Cognitive Neuroanatomy of Language

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Language-related functions were among the first to be ascribed a specific location in the human brain (Broca, 1861). Recently, high-resolution MR images were obtained (1994) by Cabanis et al., from the still preserved brain of the first patient described one hundred and thirty years before by Paul Broca, in 1865. The patient, called Leborgne, was also known by his nick-name «Tan-Tan», which was the only stereotypic oral production he could produce after his stroke.

It is possible to see on MR images how the very large lesion destroys a fair amount of frontal cortex and the underlying white matter, and spreads towards the head of the caudate, far beyond the limits of what we call Broca's area.

Brain/language Relationships : The «Aphasia Model»

Over the past century, many attempts have been made to find clear relationships between aphasia and brain lesions, that is to use aphasia as a pathophysiological model to study brain/language relationships. As we all know, some aspects of this model are well-established; the exact site of the lesion, its size and etiology strongly influence the observed aphasia and its prognosis. There are few critical regions such as the posterior part of the left superior temporal region —also called Wernicke's area— whose lesions usually cause massive deficits on several language dimensions.

However, most of aphasic symptoms, such as anomia, are related to various lesion sites corresponding to a «distributed anatomy of symptoms», suggesting that a given symptom may arise from lesions localized at different points of a network distributed over the left hemisphere if not the entire brain.

Besides, the relationships between lesion anatomy and language disorders appear more stable when symptoms, rather than syndromes, such as Broca or Wernicke's aphasia, are considered.

In fact, the classical dogma on brain and language is often challenged by clinical observations that Anna Basso and co-workers (1985) called Exceptions, such as fluent aphasias with pre-rolandic lesions and vice-versa or even more paradoxical cases showing no aphasia at all despite destruction of the whole left perisylvian area, or crossed-aphasia resulting from right-sided lesions in right-handed subjects.

Many factors have been invoked to explain such exceptional cases, not really so exceptional as they were about 12 % in the Basso series.

Apart from handedness, other subject-specific factors such as age and gender may influence aphasia type and severity.

Cultural factors starting from literacy to bilingualism and familiarity with language material or language exercises are obviously major factors.

The dynamics of post-lesional phenomena should also be considered in this model, both in their neural and linguistic dimensions.

And finally, the effects of patient motivation and the influence of aphasia therapy should certainly not be overlooked.

Brain/language Relationships : Functional Imaging Data

Functional imaging techniques, and in particular PET, are potentially of great heuristic value to try to disentangle all these complex influences on the brain/language model. In particular, these techniques should, sooner or later, help us to understand more about recovery of language functions.

Indeed, aphasia should be considered not only from a negative viewpoint, as a set of deficits caused by brain lesions, but also from a positive viewpoint, as the behavioral consequences of both reorganization of neural systems and cognitive compensatory strategies.

In fact, there are different ways to use functional brain imaging to expand our knowledge beyond the limits of the classical lesion-based model.

Activation in Normal Subjects.

The first one is to address whether the regions related to impairments of specific language functions when damaged, might be activated in normal subjects during language tasks relying on the same functions.

For instance, several authors such as Geschwind (1965) or Cappa et al. (1981) claimed that phonological disorders are associated with lesions close to the left sylvian fissure whereas lexical semantic disorders are linked to lesions of regions that are more distant to the fissure, such as the inferior parts of the parietal (Brodmann area 39) or the temporal lobes (Brodmann area 37).

Using PET and a language activation experiment, we addressed (Démonet et al., 1992a, Démonet et al., 1994a, Démonet et al., 1994b) whether such a topographical segregation between phonological and lexical semantic processes might be observed in normal subjects when performing two language tasks, respectively related to each of these processes.

We used monitoring tasks with 30% targets among distractors in series of stimuli presented binaurally at a constant rate (1 per 3s); subjects responded by clicking on a button with right fingers.

In the Phoneme task, stimuli were 3- or 4-syllable non-words and the target was the phoneme /b/ if, and only if, the phoneme /d/ was detected in a preceding syllable.

For example, subjects had to detect /b/ in the non-word REDOIZABU since both /d/ and /b/ are present, but they should not click on the non-words IDOFUPO as /d/ is present but the target /b/ absent, in ZOTAFABI since the target /b/ is present but not preceded by /d/ nor in MOIGAJOPO that represents a complete distractor.

