.) tests.

**Correlation significant at $P < 0.01$ level; *Correlation significant at $P < 0.05$ level; n.s. = correlation not significant.

correlated processes. These commonalities in turn may be direct (e.g. some common brain areas are involved in the processes of interest) or indirect (e.g. the processes have some more basic components in common), or a combination. It is not possible from such data alone to determine whether the associations between correlated measures are direct or indirect, but it is possible to say that for the present data, the high correlations are indicative of shared neural resources and processes.

Hemisphere of lesion and distracter effects

Like some previous studies (e.g. Spinnler and Vignolo, 1966; Faglioni *et al.*, 1969), but unlike Schnider *et al.* (1994), we observed significant differences between LHD and RHD groups in our task. The RHD group (all non-aphasic) performed overall at a very similar level to the mildest aphasic group (anomics), but faster and more accurately than either the Broca's or the Wernicke's patients. However, LHD patients were significantly more affected by the semantic distracter manipulation. On closer inspection, this effect is seen to be driven by the two more severely language impaired LHD groups (Broca's and Wernicke's; see Fig. 3). Interestingly, this distracter effect did not interact with domain. Thus, not only did performance levels go hand-in-hand in the verbal and nonverbal domains, but the two domains also display similar effects of semantic distance. Furthermore, while there is some evidence that deficits in semantic processing follow posterior lesions of the left hemisphere (Cappa *et al.*, 1981; Hart and Gordon, 1990; Chertkow *et al.*, 1997), a differential impairment in dealing with semantic competition was not seen in this study even on the subset of our patients with posterior lesions (see Saygin, 2001). That a semantic manipulation affected performance more in the aphasic subjects but did not differentially affect language processing is an outcome that agrees with several prior studies (e.g. De Renzi *et al.*, 1972; Duffy and Duffy, 1981). Such results may support the more general hypothesis advanced by earlier pioneers in neurology (e.g. Jackson, 1878; Head, 1926) that aphasia is correlated with or is itself a more general symbolic or conceptual deficit rather than being

restricted only to the linguistic domain. However, these hemispheric findings should be interpreted with some caution because of the disparity in sample sizes in the present study.

On dissociations

In an earlier study, Varney (1980) reported deficits in nonverbal comprehension only in patients who also exhibited deficits in verbal comprehension. However, he did find dissociations in the opposite direction, i.e. aphasic patients who were impaired in verbal comprehension but not in sound recognition. In contrast, Clarke *et al.* (1996) did find one patient who was deficient in the nonverbal auditory domain but had no diagnosed verbal comprehension deficits. Clarke *et al.* (1996, 2000) also report on subjects with impaired language comprehension who performed well on nonverbal sounds, implying that there could be dissociations of verbal and nonverbal comprehension in aphasic subjects, in both directions.

In our experiment, both task and items were closely matched across domains, response latencies as well as accuracy were recorded, and outliers were analysed quantitatively taking correlations at the group level into account. Under these conditions, we saw that deficits in the two domains largely went hand-in-hand. Three outliers for accuracy (patients J.W., R.S., W.G.) and one for RT (patient J.W.) were identified. Subsequent testing confirmed that J.W. has a persistent and reliable nonverbal auditory agnosia. Patient R.S. exhibits some evidence for a weaker dissociation in the opposite direction. W.G. was classified as an outlier based on very low scores in both domains and thus does not represent a theoretically interesting dissociation. R.S. and J.W. both have extensive lesions that are largely overlapping and thus we cannot make any localization inference based simply on the dissociations we identified.

We believe that the differences between our results and others' are due primarily to task differences, to differences in experimental design and, perhaps, partially to the random distribution of patients studied. Note that previous dissociations suggested by Varney (1980) and Clarke *et al.* (1996) were both based on a classification of impaired performance

