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PET evaluation of bilingual language compensation following early childhood brain damage

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Abstract

We report a positron emission tomography (PET) study in a 37-year-old, right handed, bilingual (English and American Sign Language) male with left frontal lobe damage, without evidence of language or general intellectual dysfunction. A brain MRI scan demonstrated an atrophic lesion of the left dorsolateral prefrontal, orbital, and opercular cortices extending from the frontal pole to precentral gyrus and including parts of anterior cingulate cortex, due to an probable infantile encephalitis. H_2 ^{15}O PET scans found evidence of increased right hemisphere activity compared to normal controls during spontaneous generation of narrative in *both* English and ASL. Neuropsychological data were within normal limits with the exception of visuospatial function. The results suggest the possibility that plasticity, unmasking of neural pathways, and or other adaptations of language function in the right hemisphere may have occurred, and are discussed with regard to the crowding hypothesis. © 2000 Published by Elsevier Science Ltd.

Keywords: Plasticity; ASL; Left frontal lobe damage; Crowding

1. Introduction

The capacity of the brain to recover from an acute focal lesion, ostensibly through plasticity of neural pathways, has been well documented, particularly if the lesion occurs in early childhood [16,24,25,29,30,40]. The unmasking of inactive or redundant pathways, or mediation of functional representation by undamaged brain tissue and neural group selection are among possible mechanisms [1,17,27].

Although neuronal plasticity in humans has been demonstrated in the recovery of visual, auditory, and motor function [24,37], the most striking example has been the recovery of language function after early lesions of the left cerebral hemisphere [26]. Children who incur left hemisphere lesions before the age of six first demonstrate a transient dysphasia, followed by a rapid and generally good, if not complete, recovery [2,14]. One possible mechanism of compensation in these children is represented by right hemisphere homologous region adaptation [11]. However, this adaptation may adversely affect the development of normal right hemisphere functions [20,35]. And the long-term prognosis for normal development in children who have suffered left hemisphere damage may be less favorable than once thought. Indeed, a number of cognitive abnormalities may become apparent with careful study [39].

The case we report demonstrates that brain damage to language-related areas early in life can be followed by a remarkable recovery and normal development of language ability. Positron emission tomography (PET) was used to evaluate the role of the contralateral hemisphere in supporting the cognitive processes that enabled language compensation to occur and possible interference with other cognitive functions was examined using neuropsychological tests.

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2. Case report

Patient MA is a right-handed 37-year-old male with 18 years of education. He is employed as a social worker. MA was participating as a normal volunteer in a language study when his lesion was incidentally discovered. His interpersonal behavior is appropriate, although he reports a 'short temper'. Gestation, labor and delivery of MA were uncomplicated. However, at 6 weeks of age he suffered from an illness characterized by high fever and was hospitalized for 12 days during which time a diagnosis of encephalitis was made. The patient's neurological condition improved rapidly following admission. He received one half pint of blood for treatment of anemia during his stay; his hospital course was otherwise uncomplicated.

Post-natal development had been normal prior to this hospitalization, and developmental milestones (head turning, visual tracking, holding head, crawling, standing and walking) were reached entirely within normal limits following discharge. MA developed receptive and expressive language skills normally, learning English and ASL in early childhood, around the age of two, because both parents were profoundly hearing impaired. MA's family history was otherwise non-contributory. MA used only ASL at home and spoke English in the community.

T1 weighted spin echo magnetic resonance images (Fig. 1) were obtained during a routine screening procedure. These revealed an encephalomalacia mainly involving the left frontal lobe. Images confirmed a widespread destruction of the medial and dorsolateral prefrontal, orbital and opercular cortices extending from the frontal pole to the precentral gyrus, which was itself spared. Evidence of some involvement of the anterior cingulate cortex was also documented. There was a concomitant enlargement of the left frontal sinus as well as the adjoining diploic space. The adjacent lateral ventricle also illustrated compensatory dilatation.

