Hemispheric specialization using SPECT and stimulation tasks in children with dysphasia and dystrophia

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Developmental dysphasia, a severe childhood learning disorder, is thought to result from problems in hemispheric specialization involving both left and right cerebral hemispheres. Regional cerebral blood flow (rCBF) was measured at rest and during stimulation of both hemispheres independently: dichotic listening for the left, dichaptic palpation for the right. Eight right-handed boys with expressive dysphasia, aged 8 to 12 years, were investigated using SPECT and compared with eight right-handed age-matched boys with Duchenne muscular dystrophy with reading disorders but normal speech. rCBF values at rest were also compared with those of five right-handed age-matched normal boys. In the dichotic task, children with dysphasia differed from children with dystrophia by failure to increase rCBF in the left hemisphere, in Broca's area, but rCBF increased in the right hemisphere, in the region homologous to Broca's area. In the dichaptic task, rCBF increased bilaterally for children with dysphasia whereas in children with dystrophia rCBF increased only in the right hemisphere. At rest the physiological asymmetry was reversed in favor of the right hemisphere in all areas except Broca's area. Surprisingly, the same applied at rest and for all areas in children with dystrophia. These results confirm that functional specialization of both hemispheres is impaired in developmental dysphasia. Moreover, they suggest that learning disabilities associated with Duchenne muscular dystrophy could also be related to abnormal hemispheric specialization.

The ontogenesis of cerebral specialization has generated a great deal of research. Dichotic listening paradigms have demonstrated that children exhibit a significant right-ear advantage (left hemisphere) for various types of linguistic material as early as in the first year of life (Bertoncini et al. 1989). These findings have been associated with neuroanatomical asymmetry: the left planum temporale is wider than the right (Geschwind and Levitsky 1968) in newborn infants and fetuses (Wada et al. 1975, Chi et al. 1977). Therefore, the left hemisphere is usually considered to be involved in the development of language in right-handed individuals, and impaired oral language development reflects incomplete or abnormal lateralization to the left hemisphere.

Developmental dysphasia is a congenital, severe, and specific language disorder of unknown etiology. Although CT and MRI demonstrate no lesion (Hier and Rosenberger 1980, Jernigan et al. 1991), recent findings suggest that the left hemisphere of patients with dysphasia may exhibit focal abnormalities. Jernigan and coworkers (1991) and Plante and colleagues (1991) reported a large number of language-impaired children whose plana temporale were symmetrical. Cohen and colleagues (1989) reported an 8-year-old girl with developmental dysphasia in whom post-mortem examination disclosed minor architectural dysplasia predominantly located in the perisylvian region of the left hemisphere and symmetry of the plana temporale. When measuring regional cerebral blood flow (rCBF) with SPECT, 14 children with dysphasia failed to activate the left hemisphere during a task of phonemic discrimination (Tzourio et al. 1994).

Hemispheric lateralization is also thought to be abnormal in developmental language disorders but few and conflicting data are available (Cohen et al. 1991). Most research involves children with learning disabilities. Children with language impairment are not clearly identified, and reports mention a lack of right-ear advantage in dichotic listening to various types of linguistic materials (Obrzut 1988). A recent neuropsychological study performed in 10 right-handed children with developmental dysphasia emphasized differences in hemisphere performances (Duvelleroy-Hommet et al. 1995). Children with dysphasia had a right-ear advantage (left hemisphere) when performing dichotic tasks, suggesting that the left-hemispheric dysfunction is not complete. But they did not provide any evidence of left-hemisphere specialization for oral language production using the verbomanual time-sharing paradigm, emphasizing a disorder that mainly involves expressive areas. Moreover, the same patients had lower performances with the left hand (right hemisphere) than control children on dichaptic tasks, suggesting that specialization was also impaired in the right hemisphere.

Functional cerebral imaging using SPECT with ^{133}Xe as a tracer ('dynamic SPECT') is a non-invasive measurement of rCBF, a parameter close to glucose metabolism and related to neuronal function. Dynamic SPECT can be adapted for children. The procedure is adequate for examinations at rest and under cognitive stimulations, and the low-radiation dose permits repetition (Chiron et al. 1992). Therefore, it is a potential technique for studying brain function in subjects with learning disabilities. To study the left- and right-hemispheric performances independently, lateralized measures of rCBF at rest and during tasks suitable for children, and SPECT were performed. It was ensured neuropsychologically that the tasks involved one hemisphere predominantly. Functional left-hemisphere specialization was investigated by dichotic listening using only the right ear (Kimura 1963) and right functional specialization by dichaptic task (Witelson 1974).

In studies of children using nuclear functional imaging such as SPECT or positron emission tomography (PET), the control group cannot be drawn from normally developing subjects because of ethical constraints. Therefore, control children, who were matched for age and sex with our dysphasic patients, were selected from the only pediatric series of normative data published using the same SPECT procedure (Chiron et al. 1992). However, these data were small in number and available only at rest. Patients with slightly different disorders may also be used as controls if participation is likely to improve the understanding of their disease. Therefore, children with Duchenne muscular dystrophy comprised the comparison group. Children with this fatal X-linked recessive myopathy frequently have specific learning disabilities of unknown etiology (Billard et al. 1992), which may involve language. But these disabilities differ from those observed in children with dysphasia because children with dystrophia experience delays in acquiring reading skills but do not experience any obvious impairment of expressive language (Billard et al. 1998).

The objective of the present work was to study hemispheric specialization in children with developmental expressive dysphasia, using SPECT functional imaging at rest and during stimulation of both hemispheres independently. The following questions were addressed: are there bilateral disorders of hemispheric specialization, are specific regions involved, and are specialization disorders detectable at rest?

