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Developmental plasticity after right hemispherectomy in an epileptic adolescent with early brain injury

Received: 26 November 2004
Published online: 26 April 2005
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Abstract *Objectives:* The authors present the case of an adolescent affected with refractory epilepsy due to a neonatal ischemic infarction of the right medial cerebral artery. Hemiplegic since the first months of life, she began presenting motor partial seizures associated with drop attacks at 4.5 years; these were initially well controlled by antiepileptic drugs, but at 10 years seizures appeared again and became refractory. Thus, at 14 years and 10 months, she was submitted to a right hemispherectomy that made her rapidly seizure free. In the post-surgical follow-up lasting 5 years, neuropsychological serial assessments showed an impressive progressive improvement of cognitive skills, namely, visuospatial abilities. This case seems to challenge the widely spread feeling that functional catch-up in brain-injured children could only occur early in life. In effect, the astonishing recovery especially of visuospatial skills in our case occurred in adolescence after a late surgical intervention of right hemispherectomy. *Methods:* Different

neuropsychological aspects are discussed. The reorganisation process recovered the spatial and linguistic abilities as well as the verbal and visuospatial memory; however, there was a persistent impairment of complex spatial and perceptual skills as well as recall abilities. Despite the deficit of complex visual stimuli processing, the patient showed a good performance in the recognition of unknown faces. *Conclusions:* Probably, the absence of seizures in the first 4 years of life could have allowed a generally adequate compensatory reorganisation, successively masked by the persistent and diffuse epileptic disorder. The seizure control produced by surgery eventually made evident the effectiveness of the brain reorganisation.

Keywords Brain reorganisation · Epilepsy · Hemispherectomy · Early brain injury

Introduction

There is good evidence that hemispherectomy in hemiplegic children with refractory epilepsy is an effective tool not only in the treatment of epileptic disorder but also in aiding functional brain reorganisation [3, 40, 43]. Independent of the laterality of lesions, verbal skills seem to show greater improvement more so than visuospatial abilities

[12, 27, 31, 38, 39]. Brain plasticity, moreover, is greater in early childhood [18, 19, 29].

Although in epileptic children left hemispherectomy, with all its associated neuropsychological consequences, has been largely investigated, [22, 41, 42] detailed neuropsychological effects of right hemispherectomy have been studied to a lesser extent [20, 32]. Unlike what happens in left hemispherectomy, language disorders after right hemi-

spherectomy appear less severe and relatively independent of the age of surgical treatment. Only when right hemispherectomy occurs early but after the speech onset, there may be some initial language disorder such as disorganized speech or minor restriction of comprehension, presumably due to an interhemispheric spread of epileptic activity. Indeed, the effect of right hemispherectomy at any age may be generally considered related to the usual lowering of cognitive competence [40]. Relatively little attention has been paid to non-linguistic abilities. Kohn and Dennis [20] reported that visual processing skills may develop in patients who had undergone right hemispherectomy up to a maximum of about 10-year-old level. In a girl who had early right hemispherectomy, Day and Ulatowska [13] reported relevant difficulties with tasks requiring visual perception or visual-motor coordination.

Our study concerns a girl who was surgically treated at 14 years and 10 months and followed up for 5 years. Her neuropsychological evolution shows an extraordinary improvement of performance IQ, from a moderate mental retardation up to the lower limit of normal IQ. The analysis of the evolution of different neuropsychological aspects, including complex visuospatial and language skills before surgery and for a long period after, can provide new information about the ability of the contralateral hemisphere to compensate for right hemispherectomy of epileptic children.

Case report

G.T., age 19 years and 6 months, had 13 years of formal education. At the time of our last observation, she had finished school and was attending a professional training course. Family history was normal. She was one of twins born after full-term pregnancy without major complications. At 5 months of age, a reduction of left motor abilities was noted and 4 months later, hemiplegic cerebral palsy was diagnosed. A CT scan showed the malacic sequelae of ischemic infarction of the right medial cerebral artery. At 4 years and 6 months, G.T. began presenting partial complex seizures several times a day. Ethosuccimide administration produced full control of seizures, but 18 months later new paroxysmal manifestations appeared. These were characterised by staring associated with generalised tremors and loss of equilibrium. The change of ethosuccimide with carbamazepine made G.T. seizure free for about 6 years. At 12 years, carbamazepine was rapidly decreased due to an increasing marked leukopenia. Seizures reappeared and occurred many times a day. Seizures were severe, especially in the morning on awakening, were preceded by an aura (malaise, perspiration and pallor), and were characterised by staring associated with limb hypertonia, often followed by falls. Interictal EEG abnormalities were characterised by slow and epileptiform activities on the right hemisphere. Ictal EEG showed a 1-min-long discharge of polyspikes in the anterior fronto-parietal regions, with a rapid ipsilateral

diffusion progressively followed by diffuse spike and poly-spike waves. Soon after, a decremental activity was usually observed. Epileptic manifestations increased during the menstrual period and under stress. For 2 years, all therapeutic trials (phenobarbital, valproate, phenytoine, benzodiazepine, lamotrigine) aimed at controlling the seizures failed. Neurosurgery was then considered and the patient was evaluated to be a good candidate. At this point, G.T. underwent anatomic right hemispherectomy.