Neurological examination revealed no evidence of peripheral hemiatrophy. Cranial nerves were intact. Muscle strength, tone, and bulk were within normal limits bilaterally. All sensory modalities were intact. Deep tendon reflexes were normal and symmetrical throughout. Toes were downgoing bilaterally. Cerebellar signs were absent; gait was within normal limits. MA reported performing all skilled manual functions with the right hand. Neurological review of systems was non-contributory.

3. Methods

3.1. Subjects

MA and 12 right handed control subjects fluent in ASL (native signers, six females, six males; mean age 41 ± 10, range 28–56 years) underwent PET evaluation of both English and ASL narrative production. All control subjects received a physical examination and medical history, laboratory evaluation, brain MRI, and were determined to be free of neuropsychiatric or medical illnesses.

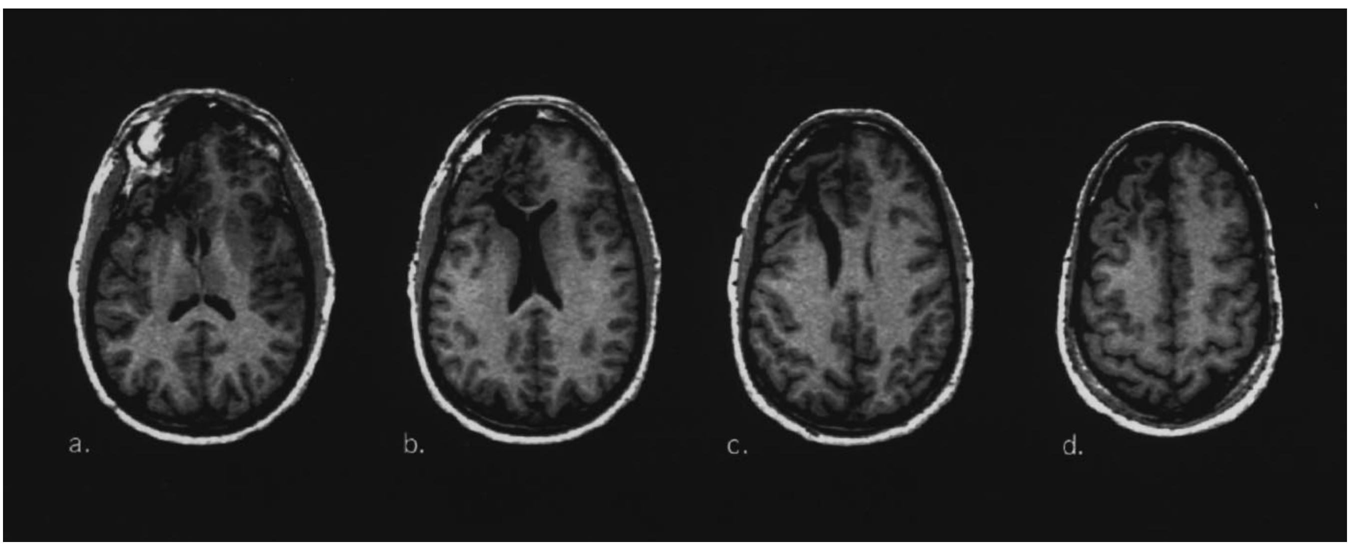

Fig. 1. MRI scan illustrating left prefrontal encephalomalacia in patient MA. The T1-weighted spin echo image is displayed at planes 8 mm (a), 14 mm (b), 24 mm (c) and 40 mm (d) above the bicommisural (AC–PC) line. The images demonstrate widespread atrophy of medial and dorsolateral prefrontal, orbital and opercular cortices, with minor involvement of the anterior cingulate cortex; the precentral gyrus appears to have been spared. The left frontal sinus and adjoining diploic space are enlarged and the lateral ventricle adjacent to the lesion shows compensatory dilatation.

3.2. Behavioral tasks

The PET tasks were designed to highlight brain regions activated during the spontaneous generation of English or ASL, by comparing narrative and motor control tasks. In the English narrative task, subjects were instructed to recount an event or a series of events from memory, using normal speech rate, rhythm and intonation. Semantic content was typically rich in visual episodic detail. Subjects were not required to complete the narrative within a fixed period of time. The ASL task was cognitively equivalent: without temporal constraints, subjects were instructed to produce a similar narrative in ASL, using standard rate, rhythm and extent of signing space.