Method

SUBJECTS

The first group comprised eight right-handed boys with developmental dysphasia (Table I), aged 8 to 12 years (mean 10.2 years). These boys were outpatients who had been referred to CB. They presented with speech disorders consisting of phonological and syntactic disturbances, resulting in expressive dysphasia. According to DSM-IV criteria, they presented with a primary disorder of oral language development, had normal hearing acuity and normal intelligence, and had neither an objective neurological disease nor an emotional or communicative disorder. MRI was normal in all subjects. The boys' neurological examinations were normal but slight clumsiness in fine motor activities such as writing and/or drawing or sport was observed. They all followed a special schooling program for children with dysphasia, which included the support of specialized teachers and speech therapists for reading, writing, and oral language rehabilitation. Although non-verbal IQ was in the normal range in all patients, three had moderate visuospatial or visuoconstructive disorders and four had mild difficulties in mathematics.

The second group (comparison group) comprised eight right-handed boys with Duchenne muscular dystrophy (Table I), aged 9 to 13.5 years (mean 10.7 years) (no statistically significant differences in age between this group and the children with dysphasia were found, Student's t test). These children were outpatients who had been referred to CB. All children had normal MRI. Three were attending mainstream school, the others had motor and reading rehabilitation in special centers for children with dystrophia. There was no significant difference for non-verbal IQ (PIQ) measured by four

Table I: Individual neuropsychological performances

	Age (y)	*Performance IQ*	*Verbal IQ*	*Syntax comprehension*[a]	*Syntax expression*[b]	*Lexical comprehension*[c]	*Phonological expression*[d]	*Reading index*[e]
Children with dysphasia								
1	7.8	99	79	33	18	48	60	87
2	11.1	107	87	35	37	58	87	62
3	10.2	94	74	36	27	56	41	68
4	11.7	101	81	37	28	54	89	74
5	8.9	106	84	34	28	54	87	74
6	11.2	105	85	37	34	41	96	65
7	12	102	76	38	32	44	91	63
8	10	109	50	29	26	49	46	66
Mean	10.3	102.9	77	34.9	28.8	50.5	74.6	69.9
Children with dystrophia								
1	10.5	116	105	38	38	60	100	105
2	12	95	92	38	38	57	96	75
3	13.5	109	102	39	35	60	100	86
4	9	102	101	33	33	42	95	84
5	10	114	81	37	36	53	100	97
6	11.5	98	88	38	35	56	100	67
7	9.5	80	86	34	36	53	100	74
8	10	114	81	36	36	55	98	97
Mean	10.7	103.3	92	36.6	35.9	54.4	98.6	86

[a] normal value for age over 8 y, >35
[b] normal value for age over 8 y, >32
[c] normal value for age over 8 y, >52
[d] normal value for age over 8 y, 100
[e] normal ratio reading index/chronological age over 8 y, 100.

subtests of WISC-R Scale (Weschler 1981) between children with dysphasia and children with dystrophia. Patients in both groups were right handed with an Auzias index (handedness test) higher than 90. The score of lexical comprehension tested by the 'Vocabulaire actif et passif' (TVAP) (Deltour and Hupkens 1980) was not significantly different between the two groups, although it was slightly low in children with dysphasia and normal in children with dystrophia. The score of syntactical comprehension tested by the comprehension part of the French version of Northwestern Syntactic Screening Test (NSST) (Weil-Harpen et al. 1983) was normal in both groups. Conversely, the scores in expressive language were significantly lower in the dysphasic group, i.e. the phonological score evaluated by the 'batterie pour le langage' (Chevrie-Muller et al. 1981) (F=11.3 $P<0.004$) and the syntactical score evaluated by the expression part of the NSST (Weil-Harpen et al. 1983) (F=12, $P<0.003$). Reading disability existed in both groups but was greater in children with dysphasia (F=4.7, $P<0.04$). Reading index was calculated by the ratio of the reading age measured by the leximetry test 'La Pipe et le Rat' (Lefavrais 1987) to the chronological age.

The third group (normal group) was only used for 'at rest rCBF' comparisons because normally developing children could not be entered in stimulation SPECT examination for ethical reasons. These children had previously been investigated using the same SPECT procedure at rest and the results have been published separately (Chiron et al. 1992). It comprised five right-handed boys aged 6 to 12 years (mean 10 years) (age of this group did not differ significantly from children with dysphasia and children with dystrophia, Student's t test), i.e. all the right-handed sex- and age-matched subjects reported in the literature were investigated with the same SPECT procedure. They were drawn from a series of 39 right-handed children under 18 years of age who underwent measurement of rCBF for transient symptoms (facial angioma, sleep myoclonia, cerebelloopsomyoclonic syndrome, syncope, headache, and so on) and were a posteriori considered normal (Chiron et al. 1997). These children all had normal cognitive development, schooling, neurological examination, and EEG and CT scan at the time of SPECT. They were followed up for at least 2 years and remained unaffected by any cognitive or neurological impairment. All attended mainstream schools.

SPECT INVESTIGATION

Informed consent was obtained for all subjects, from either the parent or guardian, after a full explanation of the investigation procedures. The study was also approved by the institutional and technical ethics committees for radiation studies.