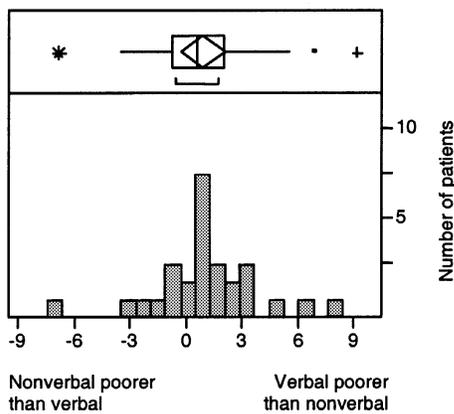


Fig. 10 Histogram depicting the distribution of z -score differences between subjects' accuracy scores in the two domains. Confirming previous findings by others and as expected given the clinical diagnosis of the population, we found aphasic patients whose performance in the verbal domain was worse than their performance in the nonverbal domain. However, we also identified several patients who exhibited the opposite pattern despite having diagnosed language disorders. Note that the histogram's outlier scale depicts the three patients identified earlier in Fig. 5A, patients J.W. (*), R.S. (+) and W.G. (-).

as performing below the level of the worst control subject. While we advocate quantifying dissociations in neuropsychology using more quantitative methods such as outlier analyses, we can compare our results to these prior studies by using the same criteria. According to these criteria, nine patients in the current study performed worse than the poorest performing control subject in the verbal domain and eight patients did so in the nonverbal domain. Furthermore, with these criteria, five of our patients would be considered to show dissociations: three impaired in verbal processing but not in nonverbal processing (M.B., P.P., C.H.) and two deficient in the nonverbal domain but not in the verbal domain (J.W., F.Y.). Note that according to this analysis, R.S.'s performance was deficient in both domains.

While Clarke *et al.* (1996, 2000) did not focus upon comparing performance in verbal and nonverbal domains and did not test or report language processing in much detail, Varney's study featured verbal versus nonverbal processing as an experimental condition (Varney, 1980). Varney also examined processing in the two domains without stipulating performance cut-offs by using standardized score differences in verbal and nonverbal tests, and found that deficits in nonverbal recognition were consistently associated with deficits in verbal recognition of equal or larger severity. We examined the distribution of standardized score differences in our sample in a similar fashion (see Fig. 10) and saw that, while the distribution is skewed in the direction Varney observed, several patients in our sample had worse impairments in the nonverbal domain. Once again, the difference between Varney's results (Varney, 1980) and ours may well be due to the fact that we used the same controlled online task across both conditions.

In summary, our data indicate that, while performance in the verbal and nonverbal domains is highly correlated, it is possible to identify not only patients who perform worse in the verbal domain (i.e. the expected result based on an aphasic sample), but we can also identify reliably patients who perform worse in the nonverbal domain—an unexpected and rarely reported outcome. However, we did not observe any systematic pattern in the lesion locations or behavioural profiles of the few patients who exhibited dissociations. It is possible that these dissociations are due to variation between individuals' pre-morbid brain organization for these functions, as well as non-uniform post-stroke recovery patterns across patients and across domains.

Localization

The strong behavioural correlations elicited by our verbal and nonverbal stimuli suggest that these two domains may utilize common brain regions and/or processes. In an effort to understand where in the brain those directly or indirectly shared resources may reside, we used lesion–symptom correlation analyses.

We performed lesion overlays on patients who exhibited specific behavioural deficits and identified some posterior regions in the middle temporal gyrus, superior temporal gyrus and IPL that were associated with impairments in our task. These regions most likely correspond to Brodmann's areas 41 and 42, posterior portions of areas 21 and 22, the superior portion of area 37, and inferior portions of areas 39 and 40. There was some indication that the insula may also be involved. The overlay maps were similar for both the verbal and the nonverbal domains. The regions of maximum overlap were more clearly defined for the nonverbal domain, whereas for the verbal condition the foci were less strong. We then re-analysed the behavioural data based on these regions to see how general the results were and to quantify any domain differences that might arise. We found that the pMTG and pSTG regions contributed significantly to performance in both domains, while the IPL region showed a tendency linked primarily to non-verbal processing. In addition, the pSTG region was significantly implicated as important for non-verbal processing above and beyond its importance for the verbal domain. Patients who performed well in the nonverbal domain all had lesions sparing the posterior areas we identified with lesion overlays, specifically the pSTG focus. We did not identify any areas for which verbal processing had quantifiably more impact compared with nonverbal processing.