In the Word task, targets were nouns of small animals (smaller than a chicken or a cat) preceded by a «positive» adjective in adjective/noun pairs. For example, target was «kind mouse», and distractors were «superb elephant» with a positive adjective but a big animal, «bad wasp». with a small animal preceded by a negative adjective, or «horrible lion» that represents the complete distractor.

Figure 1 represents statistical maps displaying vowe in the brain in which significant changes were observed.

In the superior part of the figure, are represented blood flow increases in the semantic task compared to the phonological one and in the lower part of the figure, blood flow increases in the phonological task compared to the semantic task.

These results are in very good accord with our hypotheses based on findings in aphasic patients.

Indeed, the topography of blood flow increases matched well the distribution of lesions generating either phonemic disorders, namely regions close to the sylvian fissure or lexical semantic disorders, namely inferior temporal and inferior parietal localizations.

I would focus my talk, for few minutes, on the data of phonological processing I have just presented.

There are several PET studies on this topic that have been published in the last years —see, for example, Petersen et al. (1988), Zatorre et al. (1992), Sergent et al. (1992), Démonet et al. (1992a) and Paulesu et al. (1993)— and all the results emerging from these works confirm the importance of left perisylvian cortex in phonological processing. The relative convergence of these results should be highlighted, as such studies came from different paradigms, and different PET machines as well !

However, the experiments implicate left perisylvian areas of activation that do not strictly overlap (Figure 2). Such different results may be explained by several factors that allow us to understand better the general paradigm of language activation.

First of all, phonological processing is not a unitary psychological operation involving a single neural system, since it can be characterized as the conjunction of acoustically based processes,

articulatory based processes, sequential or global computation of phonological analysis ... and the description is not exhaustive.

Two additional, but important, factors can account for the difference:

— First, the nature of stimulation modality, either auditory or visual, of course induces activation of neural networks that differ in some aspects

— Second, the choice of the references task, *id est* the task that will be compared to the phonological condition is of crucial importance. Resting state (no stimulation, no mental activities, no motor output) so resembles «brain death condition» that it seems unrealistic. On the other hand, references task involving some cognitive processes, such as passive listening or detection of tones, may obviously obscure the activities of neural structures equally engaged in both references and phonological tasks.

Finally, two factors that are not specific to language activation have to be mentioned since they may strongly alter brain activation results.

The first one is related to the influence of stimulating conditions such as rate of presentation and exposure duration of stimuli. These factors have been recently investigated in great detail by Price et al. (1992, 1994).

For example, results from Price et al. (1992) showed that there is a linear relationship between the amount of activation in the primary auditory cortex and the increasing number of words that subjects were listening to.

Such linear relationship is not observed however in Wernicke's area which tends to respond equally to word presentation whatever the rate of presentation.

Another very important factor is related to the degree of familiarity with the task, the identification of the neural correlates of learning mechanisms during a cognitive task being obviously a crucial issue. Comparing the same language task (verb generation task) in naive and over-practiced conditions, Raichle and his co-workers (1994) demonstrated a marked influence of practice effects on the activation pattern observed with the verb generation task. The activation observed in subjects who performed a verb generation task for the first time, in particular that in the left frontal cortex, almost completely vanished after subjects had over-practiced the task and the same word list stimuli. But when another word list stimuli is presented to the same subjects, the first pattern of activation reappears.

All these factors should certainly be controlled in any activation studies and particularly in aphasic patients.

Resting State in **Patients**

The second way to use functional imaging and explore brain correlates of aphasia is to investigate the metabolic abnormalities that are induced by the lesions and are seen in functional images during a resting state.

A fair number of studies have been done especially in the States during the eighties. To my view, one of the major contributions of these studies was to demonstrate the existence of massive remote effects of lesions with metabolic depression spreading far away from the anatomical site of the actual lesion. The most striking example of these remote effects relates to so-called subcortical aphasia in which hypometabolism in the ipsilateral cortex is very frequently observed.

Results from one of our previous studies (Démonet et al. 1992b), based on SPECT data, highlighted examples of such remote effects with, in particular, a marked hypoperfusion in left cortical regions distant from the subcortical lesion restricted to the left striato-capsular region.