SPECT was performed using a highly sensitive tomographic system specifically designed for use on the brain, TOMOMATIC 564, which provides five contiguous axial slices, 20 mm thick, from the orbitomeatal level + 20 mm to the orbitomeatal level + 100 mm, with a spatial resolution of 12 mm. rCBF was assessed by the dynamic SPECT technique using ^{133}Xe as a tracer (Lassen 1986). ^{133}Xe was injected through an intravenous cannula, which had been previously inserted, at a mean dose of 56×10^6 becquerel/kg/injection. Tomographic imaging is performed during the washout of ^{133}Xe. ^{133}Xe is metabolically inert and freely diffusable, therefore the kinetics of its disappearance from a given brain region is a measure of blood flow in that region. Absolute values can be measured by means of the Celsis algorithm (Celsis et al.1981). The acquisition of images lasted 4.5 minutes after the ^{133}Xe injection and was performed according to a preestablished non-invasive procedure, at rest, in dimmed light, and without any external stimulation (Chiron et al. 1992). For each examination, the radiation dose was 3.5 milliGrey for the lung, the target organ for Xe, and it was very low for the brain.

EXPERIMENTAL PROTOCOL

The child's anxiety was evaluated by MCM, using the Covi scale (Covi and Lipman 1984). Evaluation was performed after inserting the intravenous cannula and before starting SPECT. The scale comprises three items measured from 0 (no anxiety) to 4 (high anxiety).

Three SPECT examinations were performed for each child with dysphasia and each child with dystrophia on the same day and at a time interval of 45 minutes – resting, dichotic listening, and performing a dichaptic task, respectively. Perfusion alternatively involved the left and right arm in consecutive children. The patient's head was placed in the same position for all investigations. At rest, the children were asked to lie still. Then, the range of dichotic and dichaptic studies was alternated to avoid any systematic time effect. The procedure was similar for both tasks. During the interval between the 'at rest' scan and the first-task scan, the child was shown how to perform the first task; the same applied to the second task between the first- and the second-task scans. The final test started about 40 seconds before the administration of the tracer and was pursued during the entire period of acquisition of the data.

The dichotic listening procedure delivered pairs of digits simultaneously to both ears via earphones connected to a stereophonic tape recorder. Monaural presentations were first balanced to ensure a comfortable subjective equality in both ears. The material used was adapted from a synthesized tape (Chevrie-Muller 1989) which contains 36 sets of different monosyllabic digits, i.e. 72 digits delivered to the left ear and 72 synchronously delivered to the right one. According to the individual conditions of SPECT examination, the number of sets delivered varied from 26 to 36 (mean in children with dysphasia, 30; in children with dystrophia, 29). The child was instructed to listen carefully to what was expressed in the right ear. After each stimulus, two digits drawn on a sheet were shown to the child. The child was instructed to cross their index fingers when both digits seen were the same as those heard by the right ear and not to move if one or both were different. Each dichotic set and response lasted 10 seconds.

During the dichaptic task, the child had to explore, without seeing, two shapes stuck onto a piece of cardboard. The test comprised 21 sets of shapes. The child was instructed to explore both shapes simultaneously, the left shape with the left hand and the right shape with the right hand. The response procedure was the same as in the dichotic listening and, according to the individual conditions of SPECT examination, the number of sets delivered varied from 13 to 21 (mean in children with dysphasia, 16; in children with dystrophia, 15). After each stimulus, two black shapes drawn on a sheet were shown to the child who was instructed to cross their index fingers if both shapes seen were the same as those explored by the hands. Each dichaptic set and response lasted about 15 seconds.

DEFINITION OF THE REGIONS STUDIED

For each child with dysphasia and dystrophia, three images of rCBF were obtained on which CBF was measured in mL/100gr/mn in 18 circular and symmetrical cortical regions of interest per slice, nine left and nine right (Fig. 1A). The hemispheric mean CBF (mCBF) was taken as the mean value of the regions of interest localized on the three slices: orbitomeatal + 40, + 60, and + 80 mm respectively, in the left and right hemispheres. rCBFs were calculated on each side in six large cerebral regions defined according to Brodmann's areas and corresponding respectively to frontal; sensorimotor; Broca, which we called 'left Broca' for Broca's area in the strictest sense and 'right Broca' for the contralateral area on the right side; auditory, including Wernicke's area; plurimodal parietotemporal; and unimodal parietotemporooccipital (TO) cortex (Fig. 1B).

DATA ANALYSIS

Both of the following were studied: the left–right indexes of mCBF and rCBFs, defined by ([left CBF – right CBF] × 2)/(left CBF + right CBF), which reflect the relative left-to-right changes in tasks and groups; and the absolute values of left and right mCBF and rCBFs, which indicate the absolute changes in left and right hemispheres for each given task and group.

The first analysis involved tasks (intragroup analysis), comparing the changes among rest, dichotic, and dichaptic values in children with dysphasia and dystrophia respectively. The second analysis involved groups (intergroup analysis). It compared children with dysphasia and children with dystrophia during each given task, and children with dysphasia, children with dystrophia, and control subjects at rest.

Statistical analysis for intra- and intergroup comparisons used one-factor ANOVA. To compare the groups with dysphasia and dystrophia at rest and after the two stimulation tasks, one-factor ANOVA with repeated measures was used. When there was a significant difference, a two-group comparison was performed using the Fisher test.

Results

ANXIETY SCALE

The mean anxiety score was 1.18 (±1.6 SD) (range 0 to 5) in children with dysphasia and 2.25 (±1.98 SD) (ranges 0 to 5) in children with dystrophia. There was no significant difference between the two groups (Mann–Whitney *U* test). Although no reference value for the anxiety scale is available for children with the tasks we used, the scores obtained suggest that anxiety was relatively low in both groups (the maximum score being 12 with the present scale).