The motor control tasks were designed to utilize all of the muscle groups activated during the production of narrative — laryngeal and oral articulatory movements for English, limb and facial movements for ASL — but to produce output devoid of linguistic content. The laryngeal/oral articulatory task has been described elsewhere [4]; subjects were instructed to hum while varying pitch and opening and closing the vocal folds at a rate that approximated that of spoken English. At the same time subjects moved the lips, tongue and mandible at a rate and range of movement, which were qualitatively similar to those produced during speech. For the limb/facial motor task, subjects produced bilateral movements of the fingers, wrists, elbows, shoulders and face; rate and range of movements were qualitatively similar to those produced during ASL. Subjects were instructed not to make any movements not commonly seen during speech or signing, such as protrusion of the tongue, hyperextension of limbs. All subjects underwent practice of these tasks prior to the PET procedure.

3.3. PET methods

PET scans were performed on a Scanditronix PC2048-15B tomograph (Uppsala, Sweden) with an axial and in plane resolution of 6.5 mm. Fifteen planes, offset by 6.5 mm (center to center), were acquired simultaneously. Subjects' eyes were patched and head motion was restricted with a thermoplastic mask. For each scan, 30 mCi of $H_2\,^{15}O$ was injected I.V. in a bolus preparation over 10 s. Speech, signing, and motor control tasks were initiated 30 s prior to injection of the radiotracer, and were continued through the 60 s scanning period.

PET scans were registered and analyzed using statistical parametric mapping (SPM) software (MRC Cyclotron Unit, Hammersmith Hospital, London, UK). The original 15 PET slices were interpolated, registered, and then stereotaxically normalized producing 26 slices parallel to the anterior–posterior comissural line in a common stereotactic space [9] and cross referenced with the Talairach standard anatomical atlas [36].

Although spatial normalization may be compromised in patients with a gross structural lesions, stereotaxic normalization of MA's PET images occurred without notable deviation from controls. Registration and normalization parameters were similar in MA and controls and satisfactory normalization of the right hemisphere — contralateral to the lesion — was verified by visual inspection. Images were then smoothed with a Gaussian filter (20 × 20 × 12 mm in x-, y- and z-axes) to accommodate intersubject differences in anatomy. Global differences in tissue activity were controlled by proportional normalization.

SPM was used to identify increases in normalized regional cerebral blood flow (rCBF) for each language

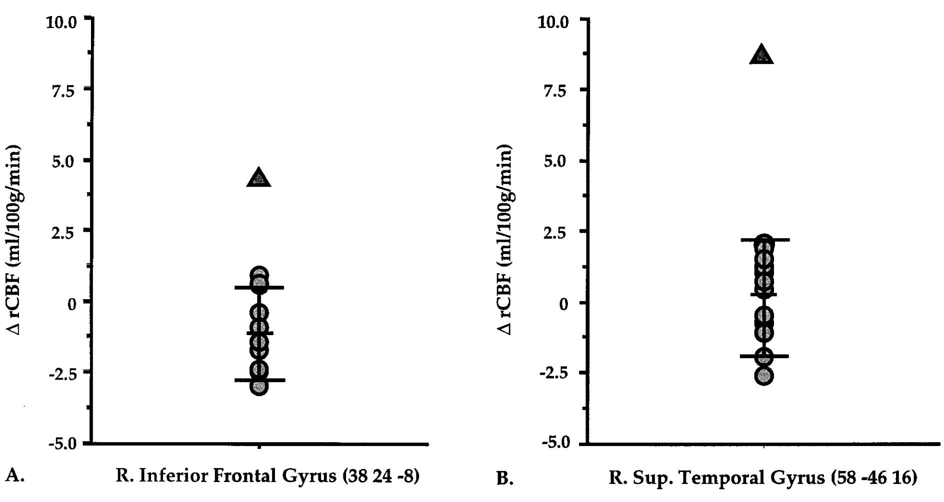

Fig. 2. Changes in rCBF values in control subjects (circles) and patient MA (triangle) when language production tasks are compared with their respective motor control baselines. rCBF values were extracted from individual stereotaxically normalized PET images at the coordinates indicated, for purposes of illustration. (a) depicts changes in the right frontal operculum during the production of English; (b) depicts changes in the right posterior superior temporal gyrus during the production of ASL. See also Table 1, Fig. 3.