Some of these studies also reinforced the previous finding that direct or indirect damage to specific lesion such as the left posterior temporal region has a critical role in both aphasia type and prognosis.

Finally, follow up studies have been done and some others are currently reported or going on. However, these longitudinal data are still unclear, if not contradictory.

In general, the functional significance of the abnormalities or longitudinal changes in brain metabolism observed at rest remains to be clarified.

For instance, remote hypometabolic effects may represent, at least, two different phenomena.

On the one hand, the affected regions may be only de-afferented but still can participate in functional activation via other connections or networks.

On the other hand, these hypometabolic regions, particularly when they lie not too far away from the actual lesion or within the same vascular territory, may be actually affected by a neuronal loss, leading to a definitive lack of function.

Activation in Patients

The shortcomings of resting state PET studies obviously incline to explore in patients the functionality of the spared regions by using activation tasks.

This will constitute the third, and last, part of my talk.

In fact very little has been done so far using up-to-date methodological standards of PET activation that is high-resolution rCBF recordings using the O15 technique.

In Figure 3 are presented the results of one of such rare studies which was published in 1995 by Weiller et al. They studied 6 Wernicke aphasic patients with retro-rolandic lesions and a good recovery.

By comparison to the activations observed in a non-word repetition task and in a verb generation task in normal subjects, aphasics demonstrated, of course, no activation in the damaged region and increased supra-normal activations in the right hemisphere, both in the superior temporal and the inferior frontal regions and in both tasks.

Although appealing at first glance, this type of studies soon appear particularly complex because they combine two main sources of variance:

— one is related to brain lesions and aphasia, and we've already seen some of these factors in the first part of this presentation

— the other source of variance comes from the many factors that may distort the results of cognitive activation even in normal subjects.

In general, such complexity suggests that activation can only be explored on the basis of single-subject studies.

However, they are also many problems for interpreting specific activation results in such studies.

For example, a massive lesion involving a major part of the left hemisphere induced in a patient, among other language disorders, a deep dyslexia.

During a reading task in which patient performance was impaired, an activation of the right hemisphere was observed. But in fact, what else could be predicted, as only very few regions were spared in the left hemisphere.

The question of the specificity of such activations in the right hemisphere can be illustrated by data recently obtained in another patient by Walburton et al. (1996).

Figure 4 shows PET activation results co-registred with the actual MRI of this particular patient who presented a left posterior lesion.

The experimental task was verb generation on which this patient performed well. Although right hemispheric activations were seen in the verb generation minus rest comparison, these were no longer apparent in the verb generation minus listening comparison.

This implies that right-sided signals do not correspond to some sort of vicarious processes that can be involved in the verb generation task but are rather related to listening to words, a process that is common to verb generation and listening.

Thus, as the key issue of such studies is the mechanism of recovery and compensation of aphasia disorders, we are facing an even more complex problem.

We have first to specify activations in terms of

— signal localization

— task-specificity

— and time curse after lesion onset

and secondly, to establish causal relationships between functional activations and recovered performance.

Many aspects of this problem remain to be addressed in the future.

I'd like to close my talk by giving you an example of activation of a particular case of aphasia in which activation data provided some hints on the mechanisms of functional compensation in aphasia.

We studied (Cardebat et al, 1994) a case of a young man who suffered from an ischemic stoke which destroyed the left posterior sylvian region. He presented a severe Wernicke's aphasia in the first stage of evolution; after few months, he evolved towards a rare syndrome called deep dysphasia in which the main symptom is a deficit of repetition.

Repetition of concrete nouns was possible but with semantic paraphasias such as fork repeated instead of plate, whereas repetition of abstract nouns, grammatical words, and non-words was just impossible.

Auditory comprehension was quite good but again far better for concrete nouns than for abstract ones.

In general, performance on semantic tasks was fairly good but on phonological tasks, he was really poor.

The patient condition can be summarized as understanding the meaning of words (at least the meaning of concrete words) without accurate processing of their phonological forms.

We activated this patient (Figure 5), unfortunately only using SPECT but still, with, I think, interesting results.

By comparison to a references condition (listening to connected speech spoken in a foreign language), we observed activations in two tasks in which performances were very different.

During a phonological task, which was phoneme monitoring in connected French speech, patient performance was at chance level, despite increases of CBF that were seen in almost all the undamaged cerebral territories.