TASK CONTROL

The percentage of correct responses was significantly different from 50% (the percentage of correct responses by chance) for each group and task, thus confirming that the patients really performed the tasks. On the dichotic task, children with dysphasia gave 81% correct responses ($P<0.001$) and children with dystrophia 83% ($P<0.001$). On the dichaptic task, children with dysphasia gave 64% correct responses ($P<0.05$) and children with dystrophia 74% ($P<0.001$).

INTRAGROUP ANALYSIS

For analysis of tasks in children with dysphasia and children with dystrophia, see Table II. Left–right indexes in the comparison group (patients with dystrophia) exhibited changes in the predicted direction although not reaching statistical significance: indexes increased on the dichotic task (supposed to stimulate the left hemisphere) and decreased on the dichaptic task (supposed to stimulate the right hemisphere). These changes were particularly evident in the temporooccipital area where the index was slightly negative at rest, positive on dichotic task, and strongly negative on dichaptic task (Table II). In children with dysphasia, the indexes tended to increase on the dichotic task (except in Broca's area where the index decreased paradoxically), but changes were more heterogeneous on the dichaptic task, with the index showing increase, decrease, or no change according to the regions studied.

Absolute CBF values confirmed these changes although only those triggered by the dichaptic stimulation reached statistical significance. Indeed, the dichotic task induced mild increase but this occurred in all the left areas in the comparison

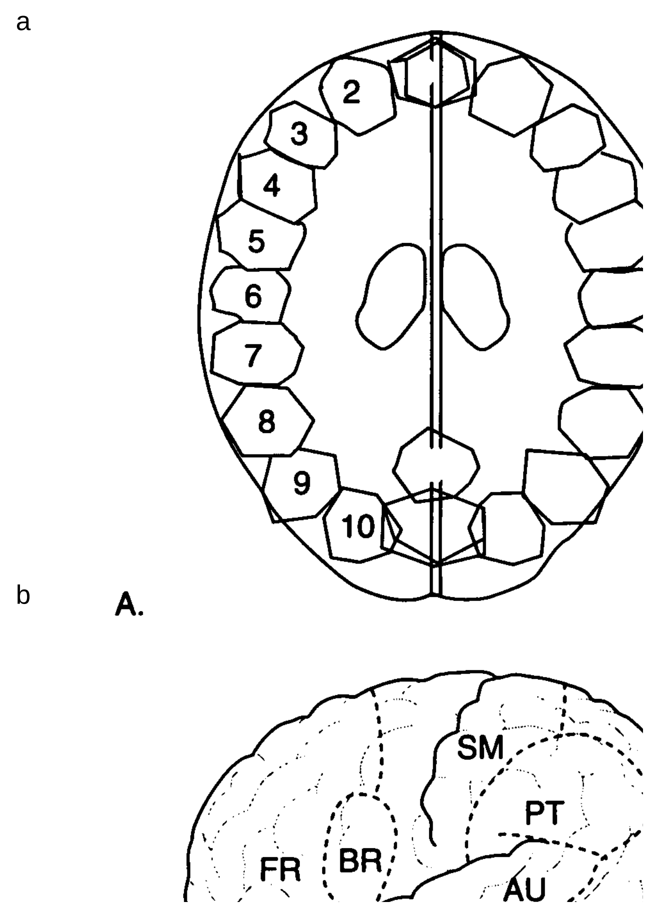

Figure 1: (a) *18 cortical regions of interest, nine left and nine right, in which regional cerebral blood flow (rCBF) was measured, in mL/100gr/min.* (b) *rCBFs were calculated on each side in six large cerebral regions defined according to Brodmann's areas and corresponding respectively to frontal (FR); sensorimotor (SM); 'Broca' (BR), which we called 'left Broca' for Broca's area in the strictest sense and 'right Broca' for area homologous to Broca on right side; auditory (AU) including Wernicke's area; plurimodal parietotemporal (PT); and unimodal temporooccipital (TO) cortex.*

group, whereas in the children with dysphasia the left Broca disclosed a paradoxical rCBF decrease. On the dichaptic task, changes were more marked and also different in both groups. In the comparison group, the rCBF value significantly increased in the right temporooccipital region (P=0.03) compared with 'at rest' and the dichotic task. By contrast, the same task induced larger changes in children with dysphasia because CBF increased not only on the right hemisphere (P=0.03) but also on the left (P=0.07). Two specific regions were more significantly involved in these changes, the right temporooccipital area (P=0.006) and the left auditory area (P=0.01). Changes were significant, not only compared with rest but also with the dichotic condition.

These results suggest that (1) dichotic and dichaptic tasks did induce rCBF increase in the predicted hemisphere, (2) children with dystrophia were a reliable comparison group for stimulation tasks because they exhibited changes similar to those predicted in normal subjects, and (3) the specialization of the right hemisphere for the dichaptic task could be abnormal in expressive dysphasia, and also partly involved the left hemisphere.

INTERGROUP ANALYSIS

Comparing children with dysphasia and dystrophia during the stimulation tasks

Both groups exhibited different patterns in two regions, Broca and TO (Fig. 2). The most discriminating effect was found in Broca's area during the dichotic task: rCBF was higher in children with dysphasia on both sides and increased on the left in children with dystrophia but not in children with dysphasia (P=0.04), the latter exhibiting rCBF increase more on the right side. In the TO region, both groups exhibited similar changes showing a positive index on the dichotic task and a negative one on the dichaptic task (P=0.009), and showing complete CBF which increased on the left on the dichotic task (P=0.04) and on the right on the dichaptic (P=0.0002), but children with dysphasia also increased on the left on the dichaptic (P=0.04).

