

environment so that we can preemptively avoid X, rather than just have to react to X's presence in an emergency. But there are other advantages of feeling one's emotional reactions and knowing of those feelings. For instance, one can generalize knowledge, and decide to be cautious with any object that looks like X. Feeling an emotion offers us flexibility of response based on the particular history of our interactions with the environment.

The key components of this hypothesis are being tested in humans, in both neurological patients with lesions and normal individuals participating in imaging experiments. Some aspects of the hypothesis are also being tested in experimental animals.

Emotions and feelings are not intangible phenomena. Their subject matter is concrete and they can be related to specific systems in body and brain, no less so than vision or speech. Nor are the responsible brain systems confined to the subcortical sector. Brain core and cerebral cortex work together to construct emotion and feeling, no less so than they do in vision.

7 Words and Concepts in the Brain

Hanna Damasio

Introduction

The goal of my work is the understanding of the neural basis for certain cognitive processes and for certain behaviors. The level at which I work is the large-scale system level in the primate brain, specifically, in the human brain. I am interested in events at other levels, as for instance at cellular level or at the level of microcircuitry, or at the purely cognitive level, all of which are obviously necessary to get to a complete understanding of mind and brain phenomena, but my work is about the large-scale system level and this is the subject of this chapter.

Work in this general area has a long tradition but the current approaches and methods are actually quite new.

Functional imaging, for instance, as practiced today, is literally just beginning as an approach. We can use it to perform experiments in normal individuals as well as in neurological patients. We take advantage of either the regional distribution of a radiolabeled tracer in the human brain; or we make use of the effects of a changing magnetic field on brain physiology. In either case, we measure an index of brain function *when* the brain is involved in performing a particular cognitive behavioral task.

With the modern *lesion method*, which remains the gold standard for bridging brain and cognition, focal areas of brain damage, which we call lesions, are used as probes to test hypotheses about the possible function of a system. The system in question is always made up of several components, and the function is always the result of the combined operation of the components within the system. The lesion is a "knock-out" of one component, and it allows us to test our prediction as to what should happen when the component is knocked out. In fact, it is the same strategy used in molecular biology when you selectively knock out a gene and verify if the results of the lack of that gene conform to your prediction.

Although lesion work is really the oldest in neurosciences, the systematic lesion method approach is quite recent. It could only appear after modern neuroimaging techniques allowed us to study the human brain *in vivo* (see H. Damasio 1995). Just as with functional imaging, and perhaps even more so, proper lesion method experiments require a complicated set up of human and technical resources. This probably explains why it is so rarely practiced.

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What I would like to report here is the result of a number of studies on the neural correlates of language, specifically, the neural systems that are possibly involved in word retrieval, and in the corresponding concept retrieval.

If you open a textbook of neurology, neuropsychology, or linguistics, in a section concerning the possible neural basis of language, you are likely to read that there is an anterior region in the left hemisphere, more precisely in the left frontal operculum, that allows the production of words, and a posterior region, in the left superior temporal gyrus, which allows the comprehension of the spoken word. These two areas are named for their "discoverers" as Broca's area and Wernicke's area, and they have been with us since the second half of the nineteenth century (Broca 1861; Wernicke 1874). In the 1960s Norman Geschwind (1965) revived the interest in these areas and added a few others, also in the left hemisphere, that he believed were involved in the production and comprehension of language. These included the inferior parietal lobule—parts of the gray matter in the supramarginal and angular gyri, as well as the white matter underneath, the famous arcuate fasciculus connecting Wernicke's and Broca's areas. He also added part of Brodmann's area 37 to the language map. Such a diagrammatic representation was fine at the time; but, unfortunately, it is still the prevailing anatomical framework for the discussion of the neural basis of language. We all know, of course, that the story is not this simple. The problem with the old anatomical account is not that it is wrong but that it is quite incomplete.

It is still useful to maintain such designations as Broca's aphasia and Wernicke's aphasia, in the sense that they predict likely loci of brain damage in a neurological patient. The designations are clinically useful. But we no longer accept the idea that there are only these two language-related areas, connected by a direct and unidirectional pathway that translates thought into words. The way we see the production of language today involves many brain regions connected bidirectionally, forming complex systems.

