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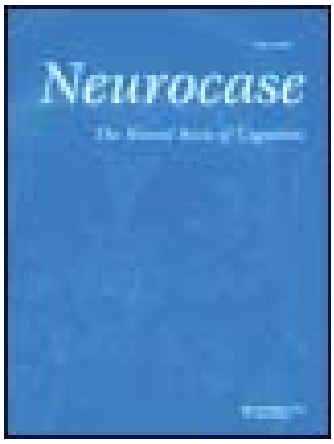

Neurocase: The Neural Basis of Cognition
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/nncs20

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Published online: 09 Aug 2010.

To cite this article: Denise Klein , Brenda Milner , Robert J. Zatorre , Regina Visca & André Olivier (2002) Cerebral Organization in a Right-handed Trilingual Patient with Right-hemisphere Speech: a Positron Emission Tomography Study, Neurocase: The Neural Basis of Cognition, 8:5, 369-375

To link to this article: http://dx.doi.org/10.1076/neur.8.4.369.16185

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Neurocase (2002) Vol. 8, pp. 369–375 © *Oxford University Press 2002*

Cerebral Organization in a Right-handed Trilingual Patient with Right-hemisphere Speech: a Positron Emission Tomography Study

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Abstract

Using the method of positron emission tomography, combined with word-generation tasks, we had the opportunity to examine the cerebral representation of multiple languages in the brain in a right-handed patient, RA, with known right-hemisphere speech representation as determined by intracarotid sodium amobarbital testing. Similar patterns of cerebral blood flow were observed across all three languages (French, Spanish and English), when synonym generation was compared with a silent resting baseline. In particular, several regions in the right inferior frontal cortex were activated. These foci are in locations corresponding to those observed in the left hemisphere in normal right-handed volunteers with presumed left-hemisphere dominance, and in patients known to be left-hemisphere dominant for speech. The lack of anatomical separation of the three languages within the same individual, who acquired two languages early and one language later in life, suggests that at least at this single-word level of analysis, age of acquisition was not a significant factor in the determining of functional organization in the brain.

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Introduction

Historically, the intracarotid sodium amobarbital procedure has been seen to confer a special advantage for the assessment of hemispheric lateralization in patients, in that it permits a direct comparison of the roles of the two hemispheres in the mediation of speech (Branch *et al.*, 1964). In recent times, several neuroimaging studies have compared the efficacy of functional imaging tools such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) with the intracarotid sodium amobarbital procedure (Binder *et al.*, 1996; Hunter *et al.*, 1999), and a correlation between lateralization measures derived from functional imaging and the intracarotid sodium amobarbital procedure (Pardo and Fox, 1993; Desmond *et al.*, 1995; Binder *et al.*, 1996) has been observed.

In addition to being non-invasive, functional neuroimaging procedures have the advantage of being able to localize functions within a hemisphere. As one example (across many laboratories), studies of word generation have produced activations in the left inferior frontal cortex in right-handed volunteers (Petersen *et al.*, 1988; Frith *et al.*, 1991; Wise *et al.*, 1991; Klein *et al.,* 1995). This demonstration of a role for the left inferior frontal cortex in lexical search and retrieval is consistent with the finding that patients with left frontal-lobe lesions show an impairment on word fluency tasks (Milner, 1964; Benton, 1968).

As an extension of functional imaging studies in unilingual subjects, several studies of bilingual volunteers have now explored whether similar patterns of cortical representation in the left inferior frontal cortex can be observed for native (L1) and second (L2) languages, and, more generally, whether the neural substrates involved in processing a second or subsequent language are similar to those of a native language. Several PET and fMRI studies have observed common patterns of activation for L1 and L2 using single-word paradigms (Klein *et al.*, 1995, 1999; Chee *et al.*, 1999a; Illes *et al.*, 1999; Hernandez *et al.*, 2000) and tasks of sentence and story processing (Perani *et al.*, 1996; Chee *et al.*, 1999b). But other studies have shown a divergence between findings for L2 and L1, depending on the proficiency of the bilingual speaker (Perani *et al.*, 1998); according to Dehaene *et al.* (1997), less proficient bilinguals are likely to show wider differences between L1 and L2. Still other investigators (e.g. Kim *et al.*, 1997) have argued for spatial separation of L1 and L2 within the left frontal cortex when the second language is acquired in adulthood, but not when both languages are

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acquired early. Several lines of evidence point to the fact that the early acquisition of language produces better linguistic competency and that the organization of L2 may be affected by age of acquisition (Harley and Wang, 1997), so that the interaction between these factors may also be contributory to the final outcome.