In the 2 weeks after the surgical treatment, the seizures acquired a new pattern characterized by short hypertonic fits of the left arm and by axial hypertonia with opisthotonus and mydriasis, once followed by a generalised tonic-clonic seizure. Vigabatrin was added to the previous treatment regimen (phenytoine, phenobarbital, and benzodiazepine) and this produced a definitive seizure control.

After surgery, EEG recordings were performed every 6 months and showed constant depression of activity on the right regions. The immediately postsurgical left background activity was characterised by irregular posterior alpha with rapid superimposed rhythms mixed with theta activity. During the follow-up the organisation of the background activity on the left side progressively improved up to normalisation.

Two years ago, a progressive weaning from benzodiazepine and phenytoine was undertaken. G.T.'s current therapy consists only of phenobarbital.

Serial magnetic resonance imaging (MRI) showed a progressive evident expansion of the healthy hemisphere (Fig. 1).

Methods

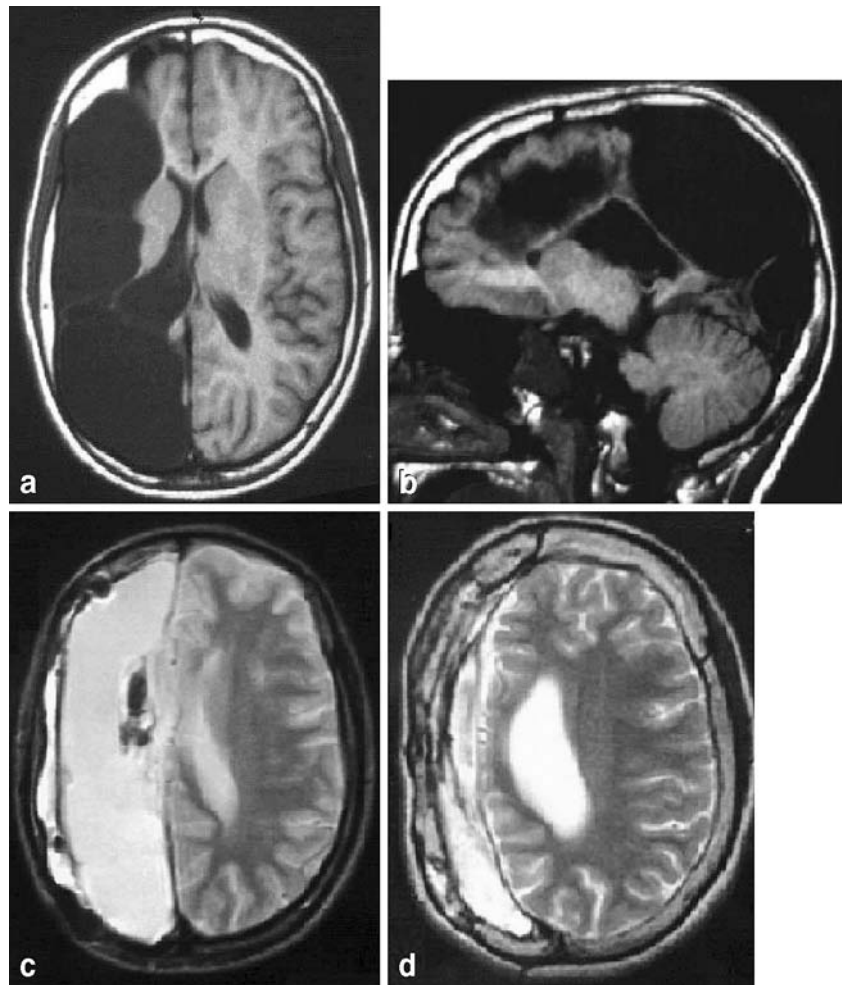
The patient underwent a full clinical examination, including pre-surgical and serial post-surgical MRI. A general neuropsychological assessment was performed before surgery, and serially during the 5-year follow-up at an interval of about 1 year. At the end of the follow-up, the neuropsychological assessment concerned a more detailed analysis of specific skills.

