Language recovery in Greek-English bilingual stroke patients: an fMRI study

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Cover image: Pieter Bruegel the Elder. The Tower of Babel. 1563. Oil on panel. Kunsthistorisches Museum, Vienna, Austria

Table of contents

Contributions....4
Abbreviations....5
List of Figures....6
List of Tables....7
Abstract....8
1. Introduction....9
1.1 Bilingualism in the world....9
1.2 In search of the bilingual....10
1.3 Insights into bilingualism....11
1.4 Why study bilingualism....17
1.5 Studying the cognitive brain I – The lesion deficit model....19
1.6 Studying the cognitive brain II – Functional imaging....19
1.7 Studying the cognitive brain III – Studying the healthy and the damaged brain....21
1.8 Our study....24
2. Materials and methods....27
2.1 Subject recruitment....27
2.2 Behavioural testing....28
2.3 fMRI Design....33
2.4 Experimental Tasks....35
2.5 Stimuli....36
2.6 Counterbalancing tasks and stimuli....37
2.7 Data acquisition....38
2.8 Data Analysis....39
3. Results....41
3.1 In-scanner behaviour....41
3.2 Functional imaging findings....42
4. Discussion....50
5. Conclusions....54
References....56

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Abbreviations

ANOVA: Analysis of Variance

BAT: Bilingual Aphasia Test

BIA/BIA+ model: Bilingual Interactive Activation model/its extended version

BOLD: Blood Oxygen Level Dependent

CAT: Comprehensive Aphasia Test

CT: Computerised Tomography

ERP: Event-Related Potentials

FIL: Functional Imaging Laboratory (our laboratory)

(f)MRI: (functional) Magnetic Resonance Imaging

HRF: Haemodynamic Response Function

IC model: Inhibitory Control model

L1: First Acquired Language

L2: Second Acquired Language

PALPA: Psycholinguistic Assessment of Language Processing in Aphasia

PET: Positron Emission Tomography

SL(T): Speech & Language (Therapy)

SPM: Statistical Parametric Mapping

List of Figures

Figure I: How lesions can cause abnormnal activations *(From Price & Friston 1999)* p.23

Figures (1a-4a) and (1b-4b): Activation conditions (a), Baseline conditions (b) p.34

Figure II: Controls reading Greek and English p.42

Figure III: Cortical grey matter of TE – stroke lesion in left parietal lobe p.43

Figure IV: TE reading Greek p.44

Figure V: TE > controls p.45

Figure VI: Controls > TE p.46

Figure VII: AP's lesion p.47

Figure VIII: AP reading in normal areas p.48

Figure IX: AP's lucky escape from aphasia p.48

Figure X: AP's overactivation (crosshair at lesion) p.49

Figure XI: Reduced activation in lesioned area of TE p.51

List of tables

Table I: How patient activations can contribute to normal and abnormal models of processing *(From Price & Friston 1999)* p.22

Table II: Mean control performance in behavioural tests p.29

Table III: TE's assessment of aphasia 6 months post-stroke p.30

Table IV: AP's CAT scores p.31

Table V: Patients vs. controls in lexical decision tests p.32

Table VI: In scanner performance during reading task p.41

Table VII: TE abnormal activation regions p.43

Abstract

As bilingualism has become more and more common, we were initially interested in how stroke impacted upon language abilities in bilingual participants. For practical reasons, the languages chosen were Greek and English. Due to unavailability of suitable patients, however, we used our experimental paradigm to answer two specific questions: (1) How does a Greek patient recover reading ability in their own language despite damage in or near the normal reading system? (2) Do neurologically normal bilinguals show the same or different activation patterns when reading in Greek or English? First, an overview of the major questions and the most widely accepted answers about bilingualism is presented as background. I then describe how functional imaging can be used to complement the classic psycholinguistic approach. Our results confirm, once again, the widely accepted notion that different languages are served by the same gross set of neuroanatomical regions in the healthy brain. The absence of significant differences between Greek and English also confirm that our subjects were highly proficient in both languages. Our patient data showed abnormal activation patterns in patients who were performing the reading task well. Patient TE, with a left parietal lesion, had the most interesting results. As expected TE showed less activation than the neurologically normal controls at the site of his lesion . In addition, he also showed less activation than normal in bilateral premotor and superior temporal regions that are associated with speech output. These areas looked structurally normal on TE's MRI. Reduced activation in the context of recovered speech output suggest that, pre-stroke, these areas relied on excitatory input from the left parietal region that was now damaged. In other words, the damaged parietal cortex and the undamaged premotor and superior temporal regions are likely to interact during normal speech output. In contrast, TE showed enhanced activation in the left frontal lobe and right cerebellum. We interpret this activation as a result of the use of a non-typical cognitive strategy in order to cope with the speech output task when the normal system is damaged. The clinical implications of our findings are also discussed.

1. Introduction

1.1 Bilingualism in the world

The emergence of language in human evolution has been a critical step towards the foundation of our civilisation. As a means of communication, language has provided members of human communities the opportunity for better co-operation enhancing their chances for survival. As soon as survival had been secured, language began to promote the preservation of knowledge and hard-earned experience from one person to another and from generation to generation over thousands of years overcoming the limitations of the short human life span. People of the 21st century can still benefit from the teachings and experience of individuals who lived thousands of years ago thanks to language. There are of course limitations which are as significant as the benefits of such a powerful ability and they have been acknowledged since very early in human history.

The Biblical story of the Tower of Babel (The Bible, 1000BC) is one of the earliest and most well known symbolic references to linguistic issues concerning different languages. Humans in their arrogant attempt to reach the Heavens reached hubris instead and were punished by God by the confusion of the tongues. Chaos and disorganisation came to humans so the arrogant task was aborted and the speakers of different languages were dispersed in the continents forming the world's nations.

Human history has demonstrated in a most dramatic way the impact of the existence of different languages. With language being the flagship of each different culture, numerous inter-cultural conflicts have broken out transforming the means of communication and creation into a means of discrimination and destruction. Although inter-cultural conflicts still remain an important problem it seems that the different language cultures are now meeting again. There is a growing awareness of bilingualism bolstered by an increasing number of bilinguals in the world. In the near future, the

globalisation of markets, the expansion of international communication networks, the heightened attention to minority rights and the blurring of geographical borders fostered by the European Union will enhance this awareness even more (Paradis 2000b). Furthermore, the use of English throughout the world as the 'universal' language of trade, science and of course the Internet has made its use as a foreign language a necessary qualification for everyone. It is more evident than ever that the use of more than one language in every day life is no longer a privilege of the scholars. There is a general agreement that bilinguals and multilinguals outnumber monolinguals in the world's population (Bot & Kroll 2002;Grosjean F 1994).

1.2 In search of the bilingual

So who is a bilingual? A typical answer would be: "a person who is able to use two languages spontaneously and with the same ease without any difference in performance". It seems though that this image of a 'perfect' bilingual has been created probably within an essentially monolingual language culture and thus proficiency in different languages alone should not be used as a criterion to classify an individual as bilingual (Fabbro 2001). There are several other aspects of bilingualism that should be taken into account but instead are easily missed or ignored.

A good example is the language acquisition history of the bilingual. Languages are acquired and used for different purposes, in different domains of life with different people and thus language acquisition histories are essentially as diverse as individuals themselves are. Then, it should also be noted that bilinguals are rarely equally fluent in all language skills in all their languages. Some may still even be in the process of acquiring a language and their repertoire may change over time depending on the skills needed during any given period. Finally, bilinguals may need to adapt their language behaviour

according to their immediate surroundings (e.g. when talking to monolinguals) (Grosjean F 1998). Thus, bilinguals are not to be considered simply as two monolinguals in the same person (Grosjean 1989). Under this scope, a good description of a bilingual which would be accepted by most researchers is that of the person who uses two or more languages or dialects in everyday life (Grosjean F 1994). There are no objective linguistic criteria to distinguish between a language and a dialect (Pinker S 1994). Neither is there evidence for differential brain representations of dialects (Paradis 1995). Thus, for the purpose of this study, dialects are incorporated to the term "language".

A final remark that needs to be made is that all verbal functions that are present in a bilingual individual have their homolog in monolingual speakers. Bilinguals are able to switch and mix different languages at will whereas monolinguals are able to switch and mix different registers of the same language i.e. are able to express the same concept either to a panel of experts or to their young children (Paradis 1998).

1.3 Insights into bilingualism

The debate about how different languages are represented in the brain has been long and uncertain. Johann Gesner (1738—1801) was probably the person who triggered it providing the first known description of dissociation in reading in different languages in a bilingual abbot (Pearce 2005). Gesner's patient was able to read Latin but not German after he had suffered brain damage. Several other reports of selective language impairment or recovery after brain damage or stroke have kept the debate alive up until today. What is particularly interesting about bilingual aphasic disorders is the diversity in their recovery patterns. Six different patterns have been identified (Paradis 1977):

1. Parallel recovery: occurs when both languages are impaired and restored at the same rate

2. Differential recovery: occurs when languages recover differentially relative to their premorbid levels

3. Selective recovery: occurs when one language is not recovered

4. Antagonistic type of recovery pattern: one language recovers to a certain extent first and it starts regressing when the other language begins to recover. The antagonistic pattern of recovery is seen to be the least common. By contrast, in selective aphasia, there is aphasia in one language without impairment evident in the other

5. Varying rates of recovery: two languages may eventually recover but recovery of the second language may only begin after the first has recovered, which is called successive recovery of one language after the other.

6. Mixed: less often, there are mixed patterns or mutual interference between the languages seen in the process of recovery

The main questions raised from this plethora of neuropsychological phenomena are trying to address the following issues:

- the existence or not in the bilingual brain of one or more lexica and their control mechanisms
- the memory functions required to sustain bilingualism
- the cerebral representation of language functions of bilinguals as compared to monolinguals

There is no final answer to any of these questions as research is ongoing and the results of the numerous studies are very often conflicting and controversial. A recent commentary provides an indicative listing of some of these studies and illustrates the contradicting nature of their results (Paradis 2003). For a discussion of some of the methodological and conceptual issues of studying bilinguals, the reader is referred to another comprehensive review (Grosjean F 1998).

In the last decades significant progress has been made in the study of bilingualism. Among the numerous controversial debates, of significant importance has been the more-or-less general agreement on the necessity of distinguishing a conceptual and a lexical level when studying language. So how are these levels organised in a bilingual? In short, evidence clearly supports that the conceptual representation in a bilingual is unique for all languages and shows a strong consensus for the existence of a single large lexicon rather than several different ones (French & Jacquet 2004).

The question of storage is not the only problem however. The debate about the control of the bilingual lexicon is another difficult one. Lexical selection in a specific context is a concept shared by monolinguals as well but the selection of the right word in the right language is a somewhat prominent manifestation of it. So is there a language-specific mechanism of lexical selection? The evidence argues against this concept and the general view favours non-selective lexical access (French & Jacquet 2004). So if lexical access is non-selective how can bilinguals efficiently control their language use? In other words how is lexical selection possible? This question has brought forward the need for creating models. One very successful attempt to model lexical selection has been the Bilingual Interactive Activation (BIA) model (Dijkstra & van Heuven 1998) and its subsequent extended version, BIA+ (Dijkstra & van Heuven 2002). Another significant contribution was the Inhibitory Control (IC) model (Green 2003). The IC model is another well-known non-selective access model which is based on inhibitory mechanisms to produce lexical selection and is in complete agreement with the BIA+. It is beyond the scope of this study to explain the details of these models but it would suffice to say that both these models enjoy wide acceptance and are quite promising. They are both successful at a low level i.e. single word handling and their major shortcomings concern their learning capabilities and handling sequences of words (French & Jacquet 2004).

Another area of long and heated debate is the concept of language lateralisation and localisation differences between the brains of bilinguals and monolinguals. The term lateralisation refers to the degree of control that each of the two hemispheres exerts on language functions. It is well established over the past hundred years that the language system is mostly left lateralised. The concept under investigation is whether bilinguals have less lateralised language control owing to a greater participation of the right hemisphere. The term localisation refers to anatomically distinct language-specific brain areas. In this case the argument is about the possible existence of language-specific areas that are unique to bilinguals.