The neural representation of multiple languages has also been investigated by electrical stimulation of the cerebral cortex in conscious bilingual patients (Ojemann, 1983), by examining aphasic bilingual subjects (Paradis, 1993), and by experimental studies of normal bilingual volunteers (Albert and Obler, 1978), but it has proven difficult to determine conclusively whether there is a common cortical substrate within which all languages operate, or whether multiple languages may be represented by different cerebral regions within the language-dominant hemisphere.

We report here a case study in which we used PET to investigate the neural representation of the three languages of a polyglot speaker, RA, a right-handed patient with familial right-handedness and with speech lateralized to the right cerebral hemisphere, as determined by intracarotid sodium amobarbital tests. RA was raised in a bilingual (French/Spanish) setting from birth, and then learned a third language (English) later in life. This particular set of circumstances gives rise to the possibility of investigating how multiple languages are organized in a person with known atypical speech representation. We wished to examine the cerebral representation of the three languages as a function of when they were acquired and also in terms of RA's level of proficiency in each language.

Case history

RA is a 37-year-old right-handed woman with a long-standing history of seizure disorder. From birth to the age of 4 years she had several brief uncomplicated febrile convulsions. At the age of 2 years she also sustained a relatively benign head trauma, but she did not lose consciousness. She was seizure free from 4 years of age until the age of 12 years, when the seizures returned in the form of two to four complex partial seizures per month, at times occurring in clusters of up to seven or eight per day. The seizures are characterized by an olfactory aura, followed by loss of contact, and the seizure activity consists of either repeated kissing of the left hand or occasionally the shaking of both legs. There is no communication during this time, but she may call out her mother's name repeatedly. These episodes last 30–60 s, with post-ictal tiredness and headache. Several medications have been tried, with little impact on her seizure frequency. An MRI of 18 March 1999 indicated globally diffuse atrophy in the cerebral and cerebellar hemispheres, most likely related to long-term usage of anti-epileptic medication. Coronal T2-weighted and inversion recovery images revealed gross asymmetry in the size of the hippocampi, with the left hippocampus being significantly atrophied compared with the right. Electroencephalography revealed a left mesio-temporal lobe focus for the epileptiform activity. On 15 April 1999 a left selective amygdalo-hippocampectomy was carried out at the Montreal Neurological Hospital with the aim of reducing the frequency of the seizures, and a year after the operation she remains seizure free. The pathology report confirmed hippocampal sclerosis.

Linguistic history

RA was born in Morocco in the small town of Canitra, where both French and Spanish are spoken. In her youth, she spoke French with both parents, but spoke only Spanish to her maternal grandmother who lived in the same house. French was the language used most regularly with the other grandparents and relatives. RA lived in Spain from the age of 4 years until the age of 9 years but attended a French school. She went to Canada at the age of 9 years and went to an English-medium school for 1 year. From this time onwards, RA attended a French-medium school where she was exposed to all three languages. RA has worked for the past 20 years as a freelance interpreter and she makes frequent use of all three languages.

Neuropsychological testing

RA gave informed consent to be tested and all aspects of the investigation were performed according to institution-reviewed medico-ethical guidelines.

Cognitive profile. Basic intellectual function, as tested in French on the Wechsler Adult Intelligence Scale-Revised (WAIS-R), was in the Low Average range (full-scale IQ = 80). Although the patient is strongly right handed, as are all members of her immediate family, she showed a small left-ear advantage on the fused words dichotic listening test, which was administered in English (Wexler–Halwes Fused Words Test: left ear = 12; right ear = 5), an asymmetry that is opposite to what is normally expected (Wexler and Halwes, 1983). This raised the possibility of atypical hemispheric dominance for language (Zatorre, 1988) and therefore intracarotid amobarbital procedures were performed.