General neuropsychological assessment

General neuropsychological assessment included Wechsler Intelligence Scales (WISC-R or WAIS) [46, 47] and specific skills tests (memory, visuospatial attention, visuo-perceptual and "frontal lobe" abilities), carried out with the following battery of neuropsychological tests:

- *Memory tasks* (digit and spatial span): immediate visuospatial recall [34], immediate and delayed recall of words [44, 33]; the normative data for the latter test were calculated using a methodology reported by Carlesimo et al. [10].

Fig. 1 **a, b** Presurgical neuroimaging: axial and sagittal T₁ MRI showing an extensive multicystic porencephaly that replaces the most part of the right hemisphere; remaining frontal cortex irrigated by the anterior cerebral artery is present. **c** Axial T₂ image soon after right hemispherectomy. **d** Expansion of the left hemisphere 3 years after right hemispherectomy



- *Visuoperceptual tasks*: the Beery Developmental Visual Motor Integration Test [4]
- *Visuospatial attention tasks*: the Bells Test Revised [8], Line Cancellation Test [1] and Zazzo’s test [48]
- *“Frontal” ability tasks*: “word fluency” [9, 37]

Specific task assessments (at the end of the follow-up)

Given G.T.’s considerable post-surgical recovery, in particular her visuospatial abilities profile, a more analytic assessment of spatial, linguistic and memory functions was performed during the last clinical observation.

Analysis of visuospatial and visuoperceptual skills

These skills were explored by the Visual Object and Space Perception (VOSP) battery [45], consisting of four items testing object perception (incomplete letters, silhouettes, object decision, progressive silhouettes) and four items of

spatial perception (dot counting, position discrimination, number location, cube analysis). Each test, standardised and validated on normal population, tries to focus on a single component of visual perception, thus minimising the participation of other cognitive abilities.

The exploration of complex visuospatial abilities was performed using the Benton’s Line Orientation Judgement [6], the Revised Minnesota Paper Form Board Test [21], and Spatial Relations subtest of the Differential Aptitude Tests (DAT) [5].

Benton’s line orientation judgement The subject has to choose two target lines among a set of particularly arranged lines; it explores an aspect of spatial reasoning.

Revised Minnesota paper form board test (RMPFBT) The task requires the subject to mentally manipulate visuospatial images and (within a time limit of 20 min) to choose five bidimensional figures among which lies the one that corresponds with the joining of two or more parts shown in the target.

Spatial relations of the differential aptitude tests (DAT) This is a subtest included in a battery that explores individual aptitudes. The patient has to imagine (within a time limit of 30 min) mental rotations and to reassemble bidimensional pictures in order to choose which one corresponds to one of five alternative three-dimensional shapes.

Finally, Benton's Unknown Faces Recognition [7], Ghent's Overlapping Figure Test [14] and Gollin's Degraded Figures Test [15] were used to explore higher level visuoperceptual abilities.

The first of these requires the subject to recognise unknown faces among a set of faces photographed in a frontal or lateral position; the second task consists in overlapping objects, animals or abstract designs that the patient has to identify when visually cued; in the last test the subject has to identify fragmented drawings presented according to an increasing completion level.

Linguistic tasks

Extensive evaluation of linguistic abilities was obtained using a test battery for aphasia [Batteria per l'Analisi dei Deficit Afasici (BADA)] [26] that includes tasks aimed at exploring phonological, lexical/semantic and morphosyntactic levels of the linguistic abilities.

- *Phonological abilities* were evaluated by auditory "same/different" discrimination and visual-verbal matching of meaningless consonant-vowel pairs (phonemic discrimination and visual-verbal matching) and transcoding tasks (repetition, reading, writing and delayed copy of legal non-words).
- *Lexical-semantic abilities* were explored by oral and written discrimination of word and legal non-word tasks (auditory and visual lexical decision), transcoding tasks (repetition, reading, writing and delayed copy of words), oral and written comprehension of single word tasks (spoken and written comprehension of nouns and verbs), oral and written naming of objects, actions and pictures tasks (oral and written objects and actions naming).
- *Morphosyntactic abilities* were examined by tasks judging whether oral and written sentences were syntactically correct (auditory and visual grammatical judgement) and by transcoding (repetition and reading of sentences) and syntactic comprehension tasks, in which the patient has to identify the picture corresponding to the meaning of oral or written stimuli sentences (auditory and visual grammatical comprehension). The foil and the target share semantic or morphological features and may appear in a reversible, active or passive form.