Table 1
Results of SPM contrasts evaluating the formulation and generation of narrative in English and ASL[a]

Regions of interest	Broadman No.	Actiation maxima in controls				Activation in patient MA > controls			
		Z-score	*x*	*y*	*z*	*Z*-score	*x*	*y*	*z*
English									
Inferior frontal operculum	47	3.12	−44	32	−8	2.59	38	24	−8
ASL									
Anterior temperal gyrus	21	3.52	−48	−54	16	4.49	58	−46	16

[a] Regions in which rCBF responses were significantly greater than baseline values in control subjects (left), and in which such responses were higher in MA than controls (right), are tabulated along with Z-scores (representing standardized differences between MA and mean for control subjects, rather than indices of statistical significance) and associated Talaraich coordinates.

task vs. its respective motor baseline (English — laryngeal/oral motor task; ASL-limb motor task) in control subjects and MA. Differences between MA and controls were described using the Multistudy: Different Conditions design type in SPM. This statistical option has been used to characterize differences between a single subject and a cohort of controls by providing a voxel-wise index of where an individuals values fall with respect to the mean and S.D. of the control group. While these measures are presented as Z-scores, they should not be taken as indices of statistical significance. In addition, differences in rCBF (language — motor task for selected voxels) were extracted from each subject's PET images in order to illustrate the individual values graphically.

Subjects' speech output was recorded along with a computer generated signal, identifying the start of the $H_2\,^{15}O$ scan. The speech samples (from 20 s before to 40 s following the start of the scan) were transcribed and speech rate, mean number of syllables/word and additional measures of syntactic complexity (mean T-unit (main clause) length, predicates/T-unit, clauses/T-unit [5,17]) were calculated. A videotape of MA's spontaneous narrative in ASL was acquired independently and analyzed by a psycholinguist experienced in evaluation of ASL production, who was unaware of the patient's condition.

3.4. Neuropsychological tests

The battery of neuropsychological tests was administered in a quiet room without distraction. The tests selected reflect measures of general intelligence and cognition, language, frontal lobe functioning, and visuospatial ability. Tests of intelligence and general cognitive function included The Wechsler Adult Intelligence Scale-Revised (WAIS-R) [41] and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [28], respectively. Language ability measures included the Boston Naming Test [18], the California Verbal Learning Test (CVLT) [6], object and figure naming, and four measures of fluency: The Controlled Oral Word Association Test (COWA), and supermarket, animals, and countries fluency. Tests of frontal lobe function include the Wisconsin Card Sorting Test (WCST) [13] and the Towers of Hanoi test. Visuospatial functioning was measured with the Rey Complex Figure Test [32].

4. Results

4.1. PET scanning

Brain activation patterns associated with the production of narrative in English and ASL were evaluated in MA and control subjects. Each narrative task was contrasted with its respective motor control condition, in order to highlight regions involved in linguistic processing, independent of motor execution. The activation patterns in MA and control subjects were then compared.

MA exhibited elevated activation, compared to controls, within the right hemisphere during spontaneous

Table 2
Wechsler adult intelligence scale-revised

	IQ	*Percentile*
Full scale score	106	66
Verbal score	113	81
Performance	98	45
	Age-scaled score	*Percentile*
Verbal subtests		
Information	14	91
Digital span	13	84
Vocabulary	12	75
Arithmetic	11	63
Comprehension	12	75
Similarites	11	63
Perfromance subtests		
Picture completion	11	63
Picture arrangement	10	50
Block design	12	75
Object assembly	10	50
Digit symbol	10	50

generation of narrative in *both* English and ASL (Fig. 2a, Fig. 3a and Table 1). During English narrative production, the right inferior frontal operculum, Brodman area 47, was more active in MA than in controls. Control subjects, on the other hand, activated homologous regions in the left hemisphere during English narrative production (Table 1). No significant activations of any regions in the right opercular cortex were detected in control subjects.