Where does the idea that there are language areas beyond Broca and Wernicke come from? As usual, individual observations gave us the first clues, long before systematic experiments could demonstrate it. For instance, we have solid evidence that a subject with damage to the anterior sector of the left temporal lobe, involving the temporal pole, in spite of perfectly fluent, non-aphasic language, will be severely impaired in the retrieval of names for specific persons. The patient knows the person and can provide verbal descriptions that allows an independent examiner, who does not know what stimulus the patient is looking at, to identify the person the patient is trying to name. On the other hand such a patient can name perfectly well other objects, either natural or man-made, and can also look at pictures depicting actions and retrieve the correct word denoting those actions. So what we find is a very circumscribed deficit of word retrieval and a circumscribed area of brain damage in the left temporal pole, away from either Broca's area or Wernicke's area, which are not damaged at all.

On the other hand a subject with a lesion in the left temporal lobe, but located posteriorly in the temporo-occipital junction away from the temporal pole, as well as from Wernicke's and Broca's area, will show a deficit in the retrieval of words denoting manipulable objects. The retrieval of words for persons or animals is entirely normal.

Many observations such as these led us to construe the following hypotheses:

General hypothesis. The retrieval of words which denote concrete entities belonging to distinct conceptual categories depends upon relatively separable regions in higher-order cortices of the left temporal lobe.

Specific hypothesis. The retrieval of words which denote concrete entities belonging to distinct conceptual categories depends upon relatively separable regions in higher-order cortices of the left temporal lobe.

In order to address these hypotheses we studied a large group of subjects with single lesions of either hemisphere so that we could sample vast sectors of the telencephalon.

1. Lesion Studies

Methods

Subjects Subjects with unilateral brain damage ($n = 116$) were selected from the Patient Registry of the University of Iowa's Division of Cognitive Neuroscience. All gave informed consent in accordance with the Human Subjects Committee of the University of Iowa. As a group, the subjects permitted us to probe most of the telencephalon—their lesions were located in the left ($n = 68$) or right ($n = 48$) hemisphere, in varied regions of the cerebral cortex. Lesions were caused by either cerebrovascular disease ($n = 95$), herpes simplex encephalitis ($n = 5$), or temporal lobectomy ($n = 16$). Handedness, measured with the Geschwind-Oldfield Questionnaire which has a scale ranging from full right-handedness (+100) to full left-handedness (-100), was distributed as follows: 109 were right-handed (+90 or greater); 4 were left-handed (-90 or lower); 3 were mixed-handed (< +90 and > -90).

All subjects had been extensively characterized neuropsychologically and neuroanatomically, according to the standard protocols of the Benton Neuropsychology Laboratory (Tranel 1996) and the Laboratory of Neuroimaging and Human Neuroanatomy (H. Damasio and A. R. Damasio 1989; H. Damasio and Frank 1992; H. Damasio 1995). All subjects had at least average verbal intelligence (as measured by the WAIS-R), a high school education or higher, and no difficulty attending and perceiving visual stimuli. Some subjects in the sample were recovered aphasics, but in no case was the residual aphasia of such severity as to preclude the production of scorable recognition

responses. Subjects with severe aphasia or with severe visual perceptual deficits were not included in the brain-damaged sample.

We studied 55 normal controls, who were matched to the brain-damaged subjects on age, education, and gender distribution.

Stimuli The unique stimuli were pictures of persons (presented as faces), drawn from the Iowa Famous Faces Test ($n=77$) (Tranel, H. Damasio, and A. R. Damasio 1995) and a modified version of the Boston Famous Faces Test ($n=56$; Albert, Butler and Levin 1979). The faces used in the experiments were of persons who would have been known to the subjects prior to the onset of their brain damage. Face pictures were prepared as black-and-white slides in which all non-face background features were deleted. The non-unique stimuli were pictures of animals ($n=90$) and tools ($n=104$) drawn from the Snodgrass and Vanderwart (1980) line drawings and from a set of photographs we have prepared (A. R. Damasio *et al.* 1990). The categories of animals and tools did not differ in word frequency, as derived from the Francis and Kucera (1982) database.