Intracarotid amobarbital speech studies. Naming and series repetition tasks, as well as subsequent memory testing, were carried out in French during the 2–6-min period of hemiparesis induced by the injection of 125 mg of 10% sodium amobarbital into the internal carotid artery on one side. A 3 cc arteriogram was also carried out so that the symmetry of the arterial supply to the two cerebral hemispheres could be assessed. The right and left carotid arteries were injected on different days. On neither day was there filling of the posterior circulation, nor was there any anterior cross-filling from left to right or right to left.

Following the left-sided injection, carried out on the first day, there was no speech arrest and no disturbance of speech on any task. After injection into the right hemisphere, speech

Table 1. Order of presentation of conditions

Block A: Spanish
(a) Word repetition 1 (SREP1);
(b) Word repetition 2 (SREP2);
(c) Synonym generation 1 (SSYN1);
(d) Synonym generation 2 (SSYN2);
(e) Silent baseline 1 (SB1)
Block B: English
(f) Word repetition 1 (EREP1);
(g) Word repetition 2 (EREP2);
(h) Synonym generation 1 (ESYN1);
(i) Synonym generation 2 (ESYN2);
(j) Silent baseline 2 (SB2)
Block C: French
(k) Word repetition 1 (FREP1);
(l) Word repetition 2 (FREP2);
(m) Synonym generation 1 (FSYN1);
(n) Synonym generation 2 (FSYN2)

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arrest was observed until 5 min 53 s, when the patient said 'oui' in response to her name. During this time, disturbances of comprehension were documented. As speech recovered, naming, spelling, and sequential speech errors were evident. Fifteen minutes after injection, residual naming errors were still being observed. It was concluded that in this patient, speech representation is exclusively in the right cerebral hemisphere.

Functional imaging study of language using PET

The patient was scanned in all three languages, the scanning session being divided into three language blocks, beginning with Spanish (L1a), then English (L2) and then French (L1b). Successive language blocks were separated by a silent baseline condition in which the subject was scanned while resting (see Table 1). In each 60-s activation scanning condition, the patient was presented with an auditory word every 4 s and was either required to repeat the word aloud or to generate a synonym. Two different stimulus lists were used for each language. To familiarize RA with each task, she was presented with 10 practice items before each scan. The task was initiated 10 s in advance of each scan, and continued until after the scan had finished. The stimuli were read at a rate of one stimulus every 4 s by a native speaker in each language. The native speaker who read the lists for the Spanish set was male, while for the English and French sets the speaker was female. The stimuli chosen for each list were matched as far as possible for frequency, part-of-speech, syllable number and word length. For the synonym-generation lists, stimuli were chosen that were good examplars for each language, and an attempt was made to avoid using the same exemplars across languages, but this was not always possible. Lights were dimmed for the duration of the scan and RA was instructed to keep her eyes closed during each scan. Response accuracy was recorded and was scored by a native speaker of each language.

PET data acquisition

PET scans were obtained with a Siemens Exact HR+ tomograph operating in three-dimensional acquisition mode. The distribution of cerebral blood flow (CBF) was measured during each 60-s scan using the H_2O^{15} water bolus method. T1-weighted structural MRI scans (160 1-mm thick slices) were also obtained with a 1.5T Phillips ACS system to provide anatomical detail. Merged images were resampled into the standardized stereotaxic space of Talairach and Tournoux (1988). Significant focal CBF changes were identified using the method of Worsley *et al.* (1992). The average of the two silent baseline conditions, and of the two repetition conditions, respectively, were subtracted from the averages of the two generation conditions, and then the subtractions for each language were directly compared with each other.

Task performance during scanning acquisition

RA was able to produce the correct phonology for each word in each language, and word repetition was 100% accurate for each language. For synonym generation, a correct response could be either the experimenter-defined synonym or a word that was closely associated with the presented item. An unrelated response or no response was marked as incorrect. RA was most accurate at generating synonyms in French (L1a = 85% correct). She was less accurate at synonym generation in both her other native language (Spanish L1b = 54% correct) and also in her second language (English L2 = 50% correct). For all three languages, all errors (except one in Spanish) were characterized by no response.