As far as the lateralisation concept is concerned, there is no evidence for a greater involvement of the right hemisphere in bilinguals. This conclusion is based on both experimental psycholinguistic methods as well as clinical data. It is possible that the methods used may detect activation patterns that relate to other aspects of language, such as pragmatics, which are handled by the right hemisphere. In such a case, any differences found between the two hemispheres should not be considered related to the core linguistic functions (Paradis 2004).

The concept of different localisation of language functions is not supported by the evidence either. Both languages of the bilingual seem to be represented as distinct microanatomical subsystems in the same gross anatomical areas and to constitute neurofunctional subsystems using dedicated neural circuits (Paradis 2004). Selective language deficits are not enough to demonstrate different anatomical representation (Paradis 1996). It is possible though that depending on the language proficiency in the second language a speaker may compensate any linguistic incompetence by relying more heavily (compared to monolinguals) on metalinguistic knowledge and pragmatic elements which could lead to activation of areas not ordinarily associated with language (e.g.

hippocampal gyri, frontal lobes, right hemisphere). This does not mean however that acquired language skills are represented in those areas (Paradis 2004). The reverse pattern is also possible and as proficiency in L2 increases, its representation and its processing profile as detected by ERP and neuroimaging converge with those of native speakers (Green 2005). The effect of proficiency has also been demonstrated in Chinese-English bilinguals where greater language proficiency correlated with smaller BOLD signal change in the participant's more proficient language (Chee et al. 2001). More evidence came from recent neuroimaging findings which indicate age of acquisition and proficiency in second language (L2) as important factors affecting L2 brain representation (Wartenburger et al. 2003). Wartenburger and colleagues demonstrated differences in activation patterns of L1 and L2 in early vs. late and highly vs. poorly proficient bilinguals. The areas of difference – when present – did not strike out as novel and unexpected however (Perani & Abutalebi 2005) but were parts of the set of language areas as these have been re-defined by neuroimaging (Price 2000) rather than the traditional set of left perisylvian areas.

This view of the existence of a single major language system in the brain comprising of minor subsystems serving to process the intricacies of each language has been well documented. A convincing set of experiments using both PET and fMRI testing of highly proficient bilinguals in English-German and English-Japanese provides more and robust evidence for the universality of cerebral representation of language across cultures (Crinion et al. 2006). Crinion and colleagues work has looked at languages that differ greatly in their most fundamental aspects and yet, during the same task, the brain activation observed was remarkably similar. At a lower statistical threshold they found differences concerning perceptual differences between languages, namely word length. The effect observed was higher activation in occipital cortices. Several other studies have

demonstrated similar findings as well. Japanese-English bilinguals of moderate fluency demonstrated significant activation overlap and the observed differences were related to linguistic processing of negative sentences (Hasegawa, Carpenter, & Just 2002), activation in late Japanese-English bilinguals differed only in the processing of passive sentences (Yokoyama et al. 2006), co-localisation of peak activation was reported for Chinese characters and English words (Chee et al. 2000), activation overlap was reported for Mandarin and English sentence processing (Chee et al. 1999). Together all these findings provide evidence in support of the view that different languages are handled by different subsystems in the same gross set of language areas.

However, these findings do not shed any light to the issue of control of the appropriate language. The work of Crinion and colleagues has elaborated on this topic and has revealed that neuronal responses within the left caudate are sensitive to changes in the language or the meaning of words – the former being of importance to bilinguals, the latter to both monolinguals and bilinguals (Crinion et al. 2006). A new role is thus proposed for the left caudate, that of monitoring and controlling the language in use. This suggestion provides even more support to the idea that the bilingual brain is not so much different from the unilingual but adapts to the changing needs by elaborating on the use of already established and successful neuronal circuits.

In summary, we can say that after considering the several diverse clinical and experimental findings bilinguals are now generally believed to maintain their languages in roughly the same brain areas as monolinguals. As far as the control of their languages is concerned, they employ more or less the same methods as monolinguals for the regulation of their single bilingual lexicon. This regulation may well be seen as a more extreme variant of the attempt to solve the universally present problem of lexical selection. The

distinctly specialised use of control areas of the brain in order to achieve this regulation is possible.

1.4 Why study bilingualism?

As mentioned earlier, bilingualism attracted attention because of the variety in patterns of recovery from aphasia in individuals speaking more than one language. What has been learned so far is the complex character of language and its neurofunctional modularity. Languages in bilinguals and sociolinguistic registers in monolinguals are now considered as being neurofunctionally fractionable (Paradis 2000a) and their relations dynamic, described either as inhibition (Green 2003;Green 1986) or as variable thresholds or unbalanced use (Paradis 2004). However, more than a century of study later, there is still no clear conclusion about what determines the pattern of recovery in bilingual aphasics. The literature is full of heated debates and non-generalisable case studies using a variety of methods and paradigms that prevent direct comparisons.

The enigmatic nature of bilingual aphasia is not of pure scientific or academic interest though. Its clinical implications are quite underestimated as reflected in the number of studies focusing on its demanding needs for specialised rehabilitation let alone the patient's point of view and quality of life issues. However, as a result of international migration, intermarriage and globalisation the numbers of bilinguals and multilinguals increase and with it as a result of stroke, head injury and neurodegenerative disease so does bilingual aphasia (Green 2005). The inefficiency of traditional approaches, the differences between languages and the unpredictable effects of brain damage to each different language (Green 2005) place extra burden on language rehabilitation. Several varied and in cases not yet properly formulated questions have risen. Should therapy be provided for both languages? If not is it ethical (Paradis 1995)? And if only one language

is to be rehabilitated which one will this be (the native, the most fluent premorbidly, the best recovered, the language of the hospital/country providing healthcare or that of the home environment)? Is there a transfer of therapeutic effects from the treated to the non-treated language and what factors determine this effect? Is there harm done during rehabilitation to a bilingual (Paradis 2004)?

A ten-year-old review on the speech and language therapy (SLT) efficiency after listing several problems in every day SLT practice concludes by underlining a key fact; that SLT is often viewed as a group of prescribed and precise activities, just like a drug (Enderby & Emerson 1996). Enderby and Emerson suggest that an important challenge SLT professionals need to face is to describe in detail the components of therapy in order to determine the best practice ensuring maximum benefit with minimum harm. Their conclusion is conveniently matching the issues raised about bilingual aphasia after stroke and yet they didn't mention bilingualism at all! Seven years later another study investigated the beliefs of SL pathologists about the assessment of bilingual individuals. It concludes that they themselves are not able to assess the needs of bilinguals properly nor are they capable of helping them even with the intervention of an interpreter (Kritikos 2003)! Although successful at uncovering a significant flaw in SLT practice this study fails again to pay attention to bilingual aphasia and focuses only on bilingual children. In fact, the literature is dominated by studies on bilingual children whereas aphasia rehabilitation in bilinguals does not seem to be equally attractive. We believe there is a growing and demanding need to design studies that will start to address these issues as well. We advocate that the combined use of the rapidly evolving and highly sophisticated neuroimaging techniques along with evidence from neuropsychology can lead to valuable conclusions with high cost effectiveness and minimal patient inconvenience.

1.5 Studying the cognitive brain I – The lesion deficit model

As is typical in cognitive science, the motivation to study the brain-mind relationship came from brain damaged patients. It was the 19th century neurologists who started documenting cases of neurologically impaired individuals that had suffered brain damage and demonstrated a selective cognitive deficit. The most famous case was Paul Broca's patient who had impaired articulation due to damage in the area of the third frontal convolution. The correlation between this brain area and the specific language impairment that it led to marked the birth of the lesion deficit model.

In short, the lesion deficit model advocates the notion that a specific brain insult points to a specific impairment. The damaged brain region is equated with the consequent impaired cognitive skill. In its enhanced version, it was extended to include damage to the white matter connecting brain regions (Price, Noppeney, & Friston 2006). This model proved to be very simplistic in its approach and has three major shortcomings. First, it does not distinguish the impact of damage to a region from the impaired performance of a remote region connected to the first. Second, its conclusions cannot be generalised because similar lesions may have different consequences and vice versa. Third, it cannot tell anything about normal brain function. At best, the conclusion that can be made from a lesion deficit study is that a damaged region or the connections passing through this region were necessary for the observed impaired cognitive function (Price, Noppeney, & Friston 2006).

1.6 Studying the cognitive brain II – Functional imaging

In the last two decades, functional imaging and mostly fMRI has become the spearhead of cognitive neuroscience research. Activation of brain regions can be demonstrated in vivo with excellent spatial and good temporal resolution. This time it is

not necessary to focus on a lesioned brain; conclusions can be drawn for the healthy brain as well. As the whole brain is scanned, the disturbed interactions between an impaired and a healthy region can also be demonstrated.

The reduction in the metabolic activity of a brain area remote from the damaged region – which can be due to either cortical or white matter insult – is referred to as *diaschisis* (from Greek *διασχίζω* = to tear apart) (Feeney & Baron 1986). Diaschisis can also be context-sensitive or task-dependent and it is then referred to as *dynamic diaschisis* (Price et al. 2001). Dynamic diaschisis occurs when a region's activation depends on the input to it. In other words, the region may activate normally when it's not receiving input from the damaged area, and abnormally when it does. When the damaged region is connected to a remote area via inhibitory connections then the result of the insult is an increase in the activity of the remote area, a phenomenon called *disinhibition* or *unmasking*.

Functional imaging, unlike classical CT or MRI, can also demonstrate the presence of residual responsiveness in a damaged brain area. This is usually arising from peri-lesional tissue and occurs either as a reactivation of the damaged tissue after the acute stage or as a result of plasticity. The activation pattern revealed may look normal or 'patchy'. Peri-lesional activity varies between patients depending on the dimensions and type of the lesion. Its presence will determine the functional validation of the lesion and possibly falsify suspicions of it being not necessary for the observed behaviour of the patient (Price, Noppeney, & Friston 2006).

However there are again some important limitations in the use of neuroimaging. First, functional imaging demonstrates sets of active regions that sustain a function but cannot tell us anything about their necessity. In other words it can only show the sufficient sets of brain areas for a particular function (Price, Noppeney, & Friston 2006).

Second, it is possible that multiple neuronal systems may be able to do the same task, a phenomenon called *degeneracy* (Edelman & Gally 2001). Degeneracy is a very important property of the brain for preserving its function. When a part of a degenerate system is knocked out, it is possible that the remaining ones can take up its task giving rise to either novel or even identical to normal patterns of activation (Price & Friston 2002). Functional imaging alone cannot discriminate among parts of a degenerate system as they may be functioning in parallel or inhibit each other (Price & Friston 2002;Price, Noppeney, & Friston 2006).

It is beyond the scope of this study to summarise the whole range of the costs and benefits of functional imaging. However, it would suffice at this point to say that from the brief summary that was attempted, it was clear that the lesion deficit model and functional imaging are complementary approaches to study brain function. The first can tell us about the necessity of brain regions and the second of the sufficiency of them in order to perform a certain function. Thus, the combined use of these two approaches is superior to each one of them in isolation (Price, Noppeney, & Friston 2006).

1.7 Studying the cognitive brain III – Studying the healthy and the damaged brain

Functional imaging of neuropsychologically impaired patients has lagged behind that of healthy subjects. This is not surprising as it is first necessary to gain some insight into normal brain function. Moreover, there are some fundamental differences in the approaches of studying the healthy and the lesioned brain and it took some time to acknowledge them. These concern all levels of the approach: study design, analysis and of course the interpretation of findings. The most significant condition that has to be met first when studying a patient is that the patient must be able to perform the experimental

tasks (Price & Friston 2002). If the patient cannot perform the experimental task then the interpretation of the findings is very difficult. The relation between the deficit in performance and the abnormal neural processing is obscured as we cannot define the causative relation between the two and each one could well be occurring as a consequence of the other (Price & Friston 1999). On the other hand, when the patient is able to perform the task then this does not necessarily mean that the underlying neural processing is normal. In fact, it could happen that the patient is activating regions that the controls do not, the controls are activating regions that the patient does not or both patient and controls activate the same regions but with different correlations between regional responses. Each pattern of activation leads to a different interpretation both for the normal and the damaged brain (see Table I).