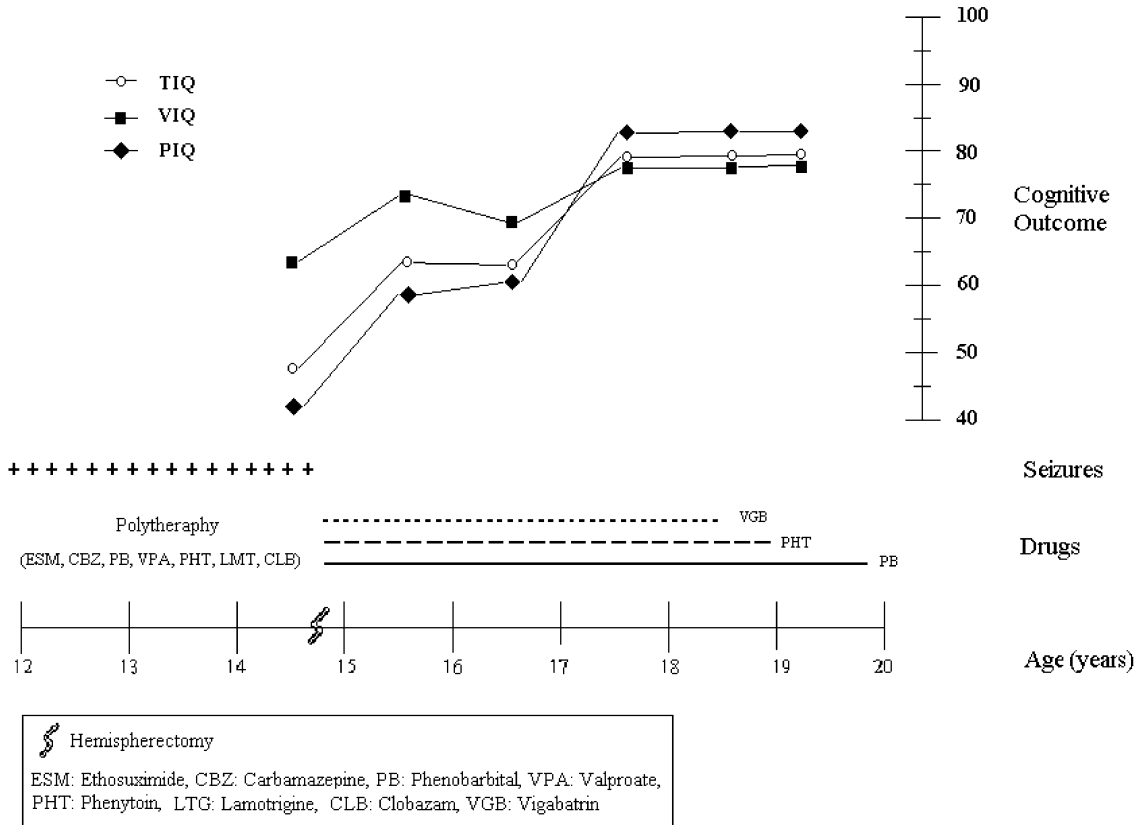


Fig. 2 Evolution of cognitive skills soon before and after hemispherectomy

Memory tasks

Memory abilities were carefully examined using the Test of Memory and Learning (TOMAL) [35]. The battery explores short-term verbal and visuospatial memory, and it is possible to score both every single subtest as well as overall general indexes of verbal and non-verbal memory.

- *Stories Recall*. This task examines episodic, semantic and temporal sequence of memory events through the immediate recall of brief oral stories.
- *Faces Recall*. The subject has to remember unknown faces of different ages, sex and race among a set of other faces.
- *Word Selective Recall*. This explores the learning and the free recall of a word list.
- *Visual Selective Recall*. In this subtest, the patient has to learn and recognise the spatial location of dots placed in a successive array.
- *Object Recall*. It consists in recalling and naming pictures of objects and animals.
- *Abstract Perceptive Recall*. This task evaluates the recognition of abstract drawings amongst a set of other drawings.

- *Forward Digits Sequence*. This task requires the subject to retain a digit sequence that increases progressively in length.
- *Visual Sequential Recall*. This task explores the sequential order recall of abstract designs.
- *Word-Coupling Recall*. This task examines the learning and the associative recall of a coupled-words list.
- *Spatial Placing Recall*. This subtest requires the patient to retain the visuospatial placing of dots randomly placed in a grid.

Furthermore, it is possible to estimate a delayed memory index by administering Stories Recall, Faces Recall, Word Selective Recall and Visual Selective Recall tests 30 min after their initial administration.

Therefore, in order to analyse learning and short- and long-term (4 h later) memory of visual stimuli whilst minimising the involvement of verbal component, a task proposed by M. Jones-Gotman et al. [17] was administered. It includes 13 abstract designs presented in succession, and in the learning phase, the patient has to copy and recall every target four times. Four hours later, the patient must reproduce the stimuli previously learned.