The choice of the three types of item was dictated by previous studies and by the fact that the entities represent varied conceptual categories and have a diverse characterization in terms of sensory and motor specifications and contextual complexity (A. R. Damasio and H. Damasio 1994). These entities vary along a number of dimensions which characterize their properties and the interactions of the individual with the entities, including sensory channels, used in the interaction: motor pattern (if applicable—for instance, manipulability); natural or artifactual status; physical characteristics; capability for self-movement; and so on (see Tranel, H. Damasio, and A. R. Damasio 1997 for a detailed explanation of these factors). 'Contextual complexity' refers to the complexity of relationships which help constitute an item, along with its physical characteristics. Contextual complexity permits us to classify a given concrete entity along a dimension that ranges from *unique* (an entity belonging to a class with $N=1$ and depending on a highly complex context for its definition), to varied *non-unique* levels (entities processed as belonging to classes with $N>1$, having many members whose definition depends on less complex contexts).

Procedure The stimuli were shown in random order one-by-one on a Caramate 4000 slide projector, in free field. For each stimulus, the subject was asked to tell the experimenter what (or who) the entity was. If the subject produced a vague or superordinate-level response (e.g. "something you can work with" or "a movie star"), the subject was prompted to "be more specific; tell me exactly what [who] you think that [thing] is." Prompting was repeated if the experimenter sensed that the subject could generate a more specific answer, or if the subject produced a paraphrastic response that might be difficult to score. Time limits were not imposed. All responses were audio-

taped and prepared as typewritten transcriptions. The transcriptions were scored by raters who were blind to the experimental hypotheses, following the procedures specified below; when necessary, the raters also used information from the audiotapes.

Neuropsychological Data Quantification and Analysis The dependent measure was a recognition score and a naming score. For each stimulus the subject's recognition/naming response was scored as follows. First, if the stimulus was named correctly, the item was scored as a correct recognition and naming. In other words, we accepted correct naming as unequivocal evidence of correct recognition. Our rationale for this approach is that we have never found a subject who would produce a correct name, and then fail to recognize the stimulus that was named. As part of one of our studies, we explored in a subset of subjects with correct naming responses whether they had retrieved the concept for an item prior to retrieving its name, and, as we expected, they had. In fact, we do not believe it is possible for someone to name, accurately and reliably, an unrecognized item, even in the extreme instance of patients with Alzheimer's disease who may seem, on the face of it, to do just that. (A severely inattentive or demented patient may produce a naming response and then, by the time the response comes under scrutiny, have lost from working memory the material recalled during concept retrieval, leading to the appearance that the patient has named but not recognized. We believe this is an artifact of the attentional/memory defect, though, and we stand by the claim that concept retrieval remains a prerequisite for accurate naming.)

Second, for items that were not named correctly, the subject's responses were presented (as typewritten transcriptions) to raters who were asked to determine what the stimulus was *from the description alone*, without having in front of them either the stimulus or its name. Thus, if the subject had provided a specific description of the entity, including information about characteristics, functions, and properties (e.g. "that's the president who was killed... his brother was also killed, later... he had an affair with that movie star who killed herself"; or "that's an animal that you find on farms; it makes an oinking sound and likes to roll in the mud"), that was sufficiently detailed so that raters could identify the entity from the description alone, without having in front of them the stimulus or its name, the response was scored as correct recognition but as a failure in naming. If on the other hand it was not possible for the rater to come up with the correct name of the stimulus based on the response of the subject, the item was classified as a failure in recognition which precluded correct naming. Therefore the item was not counted as a failure in naming.

For each subject and each category, the number of correct recognition responses was divided by the number of stimuli in the category and multiplied by 100 to yield a percent correct recognition score. The naming score

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was calculated by summing the number of correct naming responses using *only* those stimuli for which the subject had produced a correct recognition response. Classification of brain-damaged subjects as normal or abnormal on the six tasks was conducted by calculating for each subject the extent to which their scores differed from the means of the normal controls.