PET results

Regions of significant CBF increase for the subtraction of a silent baseline from synonym generation for each of the three languages are enumerated in Tables 2 and 3, and the strongest cortical sites of activation are shown across conditions in Fig. 1, for purposes of comparison.

L1a: French synonym generation minus silent baseline. Several significant blood flow increases were observed unilaterally in the right frontal cortex: in the inferior frontal gyrus (pars triangularis and orbicularis and in the short gyri of the insula); in the medial superior frontal gyrus; in the posterior orbital frontal gyrus and in the cingulate cortex. Posteriorly, a unilateral peak was observed in the right angular gyrus and in the left superior temporal gyrus, and bilateral activations were seen in the middle temporal and inferior temporal gyri. Significant CBF increases were observed bilaterally in the cerebellar cortices.

L1b: Spanish synonym generation minus silent baseline. Several significant blood flow increases were observed unilaterally in the right frontal cortex: in the inferior frontal gyrus (pars triangularis and opercularis); in the superior frontal

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Table 2. Synonym generation minus silent baseline: right-hemisphere activations

	x	*y*	*z*	*t*-value
Frontal cortex				
IFG: pars triangularis				
English	38	36	17	6.9
French	38	39	18	6.3
Spanish	39	27	17	4.2
Spanish	39	39	17	3.7
IFG: pars orbicularis				
English	35	46	–2	6.2
French	38	48	–2	4.6
French	47	39	–2	4.8
IFG: pars opercularis				
English	47	12	12	4.6
Spanish	50	10	14	3.8
English (IFS)	44	15	–2	4.2
French (short gyri of insula)	40	17	–3	4.8
IFG: pre-central gyrus				
English	40	12	27	5.1
SFG: frontal pole				
English	24	49	21	4.6
Spanish	21	48	21	4.1
Spanish	35	48	26	3.5
SFG: medial				
French	12	29	47	3.6
Orbital frontal cortex				
English (posterior)	17	20	–18	4.0
French (posterior)	20	20	–19	4.9
Spanish (posterior)	17	24	–19	4.6
Spanish	32	48	–8	4.9
Cingulate cortex				
English	9	27	26	4.7
French	7	29	27	5.7
Spanish	9	27	32	3.8
Globus pallidus				
Spanish	15	6	–6	4.1
Gyrus rectus				
Spanish	13	49	–16	3.8
Parietal cortex				
Angular gyrus				
English	54	–36	47	3.9
English	52	–47	50	3.8
French	44	–45	48	5.6
Temporal cortex				
Middle temporal gyrus				
English	62	–31	–13	4.1
French	63	–33	–12	4.4
Inferior temporal				
French (ITG)	58	–41	–16	4.4
Spanish (ITS)	64	–33	–15	4.8
Lateral cerebellum				
French	38	–57	–21	4.0
Spanish	36	–57	–21	4.0

Activation foci in this table represent peaks of statistically significant increases in normalized cerebral blood flow (CBF) for each language for the subtraction of a silent baseline from synonym generation.
The anatomical region reported refers to the position of the peak based on the merged registration image of the patient's own positron emission tomograph and magnetic resonance image.
IFG, inferior frontal gyrus; SFG, superior frontal gyrus; *x*, medial–lateral distance relative to the midline (positive = right); *y*, anterior–posterior distance relative to the anterior commissure (positive = anterior); *z*, superior–inferior distance relative to the anterior commissure line (posterior = superior).

Table 3. Synonym generation minus silent baseline: left-hemisphere activations

	x	*y*	*z*	*t*-value
Frontal cortex				
Short gyri of insula cortex				
Spanish	–29	24	8	4.0
Medial superior frontal gyrus				
English	–10	30	42	4.0
Temporal cortex				
Superior temporal gyrus (STG)				
French	–60	–29	6	3.6
Spanish	–57	–28	6	4.3
English (STS)	–53	–38	–5	4.6
Middle temporal gyrus (MTG)				
English (MTG)	–60	–38	–16	5.2
French (MTS)	–53	–36	–2	3.7
Inferior temporal gyrus (ITG)				
French (ITG)	–57	–45	–18	5.1
Spanish (ITG)	–60	–41	–21	4.1
Spanish (ITG)	–54	–52	–18	4.0
Cerebellum				
English	–41	–60	–22	5.4
French	–40	–65	–24	3.6
Spanish	–37	–64	–24	5.2

MTS, medial temporal sulcus.

gyrus (frontal polar area); in the posterior orbital frontal gyrus; in the gyrus rectus, cingulate cortex and globus pallidus. A peak was also observed in the left hemisphere in the short gyri of the insula. Posteriorly, a unilateral peak was seen in the left superior temporal gyrus, and bilateral activations were seen in the inferior temporal gyri. Significant CBF increases were observed bilaterally in the cerebellar cortices.