Similarly, the SPM analysis indicated that during formulation and expression of narrative using ASL, the right posterior superior temporal gyrus, Brodman area 22, was more active in MA than in controls (Fig. 2b, Fig. 3b and Table 1). Control subjects, on the other hand, activated the homologous region in the left hemisphere (Table 1). No significant activation of the right posterior superior temporal regions were detected in control subjects.

The patient was cooperative and did not appear agitated or anxious during the PET procedure. Measures of spoken language production in MA did not differ notably from control values (mean $\pm$ S.D.): while the patient spoke at a slower rate, the value was still within 2 S.D. of the mean for control subjects (patient = 2.75 syllables/s; controls = 4.00 ± 0.66). On measures of syntactic/semantic complexity, the patient scored higher than (but still within 1 S.D. of) the mean (mean T-unit (main clause) length, patient = 14.33 words; controls = 13.57 ± 2.21; predicates/T-unit, patient = 6.11; controls = 4.93 ± 0.86; clauses/T-unit, patient = 2.00, controls = 1.53 ± 0.58; syllables/word patient = 1.45, controls = 1.38 ± 0.15).

Blinded rating of MA's ASL narrative revealed him to be a skilled and fluent signer who used a wide and appropriate range of grammatical and expressive devices reflecting a native command of the language. This was evident in his fluent use of ASL classifier constructions, typically difficult for non-native signers. MA also used a wide range of lexical items, and a variety of sentence structures. His overall style was judged to be relaxed and natural; fingerspelling was smooth and natural, and used in appropriate contexts.

4.2. Neuropsychological tests

Neuropsychological examination found patient MA to be anxious and mildly agitated, with occasional outbursts of anger. He abruptly withdrew from the initial testing session, yet later completed the entire test battery. The results (Tables 2 and 3) are deemed valid and reliable. His neuropsychological test scores indicated that general intelligence/cognition and language function were within normal limits, while his performance on tests of visuospatial ability was impaired.

4.2.1. General intelligence/cognition

General intelligence assessed by the WAIS-R was within normal limits but MA's scores revealed a differ-