During a semantic task, which was monitoring for animal names in connected speech, his performance was fairly good and was specifically associated with an activation in the right posterior temporal region just as if the activation of this right-sided region could compensate for the lesion effects in a semantic task but not in a phonological task.

Whatever the technical limitations of this work, I think it shows how the combination of brain imaging methods with single-case studies of clear-cut psycholinguistic dissociations may have a major impact on the understanding of the brain correlates of language functions and dysfunctions.

In any case, this would give us the opportunity to reconcile two sometimes antagonistic approaches to cognitive neuroscience.

References

BASSO A., LECOURS A-R., MORASCHINI S., VANIER M. (1985) «Anatomo-Clinical Correlations of the Aphasias as Defined through Computerized Tomography: on Exceptions», *Brain and Language*, 26: 201-29.

BROCA P. (1861) «Remarques sur le siège de la faculté du langage articulé, suivies d'une observation d'aphémie», *Bulletin de la Société Anatomique de Paris* 36 VI: 330-357.

CABANIS EA, IBA-ZIZEN MT, ABELANET R, MONOD-BROCA P, SIGNORET JL. (1994) «"Tan-Tan" the first Paul Broca's patient with aphemia (1861), CT (1979) and MRI (1994) of the brain», European Society of Neuroradiology, 4th Refresher Course «Language and Aphasias», Picard L and Salamon G (eds), 9-22. Edizioni del Centauro, Udine.

CAPPA, S., CAVALOTTI, G., VIGNOLO, L.A. (1981) «Phonemic and Lexical Errors in Fluent Aphasia: Correlation with Lesion Site», *Neuropsychologia*, 19:171-177.

CARDEBAT, D., DÉMONET, J.-F., CELSIS, P., PUEL, M., VIALLARD, G., & MARC-VERGNES, J.-P. (1994) «Right Temporal Compensatory Mechanisms in a Deep Dysphasic Patient: a Case Report with Activation Study by SPECT», *Neuropsychologia*, 32: 97-103.

DÉMONET, J.-F., CHOLLET, F., RAMSAY, S., CARDEBAT, D., NESPOULOUS, J.-L., WISE, R., RASCOL, A., & FRACKOWIAK, R.S.J. (1992a) «The Anatomy of Phonological and Semantic Processing in Normal Subjects», *Brain*, 115, 1753-1768.

DÉMONET, J.-F., CELSIS, P., NESPOULOUS, J.-L., VIALLARD, G., MARC-VERGNES, J.P., & RASCOL, A. (1992b) «Cerebral Blood Flow Correlates of Word Monitoring in Sentences: Influence of Semantic Incoherence. A SPECT Study in Normals», *Neuropsychologia*, 30, 1-11.

DÉMONET, J.-F., PRICE, C., WISE, R., & FRACKOWIAK, R.S.J. (1994a) «A PET Study of Cognitive Strategies in Normal Subjects during Language Tasks: Influence of Phonetic Ambiguity and Sequence Processing on Phoneme Monitoring», *Brain*, 117: 671-682.

DÉMONET, J.-F., PRICE, C., WISE, R., & FRACKOWIAK, R.S.J. (1994b). «Differential Activation of Right and Left Posterior Sylvian Regions by Semantic and Phonological Tasks: a Positron-Emission Tomography Study in Normal Human Subjects», *Neuroscience Letters*, 182: 25-28.

DÉMONET, J.-F., FIEZ, J.A., PAULESU, E., PETERSEN, S.E., & ZATORRE, R.J. (1996) «PET Studies of Phonological Processing. A Critical Reply to Poeppel», *Brain and Language*, 28 (in press)
FIEZ, J.A., RAICHLE, M.E., MIEZIN, F.M., PETERSEN, S.E., TALLAL, P., & KATZ, W.F. (1995). «PET Studies of Auditory and Phonological Processing: Effects of Stimulus Characteristics and Task Demands», *Journal of Cognitive Neuroscience*, 7: 357-375.

FIEZ, J.A., RAICHLE, M.E., BALOTA, D.A., TALLAL, P., & PETERSEN, S.E. (1996). «PET Activation of Posterior Temporal Regions during Auditory Word Presentation and Verb Generation», *Cerebral Cortex*, 6: 1-10.

GESCHWIND, N. (1965) «Disconnexion Syndromes in Animals and Man», *Brain*, 88: 237-294 and 585-644.