L2: English synonym generation minus silent baseline. Several significant blood flow increases were observed unilaterally in the right frontal cortex: in the inferior frontal gyrus (pars triangularis, orbicularis, opercularis and in the pre-central gyrus); in the superior frontal gyrus (frontal polar area); and in the cingulate cortex. A peak was noted in the left hemisphere in medial superior frontal gyrus. Posteriorly, unilateral peaks were observed in the right angular gyrus and in the left superior temporal sulcus, and bilateral activations were seen in the middle temporal gyri. A significant CBF increase was observed in the left lateral cerebellum.

Word repetition minus silent baseline and synonym generation minus word repetition. Regions of significant CBF change were also analysed for the subtraction of a silent baseline from word repetition. The CBF changes in relation to word repetition were similar to those observed for synonym generation. With respect to the frontal cortex, for all languages, strong activity was again observed in the right inferior frontal region.

For the subtraction of word repetition from synonym generation, low magnitude CBF increases in the right frontal cortex were visible for each language; the lack of the

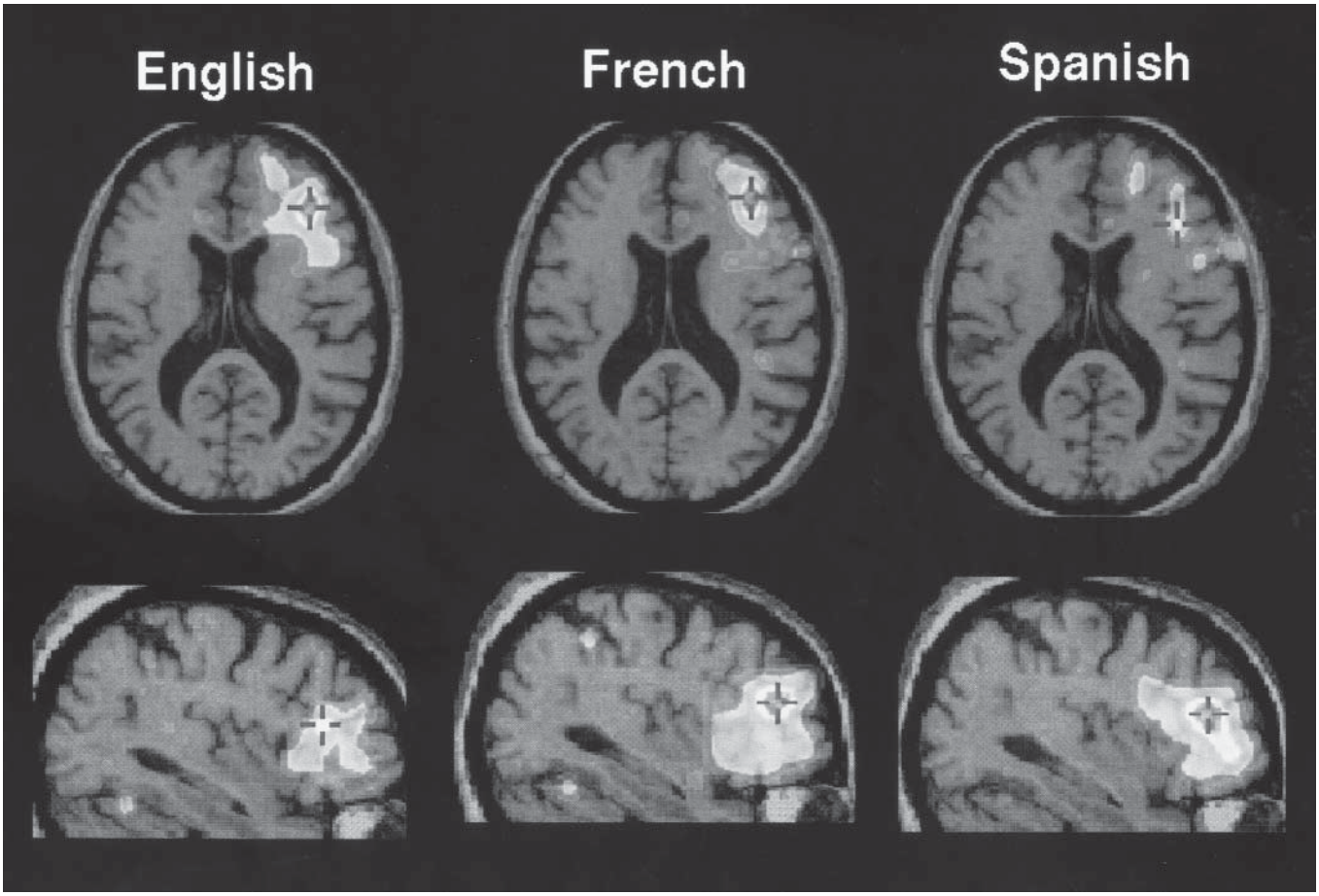

Fig. 1. Synonym generation minus silent baseline. Positron emission tomography (PET) subtraction image showing cerebral blood flow (CBF) increases for each language superimposed upon the magnetic resonance image (MRI). Overall there are similar configurations of CBF visible across languages. A series of distinct foci was observed in the right frontal cortex in each language, as compared with the silent baseline. Direct comparison of the subtractions for each of the languages failed to reveal any spatial separation of Spanish, French or English within the right frontal cortex. The CBF increases are in corresponding locations to those observed in normal volunteers, but are in the right hemisphere.

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predicted strong activation in the right inferior frontal cortex was presumably due to the recruitment of this region even for word repetition.