These results suggest that (1) the main functional effects induced by dichotic and dichaptic tasks as performed in the present study were observed in TO regions; (2) the specialization of the left hemisphere for dichotic tasks is abnormal in expressive dysphasia, the abnormality specifically involving Broca's area; and (3) specialization disorders also involve the right hemisphere for dichaptic tasks in patients with dysphasia.

Comparing children with dysphasia, dystrophia, and normal children at rest

Unlike the previous conditions of stimulation, studying the index was the most helpful in detecting significant differences between groups. Left–right indexes were negative in

Table II: Mean rCBF values in the different groups

	Control subjects	*Children with dysplasia*			*Children with dystrophia*		
	Rest Mean (SD)	*Rest Mean (SD)*	*Dichotic Mean (SD)*	*Dichaptic Mean (SD)*	*Rest Mean (SD)*	*Dichotic Mean (SD)*	*Dichaptic Mean (SD)*
mCBF							
Left	65 (9)	64 (7)	66 (7)	71 (10)	62 (9)	64 (6)	68 (6)
Right	62 (8)	68 (8)	69 (6)	75 (9)	65 (9)	66 (9)	72 (10)
Index	0.05 (0.023)	–0.062 (0.032)	–0.038 (0.036)	–0.061 (0.045)	–0.047 (0.052)	–0.02 (0.088)	–0.055 (0.049)
Frontal							
Left	60 (10)	58 (9)	61 (6)	64 (8)	58 (12)	58 (4)	62 (7)
Right	57 (7)	60 (8)	61 (6)	65 (8)	58 (10)	59 (8)	64 (7)
Index	0.048 (0.078)	–0.031 (0.104)	–0.018 (0.068)	–0.018 (0.081)	–0.003 (0.063)	–0.01 (0.114)	–0.029 (0.058)
Broca							
Left	74 (13)	78 (12)	76 (18)	80 (18)	63 (10)	68 (13)	69 (9)
Right	65 (11)	74 (10)	81 (15)	88 (14)	68 (9)	66 (6)	75 (13)
Index	0.132 (0.149)	0.056 (0.176)	–0.078 (0.224)	–0.11 (0.205)	–0.078 (0.082)	0.011 (0.187)	–0.079 (0.126)
Sensorimotor							
Left	70 (14)	69 (9)	70 (9)	75 (11)	65 (8)	69 (9)	70 (6)
Right	66 (11)	74 (8)	75 (8)	81 (10)	72 (11)	73 (13)	79 (14)
Index	0.058 (0.078)	–0.072 (0.062)	–0.064 (0.092)	–0.071 (0.103)	–0.09 (0.083)	–0.054 (0.145)	–0.117 (0.132)
Auditive							
Left	67 (11)	65 (8)	64 (9)	75 (15)	62 (11)	66 (6)	68 (8)
Right	63 (9)	80 (12)	73 (9)	82 (7)	70 (16)	68 (10)	73 (9)
Index	0.06 (0.097)	–0.215 (0.091)	–0.151 (0.097)	–0.095 (0.139)	–0.121 (0.192)	–0.024 (0.118)	–0.081 (0.156)
PT							
Left	65 (8)	65 (8)	69 (7)	74 (18)	67 (10)	67 (7)	73 (9)
Right	61 (9)	68 (9)	70 (7)	74 (10)	69 (13)	69 (13)	75 (12)
Index	0.076 (0.066)	–0.047 (0.105)	–0.01 (0.05)	–0.019 (0.16)	–0.034 (0.109)	–0.024 (0.105)	–0.011 (0.122)
TO							
Left	62 (9)	56 (7)	59 (6)	63 (10)	54 (7)	59 (7)	57 (8)
Right	59 (8)	57 (8)	59 (9)	70 (13)	56 (7)	57 (5)	65 (11)
Index	0.038 (0.039)	–0.021 (0.071)	0.004 (0.139)	–0.105 (0.127)	–0.045 (0.05)	0.036 (0.095)	–0.127 (0.19)

Measurements are expressed in mL/min/100 g.
mCBF, hemispheric mean cerebral blood flow; PT, plurimodal parietotemporal; TO, unimodal parietotemporooccipital.

both children with dysphasia and dystrophia whereas they were positive in normal subjects, thus suggesting that the physiological asymmetry (left predominance) was reversed in both diseases (Fig. 3). The Broca index provided an exception because it remained positive in children with dysphasia whereas it was negative in children with dystrophia. Reversed asymmetry was significant for mCBF (P=0.0002) and for sensorimotor (P=0.0064), Broca (P=0.0416) and auditory (P=0.0104) regions. Patients with dysphasia and dystrophia did not differ from each other but differed significantly from normal subjects (except for the Broca region in which only children with dystrophia differed from normal subjects).

These results suggest that (1) disorders of hemispheric specialization were detectable at rest in developmental dysphasia, and (2) hemispheric specialization was also abnormal at rest in children with Duchenne muscular dystrophy.

Discussion

This study provides the first attempt to examine hemispheric specialization at rest and during specific stimulation tasks using functional cerebral imaging in children with developmental dysphasia. Measures of hemispheric and regional cerebral blood flow during the dichotic task (left stimulation) confirm that specialization of the left hemisphere is impaired. The abnormality mainly involves Broca's area, rCBF increasing on the right side instead of the left in patients with expressive dysphasia. In the right hemisphere, specialization is also abnormal as the dichaptic task (right stimulation) induces activation in both hemispheres of a patient with dysphasia. Moreover, abnormalities in hemispheric specialization are detectable at rest in these patients when compared with normal sex- and age-matched children. Physiological predominance of left rCBF is reversed in all regions but Broca's area.