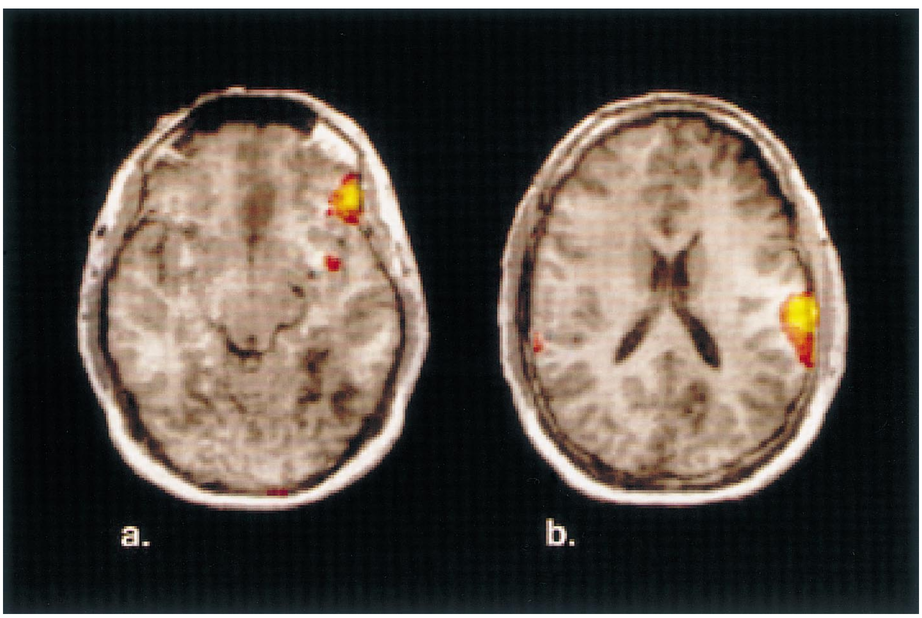

Fig. 3. Brain maps illustrating rCBF activations that were greater in patient MA than in control subjects during the formulation and expression of narrative in: English (a) at the level of the inferior frontal operculum, 8 mm below the bicommissural line. And ASL (b) at the level of the superior temporal gyrus, 16 mm above the bicommissural line. Using SPM, language tasks were contrasted with their respective motor baseline in controls and then compared with activations in patient MA. Z-scores derived from this analysis do not denote statistical validity, but simply indicate MA's values with respect to control subjects' mean and S.D. In (a) red represents voxels in which $Z > 1.5$; yellow represents voxels in which $Z > 2$; in (b) red represents voxels in which $Z > 3$, yellow voxels in which $Z > 4$. These are represented on a standardized MRI scan from a control subject that has been transformed into the same stereotaxic (Talairach) space as the SPM$\{Z\}$ data.

Table 3
Neuropsychological test scores[a]

	Raw score	Percentile
Language		
CVLT		
Trails 1–5 total	60	75
Short delay	14	87
Long delay	12	75
Recognition	16	100
Boston naming test	58/60	–
Object and figure naming	40/42	–
Fluency measures		
COWA (FAS)	44	75
Supermarket	38	90s
Animals	37	90s
Countries	26	90s
Frontal lobe function		
WCST		
total errors	16	32
Perseverative responses	16	9
Tower of Hanoi		
Correct	6 of 9	–
Mean score	1071.3s	–
Visuospatial fuction		
Rey Complex Figure		
Copy	32	50
Immediate recall	15	10
Delayed recall	17	30
Overall cognition		
RBANS total score	92	30

[a] FAS, supermarket, animals, countries, allow 90 s for patient response.

ence of 1 S.D. between verbal and performance IQ (verbal = 113, 81st percentile, and performance = 98, 45th percentile) indicating a significant dissociation between verbal ability and visuospatial skill level (Table 2). His RBANS score was below the normal mean but within normal limits.

4.2.2. Language

MA's results on fluency tests were in the high normal range. His Boston Naming Test and Object and Figure Naming scores also fell in the high normal range. CVLT scores for immediate recall, short delay, long delay, and recognition were in the above average range (Table 3).

Frontal lobe function: MA attained six categories on the WCST, which is within normal limits. Despite this score, he also demonstrated moderate perseveration as indicated by his total errors and a perseverative response score. MA's Tower of Hanoi performance was within normal limits.

4.2.3. Visuospatial function

MA was administered the Rey Complex Figure Test and scored at the 50th percentile with his copy, the 10th percentile after immediate recall, and 30th percentile for delayed reproduction. Other visuospatial tests (clock drawing, ADAS-Cog drawings) scores were within normal limits.

5. Discussion

We report here, using H_2 ^{15}O PET, physiological evidence suggesting adaptation in homologous regions within the right hemisphere following left hemisphere damage in early childhood in a patient fluent in both spoken and signed languages (English and ASL). Furthermore, when directly compared to normal controls, the adaptation appears to be divided among different regions of the right hemisphere in order to support the normal development of both individual languages and their distinctive modes of expression.

Language recovery following injury to brain regions that subserve linguistic functions has been amply documented in adults [10] and in children in whom more dramatic results can be observed [7,15,25]. The superior recovery in young children may be attributed to the extraordinary plasticity of CNS tissue in early life, which subserves the normal unfolding of developmental processes that occur during this time.