TABLE I. How patient activations can contribute to normal and abnormal models of processing

	Interpretations for:	
Patient activations	Patients	Normals
Normal:	Recovery to normal	—
Abnormal:		
1. Patients not normals:	(a) Neuronal change	Duplicate system
	(b) Cognitive change	Alternative system
2. Normals, not patient		
(a) In lesion only:	—	Redundancy
(b) Distant to lesion:	Dys-integration	Connections
3. Correlation changes:	Disconnection	—

From Price & Friston 1999

When there is abnormal activation in patients this can be either to a cognitive change or a change on the neuronal level. As for the cognitive change, the patient uses a different strategy to perform the task because, as a result of the lesion, he cannot cope or because he has learned a new skill. As for the neuronal change, this is mediated by changes in the strength of pre-existing connections and may be the result of either learning or of the direct consequences of the brain lesion (see Figure I). In any case, when

studying the possibility of one type of change, cognitive or neuronal, occurring in the patient's brain it has to remain certain that the other one remains unaffected throughout the study.

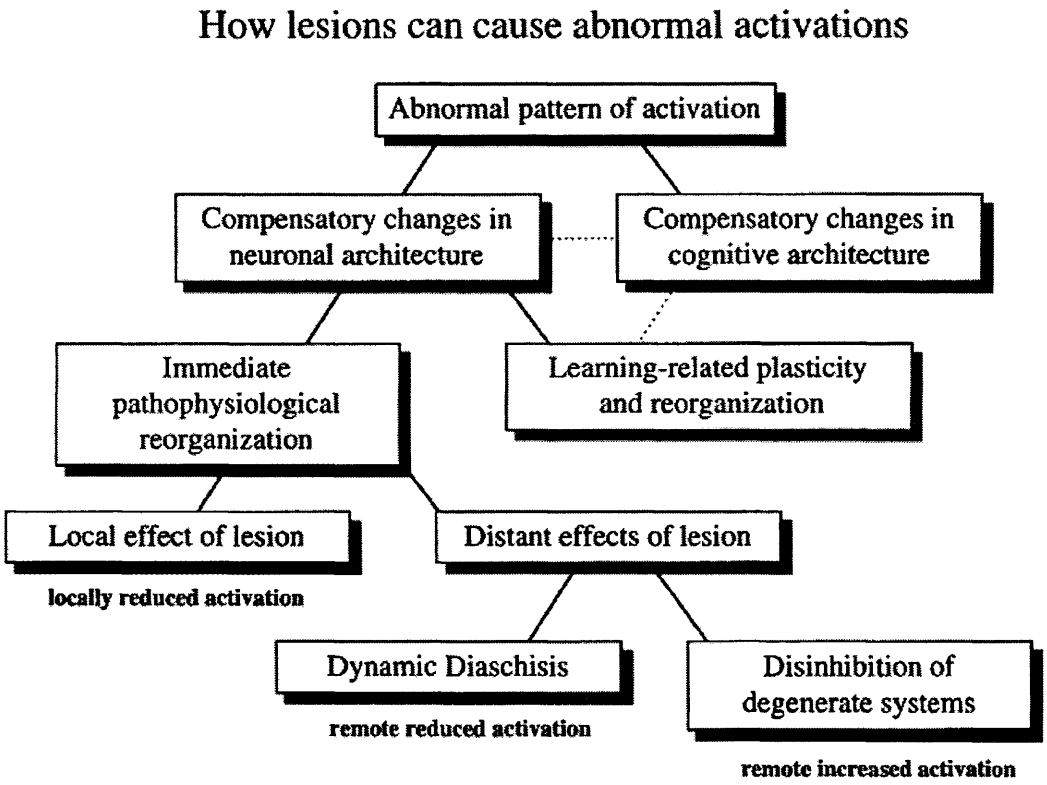


Figure 1.

From Price & Friston 1999

When the patient overactivates as compared to normal this may mean that either a normally activating region is enhanced or that there are novel activation regions. The former may be explained by increased demands from that region or by the disruption of inhibitory inputs to it i.e. disinhibition. The new areas are not easy to explain. They may represent change in cognitive strategy or neuronal changes. Underactivation may be complete absence or reduction in activity. When the patient fails completely to activate a region as compared to normals then, given normal task responses, this means that the area was not necessary for that task. Moreover, in that same case, another issue of great importance would be the exclusion by the imaging study of the possibility of residual peri-lesional activity that could confound the results. Thus, by collecting

neuropsychological data from patients with different lesions which prove to be not necessary for a task and 'subtracting' them from the set of areas observed in imaging studies of healthy subjects, it is possible to identify a minimal sufficient set of regions capable of sustaining the task. It is important to keep in mind though that the presence of multiple degenerate systems might result in no areas being necessary for a task as long as the other areas in those systems are intact (Price & Friston 1999).

In summary, it has been pointed out that in order to better understand brain function the combined use of different methods is very promising. Functional imaging can be used to identify sets of brain areas that are sufficient to sustain a certain task in patients and healthy subjects and to confirm the presence or absence of peri-lesional activity in the former. After the differences between patients and controls are identified, neuropsychological testing can be used to point out which areas are necessary for the experimental tasks used. In that way, conclusions can be drawn about degenerate neural systems in the healthy brain and patterns of recovery in patients. The latter can be used in order to identify new targets for rehabilitation. Although large patient and control databases are necessary to reach these objectives, this approach is nonetheless a promising step forward that surpasses the traditional structural CT and MRI scans and the single-sided neuropsychological assessments.

1.8 Our study

We set out to study bilingual aphasia after stroke with the use of functional imaging applying the principles mentioned above. As the author is a native Greek speaker, we studied Greek-English bilingual stroke patients. The patients we were looking for would possibly differ greatly and demonstrate a loss of any type of language related skill following stroke, but would have then made a recovery of some, if not all, of their lost

language functions. In other words, the patients of interest would be those who had recovered Greek and English to a similar degree; Greek more than English, or English more than Greek. Within these groups, the difficulty might be with speech comprehension or speech production. We set up a battery of tests that included a range of different tasks such as picture naming, reading, semantics, perceptual judgments and articulation in order to match the variety of the patients. A control group consisting of neurologically normal Greek-English bilingual subjects was also recruited and they were tested in these tasks using functional imaging.

Patient recruitment took time and involved a number of different attempts (see Materials and methods) which were not nearly as fruitful as hoped because of the rarity of patients meeting our criteria. We eventually got responses from three patients in total. One of them took an interest in our study because his family was motivated by the absence of bilingual language rehabilitation services and wanted to promote the study of bilingual aphasia. However, this patient eventually backed out because of the time commitment required to participate in both behavioural and imaging tests. Another patient (AP) was willing to participate but had a right hemisphere lesion that had resulted in only temporary speech output difficulties (dyspraxia). The third patient (TE) had a large left hemisphere lesion with impaired speech production. Although he understood and spoke English well, he claimed that he had never been taught to read English and didn't have a great necessity for it. Therefore, although his Greek reading was better than his English reading, this was more likely to be due to a proficiency difference than a selective deficit in English that was caused by his stroke. When assessed on the functional imaging paradigms that we had available for bilinguals, patient TE was only able to perform two: (1) perceptual decisions and (2) reading in Greek. His naming ability was

not sufficiently recovered to provide meaningful data and he also had difficulty following and remembering instructions for the semantic decision and articulation tasks.

In summary, although this study was designed to assess bilingual Greek-English patients who had different types of language recovery following stroke, we were unable to find patients who would fulfill our criteria. Consequently, the study focused mainly on patient TE and asked how he managed to recover his ability to read in Greek despite (i) his stroke and (ii) his naming and speech output difficulties. To assess the normality of TE's reading activations, it was necessary to compare him to neurologically normal Greek-English bilingual controls reading the same Greek words. Although we did not eventually manage to test TE in English because of patient inconvenience, patient AP was tested in both Greek and English which allowed us to assess whether his right hemisphere lesion had any impact on his activation pattern in either language.

Only two other studies were found in the literature focusing on Greek-English bilingual aphasics (Alexiadou & Stavrakaki 2006;Kambanaros & Steenbrugge 2006). However none of them has used functional imaging. Thus, our study is the first to report results of this kind and our control data provided a novel data set that allowed English and Greek reading to be compared for the first time. The words we used were chosen initially in English and had to be short, high frequency words to maximise accuracy during the task. They were then translated in Greek. A major difference between the two languages that was noted very early was the length of the words (see Materials and methods). Greek words were significantly longer so we expected this to have an effect in our results.

2. Materials and methods

2.1 Subject recruitment

Patients: 1) TE, a 73 year old gentleman who had a stroke in March 2005. He was originally born in Cyprus (Greek L1), and had been living and working in the UK for over 50 years (English L2). He left school at an early age, so his reading and writing skills were basic in Greek, and poor in English. With this poor pre-morbid reading and writing proficiency, it was difficult to interpret the tests based on written material. Within one year he has marked a significant language recovery in both languages based only on personal effort as he did not receive any SLT. TE was tested twice, both one month post-stroke (April 2005) and six months post-stroke (November 2005). He was impaired in all modalities, though comprehension was the most affected. Naming was only mildly impaired. TE is right-handed.

2) AP, a 50 year old gentleman who had a stroke in 2003 with reported speech impairment. He was born in Cyprus (Greek L1), and had been living and working in the UK for 27 years (English L2). He attended formal education in Greece for 9 years completing primary and half of secondary education. He admitted to having low proficiency in English, especially in written English. Thus, it was difficult to interpret his written skills as well. He has recovered from his language deficit based on his personal effort and the support of his family and did not use SLT either. He was found to be impaired in English but this most likely reflects a low pre-morbid proficiency. He did very well in Greek. As AP's profession involved cutting metals and there could be a risk of eye injury in the scanner, we requested special ethics approval and did an orbital x-ray to him which showed no presence of metal. AP is right-handed.

Controls: The requirements for control recruiting were that Greek should be the first language and that the subject should be living in the UK for at least a year. There was no

history of neurological or psychiatric disorders. All controls were right-handed. Subjects' consent was obtained according to the declaration of Helsinki. Nineteen controls were contacted in total. Of them, 8 declined participation and 11 accepted. There were 6 females and 5 males. The mean age was 28.8 years *(=10.69)*. All the controls had a structural scan and on the same day half of them did the Greek version of the experiment and the other half did the English. Each language was tested on a different date to avoid biasing the subjects and affecting the brain activation levels. This arrangement increased dramatically the number of scanning sessions. One control subject didn't do the English version.

Study advertising: Greek volunteers that were found in the FIL's volunteer database were contacted. There was also recruitment from personal contact and from advertising the study in areas of London where many Greek speakers were living (Bayswater, Wood Green). The study was advertised using leaflets in Greek (see appendix) that were distributed in person or were left in public places in the above areas. There was also an advertisement appearing in a Greek local newspaper for at least six weeks. The advertisement was granted special ethics approval as it was concerning patients as well and involved releasing in the media. A short article in Greek about bilingualism and stroke aphasia was published in this newspaper in order to attract more interest.

2.2 Behavioural testing

The patients were tested in English with the Comprehensive Aphasia Test (CAT) (Swinburn, Porter, & Howard 2004) and in Greek with the Greek version of the Bilingual Aphasia Test (BAT) (Paradis 1987). They also did a number of computerised tests including two lexical decision tasks to distinguish English words from non-words; one taken from the PALPA (Kay, Coltheart, & Lesser 1992) and one from Meara & Jones

(1990). The two lexical decision tests were used as informal measures of language proficiency. The controls did the computerised tests as well and were also given a small battery of psycholinguistic tests comprising of:

- verbal fluency tests in both Greek and English where the subject had one minute to recite as many words as possible starting from a certain letter or belonging to a certain category (e.g. fruits or animals)
- Oral and written composite picture description in Greek and English. We used the 'cookie theft' picture from the Boston Diagnostic Aphasia Examination (Goodglass, Kaplan, & Barresi 2001) and the composite picture from the CAT. A summary of the controls performance can be seen in table II.