Interestingly, the left-hemisphere regions we identified using overlays and further verified with quantitative analyses are typically considered to be language-specific areas of the human brain. Indeed the pSTG region we identified in the current study (the posterior portion of Brodmann's area 22) corresponds to the original Wernicke's area held since the early days of neurology to be crucial for language comprehension. We now see that Wernicke's area and the surround-

ing mid-temporal and parietal regions are implicated strongly in environmental sound processing as well. What is rather surprising is the finding that Wernicke's area itself, while it is significantly associated with deficits in both domains, is identified to be significantly more associated with deficits in the nonverbal domain above and beyond the deficits in the verbal domain. Our claim is not that Wernicke's area is selectively involved in environmental sound processing; but it is reliably and significantly implicated in our data in relation to deficits in the processing of familiar environmental sounds.

The finding that environmental sound processing relies on the same areas that are known to be important for linguistic comprehension is difficult to reconcile with very strong views on domain-specific brain regions for language. However, it is consistent with recent research on the superior temporal region. Mammalian temporal lobes contain multiple auditory areas that respond to different types and complexities of auditory stimuli (Rauschecker and Tian, 2000). Human imaging studies are revealing that different kinds of auditory stimuli are processed in various regions of the brain (e.g. Belin *et al.*, 2000). In fact, a recent functional MRI (fMRI) study by Binder *et al.* (2000) concludes that the human superior temporal region consists primarily of auditory sensory cortex. Considering the fact that speech sounds and environmental sounds are both complex auditory signals that have rich semantic associations, they could indeed be expected to share neural representations and resources. Indeed, language-related areas in the left hemisphere have recently also been implicated in the processing of environmental sounds in other lesion studies (Schnider *et al.*, 1994) and fMRI studies (e.g. Lewis *et al.*, 2001; Adams and Janata, 2002; Dick *et al.*, 2002b).

Note that we did not find a specific region that was clearly more important for performance in the verbal domain in this task. Instead, we saw that verbal deficits are associated with similar lesion locations to nonverbal deficits but less uniformly and less focally. Again, this finding is perhaps not surprising given that language is a complex phenomenon, relying perhaps upon more diverse and diffuse neural and cognitive resources. Thus following brain damage, there may be more ways for language processes to break down compared with environmental sound processing.

Conclusion

Although aphasia is often characterized as a selective impairment to language, we found that patients typically have nonverbal auditory comprehension deficits as well. In a carefully normed and controlled task involving the matching of environmental sounds and corresponding phrases to pictures, Broca's and Wernicke's aphasics were the most impaired, while anomic and right hemisphere-damaged patients showed less severe deficits. Interestingly, we found no sparing of nonverbal processing in the aphasic patients; instead, impairments in verbal and nonverbal domains went

hand-in-hand. Lesion analysis revealed that the patients with pMTG, pSTG and IPL lesions were especially impaired, suggesting a role for these regions in the processing of not only verbal but also nonverbal sounds. Furthermore, we identified the posterior part of the left superior temporal gyrus (corresponding to Wernicke's area) to be important for nonverbal sound processing above and beyond verbal sound processing. Our results and others suggest that aphasia is not a circumscribed linguistic deficit and that language may share neural resources utilized for the processing of meaningful information across cognitive domains.

Further investigation will expand on the current results, exploring for instance whether they reflect general impairments in auditory comprehension, deficits in associating auditory and visual information, or problems in accessing from memory the semantic associations of auditory input. It would also be ideal to test more patients with right hemisphere damage to gain more insight on hemispheric differences as well as to study patients with left-hemisphere damage without a diagnosis of aphasia to examine verbal and nonverbal auditory processing in a sample without a priori language disorders. We are currently carrying out related fMRI experiments with normal controls in order to shed more light on the nature of the interactions between verbal and nonverbal processes in the human brain (Dick *et al.*, 2002b).

Author note

The experimental stimuli and norms can be made available to researchers who wish to study or contrast verbal and nonverbal auditory processing in different subject populations (Saygin *et al.*, 2002). For more information on running this test on new populations, please contact the corresponding author.

Acknowledgements

We wish to thank Marta Kutas, Carl Ludy, Suzanne Moineau and Marty Sereno for helpful comments and/or assistance with testing. This research was supported by NIH/NIDCD 2RO1 DC00216 to E.B.

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Received June 16, 2002. Revised October 16, 2002.
Accepted November 20, 2002