This recovery may manifest itself by means of activation of the pluripotential tissue in both the ipsilateral and contralateral hemispheres, with lesion size, location, and age of onset determining site and extent of recovery [12,23,42]. The profound left cortical atrophy seen in MA makes it unlikely that language development would be accommodated in adjacent areas of the ipsilateral frontal cortex. Indeed, reorganization or unmasking of relatively inactive pathways or neural networks in the contralateral hemisphere have been suggested as the main mechanism of language recovery [17,38] following left hemisphere lesions and is one explanation for the results observed in MA.

The right hemisphere has been regarded as more plastic than the left hemisphere due to slower functional maturity and more diffuse organization, particularly in early childhood [21,23,33,34,43]. Preschool children with both left and right hemisphere lesions perform at near normal levels on simple visuospatial tasks, although children with right hemisphere lesions demonstrate greater developmental delay [34]. An early left hemisphere lesion, therefore, may still allow for the normal development of abstract language in the non-dominant right hemisphere, permitting fundamental language constructs to develop in a homologous brain region. Lenneberg (1967) defined the critical period of optimal contralateral recovery as before the age of three [21].

Contralateral regions in which activity is higher in MA than controls during the formulation and expression of English narrative are precisely homologous to those activated in the control subjects. Increased activation of the right inferior operculum and superior dorsolateral prefrontal cortex in MA during language expression supports the hypothesis that neuronal pathways and architecture in the right hemisphere may have been unmasked to subserve language function.

While compensation for English occurred in areas homologous to those damaged in MA, the apparent compensatory activation of right hemisphere areas for ASL occurred even though the homologous left hemisphere regions were spared. That is, while his left anterior middle temporal gyrus remained intact as evidenced by his MRI, activity in the right posterior superior temporal gyrus was nevertheless significantly elevated in MA compared to controls during production of ASL. Once again, MA's right hemisphere activation occurred in areas that were precise homologues of regions activated by control subjects in the production of ASL. This surprising finding suggests the possibility that unmasking of 'additional' contralateral pathways may have occurred even though their homologous left hemisphere regions remain undamaged. The inference is that some aspects of language (in MA's case, ASL) may somehow be prevented from developing in an intact cortical region in order to be ipsilaterally linked with other fundamental linguistic processes in the right hemisphere.

MA's data also suggests that his development of language function in the right hemisphere may have occurred at some expense to his usual right hemisphere functions, particularly visuospatial ability. This is evidenced by MA's relatively poor Rey Complex Figure results and the modest dissociation between his performance and verbal IQ scores. However, his Block Design score remains at the 75 percentile. Strauss et al. (1990) stated that interhemispheric reorganization in the case of left hemisphere damage may interfere with the development of non-verbal abilities. Our case is consistent with this crowding hypothesis [20,22,37], which states that the contralateral non-language hemisphere will assume processes of the lesioned hemisphere at the expense of normal cognitive function associated with the undamaged region. This explanation is also consistent with data reported by Levin et al. [22] who observed an analogous transfer of function to the contralateral hemisphere following a large right posterior lesion that was incurred early in childhood. In their case, visuospatial function appeared surprisingly intact when the patient was evaluated as a teenager whereas there was a cost to the normal cognitive processes stored in left temporal–parietal cortex — especially calculation.

MA also demonstrated modest impairment of prefrontal function as evidenced by his increase in perseverative errors on the WCST. Although frontal lobe function tasks such as the WCST may require the participation of both frontal lobes [3,8,19,31], because of its earlier development and importance, language function would still be expected to take precedence in occupying a cortical region. However, in the case of MA, it is difficult to determine whether this modest dysfunction is due to the lack of left hemisphere input or if his right frontal input to performance on this task was limited due to having to share cortical space and resources with language functions.

In summary, neuropsychological and PET data suggest that MA's apparently normal acquisition of two distinct languages occurred through development of linguistic capacity within the right hemisphere, mediated by neuronal plasticity and possibly by the mechanism of unmasking. MA's disproportionately limited visuospatial ability suggests that right frontal functional crowding may have occurred. Furthermore, the data presented here suggest that some aspects of cognition may be inhibited from functioning in an intact cortical region in order to be preferentially linked with other, related cognitive processes that were shifted to the contralateral hemisphere due to early childhood brain damage.

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