Synonym generation: direct comparison across languages. To determine the presence of statistically significant differences among the languages tested, an analysis of variance was performed comparing the languages directly with one another. No significant activation in the frontal lobe was detected when English was compared with French or Spanish, or when Spanish and French were compared with each other.

Discussion

This study demonstrates agreement between the PET results and the sodium amobarbital procedure in this patient with right-hemisphere speech representation. Overall there were similar configurations of blood-flow change visible across the languages examined (see Fig. 1 for a comparison). The CBF increases in the anterior inferior frontal cortex are in corresponding locations to those observed in a group of normal right-handed volunteers with presumed left-hemisphere language dominance [*x*; *y*; *z*: –40; 25; 18; see Klein *et al.* (1996)], but are in the right hemisphere (English: 38, 36, 17; French: 38, 39, 18; Spanish: 39, 27, 16). These results are consistent with the notion of common cortical representation for native and second languages in lexical search and retrieval (Klein *et al.*, 1995, 1999; Chee *et al.*, 1999a; Illes *et al.*, 1999).

To test the hypothesis that the areas activated by the three languages represented different anatomical substrates, we compared the languages directly against one another. Within the resolution of the technique, no significant activation in the frontal lobe was detected when English was compared with French or Spanish, or when Spanish and French were compared with each other, suggesting that the underlying frontal-lobe activations were similar. It should also be noted that spatially overlapping networks for processing L1 and L2 should not be equated with similarity in competence or performance skills. In our data we do obtain different behavioural scores for performance accuracy across languages, despite the observation of overlapping brain regions for L1a, L1b and L2. Although conversationally RA is fluent in all three languages, under conditions requiring rapid

processing and retrieval of synonyms, it is clear that RA is most proficient in French (L1a). Nevertheless, we failed to observe differences in activation across languages, despite RA's differing levels of success at word generation across languages, and despite the fact that she had learned her L2 later in life.