Table II: Mean control performance in behavioural tests

TEST	ENGLISH			GREEK
Lexical Decision	Real words correct	Non-words correct	Total correct	
PALPA	89.28%	87.19%	89.44%	n/a
Meara	67.96%	80.72%	72.21%	n/a
Verbal fluency				
Letter fluency	14.45			12.84
Instance-category	16.35			18.26
Composite picture				
Oral	39.61			35.65
Written	27.61			25.2

TE's summary of aphasia testing scores six months after the stroke can be seen in Table III. Interpretation needs much caution due to his low pre-morbid proficiency. During our first assessment of TE, one month after his stroke, he was found more severely impaired

but the number of tests that could be performed at that time was significantly smaller and there was no opportunity to test the Greek language.

Table III: TE's assessment of aphasia 6 months post-stroke - Cut-off points for aphasic performance are reported in brackets. In square brackets are the scores of his assessment one month after the stroke (* = abnormal scores)

	English	Greek
Production		
Verbal fluency	7 [4]	14
Category fluency	7 [6]	17
Total word fluency (13)	14 [10*]	31
Spoken composite picture* (33)	22	30
Naming* (43)	40/48 [30*]	
Spoken Comprehension		
Words* (25)	24/30 [18*]	
Sentences (27)	28/32 [22/30*]	
Paragraph* (2)	2/4 [2*]	
Written Comprehension		
Words (CAT) (27)	26/30 [24]	
Sentences (CAT) (23)	24/32 [8]	
Words (BAT)	8/10 [9]	9/10
Sentences (BAT)		10/10
Reading		
Words (CAT) (45)	34/40 [35]	
Non-words (6)	6/10 [4]	
Complex words (4)	0/6 [5]	
Words (BAT)		10/10
Sentences (BAT)	10/10 [4]	10/10
Writing		
Written composite picture (19)	5	16
Dictation (24)	9/28	
Writing picture names (15)	8/21	18/39
Translation	English to Greek	Greek to English
Words	9/10	9/10
Sentences	14/18	15/18

Patient AP scored quite low in the CAT but this was questioned again because of his low pre-morbid competence in English. Table IV shows a summary of his scores.

Table IV: AP's CAT scores - Cut-off points for aphasic performance are reported in brackets

(* = abnormal scores)

Modality Tested	English
Production	
Verbal fluency – Letter	2
Verbal fluency – Category	18
Total word fluency (13)	20
Spoken composite picture* (33)	23
Naming* (43)	43/48
Spoken Comprehension	
Words (25)	27/30
Sentences (27)	30/32
Paragraph (2)	¾
Written Comprehension	
Words (CAT) (27)	28/30
Sentences (CAT) (23)	32/32
Reading	
Words (CAT)* (45)	42/48
Non-words* (6)	2/10
Complex words* (4)	0/6
Writing	
Written composite picture* (19)	-1
Dictation* (24)	16/28
Writing picture names* (15)	9/21

AP's scores were very high throughout the Greek BAT including the translation section (to and from English) and are thus omitted. He was challenged only by writing (which he admitted being weak in) and had also some difficulty in verbal fluency tasks.

Finally, the performance of both patients against controls in computerised lexical decision tests can be seen in table V.

Table V: Patients vs. controls in lexical decision tests

Test	TE (6 mo post stroke)	AP	Controls (mean)
PALPA total correct	61.5%	76%	89%
PALPA real words correct	83.3%	88%	89.28%
PALPA non-words correct	36.7%	60%	87.19%
Meara total correct	-	61.67%	72.21%
Meara real words correct	-	56%	68%
Meara non-words correct	-	74%	81%

2.3 fMRI Design

The variables of interest were (1) task (Semantic decisions or Name) and (2) stimulus modality (Pictures of familiar objects or their written names). This resulted in four activation conditions. In each of these conditions, triads of stimuli were presented (one above in the centre of the screen and two below: "lower left" and "lower right"). For each activation condition there was a stimulus and task specific baseline that involved the presentation of triads of meaningless symbols or nonobjects (see figures below)

Activation conditions (a)	***Baseline conditions (b)***
(1a) Semantic decisions on Words	(1b) Perceptual decisions on triads of meaningless symbols
(2a) Semantic decisions on Pictures	(2b) Perceptual decisions on triads of meaningless nonobjects
(3a) Reading aloud Words	(3b) Saying "one, two three" to triads of meaningless symbols
(4a) Naming aloud Pictures	(4b) Saying "one, two three" to triads of meaningless nonobjects

All eight stimulus conditions were blocked, with 4 triads per block. Each triad remained on the screen for 4.32 seconds followed by 180ms of fixation. The resulting block length was therefore 18 seconds for each condition. Each block was preceded by 3.6 seconds of instructions (see below for details). Over the experiment there were 8 blocks of each activation condition, 4 blocks of each baseline condition, and 20 blocks of fixation. Each block of fixation lasted 14.4 seconds.

1a

Anchor

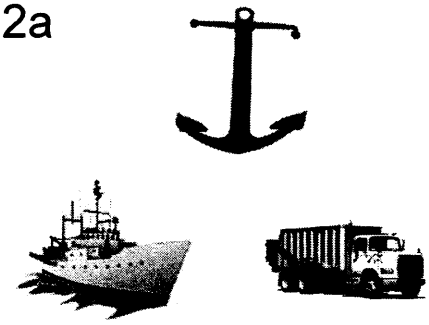
Ship Truck

1b

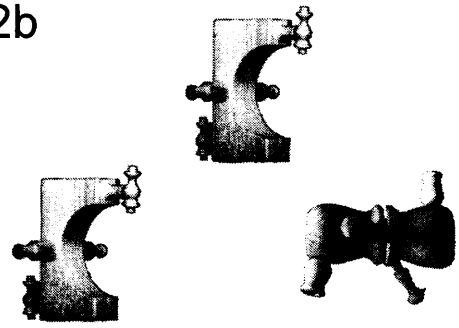
υιυιυ

δδδδ υιυιυ

2a



2b



3a

Cup

Axe **Slide**

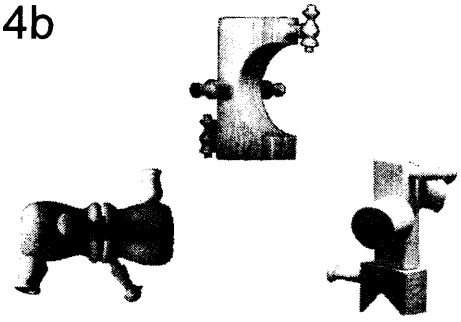
3b

δθξ

διυ υθδυ

4a

4b



2.4 Experimental Tasks

Naming task

In the naming task, subjects were instructed to read aloud or name all three words or pictures in the triad, starting with the top stimulus, then the lower left stimulus and finally the lower right stimulus. A microphone was used to record the vocal responses and subsequently distinguish between correct and incorrect trials. However, it was not possible to record reaction times due to interference from the noise of the scanner. The instruction for the naming blocks was either ***READ*** or ***NAME*** and either ***ΔΙΑΒΑΣΤΕ*** or ***ΚΑΤΟΝΟΜΑΣΤΕ.***

Baseline for Naming task

To control for visual input and motor output, the naming baseline task required subjects to say "one, two, three" or "ένα, δύο, τρία" while looking at the three meaningless stimuli in the triad (see Figure 3b and 4b). Responses were recorded as in the naming task. The instruction for the blocks of naming baseline was *either* ***1-2-3 LETTERS*** or ***1-2-3 PICTURE*** and ***Γράμματα_1_2_3*** or ***Εικόνες_1_2_3.***

Semantic task

In the semantic decision task, subjects were required to decide whether the stimulus above was more closely related in meaning to the lower left or lower right stimulus (see Figure 2a). Half of each group of subjects responded with a key pad in their right hand (forefinger press for lower left/middle finger press for lower right); the other half of each group responded with a key pad in their left hand (middle finger press for lower left; forefinger press for lower right). Reaction times and accuracy were recorded. The instruction for the semantic blocks was either ***WORD-MATCH*** or ***PICTURE-MATCH*** and either ***ΤΑΙΡΙΑΣΜΑ ΛΕΞΕΩΝ*** or ***ΤΑΙΡΙΑΣΜΑ ΕΙΚΟΝΩΝ.***

Baseline for semantic task

To control for visual input and motor output, the semantic baseline task required subjects to decide whether a meaningless stimulus above looked identical to the meaningless stimulus on the lower left or lower right (see Figures 1b and 2b). The finger press response was identical to that in the Semantic task. Reaction times and accuracy were recorded. The instruction for the blocks of semantic baseline was either ***SAME SYMBOL*** or ***SAME-PICTURE*** and either ***ΟΜΟΙΑ ΣΥΜΒΟΛΑ*** or ***ΟΜΟΙΕΣ ΕΙΚΟΝΕΣ.***

2.5 Stimuli

The activation stimuli were pictures, or the written names of 192 familiar objects. The objects were selected on the basis of their familiarity and the number of letters in their names. Specifically:

33 had three letter names (e.g. CAT, ANT, BAG, BUS)

65 had four letter names (e.g. CAKE, BELL, BATH)

58 had five letter names (e.g. CAMEL, TRAIN, TEETH)

35 had six letter names (e.g. SPIDER, TOMATO, WINDOW) and one word had seven letters (BALLOON). In Greek, the words were significantly longer. Specifically there were:

26 words with four letters

42 words with five letters

44 words with six letters

37 words with seven letters

23 words with eight letters

14 words with nine letters

3 words with ten letters

1 word with eleven letters and 2 words with thirteen letters.

The 192 stimuli were then arranged in 64 different triads such that there was a strong semantic relationship between two of the objects in the triad but not the third object; e.g. WALL (above) FENCE (lower left), SOFA (lower right). We ensured that semantically related items were neither visually similar to one another (to prevent the decision being made on the basis of perceptual attributes) nor verbally associated with one another (e.g. CAT and DOG, KNIFE and FORK, SOCK and SHOE). In addition, a pilot study with 8 subjects ensured inter-subject agreement on all correct responses.

The full set of 64 semantically related triads was divided into set 1 (with 36 triads) and set 2 (with 36 triads). The items within Set 1 and Set 2 were then reassigned into new triads that did not have a semantic relationship; e.g. LEMON (above), COW (lower left), PIPE (lower right). These unrelated triads were created for the naming conditions and were intended to prevent subjects from focusing on semantic relationships when they were naming. The end result was four different sets of stimulus items:
(i) Set 1-semantic, (ii) Set 1-name, (iii) Set 2-semantic, (iv) Set 2-name.

The baseline stimuli were either symbols or non-objects. The symbols were Greek letters. The frequency of the symbol lengths was controlled to be analogous to the frequency of the word lengths in each language i.e. in Greek the symbols were longer. The non-objects were photographs of three-dimensional wooden blocks or lego constructions. In the semantic baseline, one of the lower stimuli was always identical to the stimulus above. In the naming baseline, three different stimuli were presented.

2.6 Counterbalancing tasks and stimuli

Data for semantic decisions and naming were acquired in different fMRI sessions. For each subject, there were two sessions of semantic decisions (S) and two sessions of

naming (N). The task order for half the subjects in each group was SNNS and for the other subjects, the task order was NSSN. Within each session, half the triads were presented as pictures of the objects and half the items were presented as the written names of objects. For the first two sessions (NS or SN), all 192 objects were presented as either words or pictures of objects. In the second two sessions, the same object was presented again but in a different stimulus modality. Thus, objects that were presented as pictures in the first two sessions were presented as written words in the second two sessions and objects that were presented as written words in the first two sessions were presented as pictures in the second two sessions. Consequently, no stimulus was repeated in any of the sessions. Within a session, there were four different types of stimuli: Pictures (P), Words (W) Symbols (S), Nonobjects (N) interspersed with fixation (F). The order of presentation was PWFSNFPWFWPFNSFWP for two sessions and WPFNSFWPFPWFSNFPW for two sessions.

2.7 Data acquisition

A Siemens 1.5T scanner was used to acquire T2*-weighted echoplanar images with BOLD contrast. Each echoplanar image comprised 40 axial slices of 2 mm thickness with 1 mm slice interval and 3 × 3 mm in-plane resolution. A total of 412 volume images were acquired in four separate sessions with an effective repetition time (TR) of 3.6 s/volume. There were 103 volumes per session. To avoid Nyquist ghost artefacts a generalized reconstruction algorithm was used for data processing. After reconstruction, the first four (dummy) volumes of each session were discarded to allow for T1 equilibration effects.

