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A fMRI study of word retrieval in aphasia

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Abstract

The neural mechanisms underlying recovery of cognitive functions are incompletely understood. Aim of this study was to assess, using functional magnetic resonance (fMRI), the pattern of brain activity during covert word retrieval to letter and semantic cues in five aphasic patients after stroke, in order to assess the modifications of brain function which may be related to recovery. Four out of five patients had undergone language recovery, according to standard testing, after at least 6 months of rehabilitation. The cerebral activation of each patient was evaluated and compared with the activation pattern of normal controls studied with the same fMRI paradigm. In the patients, the pattern of brain activation was influenced by the site and extent of the lesion, by the degree of recovery of language, as reflected by task performance outside the scanner, and by task requirements. In the case of word retrieval to letter cues, a good performance was directly related to the activation in Broca's area, or in the right-sided homologue. On the other hand, in the case of semantic fluency, the relationship between performance level and activation was less clear-cut, because of extensive recruitment of frontal areas in patients with defective performance. These findings suggest that the performance in letter fluency is dependent on the integrity of the left inferior frontal cortex, with the participation of the homologous right hemispheric region when the left inferior frontal cortex is entirely of partially damaged. Semantic fluency, which engages the distributed network of semantic memory, is also associated with more extensive patterns of cerebral activation, which however appear to reflect retrieval effort rather than retrieval success.

Keywords: Recovery; Aphasia; fMRI; Verbal fluency

1. Introduction

The neurological mechanisms responsible for the recovery of aphasia due to acute vascular damage of the language-dominant hemisphere are largely unknown. In the early phase after a stroke, the functional impairment of brain networks not directly affected by the lesion (diaschisis), both in perilesional and contralateral brain areas, might contribute to the global severity of language impairment (Perani, Vallar, Cappa, Messa, & Fazio, 1987; Vallar et al., 1988). The recovery of these "distant effects" has been suggested to play a role in the "early," partial recuperation stage, which takes place in many aphasic patients, in the weeks and months immediately following the stroke (Cappa et al., 1997).

Although recovery may be observed also many years after a stroke, the following stages of aphasia are usually characterised by a slower recovery rate, which has been suggested to be related to functional re-organisation. The hypothesis of a "take-over" of function by homotopic areas in the right hemisphere as the mechanism underlying aphasia recovery goes back to the last century (Gowers, 1895). On the basis of the results of positron emission tomography activation studies (Weiller et al., 1995), a functional re-organisation, involving

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in particular the regions homotopic to the language areas in the contralateral hemisphere, has been suggested to be responsible for long-term recovery. However, other recent neuroimaging investigations have reported more complex patterns of activation in recovered patients. In particular, several studies have indicated that the reactivation of ipsilateral, perilesional areas is often associated with good recovery (Belin et al., 1996; Cao, Vikingstad, George, Johnson, & Welch, 1999; Heiss, Kessler, Thiel, Ghaemi, & Karbe, 1999; Hund-Georgiadis, Lex, Morris, & von Cramon, 2000; Rosen et al., 2000; Warburton, Price, Swinburn, & Wise, 1999). Besides performance level, another crucial determinant to be considered to interpret the pattern of activation in aphasia is the type of task. As suggested by Gold and Kertesz (2000), it is plausible that tasks, which are known to involve the right hemisphere in normal controls, may be associated with more extensive right-sided activation in aphasics. These typically include semantic comprehension tasks, rather than speech production and word generation. Even within relatively simple tasks, modifications of the linguistic requirements may change the cognitive strategy and result in different pattern of cerebral reorganisation.

In the present study, we took advantage of the well-known difference in word retrieval to letter and to semantic cues. Different component processes are involved in the two tasks. In particular, letter fluency has been suggested to place greater demand on "frontal" strategic processes, while semantic fluency is more dependent from semantic memory, in which the temporal lobe plays a crucial role. There is both behavioral (Martin, Wiggs, Lalonde, & Mack, 1994) and imaging (Mummery, Patterson, Hodges, & Wise, 1996; Paulesu et al., 1997) evidence to support this claim. The two tasks can thus be considered as "probes" for two partially independent networks, involving different brain regions, which may have different potential for reorganisation. Here, we report the anatomo-functional correlates of cued lexical retrieval in five aphasic patients, who showed different degrees of recovery in the late stage of stroke after rehabilitation therapy. The patterns of brain activation were assessed with functional Magnetic Resonance (fMRI) during verbal fluency tasks.

2. Methods

The experimental protocol was approved by the local hospital Ethics Committee, and all the subjects signed the informed consent.

2.1. Normal controls

The pattern of brain activation observed in six normal volunteers during the same tasks has been reported in another paper (Paulesu et al., 1997). For the present study, we studied four additional right-handed male volunteers. All subjects had no history of neurological or psychiatric disorders. Right-handedness was verified using the Edinburgh Inventory (Oldfield, 1971).

2.2. Aphasic patients

Subjects were selected from a large pool of outpatients attending the Language Rehabilitation clinics of Brescia and Milano. They all read and signed an informed consent to the study protocol, which was approved by the local ethical committee. We considered patients in the chronic phase after stroke (time interval range: 10 months–6 years), who had been submitted to an intensive language rehabilitation program for a minimum of six months. In order to be included, the patients had to provide evidence of being able to perform the fluency tests by producing a minimum of four correct responses in at least one of the tests. Patient (4) who was severely aphasic and not able to perform the fluency tasks, was included in the protocol for comparison with the recovered patients. No attempt was made to standardise the therapeutic protocol followed by the patients, which consisted in general of a language stimulation program supplemented, when appropriate, by a cognitive (model-driven) approach: however, they all had attended regularly therapy for a minimum of three weekly sessions.

These criteria resulted in the inclusion of five patients: four were right-handed male subjects (age range 45–69), with left hemispheric ischemic lesions, while one was a right-handed male with no history of familial sinistrality who had become aphasic after a right hemispheric lesion (crossed aphasia).

The clinical features, lesion sites, time of fMRI examination and neurolinguistic data are summarised in Tables 1 and 2.

Brief clinical summaries follow:

Case 1 (full recovery): Forty-six year-old, right handed male, medical doctor (general practitioner) with unremarkable medical history was admitted to the hospital with a sudden onset of mild right-sided weakness and language disturbances. The CT scan showed an infarction in the left temporoparietal cortex. Immediately referred for neuropsychological evaluation, he showed a normal performance on Raven's Coloured Progressive Matrices (RCPM); no evidence of apraxia, and a fluent aphasia with impaired auditory comprehension. An intensive rehabilitation program was started. The patient recovered very quickly, and after one month was not aphasic on standard testing (see Table 1). He decided to quit the rehabilitation program, and to go back to work. At reassessment after 1 year he complained of mild residual difficulties with written language, but was working full time on a very busy schedule.