The present study also provides original data regarding hemispheric specialization in children with dystrophia, a population known to experience reading disability, and selected here as the comparison group. Consistent with preliminary neuropsychological data on this disorder (unpublished personal data), the left hemisphere exhibits low functioning at rest but seems to be activated normally during tasks.

In addition to the predicted disorders of left hemispheric specialization, we provide evidence of disorders associated

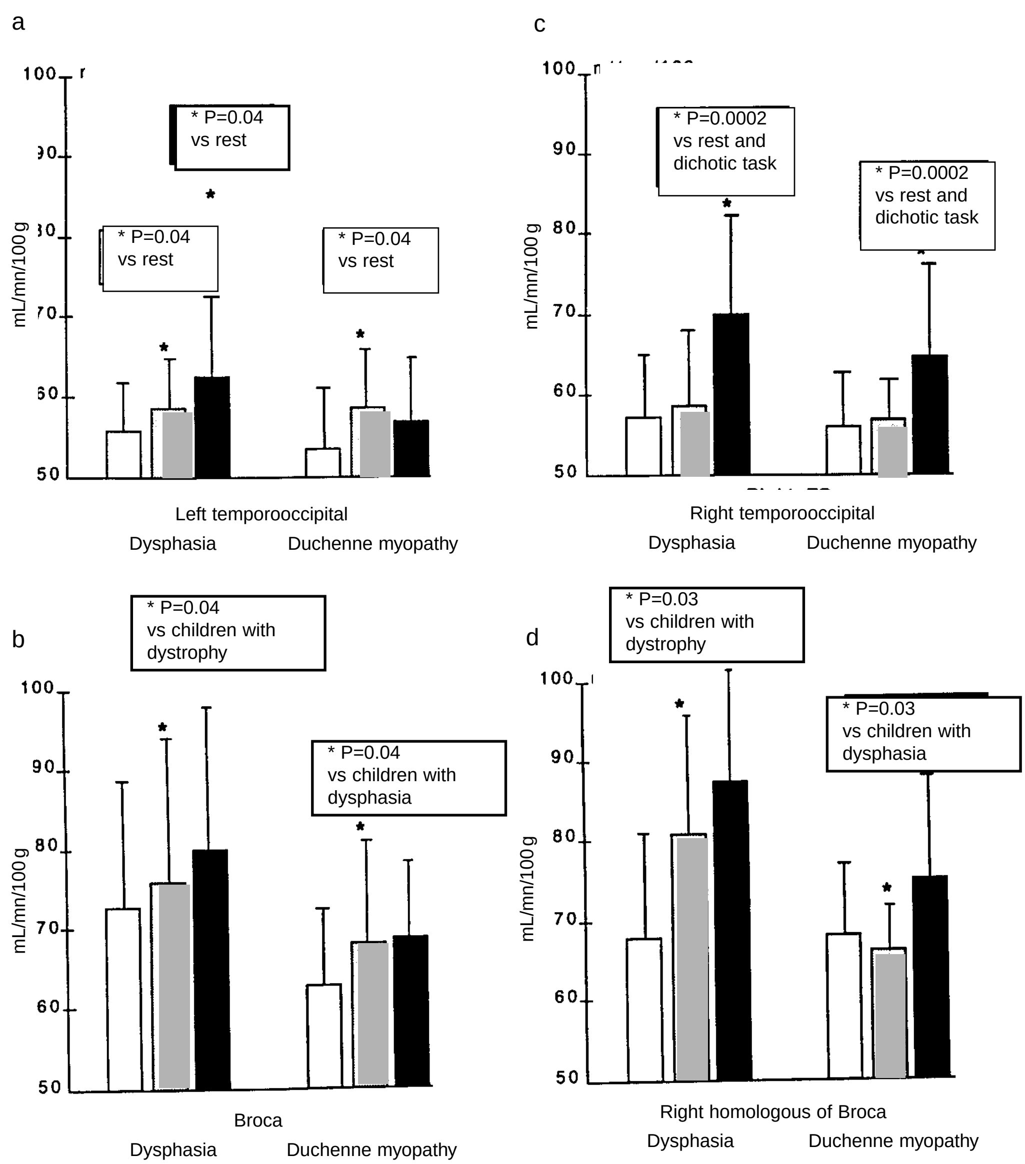

Figure 2: *Absolute values of CBF expressed in mL/mn/100 g, in left temporooccipital (TO) region* (a), *Broca's area* (b), *right temporooccipital region* (c), *and right homologous area of Broca's area* (d), *at rest* □ *and on the dichotic* ■ *and dichaptic* ■ *tasks, in children with dysphasia and Duchenne myopathy. rCBF values exhibit similar changes in TO region for both dysphasic and dystrophic groups (except in left TO on dichaptic task for children with dysphasia)* (a, c) *whereas changes are different in Broca's area and right homologous region during dichotic task between the two groups. Significant differences between both groups are noticed in the bold boxes.*

with the right. On dichaptic stimulation, CBF increase is poorly localized compared with the reference group. It not only involves the right hemisphere but also the left one. This is consistent with the poor right-hemisphere specialization of children with dysphasia suggested by the lower left-hand performance (right hemisphere) on the dichaptic task performed during neuropsychological evaluation (Duvelleroy-Hommet et al. 1995).