2.8 Data Analysis

2.8.1 Pre-processing. Data were analyzed with statistical parametric mapping (SPM2: Wellcome Department of Imaging Neuroscience, London, UK. http//www.fil.ion.ucl.ac.uk), running under Matlab 6.5.1 (Mathworks, Sherbon, MA, USA). All volumes from each subject were realigned and unwarped, adjusting for residual motion-related signal changes. The functional images were spatially normalized (Friston et al. 1995a) to a standard MNI-305 template using nonlinear basis functions (to allow intersubject averaging and comparisons) and spatially smoothed with a 6-mm full width half maximum isotropic Gaussian kernel to compensate for residual variability after spatial normalization and to permit application of Gaussian random-field theory for corrected statistical inference (Friston et al. 1995b).

2.8.2 Statistical Analysis. At the first level, the data were analyzed in a subject-specific fashion. Each of the eight conditions and the instructions were modelled separately, with event-related delta functions for each trial, convolved with a canonical hemodynamic response function (HRF). The nine regressors were then entered into the design matrix and condition effects were estimated according to the general linear model. To exclude low frequency confounds, the data were high-pass filtered using a set of discrete cosine basis functions with a cut-off period of 128 seconds. The contrasts of interest at the first level were each of the 8 experimental conditions (4 activation and 4 baseline) relative to fixation. These contrast images were then entered into a second level ANOVA to permit inferences about condition effects across subjects (i.e., a random-effects analysis) (Holmes & Friston 1998). From this second level ANOVA, the following contrasts were computed for each subject group:

1) Semantic decisions Words – Perceptual decisions on Symbols
2) Semantic decisions on Pictures – Perceptual decisions on Nonobjects
3) Reading aloud words – Saying 1-2-3 to Symbols
4) Naming pictures of objects – Saying 1-2-3 to Nonobjects.
5) Semantic decisions Words – Fixation
6) Semantic decisions Pictures – Fixation
7) Naming pictures – Fixation
8) Reading aloud > fixation

The Effects of interest are those that were stronger in one group than another (i.e. the group by condition interactions). The threshold for significance was set at $p<0.05$ corrected for multiple comparisons across the whole brain.

3. Results

3.1 In-scanner behaviour

The performance of the subjects was not very good across the different conditions. Many of the controls and both patients didn't perform well in at least one or two blocks during the task where they had to name pictures and thus we had to exclude several sessions due to low accuracy scores. Due to the small number of controls we could not use any results from the picture naming task in either language even after excluding the subjects with low accuracy scores. As TE was unable to follow the instructions for the semantic task and due to a malfunction of the keypad during the scanning session of AP we were forced to abandon the data from the semantic task as well. However, the performance in the word reading task was very high for both controls and patients (see Table VI).

Table VI: In scanner performance during reading task

CONTROLS	WORD READING ACCURACY (GREEK)	WORD READING ACCURACY (ENGLISH)
1	100%	100%
2	100%	100%
3	100%	100%
4	100%	-
5	100%	100%
6	100%	100%
7	99%	100%
8	100%	100%
9	100%	100%
10	100%	100%
11	100%	99%
PATIENTS		
TE	93%	-
AP	99%	99%

3.2 Functional imaging findings

We first attempted to look for differences between reading in each language in the healthy subjects. As can be seen in Figure II, during the reading sessions, the activation patterns observed in the controls were impressively similar. Red represents areas activated during reading in English, green reading in Greek and yellow areas that are active during both English and Greek reading.

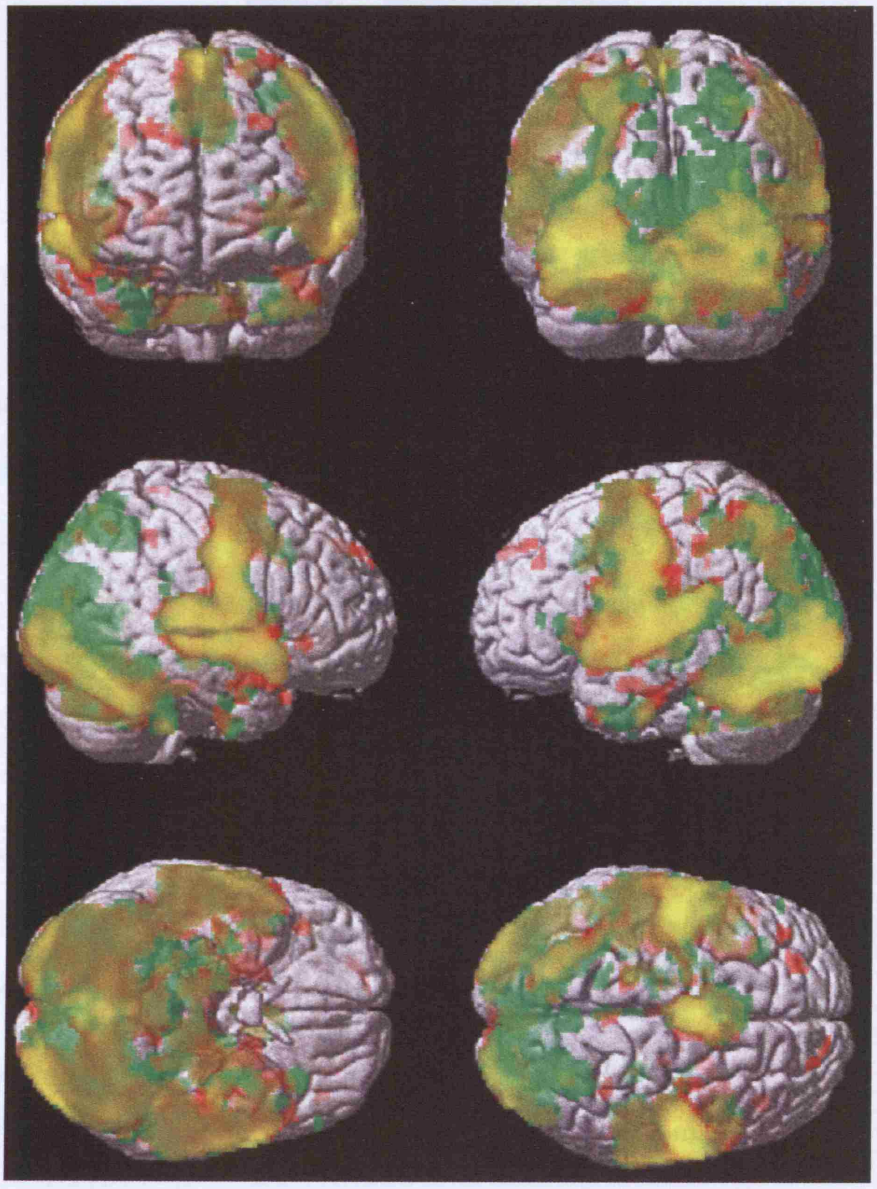


Figure II: Controls reading Greek (green) and English (red) – yellow = overlap

We then examined patient findings. The structural scan of TE revealed extensive damage in the left parietal lobe (Figure III). There was also a significant degree of cortical atrophy bilaterally.

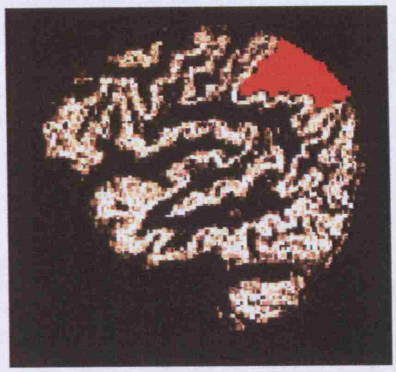


Figure III: Cortical grey matter of TE – stroke lesion in left parietal lobe

TE – functional imaging findings

The activation pattern of TE during reading in Greek can be seen in figure IV. The extent of activation resembles very much that of a normal individual. However, when contrasted with controls, TE showed an abnormal activation pattern. The locations of the abnormal activations are summarised in Table VII.

Table VII: TE abnormal activation regions

	Brain region	x	y	z	z-score
Underactivations	Left parietal (lesion)	-46	-36	52	5.3
		-44	-44	56	4
	Left dorsal premotor cortex	-42	4	40	4.9
	Left temporal	-46	-18	10	3.7
	Right dorsal premotor cortex	44	-14	40	4.5
	Right temporal	58	2	-8	4.9
	Right thalamus	14	-8	-4	4.8
Overactivations	Left frontal	-48	46	2	6.5
		-36	-10	32	6
		-38	8	56	5.7
	Right cerebellum	10	-70	-30	5.7
	Right thalamus	16	-8	-12	5.8

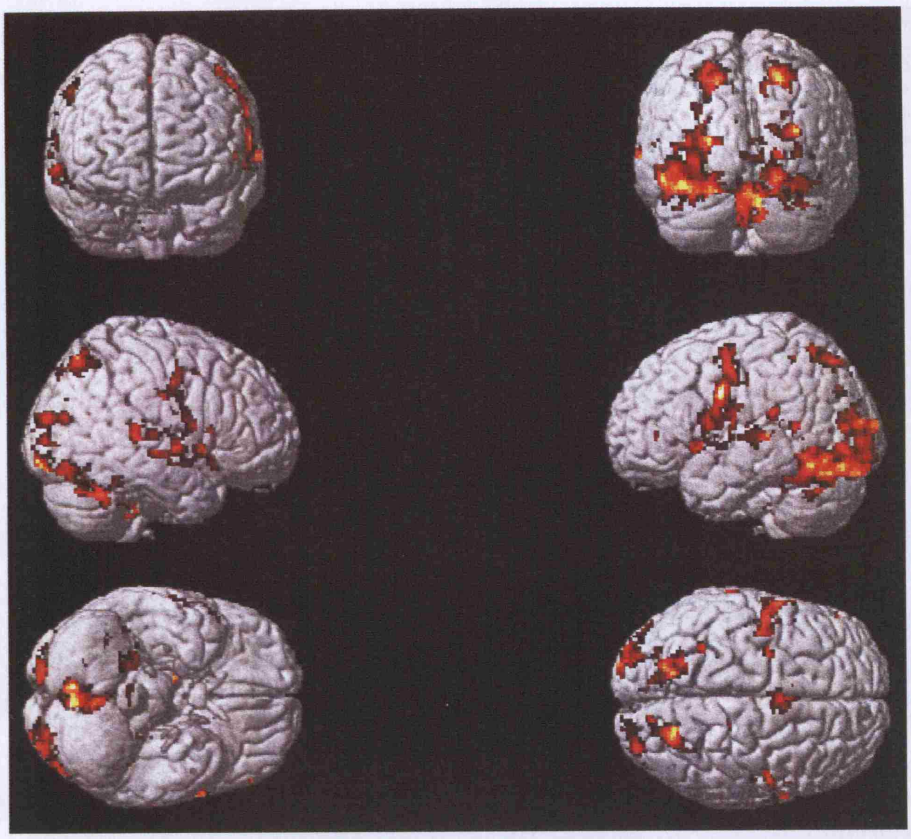


Figure IV: TE reading Greek

There were regions that were overactive and others that were underactive relative to controls. Figure V shows the areas where TE was activating more than controls and Figure VI shows the areas where he was activating less than controls.