Neuroanatomical Data Quantification and Analysis The neuroanatomical analysis was based on magnetic resonance (MR) data obtained in a 1.5 Tesla scanner with an Spg sequence of thin (1.5 mm) and contiguous T₁ weighted coronal cuts, or in those subjects in whom an MR could not be obtained on computerized axial tomography (CT) data. All neuroimaging data were obtained in the chronic epoch (at least three months post-onset of lesion). Each subject's lesion was reconstructed in three dimensions using Brainvox (H. Damasio and Frank 1992; Frank, H. Damasio, and Grabowski 1997). The anatomical description of the lesion overlap and of its placement relative to neuroanatomical landmarks was performed with Brainvox, using the MAP-3 technique. All lesions in this set were transposed and manually warped into a normal 3-D brain, so as to permit the determination of the maximal overlap of lesions relative to subjects grouped by neuropsychological defect. A detailed description of MAP-3 is provided in Frank, H. Damasio and Grabowski 1997; in brief, it entails: (1) a normal 3-D brain (the template brain) is resliced so as to match the slices of the MR/CT of the subject and create a correspondence between each of the subjects' MR/CT slices and the normal resliced brain; (2) the contour of the lesion on each slice is then transposed onto the matched slices of the normal brain, taking into consideration the appropriate anatomical landmarks; (3) for each lesion the collection of contours constitutes an "object" that can be co-rendered with the normal brain. The objects in any given group can intersect in space, and thus yield a maximal overlap relative to both surface damage and depth extension. The number of subjects contributing to this overlap is thus known.

Results

Impaired Word Retrieval The subjects were first classified according to their task performance, which was normal (within 2 standard deviations of the mean of the normal controls) in 97 subjects (47 with left hemisphere damage, 50 with right) and abnormal (2 or more standard deviations below normal) in 19. All but 1 of the latter had damage in left hemisphere, thus supporting the prediction that disruption of word retrieval for all three categories would be correlated with lesions in left but not right hemisphere. The scores of brain-damaged subjects who performed abnormally in each of the three word categories were significantly lower (all P 's < 0.001) than those of the brain-damaged subjects who performed normally.

In addition to isolated word retrieval defects for unique persons, for animals, or for tools, the instances of two combined defects always involved "persons/animals" or "animals/tools", but never "persons/tools". When naming of persons and tools was impaired in the same individual, naming of animals was impaired as well. The nonoccurrence of instances of the persons/tools combination is statistically significant ($P < 0.001$). The anatomical evidence that follows shows why this combination of defects is not possible on the basis of a single lesion.

The lesions of the 18 left hemisphere subjects with abnormal performance revealed the following: maximal overlap of lesions for abnormal retrieval of words for persons was found in left temporal pole (TP); maximal overlap of lesions for abnormal retrieval of words for animals was found in left inferior temporal cortex (IT; mostly anterior); maximal overlap of lesions for abnormal retrieval of words for tools was found in posterolateral IT, along the junction of lateral temporo-occipito-parietal cortices (a region we have designated as "posterior IT+"). In all instances the lesion overlap encompassed both cortical and subcortical white matter. Thus the prediction that the disruption of word retrieval for each category would be correlated with partially separable neural sites within left higher-order cortices of the temporal region was supported, qualified only by noting that impaired retrieval of words for tools was correlated with damage that extended into left inferior parietal cortex and the temporo-occipital junction. To assess the reliability of the findings, we conducted a test using anatomical placement of lesion as the independent variable, and compared, for each word category, the naming scores of three groups of subjects: those with lesions in TP only; those with lesions in posterior IT+ only; and those with lesions centered in IT (whose outer borders trespassed, in some instances, into either TP or posterior IT+, but not into both). A MANOVA yielded highly significant results for persons ($F(2,20) = 14.85, P < 0.001$) and tools ($F(2,20) = 6.65, P < 0.01$), and a marginally significant result for animals ($F(2,20) = 3.30, P = 0.058$), supporting the conclusion that the anatomical placement of lesion is a crucial factor determining word retrieval performance. The close link between neuroanatomical structure and lexical category is also evident at individual subject level.