Table 1 Pre and post-operative neuropsychological profiles

	Age (years, months)					
	Preoperative	Postoperative				
	14.10	15.8	16.8	17.7	18.7	19.6
Memory						
Word recall						
Immediate	37.3 (27.3)	49.3 (27.3)	55.9 (28.5)	42.9 (28.5)	51.9 (28.5)	46.1 (28.5)
Delayed	8.1 (5.1)	8.1 (5.1)	9.2 (4.6)	7.2 (4.6)	12.2 (4.6)	10.5 (4.6)
Rey–Osterreith Complex Figure						
Immediate	15.0^a (17.1)	15.0^a (17.1)	15.0^a (17.1)	15.0^a (17.1)	18.0^a (17.1)	15.0^a (17.1)
Span						
Digit	4; 3	4; 4	4; 3	4; 4	4; 3	5; 3
Spatial		4; 4	3; 5	4; 4	4; 4	3; 4
Visuospatial Attention						
Bells Test Revised						
Speed score	21.0^a (49.2)	51.0 ^a (49.2)				
Accuracy score	87.0^a (124.7)	114.0 ^a (124.7)				
Omissions	30	14				
Line Cancellation Test						
Time/Omission			40 s/0	35 s/0	45 s/0	35 s/3
Zazzo's test						
Time/Omission			70s/6	60 s/2	120s/2	90s/2
Construction Apraxia						
Rey–Osterreith Complex Figure						
Copy		27.0^a (29.9)	30.5 ^a (30.2)	30.5 ^a (30.2)	29.0^a (30.2)	30.0 ^a (30.2)
VMI	< 1.0 (7.0)	2.0 (7.0)	2.0 (7.0)	1.0 (7.0)	2.0 (7.0)	
Word fluency						
Letters						
B	5^a (6.9)	6^a (6.9)	6^a (6.9)			
F/A/S				23.0^a (17.3)	26.0^a (17.3)	22.0^a (17.3)

Word recall performance was evaluated as standard scores. Abnormal performance is in bold. Cut-off scores are in parentheses

^aRaw scores

Results

General neuropsychological assessment

Pre-surgical observation

G.T.'s pre-surgical profile (14 years and 10 months) showed a moderate delay in IQ (total, 48) with a non-homogeneous profile of intellectual abilities with a significantly greater impairment of visuospatial skills compared with verbal abilities (performance IQ <45 vs verbal IQ 64) (Fig. 2).

Neuropsychological assessment showed normal results for the screening tasks exploring immediate and delayed verbal memory, whereas G.T.'s scores were pathological on visuo-perceptual, visuospatial and word fluency tasks; moreover, Forward Digit Span was slightly impaired (Table 1).

Post-surgical follow-up

After surgery, the patient was assessed yearly up to 19 years and 6 months.

On first observation (age, 15 years and 8 months), the patient showed a remarkable improvement of overall development; in particular, total and performance IQ increased by 16 and 13 points, respectively, with verbal skills still being better than visuospatial abilities. One year later (age, 16 years and 8 months), G.T.'s visuospatial scores improved further, and her cognitive profile became homogeneous. In the following observation (age, 17 years and 7 months), aside from seizure control, total and performance scores again improved (by 14 and 20 points, respectively), and verbal/performance scores were equal. During this progressive and spectacular cognitive improvement, AED assumption had not been modified. This profile was confirmed in the latest controls, at 18 years and 9 months and 19 years and 6 months of age, respectively.

Postoperative neuropsychological specific tasks improved too. At 15 years and 8 months of age, G.T. improved her immediate verbal recall abilities and her speed score in the visual neglect test (the Bells Test Revised). On the other hand, she showed reduced performances in a spatial span test, and pathological and unchanged scores in tasks exploring visuomotor integration and word fluency abilities. Moreover, the Rey–Osterreith Complex Figure [34] was administered for the first time, and the scores concerning both copy and immediate recall trials were below the average. The following year (age, 16 years and 8 months) G.T.'s neuropsychological profile was unchanged, and at 17 years and 7 months of age she reached a normal performance in the word fluency task. The same results were confirmed in the following assessments, at 18 years and 7 months and 19 years and 6 months of age, respectively (Table 1).

Specific task assessments (at the end of the follow-up)

Visuospatial and visuo-perceptual abilities

In the VOSP tasks, the patient obtained below average-performances in most of the visuo-perceptual subtests (Silhouettes, Object Decision, Progressive Silhouettes); on the contrary, the scores obtained in all visuospatial tasks (Dot Counting, Position Discrimination, Number Location, Cube Analysis) were normal and comparable to controls. However, both kinds of abilities showed an impairment on tests exploring “higher level” visuospatial and visuo-perceptual abilities. In particular, the scores among visuospatial tests were dramatically impaired particularly on tests of spatial rotation (reasoning about drawings of two-dimensional and three-dimensional shapes; RMPFB, DAT) and of line orientation judgement (Benton's Line Orientation). Regarding visuo-perceptual tests, the performances were markedly reduced on stimulus perception tasks reproduced with an irregular outline or overlapped (Gollin's Degraded Figures and Ghent's Overlapping Figures).