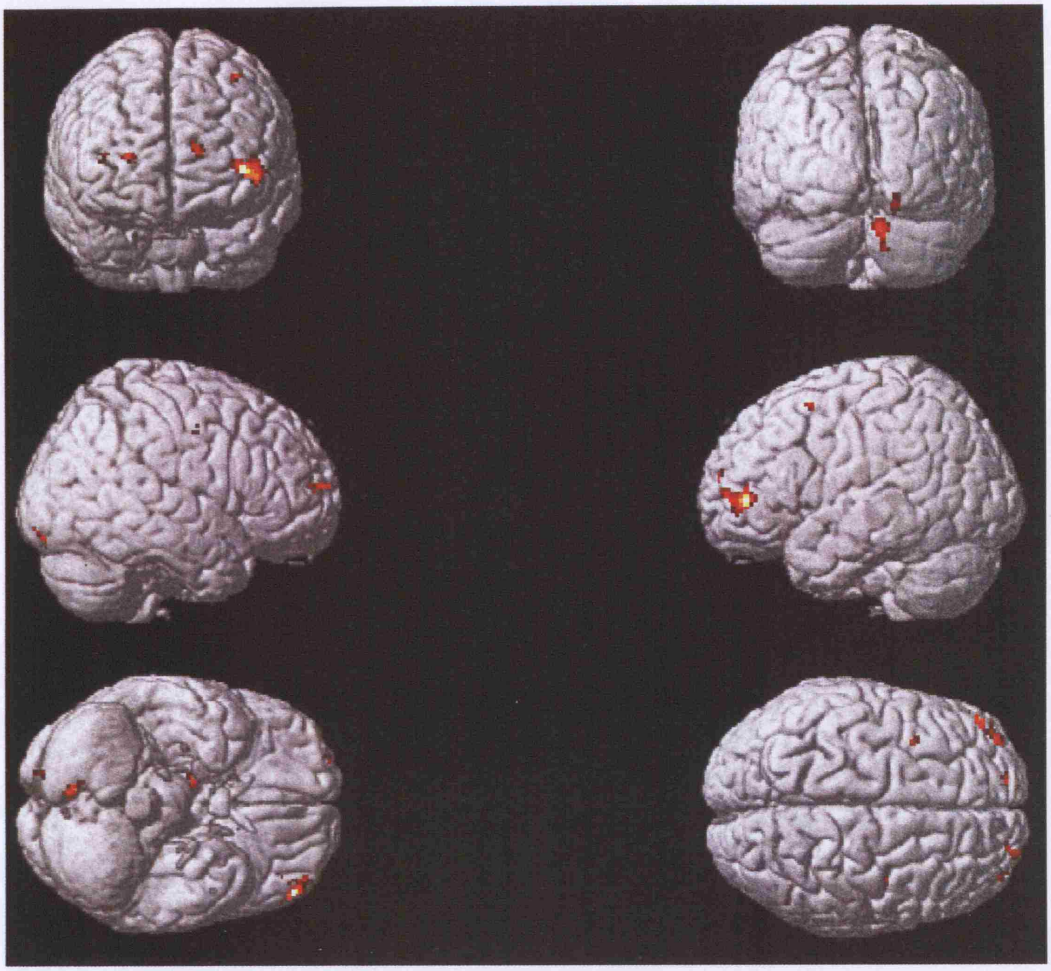


Figure V: TE > controls

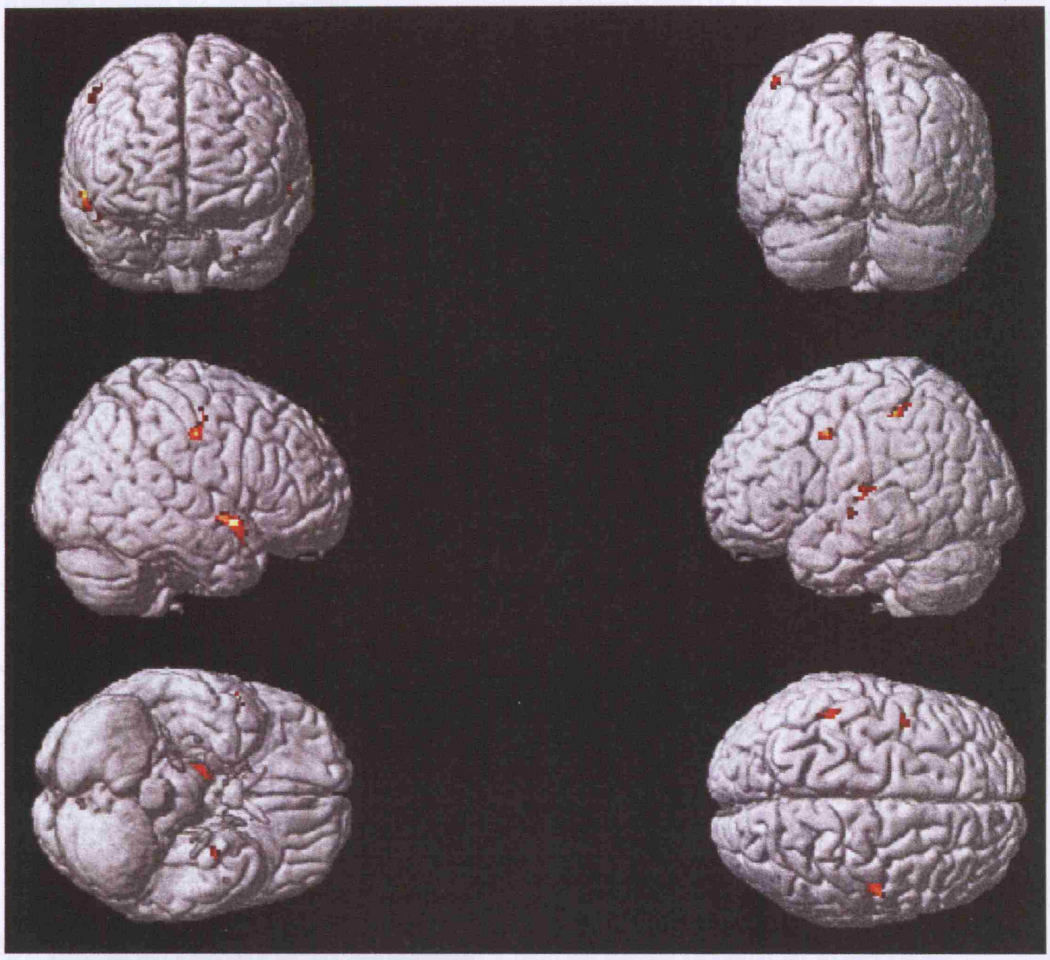


Figure VI: Controls > TE

A rather unexpected finding came from the right thalamus of TE where a region that overactivated and another one that underactivated were found.

As for patient AP the structural scan revealed a lesion in the right parietal lobe (Figure VII)

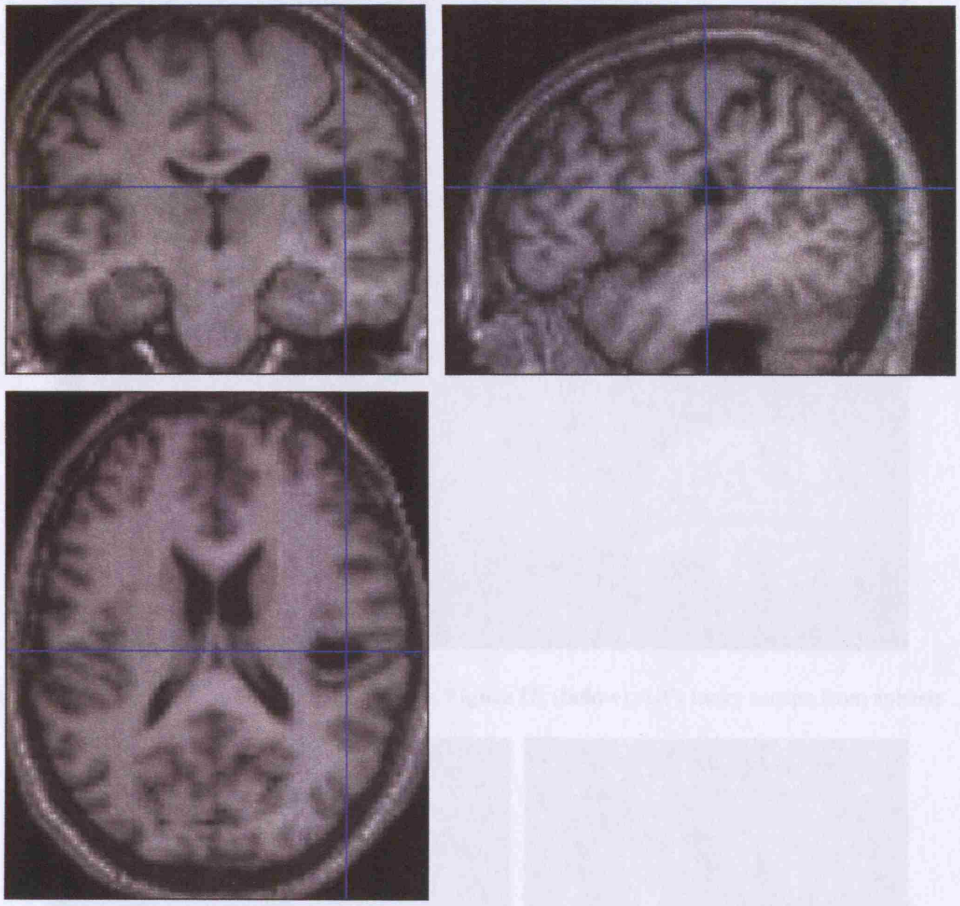


Figure VII: AP's lesion

AP – functional imaging findings

AP showed a pretty normal activation pattern while reading. This can be seen in Figure VIII. When the activation pattern was superimposed to the structural image, it became obvious that AP has been very lucky as the lesion has occurred in between the language related areas of the right hemisphere (Figure IX).

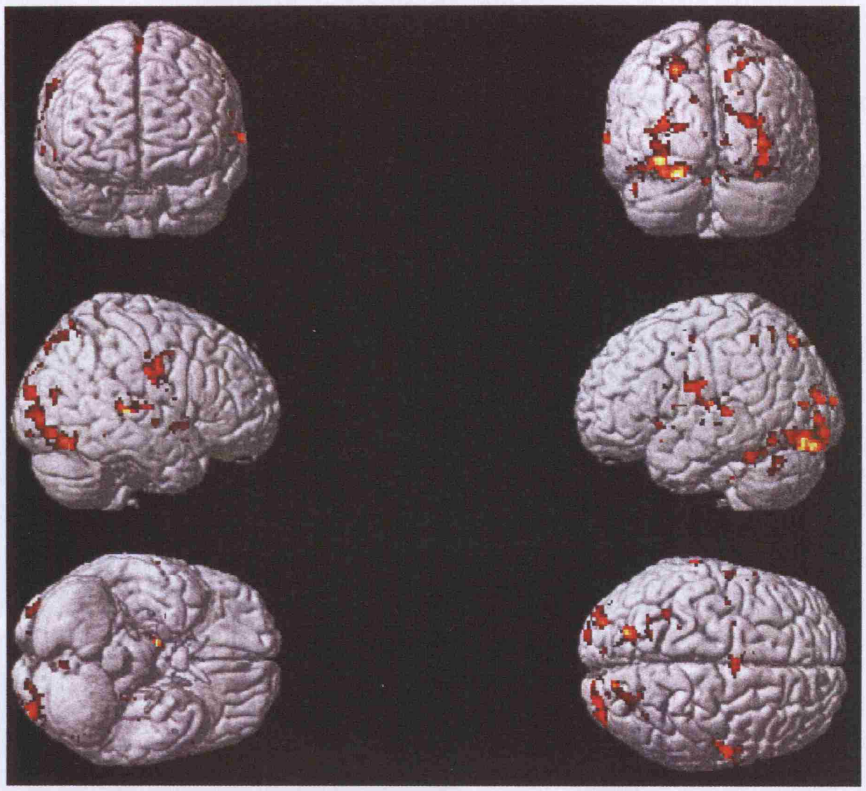
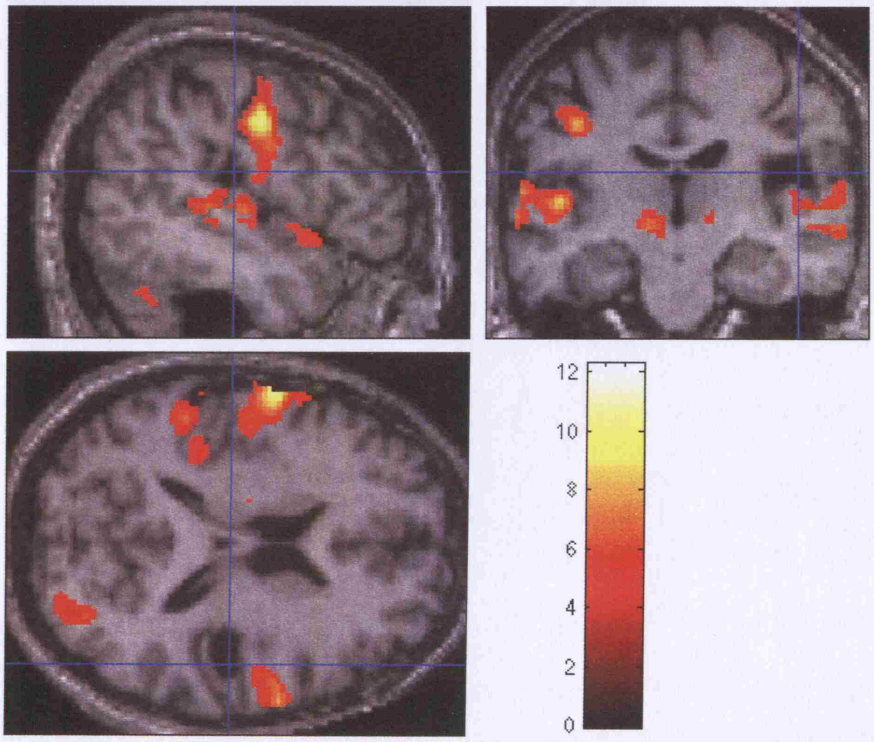


Figure VIII (above):AP reading in normal areas, **Figure IX (below):**AP's lucky escape from aphasia



When AP's activation was contrasted to the controls, however, an area with enhanced activation was found but no areas with reduced activation. The overactivating area was located very close to the lesion at location x=44, y=-22, z=26, z-score=5.03 (Figure X).