The anterior inferior frontal region was the main focus of the analysis because this region has been activated robustly and consistently in relation to word-generation tasks, and because differences in the cortical organization of language in early and late bilinguals have been shown in the frontal (Kim *et al.*, 1997) but not temporal (Kim *et al.*, 1997; Perani *et al.*, 1998) regions. We did, however, observe several other brain regions that were active in relation to synonym generation which were not consistently found across all three languages. Activity in the right angular gyrus was observed for L1a and L2, but not for L1b. Bilateral activity was observed in the middle temporal gyrus for L1a and L2, but not L1b, and bilateral activity in the inferior temporal gyrus was observed for L1a and L1b, but not L2. For all languages, activity was observed in the left superior temporal gyrus. Bilateral cerebellar activity was noted for L1a and L1b, but only left cerebellar activity was observed for L2. These differences are difficult to interpret in the context of a single case study and without clear understanding of the functional significance of these regions in relation to language tasks.

Unlike our previous study (Klein *et al.*, 1994, 1995), in which we observed increased activity in the left putamen when subjects produced responses in their L2, in the present investigation we did not observe increased activation in the putamen for speaking in L2 (English). Interestingly, we did observe an increase in activity in the right globus pallidus (*x*; *y*; *z*: 15; 6; –6) for L1b (Spanish), in this patient with right-hemisphere speech, in similar locations to those reported previously for articulation in L2 (Klein *et al.*, 1995: *x*; *y*; *z*: –15; 10; –6; Klein *et al.*, 1994: *x*; *y*; *z*: –21; 12; –9). However, other functional imaging studies comparing L1 and L2 (Klein *et al.*, 1999; Price *et al.*, 1999) have not observed activation in this region. On the basis of work with patients, Watkins *et al.* (1999) and Aglioti and Fabbro (1993) have posited a role for the left basal ganglia in speech production. Functional imaging (Wise *et al.*, 1999) and lesion reconstruction analysis (Dronkers, 1996) studies have also supported a role for the 'lenticular zone', which includes the basal ganglia [see Pierre Marie in Head (1926)], in the co-ordination of speech articulation. It is unclear what factors contribute to increased activity in the basal ganglia in relation to articulation, and more research is necessary to determine under what conditions differences related to articulation in L1 and L2 are evident.

Conclusion

Although this is a single case report and only limited aspects of language processing have been sampled, this study highlights the convergence within the right frontal cortex in the representation of the three languages in a patient with atypical language representation. The findings are consistent with the prediction that similar brain regions are active even when the L2 is acquired later in life and despite differences in levels of performance accuracy across languages, and even when language representation develops in the right cerebral hemisphere.

Acknowledgements

We thank Manuel Castro-Alamancos and Alexander Bastos for their assistance. We thank RA for her willingness to participate. This study was supported by grants from the Medical Research Council of Canada (MT2624, SP30, MT11541), the McDonnell-Pew Program in Cognitive Neuroscience and the Fonds de la Recherche en Santé du Québec.

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Cerebral organization in a right-handed trilingual patient with right-hemisphere speech: a positron emission tomography study

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Abstract

Using the method of positron emission tomography, combined with word-generation tasks, we had the opportunity to examine the cerebral representation of multiple languages in the brain in a right-handed patient, RA, with known right-hemisphere speech representation as determined by intracarotid sodium amobarbital testing. Similar patterns of cerebral blood flow were observed across all three languages (French, Spanish and English), when synonym generation was compared with a silent resting baseline. In particular, several regions in the right inferior frontal cortex were activated. These foci are in locations corresponding to those observed in the left hemisphere in normal right-handed volunteers with presumed left-hemisphere dominance, and in patients known to be left-hemisphere dominant for speech. The lack of anatomical separation of the three languages within the same individual, who acquired two languages early and one language later in life, suggests that at least at this single-word level of analysis, age of acquisition was not a significant factor in the determining of functional organization in the brain.

Journal

Neurocase 2002; 8: 369–75

Neurocase Reference Number:

O270

Primary diagnosis of interest

Epilepsy

Author's designation of case

RA

Key theoretical issue

- Common neural substrate across three languages for lexical search and retrieval

Key words: bilingualism; imaging; language; PET

Scan, EEG and related measures

PET, MRI, EEG, intracarotid sodium amobarbital testing

Standardized assessment

WAIS-R

Lesion location

- Left hemisphere—hippocampus

Lesion type

Hippocampal sclerosis

Language

English