The Broca region appears to exhibit the most relevant abnormalities found in the group with dysphasia. It is the only region to have a different pattern between both groups during the dichotic task: left Broca fails to be activated whereas rCBF increases in the right homologous region. Activation of Broca's area in such a receptive task is quite surprising but it could be sustained by the alphabetical reading associated in the present procedure. The lack of Broca activation is consistent with the pattern of language disorder in the subtype of dysphasia we studied. These patients experienced an expressive form of dysphasia, the most frequently occurring one. Their disability mainly affects phonological and syntactic expressive language with better performances in lexical and syntactical comprehension (Duvelleroy-Hommet et al. 1995), thus suggesting a predominant involvement of the Broca region. Although previous rCBF studies of children with dysphasia were not dedicated to hemispheric specialization, they already disclosed left abnormalities. Hypoperfusion involving the left hemisphere was present at rest. It was bilateral perisylvian in 13 patients (Lou et al. 1984), left parietotemporal in 14 (Denays et al. 1989), or left temporofrontal in 24 (Lou et al. 1990). Children with dysphasia significantly increased global flow during a language task or a simple auditory task compared

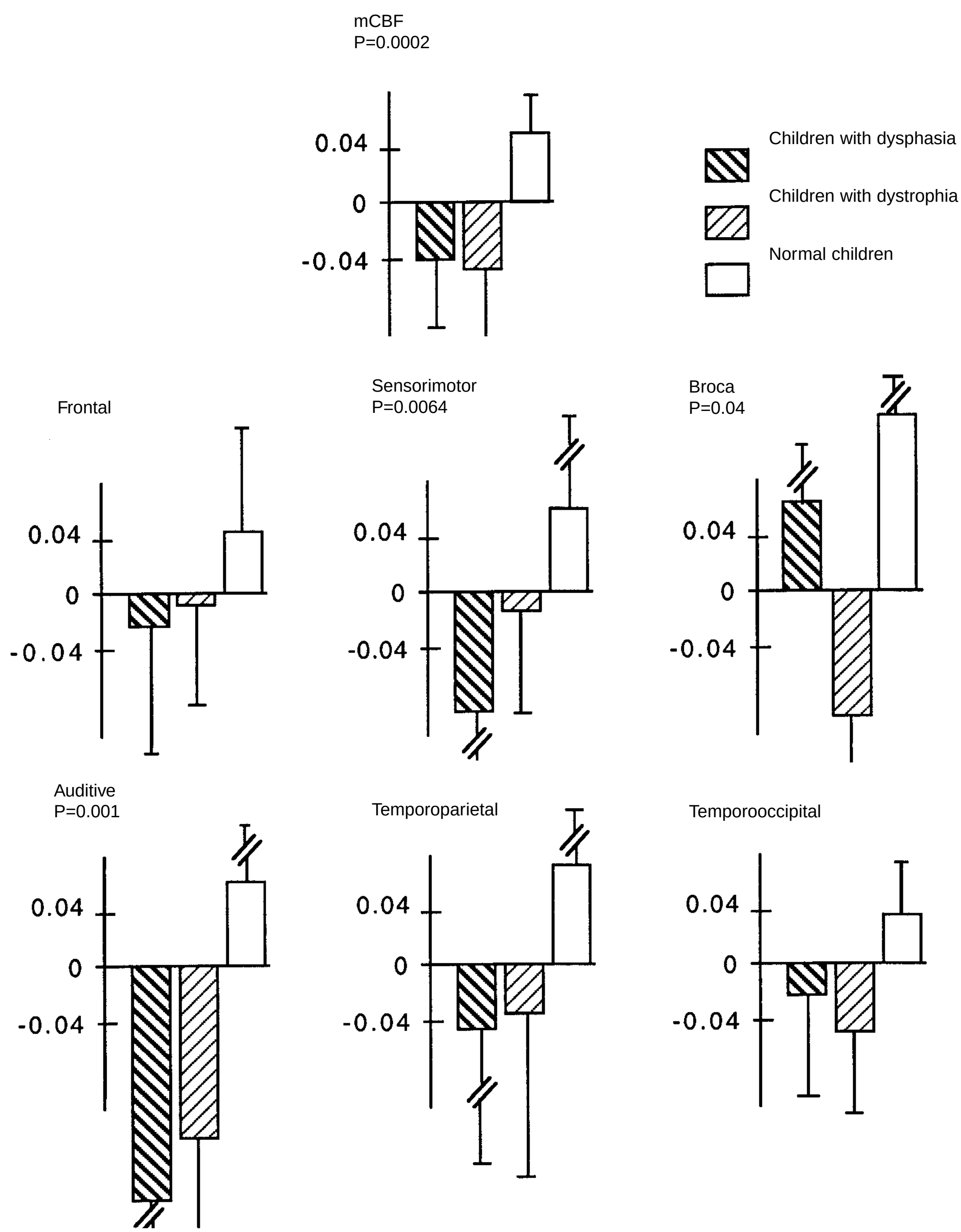

Figure 3: *Left–right index was calculated as ([left CBF – right CBF] × 2)/(left CBF + right CBF). Index was represented at rest for mean CBF (mCBF) (see text) and each region (see Fig. 1B). P expresses the significant differences between normal children and children with dysphasia and dystrophia, except for Broca where only children with dystrophia differed from normal children.*

with 'at rest' (Raynaud et al. 1989, Tzourio et al. 1994). The latter study emphasizes lack of activation of the left hemisphere during a phonemic discrimination task in a dysphasic population similar to ours, compared with a group of hyperactive children with attention deficit (Tzourio et al. 1994). Therefore, using a task different from but complementary to the one of this report, the authors demonstrate left-hemispheric dysfunction during oral language in developmental expressive dysphasia.