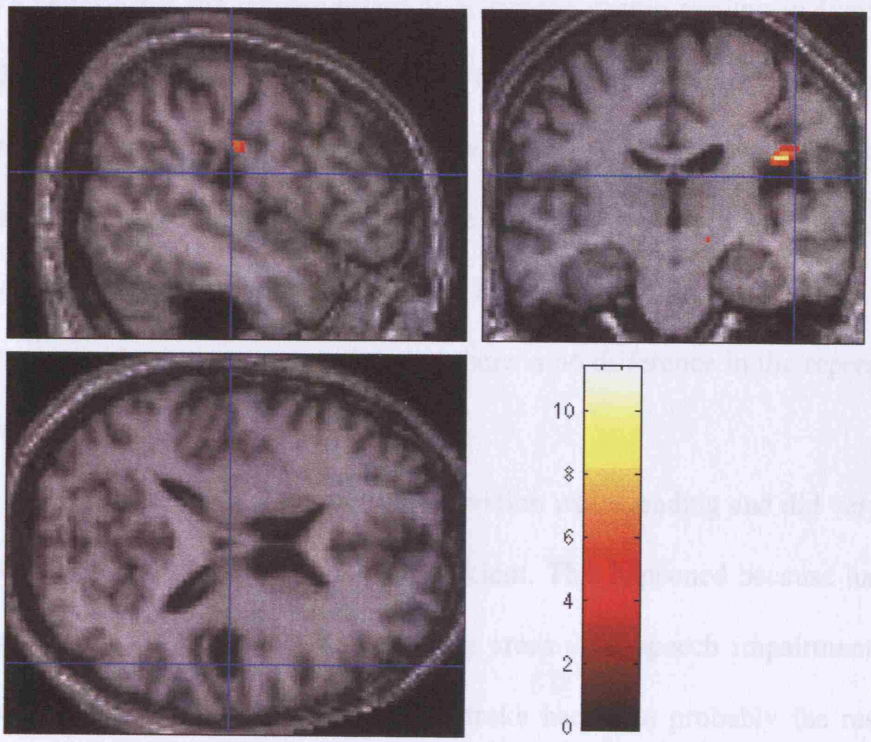


Figure X: AP's overactivation (crosshair at lesion)

4. Discussion

The imaging data although limited to the reading task only have revealed some useful findings. First, they show that there is no language effect in normal subjects while reading. We believe that the greater extent of activation during reading in Greek that is visible in the occipital lobe in Figure II is due to the significant difference in word length. Greek words were much longer and hence, the area they occupied in the visual field during presentation was larger so we believe we replicated the findings of Crinion et al. (2006). The absence of a language effect is also in agreement with the literature. Most of the evidence available so far is suggesting that there is no difference in the representation of languages in bilinguals.

Patient AP showed pretty normal activation while reading and did very well in the aphasia testing in the language he was proficient. This happened because luckily his right parietal lesion did not affect his language areas. The speech impairment that he presented with during the acute phase of his stroke had been probably the result of a temporary dysfunction of the nearby language areas, which happened to be in the ischemic penumbra. The area of overactivation represents probably a compensatory increase in the demands of the peri-lesional tissue.

The most interesting findings came from patient TE, as there were several areas of both reduced and enhanced activation despite the fact that TE's reading performance was good.

TE's Underactivations

As can be seen in Figure XI, the area in the rectangle coincides clearly with the lesioned area in the left parietal cortex. As seen previously in Figure IV there is no activation at all in this area. These findings suggest two things. First that there is no peri-lesional activity and second that this area was not necessary for the reading task.

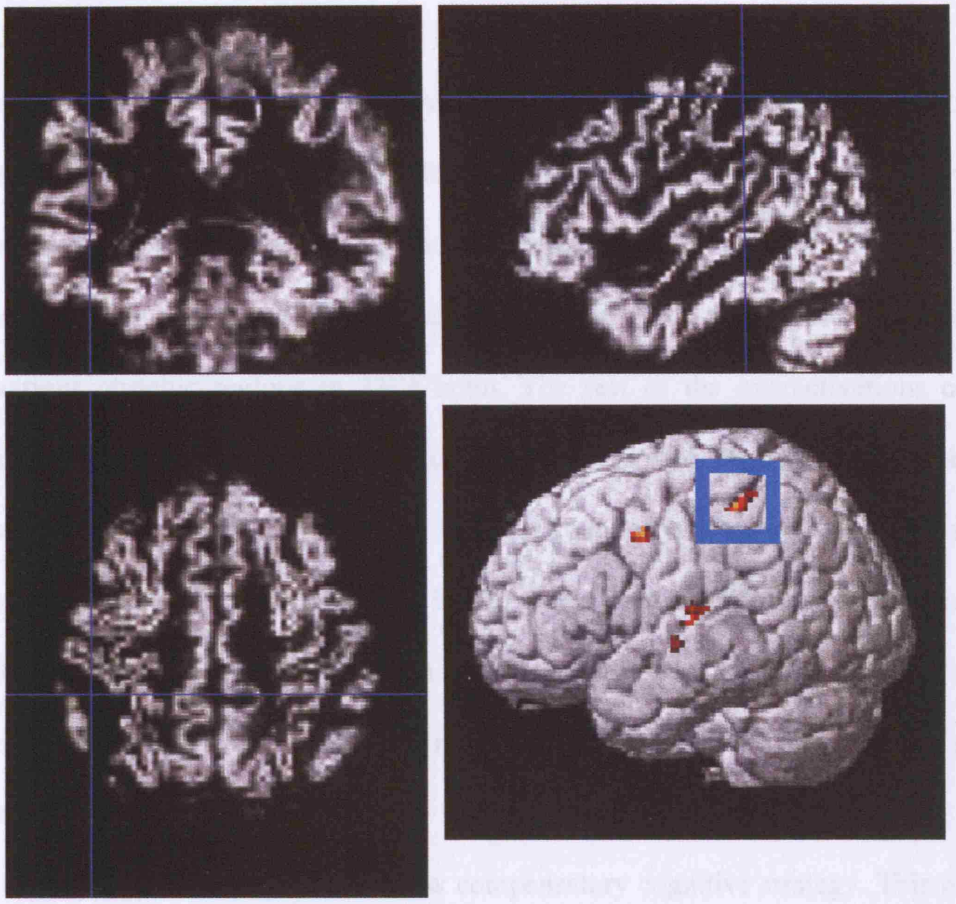


Figure XI: Reduced activation in lesioned area of TE

The rest of the underactivating areas do not correspond to lesions. This might be explained in two ways again:

(1) these areas may be receiving excitatory parietal inputs or

(2) they may be reflecting an abnormal pattern of articulation control. In fact, both these interpretations are possibly two different ways of describing the effect of the parietal lesion with the first speaking mostly in neuronal terms and the second in functional terms. Thus, the lesion seems to disrupt articulation control and this in turn disrupts activation in other areas involved in articulation and speech output (i.e. bilateral premotor and superior temporal gryi).

TE's Overactivations

As for the areas of TE's brain that showed enhanced activation relative to controls, they are located in the left anterior frontal lobe, the right cerebellum and the right thalamus. The areas in the right thalamus that showed abnormal activation were a bizarre finding and we believe that they could be artefactual due to an image registration error because of the various atrophic regions in TE's brain. The rest of the overactivations could be interpreted in two ways. First they could correlate with areas that were receiving inhibitory inputs from the lesioned area and thus could represent an effect of disinhibition. However, a recent review of functional imaging evidence in aphasic stroke concludes that disinhibition is usually associated with contra-lateral activation (Price & Crinion 2005) (i.e. in right hemisphere in TE's case) which was not observed. The second possible explanation of the overactivating areas is that they could be the effect of trying to cope with the task with the adoption of a new compensatory cognitive strategy. This is a quite convincing explanation if we consider the plethora of evidence available for these two brain regions. Frontal lobe activation has been associated with semantic maintenance (Shivde & Thompson-Schill 2004) and contributes to semantic retrieval and selection (Thompson-Schill 2003). The right cerebellar hemisphere has been associated with covert articulation (Silveri et al. 1998). Moreover, there is neuroanatomical evidence for connections between the left frontal lobe and right cerebellar hemisphere and for their activation in tandem (Schmahmann 1996). Within this coupled activation it has even been possible to dissociate two different roles; left frontal lobe being more involved in response selection and right cerebellum being more involved in search for responses (Desmond, Gabrieli, & Glover 1998). All these findings converge to suggest that TE is probably using a non-typical approach to reading. Given that he is able to read but on the other hand unable to do naming, we could suggest for example that he first visualises the

names of words and then reads them. A more detailed neuropsychological assessment of TE and patients with lesions in left frontal lobe or right cerebellum would definitely be essential to confirm this and any similar suggestion. They would also help to determine the necessity of these regions for the reading task. However, any conclusion of this kind when confirmed, could be used to devise an intervention for rehabilitation targeting the underlying cognitive functions.

5. Conclusions

The study of bilingualism has very important clinical implications. We focused on bilingual aphasia using functional imaging. The language pair we studied, Greek and English, has not been studied before in a similar paradigm. We studied healthy Greek-English bilinguals as well as two bilingual stroke patients who had recovered both languages.

The results of the healthy volunteers are in accordance with the so far available evidence and show highly significant overlap in activation patterns between the two languages while reading. The only difference observed was higher occipital activation during Greek reading and was attributed to the difference in word length, a finding that was again expected from the literature.

Both patients showed abnormal activation patterns while reading despite the fact that they performed well. Patient AP had a right hemisphere lesion which spared his right language areas and thus explained the temporary language deficit he experienced as well as his excellent recovery. There was only one area with enhanced activation near his right hemisphere lesion probably reflecting a compensatory increase in the demands of the peri-lesional tissue. Patient TE had reduced activation in his lesion while reading, confirming the absence of peri-lesional activity. He also showed reduced activation in other areas which suggests that, pre-stroke, these areas relied on excitatory input from the left parietal region. Moreover, there was abnormal enhanced activation of the left frontal lobe and right cerebellum, which is a known functional pair of neuroanatomical regions. This was suggestive of the use of a novel cognitive strategy used for reading.