HOWARD, D., PATTERSON, K., WISE, R., BROWN, W.D., FRISTON, K., WEILLER, C., & FRACKOWIAK, R. (1992) «The Cortical Localisation of the Lexicons: PET Evidence», *Brain*, 115, 1769-1782.

PAULESU, E., FRITH, C.D., & FRACKOWIAK, R.S.J. (1993) «The Neural Correlates of the Verbal Component of Working Memory», *Nature*, 362: 342-344.

PETERSEN, S.E., FOX, P.T., POSNER, M.I., MINTUN, M., & RAICHLE, M.E. (1988) «Positron Emission Tomographic Studies of the Cortical Anatomy of Single-word Processing», *Nature*, 331: 585-589.

PETERSEN, S.E., FOX, P.T., SNYDER, A.Z., & RAICHLE, M.E. (1990) «Activation of Extrastriate and Frontal Cortical Areas by Visual Words and Word-like Stimuli», *Science*, 249: 1041-1044.

PRICE, C., WISE, R., RAMSAY, S., FRISTON, K., HOWARD, D., PATTERSON, K., & FRACKOWIAK, R. (1992) «Regional Response Differences within the Human Auditory Cortex when Listening to Words», *Neuroscience Letters*, 146: 179-182.

PRICE, C.J., WISE, R.J.S., WATSON, J.D.G., PATTERSON, K., HOWARD, D., & FRACKOWIAK R.S.J. (1994) «Brain Activity during Reading. The Effects of Exposure Duration and Task», *Brain*, 117: 1255-1269.

PRICE, C.J., MOORE, C.J., & FRACKOWIAK R.S.J. (1996a) «The Effect of Varying Stimulus Rate and Duration on Brain Activity during Reading», *NeuroImage*, 3: 40-52.

RAICHLE, M.E., FIEZ, J.A., VIDEEN, T.O., MACLEOD, A.K., PARDO, J.V., FOX, P.T., & PETERSEN, S.E. (1994) «Practice-related Changes in Human Brain Functional Anatomy during Non-motor Learning», *Cerebral Cortex*, 4: 8-26.

SERGENT, J., OHTA, S., MAC DONALD, B. (1992a) «Functional Neuroanatomy of Face and Object Processing», *Brain*, 115:15-36.

SERGENT, J., ZUCK, E., LEVESQUE, M., & MAC DONALD B. (1992b) «Positron Emission Tomography Study of Letter and Object Processing: Empirical Findings and Methodological Considerations», *Cerebral Cortex*, 2: 68-80.

TALAIRACH, J., & TOURNOUX, P. (1988) «Co-Planar Stereotaxic Atlas of the Human Brain. 3-Dimensional Proportional System: An Approach to Cerebral Imaging», Translated by Mark Rayport. New York: Thieme Medical Publishers, Inc. Stuttgart, New York: George Thieme Verlag.

WARBURTON, E., WISE, R.J.S., PRICE, C.J., WEILLER, C., HADAR, U., RAMSAY, S., & FRACKOWIAK R.S.J. (1996) «Noun and Verb Retrieval by Normal Subjects. Studies with PET», *Brain*, 119:159-179.

WEILLER, C., ISENSEE, C., RIJNTJES, M., HUBER, W., MÜLLER, S., BIER, D., KRAMS, M., FAISS, J.H., NOTH, J., & DIENER, H.C. (1995). «Recovery from Wernicke's Aphasia: a Positron Emission Tomography Study», *Annals of Neurology*, 37: 723-732.

WISE, R.J., CHOLLET, F., HADAR, U., FRISTON, K., HOFFNER, E., & FRACKOWIAK, R. (1991) «Distribution of Cortical Neural Networks Involved in Word Comprehension and Word Retrieval», *Brain*,114: 1803-1817.

ZATORRE, R.J., EVANS, A.C., MEYER, E., & GJEDDE, A. (1992) «Lateralization of Phonetic and Pitch Discrimination in Speech Processing», *Science*, 256: 846-849.

ZATORRE, R.J., MEYER, E., GJEDDE, A., & EVANS, A.C. (1996) «PET Studies of Phonetic Processing of Speech: Review, Replication and Reanalysis», *Cerebral Cortex*, 6: 21-30.