We found negative left–right indexes 'at rest' in both disorders. These findings are very robust regarding the level of significance reached, given the small size of the normal group. They contrast with the asymmetry usually observed 'at rest' after 3 years of age: rCBF has been demonstrated to be significantly higher in the left than in the right hemisphere (positive left–right index), mainly in the sensorimotor and parietooccipital areas (Chiron et al. 1997).

In patients with developmental dysphasia, we found hemispheric and regional asymmetry to be reversed. Only Broca's area exhibits a positive index, perhaps due to the selection of patients according to manual lateralization. The lack of left rCBF predominance could be related to the anatomical findings recently reported in developmental dysphasia, particularly the absence of asymmetry of temporal areas. However, decrease in brain volume is unlikely to be the unique explanation as rCBF predominance can switch from right to left around 3 years of age without any anatomical change (Chiron et al. 1997).

Inverse asymmetry is more surprising in children with dystrophia. It could be partly related to the frequent dyslexia reported in this disease (Billard et al. 1992) and the lack of asymmetry of the planum temporale described in dyslexic populations (Geschwind and Galaburda 1985). Hemispheric asymmetry may also be modified by the progressive motor deficit. However, appropriate activations were obtained during both stimulations, involving the left hemisphere during the dichotic task and the right during the dichaptic task. An eventual relation between the lack of functional asymmetry and the degree of reading or motor disabilities could not be tested in our dystrophic group because it was too small.

METHODOLOGICAL ISSUES

The technique of dynamic SPECT was adapted for children by administering ^{133}Xe intravenously instead of by inhalation, and this does not induce significant changes in rCBF values (Chiron et al. 1992). It was compatible with stimulation tasks, whereas the classical static SPECT method using ^{99m}Tc-labelled tracers was not, because the image reflects the brain function limited to the time of the injection. The disadvantage of the dynamic SPECT method lies in the relatively low resolution of images which could explain why no focal rCBF defect and no asymmetry could be visually detected in our study. However, quantifying rCBF has made this technique sensitive enough to detect subtle changes, such as hemispheric asymmetry 'at rest', in more than 60 subjects (Gur et al. 1982, Chiron et al. 1995, Chiron et al. 1997).

The choice of the control group is a key point in functional imaging studies. In adults, control populations for PET and SPECT studies are rather easily obtained among normal volunteers. Such a practice is ethically and legally prohibited in healthy children because of the administration of a radioactive isotope. The only means of obtaining control values are to study an age-paired group with a different disorder (comparison group) (Tzourio et al. 1994) or to collect a population of children 'a posteriori' considered normal, which means a series of patients exhibiting transient neurological or apparently neurological events but who proved to develop normally later on (normal group). Both solutions were used for the present study. The normal rCBF values at rest were drawn from the only study performed in 39 children considered normal 'a posteriori', with the same SPECT procedure (Chiron et al. 1997). Due to no available data for children performing hemispheric tasks, we compared patients with dysphasia with a population with another disorder. Patients with dystrophia were selected because they also experience language disorders but the latter are different because they affect reading rather than oral language. Etiology is unknown for both disorders, so SPECT examination provides direct benefit to subjects with dystrophia as well as dysphasia. Children with dystrophia can, therefore, be considered as an adequate comparison group, both scientifically and ethically.

The stimulation tasks used in the present study could also be queried. There are relatively few validated tasks for hemispheric specialization. Using $^{15}O_2$ PET, functional MRI, and evoked potentials, several speech paradigms have been shown to predominantly activate the left hemisphere (Frith et al. 1991, Mazoyer et al. 1993, McCarthy et al. 1993) whereas face processing and selected spatial tasks activate the right hemisphere (Horwitz et al. 1992). However, none of these tasks has proved to be strictly lateralizing and very few have been validated in children (Tzourio et al. 1992, Dehaene and Dehaene 1994, Hertz-Pannier et al. 1997). For the present study we selected the classical paradigms used in neuropsychological evaluation, forced dichotic listening, and dichaptic recognition because they provided the highest lateralizing value in a normal population (Duvelleroy-Hommet et al. 1995), were feasible in children, and compatible with the SPECT procedure.

The type of response we used in the present series implicates visual modality. It could explain the predominant activation found in the visual associative area, namely the TO region. It could also sustain the left to right differences we observed in this region, i.e. left activation by visually recognizing digits and right activation by visually recognizing nonsignificant shapes.

Conclusion

The present study shows lack of rCBF predominance in the left hemisphere at rest in children with developmental dysphasia. This could be partly related to a lack of anatomical asymmetry in favor of the left hemisphere, a feature considered as a biological marker for specific developmental disorders of language. Functional brain activation is different in children with dysphasia and dystrophia but consistent with the relative neuropsychological disorders. The lack of left activation on the dichotic task and the lack of lateralization on the dichaptic task show that the functional specialization of both hemispheres is impaired in dysphasia. The predominant involvement of Broca's area in abnormal responses to the dichotic task suggests that left-hemisphere dysfunction is not complete but has a regional component. In children with Duchenne muscular dystrophy, a population without any oral expression impairment, the brain areas activated are consistent with the hemispheric tasks performed. Surprisingly, these patients also show a lack of hemispheric asymmetry at rest, which needs further investigation.

Accepted for publication 29th January 1999.

Acknowledgements
This study was supported by a grant from Recherche et Partage. We are indebted to Dr Chevrie-Muller who prepared and validated the tape of dichotic listening, Pr O Dulac for his advice in reviewing the paper, and AFM, the Centers of rehabilitation, the children and their families who participated in the study.

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