In sum, impaired retrieval of words for concrete entities correlated with damage in higher-order cortices outside classic language areas; moreover, impairments in the three word categories were correlated in a consistent manner with separable neural sites. Two of the latter, TP and posterior IT+, are not even contiguous, do not overlap cortically or subcortically, and are so distant as to make it virtually impossible for a single lesion to compromise them without also compromising the intervening region. This explains why a combined defect for persons and tools never occurred in our sample.

Impaired Retrieval of Concepts What if instead of looking at the maximal overlap of lesions in relation to defective word retrieval we looked at maximal overlap of lesions relative to defective recognition of the presented item, that is, defective concept retrieval? I should mention here that all subjects are tested for strictly visual perceptual defects with a large battery of psychophysical experiments and that none of the subjects in this group has a perceptual visual defect that could explain the failure to recognize a visually presented stimulus.

The subjects were first classified according to their task performance, which was normal (within 2 standard deviations of the mean of the normal controls) in 76 subjects (27 with right hemisphere damage, 49 with left) and abnormal (2 or more standard deviations below normal) in 40 (21 with right hemisphere damage, 19 with left). The scores of brain-damaged subjects who performed abnormally in each of the three conceptual categories were significantly lower (all P s < 0.0001) than those of the brain-damaged subjects who performed normally.

A number of subjects had concept retrieval defects for one single category: persons ($n = 7$), animals ($n = 19$), or tools ($n = 5$). There were also subjects in whom concept retrieval was affected in two categories. The combination "person/animals" was found in 6 subjects; the combination "animals/tools" was found in 3 subjects. However, no subject showed a combined "person/tools" defect, and in no instance were all three categories involved. In order to test the reliability of the negative findings concerning the persons/tools and persons/animals/tools combinations we conducted a Fisher Exact Probability Test on the following matrix (where n is the number of subjects with the designated set of defects): persons and tools ($n = 0$), persons but not tools ($n = 13$), tools but not persons ($n = 8$), neither tools nor persons ($n = 19$). The test yielded a P -value of 0.029, supporting the conclusion that the nonoccurrences of combined persons/tools and persons/animals/tools defects were not due to chance. Once again, the anatomical evidence given next will show why these combinations cannot be found with single unilateral lesions.

The overlap of lesions of the 40 subjects with abnormal performance revealed that: (a) in subjects with abnormal retrieval of concepts for persons, lesion overlap was maximal in right temporal polar region; (b) in subjects with abnormal retrieval of concepts for animals, lesion overlap was maximal (i) in right mesial occipital (mostly infracalcarine), extending into mesial ventral temporal region, and (ii) in a second locus (with a smaller number of overlaps) in the left mesial occipital region; (c) in subjects with abnormal retrieval of concepts for tools, lesion overlap was maximal in left lateral occipital—temporal—parietal junction. In all cases, the maximal overlaps concerned both cortex and subcortical white matter, as was seen for abnormal word retrieval.

In sum, impaired retrieval of concepts for concrete entities correlated principally with damage in higher-order cortices in right temporal polar

and mesial occipital/ventral temporal regions, and in lateral occipital-temporal-parietal regions. The spatial distribution of the lesion loci critical for the appearance of these defects explains why a defect involving persons and tools could not be found in subjects with unilateral lesions. The loci for those two categories are in different hemispheres. Hence, only a suitable bilateral lesion is likely to produce this combination. The same applies to an impairment involving persons, animals, and tools.

2. PET Studies

What happens in normal subjects when they perform the same tasks used in the lesion studies? Are the areas revealed by the lesion overlaps particularly engaged during the performance of comparable word retrieval tasks? In order to answer this question we have been performing PET studies in normal individuals, using subsets of the same stimuli and precisely the same paradigm. The hypotheses remain the same:

General hypothesis. Access of word forms for visually presented concrete entities depends on activation of the left inferior temporal cortex and/or the left temporal pole.