In summary, we demonstrated that it is feasible to use functional imaging in every-day clinical practice in order to better understand a patient and draw conclusions for the healthy brain as well. We suggest that our study could be used as a model for

increasing our awareness about bilingualism and bilingual aphasia. With a large database of bilingual controls using different pairs of languages and the systematic scanning of patients with fMRI paradigms similar to ours, a lot can be learned about how the brain creates language and recovers it when it's damaged. It would be of course not reasonable to expect the findings in patients to be generalisable as each patient tells a unique story. Thus, there is poor statistical value in these studies. On the other hand, the focus is placed on what statistics usually misses or purposefully eliminates: individual variance. When it comes to treating an individual, it is also good practice to respect its individuality and unique characteristics. With the combined use of traditional neuropsychology testing and methods like ours the benefit can be maximised. Such approaches, especially when they grow on large scales, can then be used in routine clinical practice and provide clinical evidence that could help design new rehabilitation strategies for bilingual aphasia.

References

1. Alexiadou, A. & Stavrakaki, S. 2006, "Clause structure and verb movement in a Greek-English speaking bilingual patient with Broca's aphasia: evidence from adverb placement", *Brain Lang*, vol. 96, no. 2, pp. 207-220.

2. Bot, C. L. J. d. & Kroll, J. 2002, "Psycholinguistics," in *An Introduction to Applied Linguistics*, Schmitt N, ed., Hodder Arnold, London, pp. 133-149.

3. Chee, M. W., Caplan, D., Soon, C. S., Sriram, N., Tan, E. W., Thiel, T., & Weekes, B. 1999, "Processing of visually presented sentences in Mandarin and English studied with fMRI", *Neuron*, vol. 23, no. 1, pp. 127-137.

4. Chee, M. W., Hon, N., Lee, H. L., & Soon, C. S. 2001, "Relative language proficiency modulates BOLD signal change when bilinguals perform semantic judgments. Blood oxygen level dependent", *Neuroimage.*, vol. 13, no. 6 Pt 1, pp. 1155-1163.

5. Chee, M. W., Weekes, B., Lee, K. M., Soon, C. S., Schreiber, A., Hoon, J. J., & Chee, M. 2000, "Overlap and dissociation of semantic processing of Chinese characters, English words, and pictures: evidence from fMRI", *Neuroimage.*, vol. 12, no. 4, pp. 392-403.

6. Crinion, J., Turner, R., Grogan, A., Hanakawa, T., Noppeney, U., Devlin, J. T., Aso, T., Urayama, S., Fukuyama, H., Stockton, K., Usui, K., Green, D. W., & Price, C. J. 2006, "Language control in the bilingual brain", *Science*, vol. 312, no. 5779, pp. 1537-1540.

7. Desmond, J. E., Gabrieli, J. D., & Glover, G. H. 1998, "Dissociation of frontal and cerebellar activity in a cognitive task: evidence for a distinction between selection and search", *NeuroImage*, vol. 7, no. 4 Pt 1, pp. 368-376.

8. Dijkstra, T. & van Heuven, W. J. B. 1998, "The BIA model and bilingual word recognition," in *Localist connectionist approaches to human cognition*, Crainger j & Jacobs A M, eds., Lawrence Erlbaum Associates, Mahwah, NJ, pp. 189-225.

9. Dijkstra, T. & van Heuven, W. J. B. 2002, "The architecture of the bilingual word recognition system: From identification to decision", *Bilingualism*, vol. 5, no. 03, pp. 175-197.

10. Edelman, G. M. & Gally, J. A. 2001, "Degeneracy and complexity in biological systems", *Proc.Natl.Acad.Sci.U.S.A*, vol. 98, no. 24, pp. 13763-13768.

11. Enderby, P. & Emerson, J. 1996, "Speech and language therapy: does it work?", *BMJ*, vol. 312, no. 7047, pp. 1655-1658.

12. Fabbro, F. 2001, "The bilingual brain: bilingual aphasia", *Brain Lang*, vol. 79, no. 2, pp. 201-210.

13. Feeney, D. M. & Baron, J. C. 1986, "Diaschisis", *Stroke*, vol. 17, no. 5, pp. 817-830.

14. French, R. M. & Jacquet, M. 2004, "Understanding bilingual memory: models and data", *Trends Cogn Sci.*, vol. 8, no. 2, pp. 87-93.

15. Friston, K. J., Ashburner, J., Frith, C. D., Poline, J. B., Heather, J. D., & Frackowiak, R. S. 1995a, "Spatial registration and normalization of images", *Human Brain Mapping*, vol. 3, pp. 165-189.

16. Friston, K. J., Holmes, A. P., Poline, J. B., Grasby, P. J., Williams, S. C., Frackowiak, R. S., & Turner, R. 1995b, "Analysis of fMRI time-series revisited", *Neuroimage.*, vol. 2, no. 1, pp. 45-53.

17. Goodglass, H., Kaplan, E., & Barresi, B. 2001, *The assessment of aphasia and related disorders*, 3rd edn, Lippincott Williams & Wilkins, Philadelphia.

18. Green, D. W. 2005, "The neurocognition of recovery patterns in bilingual aphasics," in *Handbook of Bilingualism: Psycholinguistic Perspectives*, Kroll JF & de Groot AMB, eds., Oxford University Press, Oxford.

19. Green, D. W. 2003, "Mental control of the bilingual lexico-semantic system", *Bilingualism*, vol. 1, no. 02, pp. 67-81.

20. Green, D. W. 1986, "Control, activation, and resource: a framework and a model for the control of speech in bilinguals", *Brain Lang*, vol. 27, no. 2, pp. 210-223.

21. Grosjean F 1998, "Studying bilinguals: Methodological and conceptual issues", *Bilingualism: Language and Cognition*, vol. 1, no. 2, pp. 131-149.

22. Grosjean F 1994, "Individual Bilingualism," in *The encyclopaedia of language and linguistics*, Asher R E, ed., Pergamon Press, Oxford, UK, pp. 1656-1660.

23. Grosjean, F. 1989, "Neurolinguists, beware! The bilingual is not two monolinguals in one person", *Brain Lang*, vol. 36, no. 1, pp. 3-15.

24. Hasegawa, M., Carpenter, P. A., & Just, M. A. 2002, "An fMRI study of bilingual sentence comprehension and workload", *Neuroimage.*, vol. 15, no. 3, pp. 647-660.

25. Holmes, A. P. & Friston, K. J. 1998, "Generalisability, Random Effects and Population Inference", *NeuroImage* p. S754.

26. Kambanaros, M. & Steenbrugge, W. v. 2006, "Noun and verb processing in Greek-English bilingual individuals with anomic aphasia and the effect of instrumentality and verb-noun name relation", *Brain Lang*, vol. 97, no. 2, pp. 162-177.

27. Kay, J., Coltheart, M., & Lesser, R. 1992, *Psycholinguistic Assessment of Language Processing in Aphasia* Lawrence Erlbaum Associates Ltd., Hove, UK.

28. Kritikos, E. P. 2003, "Speech-language pathologists' beliefs about language assessment of bilingual/bicultural individuals", *Am.J.Speech Lang Pathol.*, vol. 12, no. 1, pp. 73-91.

29. Meara, P. & Jones, G. 1990, *Eurocentres vocabulary size test 10K* Eurocentres, Zurich.

30. Paradis, M. 2000a, "Generalizable outcomes of bilingual aphasia research", *Folia Phoniatr.Logop.*, vol. 52, no. 1-3, pp. 54-64.

31. Paradis, M. 2003, "The bilingual Loch Ness Monster raises its non-asymmetric head again-or, why bother with such cumbersome notions as validity and reliability? Comments on Evans et al. (2000)", *Brain Lang*, vol. 87, no. 3, pp. 441-448.

32. Paradis, M. 1995, "Introduction: The need for distinctions," in *Aspects of bilingual aphasia*, M. Paradis, ed., Pergamon Press, Oxford, UK, pp. 1-9.

33. Paradis, M. 2000b, "The neurolinguistics of bilingualism in the next decades", *Brain Lang*, vol. 71, no. 1, pp. 178-180.

34. Paradis, M. 1998, "Language and communication in multilinguals," in *Handbook of neurolinguistics*, B.Stemmer & H.A.Whitaker, eds., Academic Press, San Diego, pp. 418-431.

35. Paradis, M. 2004, *A neurolinguistic theory of bilingualism* John Benjamins Publishing Company.

36. Paradis, M. 1987, *The Assessment of Bilingual Aphasia* Lawrence Erlbaum, Hillsdale NJ.

37. Paradis, M. 1977, "Bilingualism and aphasia," in *Studies in Neurolinguistics*, vol. 3 Whitaker H & Whitaker HA, eds., Academic Press, New York, pp. 65-121.

38. Paradis, M. 1996, "Selective deficit in one language is not a demonstration of different anatomical representation: comments on Gomez-Tortosa et al. (1995)", *Brain Lang*, vol. 54, no. 1, pp. 170-173.

39. Pearce, J. M. 2005, "A note on aphasia in bilingual patients: Pitres' and Ribot's laws", *Eur.Neurol.*, vol. 54, no. 3, pp. 127-131.

40. Perani, D. & Abutalebi, J. 2005, "The neural basis of first and second language processing", *Curr.Opin.Neurobiol.*, vol. 15, no. 2, pp. 202-206.

41. Pinker S 1994, *The language instinct* Penguin Books, London.

42. Price, C. J. 2000, "The anatomy of language: contributions from functional neuroimaging", *J.Anat.*, vol. 197 Pt 3, pp. 335-359.

43. Price, C. J. & Crinion, J. 2005, "The latest on functional imaging studies of aphasic stroke", *Curr.Opin.Neurol.*, vol. 18, no. 4, pp. 429-434.

44. Price, C. J. & Friston, K. J. 1999, "Scanning patients with tasks they can perform", *Hum.Brain Mapp.*, vol. 8, no. 2-3, pp. 102-108.

45. Price, C. J. & Friston, K. J. 2002, "Functional imaging studies of neuropsychological patients: applications and limitations", *Neurocase.*, vol. 8, no. 5, pp. 345-354.

46. Price, C. J., Noppeney, U., & Friston, K. J. 2006, "Functional Neuroimaging of Neuropsychologically Impaired Patients," in *Handbook of Functional Neuroimaging of Cognition*, 2nd edn, Cabeza R & Kingstone A, eds., The MIT Press, pp. 455-480.

47. Price, C. J., Warburton, E. A., Moore, C. J., Frackowiak, R. S., & Friston, K. J. 2001, "Dynamic diaschisis: anatomically remote and context-sensitive human brain lesions", *J.Cogn Neurosci.*, vol. 13, no. 4, pp. 419-429.

48. Schmahmann, J. D. 1996, "From Movement to Thought: Anatomic Substrates of the Cerebellar Contribution to Cognitive Processing", *Human Brain Mapping*, vol. 4, pp. 174-198.

49. Shivde, G. & Thompson-Schill, S. L. 2004, "Dissociating semantic and phonological maintenance using fMRI", *Cogn Affect.Behav.Neurosci.*, vol. 4, no. 1, pp. 10-19.

50. Silveri, M. C., Di Betta, A. M., Filippini, V., Leggio, M. G., & Molinari, M. 1998, "Verbal short-term store-rehearsal system and the cerebellum. Evidence from a patient with a right cerebellar lesion", *Brain*, vol. 121 (Pt 11), pp. 2175-2187.

51. Swinburn, K., Porter, G., & Howard, D. 2004, *Comprehensive Aphasia Test* Psychology Press.

52. The Bible, 1000BC, "Genesis," in *Genesis*, vol. 11 pp. 1-8.

53. Thompson-Schill, S. L. 2003, "Neuroimaging studies of semantic memory: inferring "how" from "where"", *Neuropsychologia*, vol. 41, no. 3, pp. 280-292.

54. Wartenburger, I., Heekeren, H. R., Abutalebi, J., Cappa, S. F., Villringer, A., & Perani, D. 2003, "Early setting of grammatical processing in the bilingual brain", *Neuron*, vol. 37, no. 1, pp. 159-170.

55. Yokoyama, S., Okamoto, H., Miyamoto, T., Yoshimoto, K., Kim, J., Iwata, K., Jeong, H., Uchida, S., Ikuta, N., Sassa, Y., Nakamura, W., Horie, K., Sato, S., & Kawashima, R. 2006, "Cortical activation in the processing of passive sentences in L1 and L2: an fMRI study", *Neuroimage.*, vol. 30, no. 2, pp. 570-579.