Although the patient had a severe impairment in processing complex visual stimuli, she obtained a normal score at the unknown faces recognition task (Table 2).

Linguistic abilities

Phonological abilities G.T. reached normal scores in most tasks exploring phonological non-words and spelling components. Only the reading performance was slightly im-

Table 2 Performances obtained at the age of 19.6 years on VOSP, Benton's Line Orientation and unknown faces recognition, DAT, RMPFB, Gollin's Pictures Test and Ghent's Overlapping Figures (standard scores)

VOSP	
Visuo-perceptual tasks	
Incomplete letters	19 ^a (17)
Silhouettes	10^a (16)
Object decision	13^a (15)
Progressive silhouettes	12^a (14)
Visuospatial tasks	
Dot counting	10 ^a (8)
Position discrimination	20 ^a (18)
Number location	7 ^a (7)
Cube analysis	10 ^a (6)
Benton's line orientation	15^a (23)
DAT	1 (23)
RMPFB	16 (26)
Benton's faces recognition	47 ^a (40)
Gollin's Pictures Test	127^a (146)
Ghent's Overlapping Figures	Abnormal

Abnormal performance is in bold. Cut-off scores are in parentheses
^aRaw scores

Table 3 Errors on the Batteria per l'Analisi dei Deficit Afasici (BADA) at the age of 19.6 years

Phonological abilities	
Phonemic discrimination (60) ^a	0 (2)
Visual-verbal matching (60) ^a	0 (2)
Non word repetition (35) ^a	0 (0)
Non word reading (35) ^a	3 (2)
Non word writing (25) ^a	1 (2)
Non word copying (6) ^a	0 (1)
Lexical-semantic abilities	
Auditory lexical decision (80) ^b	4 (2)
Visual lexical decision (80) ^b	6 (2)
Word repetition (45) ^b	0 (0)
Word reading (92) ^b	2 (2)
Word writing (46) ^b	1 (2)
Word copying (10) ^b	0 (0)
Spoken noun comprehension (40) ^b	2 (2)
Written noun comprehension (40) ^b	0 (1)
Spoken verb comprehension (20) ^b	1 (2)
Written verb comprehension (20) ^b	0 (2)
Object oral naming (30) ^b	6 (2)
Action oral naming (28) ^b	9 (2)
Object written naming (22) ^b	3 (2)
Action written naming (22) ^b	4 (2)
Morphosyntactic abilities	
Auditory grammar judgement (48) ^c	2 (2)
Visual grammar judgement (24) ^c	0 (2)
Sentences repetition (20) ^c	3 (0)
Sentences reading (6) ^c	0 (0)
Auditory grammatical comprehension (60) ^c	1 (2)
Visual grammatical comprehension (45) ^c	7 (2)

Abnormal performance is in bold. Cut-off scores are in parentheses

^aNumber of sublexical units

^bNumber of words

^cNumber of sentences

paired and this was because of some spelling errors that were made in equal measure on the left or right half of the target.

Lexical-semantic abilities G.T. showed a few difficulties in auditory and visual lexical decision tasks; the pattern of errors revealed the same amount of inaccuracies between high- and low-frequency words. In contrast, the scores in transcoding tasks (repetition, reading, written and copying) were within the average. The patient performed visual, semantic and anomic errors in the low-frequency targets of naming tasks (nouns and actions) and the scores were abnormally low.

Morphosyntactic abilities When requested to judge if sentences presented in spoken or written form were syntactically correct or not, G.T. performed correctly; a normal score was obtained in a reading task too. She produced some morphological errors in a repetition subtest and the

score reached was below the average. G.T. performed correctly in a task exploring auditory grammatical comprehension. She showed pathological performance in the same test with stimuli presented in a written form; in particular, she presented severe difficulties with passive and reversible sentences (Table 3).