Specific hypothesis. Accessing proper nouns will activate the left temporal pole; accessing common nouns the left IT. Activation patterns in IT will be different for retrieval of words denoting animals and tools/utensils.

Methods

Stimuli We used stimuli from the test batteries employed in the lesion study for the target tasks and a set of unknown human faces presented either right-side up or upside down for the control task. They were presented in black and white on a video screen suspended 15 inches from the subject, using a microcomputer-driven video laser disk. In a pilot study with normal subjects, we determined empirically the rate of presentation for each set of stimuli that would produce error rates of approximately 10 percent. In order to achieve similar levels of performance, the rate of stimulus presentation had to be different among the tasks. Familiar faces were presented every 2.5 sec., tools every 1.8 sec., and animals every 1.5 sec. (stimuli for the control task were presented every 1.0 sec.). Each stimulus was on screen for 25 percent of the stimulus time cycle; otherwise the screen was black. Faces for the person naming task were selected during a pilot session 24–48 hours before PET by having the subjects view a collection of famous faces from the lowa and Boston Famous Faces tests and indicate whether they recognized each person. During the pilot session, subjects were told that they should not name any of the persons, and no names were provided by the experimenters. For each

subject, the set of faces chosen for the PET experiment was composed from those that the subject recognized. All other items were derived from the standardized set of stimuli used in our laboratory. In the PET scanning session, subjects performed each task twice, in random order, from 5 seconds until 65 seconds after injection of [^{15}O] H_2O . Subjects named approximately 85 percent of stimuli in each category, and task performance success was not significantly different among the naming tasks (nonresponse rates for naming persons, animals, and tools were 17.0%, 14.8%, and 11.7%).

Procedure PET data were acquired with a General Electric 4096 Plus whole body tomograph, yielding 15 transaxial slices with a nominal interslice interval of 6.5 mm and an intrinsic resolution of 6.5 mm in all axes using the [^{15}O] H_2O bolus technique. The labelled water was continuously available in the scanner room. Approximately 50 mCi of [^{15}O] H_2O was administered for each of eight injections. Regional cerebral blood flow was estimated according to the autoradiographic method (Herscovitch, Markham, and Raichle 1983; Hichwa, Ponto, and Watkins 1995).

All subjects also underwent MR procedure using the parameters mentioned in the section on lesion studies. The MR images were used to reconstruct the brain in 3-D. This data set was used to orient the PET slices parallel to the longitudinal axis of the temporal lobe, in an orientation parallel to the plane that would intercept both the lowest points in the temporal poles and the lowest points in the occipital lobes. It also allowed us to define our region of interest.

We restricted the search volume, in the first phase of the study, to the overall region hypothesized for the lesion study: IT and TP. The limits of the TP/IT region were defined as the middle, inferior, and fourth temporal gyri, bounded superolaterally by the superior temporal sulcus and inferomedially by the collateral sulcus. The posterior boundary of the temporal lobe conformed to the definition in the atlas of Ono, Kubik, and Abernathy (1990). Anteriorly, TP was separated from the superior temporal gyrus by a plane perpendicular to the longitudinal axis of the temporal lobe at the level of the anterior ascending ramus of the Sylvian fissure.

The search volume used in the PET analysis was defined as all stereotactic voxels that corresponded to TP/IT in the majority of the subjects, and was determined as follows: (1) Talairach space was constructed for each subject (Talairach and Tournoux 1988; Grabowski, Damasio, and Damasio 1995); (2) The TP/IT regions of interest of each subject were converted into binary volumes, Talairach-transformed, and summed. Pixels with values reflecting the overlap of at least five subjects comprised the search volume.

The collection of 3-D MR data enabled us to avoid several potential technical artifacts in this study. We eliminated extracerebral pixels from the data set and we included in the search volume only those pixels which

corresponded to TP/IT in the majority of the subjects. We are confident that all of the regions of activation which we detected were either exclusively in TP/IT or, if they spilled beyond its boundary, were centered within it.

Data Analysis MR and PET data were coregistered using PET-Brainvox (H. Damasio *et al.* 1993; Grabowski, Damasio, and Damasio 1995) and Automated Image Registration (AIR) (Woods, Mazziotta, and Cherry 1993). PET data were subjected to Talairach transformation and then smoothed with an isotropic 16 mm Gaussian kernel. The final calculated image resolution was $19 \times 19 \times 18$ mm. PET data were analyzed with a pixelwise linear model which estimated coefficients for global flow (covariable) and task and block/subject effects (classification variables) (Friston *et al.* 1995; Grabowski *et al.* 1996). Global flow did not differ significantly across tasks. We compared adjusted mean activity in each of the three naming conditions to the control task using pixelwise *t*-statistics.

The common intracerebral stereotactic volume was 1106.3 cm^3 . The search volume (bilateral TP/IT) was 123.4 cm^3 . Using Worsley's theory of Gaussian fields (Worsley *et al.* 1992; Worsley 1994), the threshold *t* value (volumetric alpha 0.05, 58 degrees of freedom, 19 resels) was 3.82. We also analyzed the *t* fields using spatial extent rather than intensity thresholding.

Results

The results are very much concordant with those obtained with the lesion method. We do find the left temporal pole active during the retrieval of names for unique persons and two regions in the inferotemporal cortex active during the retrieval of words denoting animals and the retrieval of words denoting tools, thus supporting our initial hypothesis.

However, this is not all. If instead of limiting the search to the regions initially hypothesized we look at the whole brain volume, we also see differential activation in the left frontal operculum.

As for IT, a region of interest, the inferior and middle frontal gyri was identified in all subjects and used as the search volume. A pixelwise analysis showed that, in fact, there were three distinct foci of activation: one centered in the pars triangularis (Brodmann's area 45) present for all three categories; two other ones, one in prefrontal region present for word retrieval of unique persons; and another, in premotor cortex in the precentral sulcus, present for word retrieval of tools.

A further analysis of this premotor activation using a different approach, local standard space, was then performed. This method allows the analysis of PET data with respect to the distribution of flow values in each subject along an axis of a region identified for each subject (Grabowski *et al.* 1995). We delineated, for each subject, the area encompassing the gray matter of the precentral sulcus between the Sylvian fissure and the superior frontal sulcus. A

2-D Cartesian coordinate system was imposed on this region with a Y-axis extending between the upper and lower limits mentioned above and an X-axis perpendicular to the Y-axis. For this type of analysis no spatial filtering of the data is performed, and analysis is done using the pixelwise linear model employed for Talairach space (see details in Grabowski, Damasio, and Damasio 1998). This analysis highlighted the differential distribution of flow values in the precentral sulcus region for the word retrieval of tools. It is also interesting to note that the Talairach coordinates of this particular region of activation are very close to the region where activation is found during verb generation tasks (Petersen *et al.* 1998; Grabowski *et al.* 1996). In other words, activations related to words for actions and for entities with characteristic actions, as in the case of manipulable tools, are clustered about the same region.

Moreover, we also have described subjects with lesions in this area who show deficits in the retrieval of words denoting actions (A. R. Damasio and Tranel 1993).

Conclusion

From the data presented we can draw the following conclusions:

1. The neural support for normal language processes, even as assessed by one single aspect of language function, such as word retrieval, does not depend only on the two classic "language areas". A number of other areas are necessary to support normal language processing.
2. Given the same entity, damage to certain areas will impair naming but not preclude satisfactory concept retrieval; while damage to other areas will impair concept retrieval and thus naming, too. Given the same entity, it is possible to separate components of the system primarily dedicated to word retrieval or to concept retrieval.
3. The optimal retrieval of words for entities belonging to varied conceptual categories depends on anatomically segregated regions. This suggests that the systems which support word retrieval for varied categories are, at least in part, segregated.
4. The same applies to the retrieval of concepts themselves. Different regions are consistently associated with the retrieval of concepts for entities within certain categories.
5. The anatomical regions identified by lesions (e.g. *dysfunction sites*) are consistent with the anatomical regions identified in PET (e.g. *activation sites*).