Memory abilities

The patient reached average overall performances in most subtests of TOMAL exploring verbal short-term memory (Word Selective Recall, Object Recall, Word-Coupling Recall). Instead, abnormal scores were observed in tasks that required the retention of brief stories read aloud by the examiner (Stories Recall) and in the forward digit sequence task (Digit Sequence Forward). Overall, the Verbal Memory Index was normal. Normal results were obtained

Table 4 Performance obtained at the age of 19.6 years on TOMAL and Gotman's test (standard scores)

TOMAL	
Immediate Recall	
Verbal Tasks	
Stories Recall	6 (7)
Selective Words Recall	11 (7)
Objects Recall	10 (7)
Digits Sequence Forward	3 (7)
Word-Coupling Recall	13 (7)
Verbal Memory Index	90 (85)
Nonverbal tasks	
Faces Recall	11 (7)
Visual Selective Recall	8 (7)
Abstract Perceptive Recall	9 (7)
Visual Sequential Recall	7 (7)
Spatial Placing Recall	5 (7)
Nonverbal Memory Index	86 (85)
Immediate Memory Index	88 (85)
Delayed Recall	
Delayed stories recall	6 (7)
Delayed faces recall	12 (7)
Delayed words selective recall	10 (7)
Delayed visual selective recall	10 (7)
Delayed Memory Index	97 (85)
Gotman's test	
Learning phase	
First trial	6 ^a [6]
Second trial	6 ^a [10]
Third trial	7 ^a [10]
Fourth trial	7 ^a [10]
Delayed recall	4 ^a [12]

Abnormal performance is in bold. Cut-off scores are in parentheses.

Control scores are in brackets

^aRaw scores

in most subtests exploring the immediate recognition of visuospatial and visuoperceptual components of visual stimuli (Visual Selective Recall, Visual Sequential Recall, Faces Recall, Abstract Perceptive Recall). Only task evaluating free recall (Spatial Placing Recall) of the spatial placing of dots revealed below average performances, although the Nonverbal Memory Index was normal.

Therefore, the Immediate Memory Index was adequate (Table 4).

Among the tasks exploring delayed recall, G.T. presented a slight impairment in Delayed Stories Recall; the scores reached in the other subtests were normal. In general, the Delayed Memory Index was normal.

G.T. obtained results similar to the reported controls in the first trial of the learning phase included in Gotman's test, but these data were not confirmed in successive trials. Four hours later, the patients' performance further worsened, since her delayed score was inferior to the ones obtained in the learning phase. This data points to a rapid loss of meaningless visual information previously acquired.

Discussion

There is evidence that whilst children with congenitally damaged right hemispheres [28], but without seizures, present only lower performance IQ compared to normal controls, those with concurrent epilepsy show both verbal and performance IQ impairment [39, 28]. This can be explained by the fact that seizures or, alternatively, seizure medication can interfere with the developing brain ability to compensate for unilateral brain injury [42, 27].

Our patient with morphological and functional sequelae of right medial cerebral artery congenital ischemic infarction presented with a partial epilepsy at 4 years of life. After a year of seizures not controlled with ethosuccimide, there was a long seizure-free window (from 6 to 12 years of age); then, she began presenting again seizures rapidly acquiring a refractory character. At that time, WISC-R revealed a total IQ of 48, with performance and verbal IQ scores of 45 and 64, respectively. After surgery, performance IQ progressively improved. This specific improvement initially paralleled verbal IQ and successively progressed to values greater than verbal IQ.

This favourable evolution, analogous to what has been observed in epileptic children who had undergone left hemispherectomy, to the best of our knowledge has never been described in those who had undergone right hemispherectomy.

It has been shown that right hemispherectomy performed in patients with refractory epilepsy due to a congenital (pre- or perinatal) brain injury generally produces an improvement of performance IQ [3] even though some minor deficit related to more sophisticated visuospatial abilities persist [20]. In our patient, this improvement was

particularly relevant, to the extent that the patient was on the borderline of normal performance.

The degree of improvement in performance and general cognitive development seems to depend on various factors, among which the age of brain primary injury and seizure onset are particularly important.

In fact, although the critical age beyond which functional reorganization takes place after a unilateral injury in childhood is not known [18, 19], most researchers report a better outcome when damage occurs early in infancy rather than in childhood or adulthood [23]. Neural plasticity indeed allows for a fairer "adjustment" of the healthy hemisphere in early age [29]. Nevertheless, since early cerebral injuries are frequently associated with severe seizures and consequent impairment of development, the age of seizure onset is another substantial factor that heavily influences cognitive outcome [40, 43]. Therefore, late-onset seizures are less detrimental to mental skills than early-onset ones [43] because the absence of paroxysmal events during the first stage of life, when neuronal plasticity is more active, allows a more effective reorganization process.

The degree of functional recovery also seems to depend on the extension of the injury. Indeed, larger injuries involve broader contralateral areas in the reorganization process with, consequently, a better functional recovery [16].

In our patient, the early occurrence of injury as well as its large extension were factors that favoured the process of contralateral reorganization. Although the injury occurred at the neonatal age, she did not present seizures before age four, and soon after, there was a long period of continuous seizure control until 12 years of age. The absence of seizures in the first years of life has thus allowed a good functional reorganization of the left hemisphere.

The detrimental effects of seizures arose when resistant epilepsy appeared (between 12 and 14.8 years). Right hemispherectomy was capable of controlling seizures and this allowed the development of the originally reorganised functions of the left hemisphere. Indeed, the rise in IQ did not seem to be related with the weaning of the antiepileptic drugs, since its relevant increase was observed in the first years after surgery when therapy had not been modified at all.

If we consider the neuropsychological profile of our patient and its evolution, firstly, one can note a non-homogenous profile in non-verbal tasks. In fact, the VOSP battery revealed normal performances in those subtests primarily exploring spatial information processing, and abnormal scores in tasks requiring the elaboration of the visuoperceptual component of targets. Indeed, Mehta et al. [25] observed different perceptual and spatial performance profiles in right-hemisphere-injured patients than left-hemisphere-injured ones. The left-injured group showed intact perceptual and impaired spatial performance, whereas, in contrast, the right-injured group generally exhibited an impairment of both perceptual and spatial performance, often more

marked for perceptual items. These findings raise the question as to whether the left hemisphere plays a major role in the processing of visuospatial, rather than visuo-perceptual, abilities [25]. Thus, in our patient, the anatomical and functional integrity of the left hemisphere might explain the preservation of “basal” visuospatial abilities and the impairment of visuo-perceptual ones.

The marked deficit in the case of more “complex” spatial and perceptual aspects of visual stimuli allows us to hypothesize that early injury may have hindered in our patient the reorganization of “high-level” processes. Other studies report that spatial reasoning, such as the mental rotation of two- or three-dimensional shapes as well as perception of pictures with irregular outlines or of objects placed in unusual positions, requires the dominant involvement of the right hemisphere in later age [11, 15]. Therefore, the low scores observed on Benton’s Line Orientation, DAT, RMPFB Gollin’s Pictures Test and Ghent’s Overlapping Figures in our patient could be primarily related to the side of injury and to its early onset.

An unexpected finding was the good performance obtained in the unknown faces recognition task, although the patient had a severe impairment in the processing of complex visual stimuli. McCarthy and Warrington [24] argued that dissociation between the perception of objects and faces pictures may occur in some patients. Reynold and Jeeves [36] reported that in early age, and up to adolescence, both hemispheres may be equally involved in processing unknown faces. In any case, the final functional organisation appears to be located in the right hemisphere. In our case, good face recognition performance might be related to a “part-whole” modality of processing information typical of the left hemisphere; it could permit, in case of right posterior damage, a fairly good, if more time-consuming, analysis of visual stimuli [30].

As to linguistic abilities, as expected, no significant impairment was observed. The linguistic scores were particularly below average only in tasks requiring the elaboration of visual stimuli. Aram et al. [2] observed almost twice the rate of anomia and visual errors in early right-hemisphere-injured children compared with age-matched

controls and explained it as a possible visual-processing deficit in right-hemisphere-injured children. Similarly, our patient produced twice the amount of errors when the same task was performed with visual, rather than oral, targets (visual lexical decision, visual grammatical comprehension); in particular, she makes a lot of anomia and visuo-semantic inaccuracies on all oral naming (oral naming of nouns and actions).

As expected, short- and long-term verbal memory was fairly preserved. As to the visuospatial memory, the patient generally reached a good performance in the TOMAL subtests; only at free recall tasks did she obtain below-average performances, possibly due to the higher needs of attentive and memory resources. Similar defective performances were observed, on the other hand, at the Gotman’s test. Differently from normal subjects or even patients who have undergone surgery on the right amygdala/hippocampus, our patient did not show any improvement in the learning phase and presented an even worse behaviour in the delayed recall trial, with a rapid loss of visual information previously acquired. The removal of the right cortex in our case could have irreversibly impaired learning and recalling of random complex visual abstract information.

In summary, our case of neonatal ischemic infarction of the middle cerebral artery with refractory epilepsy shows that cerebral reorganisation can effectively take place even when hemispherectomy is performed relatively later on. The full control of seizures during the early years of life, when brain organisation is more active, could explain the good post-surgical cognitive recovery.

The reorganisation process has saved the spatial abilities as well as the linguistic abilities and verbal and visuo-spatial memory, but not the “complex” spatial and perceptual skills as well as recall abilities. Oddly, despite the severe impairment in complex visual stimuli processing shown by patients who had undergone right hemispherectomy, a good performance in the recognition of unknown faces was noted that may be explained by the presence of a part-whole information processing modality more typically associated with the left hemisphere.

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