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The right brain hemisphere is dominant in human infants

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Summary

The development of functional brain asymmetry during childhood is confirmed by changes in cerebral blood flow measured at rest using dynamic single photon emission computed tomography. Between 1 and 3 years of age, the blood flow shows a right hemispheric predominance, mainly due to the activity in the posterior associative area. Asymmetry shifts to the left after 3 years. The subsequent time course of changes appear to follow the emergence of functions localized initially on the right, but later on the left hemisphere (i.e. visuospatial and later language abilities). These findings support the hypothesis that, in man, the right hemisphere develops its functions earlier than the left.

Keywords : hemispheric specialization; cerebral functional imaging; SPECT; child; brain development

Abbreviations: mCBF = hemispheric mean cerebral blood flow; OM = orbitomeatal (level); rCBF = regional cerebral blood flow; SPECT = single photon emission computed tomography

Introduction

Despite the apparent symmetrical anatomical appearance of the two cerebral hemispheres in humans, many asymmetries have been demonstrated ever since Broca first reported the left-sided dominance for language function (Broca, 1861). Several structures are anatomically asymmetrical: the planum temporale, the parietal opercule and the pars opercularis of the frontal lobe ('Broca's region') are larger in the left than in the right hemisphere in most right-handed subjects (Geschwind and Levitsky, 1968; Geschwind and Galaburda, 1985). These asymmetries are reflected at the structural level: the extent of higher-order dendritic branching is greater in 'Broca's area' than in the homologous area of the right hemisphere (Scheibel *et al*., 1985).

Hemispheric asymmetry also has a functional component since different regions of the brain are lateralized and specialized for different cognitive processes. A much debated question is 'At what point in time does functional asymmetry develop?' Lenneberg (1967) hypothesized that the two hemispheres are equipotential for language until ~2 years of age, at which time left dominance begins to develop gradually until puberty. Further studies contradicted this theory showing that children with left or right injuries acquired before 6 months of age displayed different deficits in language abilities (Witelson, 1987; Thal *et al*., 1991). An earlier development of the right hemisphere was first suspected in EEG studies of development (Grey Walter and Dovey, 1947, quoted by Rey *et al*., 1949), and it was later used in the phylogenic hypothesis of 'right-hemisphere conservatism': the right hemisphere sustains the functions necessary to the survival of species, like visuospatial and emotional abilities, which are less likely to be impaired if they develop early during a short period of time (Geschwind and Galaburda, 1985). According to this hypothesis, the period of vulnerability would be more prolonged in the left hemisphere, accounting for the more frequent left than right sided post-epileptic lesions (Rey *et al*., 1969). Indeed, brain damage would be more likely to affect the left hemisphere still undergoing rapid maturation than the right one which has already reached a high level of maturation. In temporal lobe epilepsy, Taylor (1969) showed a transient left hemisphere vulnerability in early life and suggested this reflected a difference of development pace. However, some authors have argued that the left hemisphere develops earlier, particularly in language areas (Corballis and Morgan, 1978). In fact, such a proposal is not in contradiction with the 'right-

hemisphere conservatism hypothesis' since we can imagine that hemispheres develop at a different speed from area to area. Further studies provide growing evidence that, during the course of foetal development, certain areas of the right hemisphere mature more quickly than homologous areas in the left hemisphere (Turkewitz, 1988; De Schonen and Mathivet, 1989; Hellige, 1993). For instance, a right dominance for the identification of faces in infants has been shown as early as 4 months of age (De Schonen and Deruelle, 1991). Additional neurobiological arguments have been reported: folds surrounding the sylvian region, like high-order dendritic branches, appear earlier on the right side than on the left (Chi *et al.*, 1977; Simonds and Scheibel, 1989).

Functional asymmetry between left and right human cerebral hemispheres has been studied mostly within the context of cognitive functions with a variety of methods including dichotic listening (Berlin *et al.*, 1973), evoked potentials related to auditory stimuli (Dawson *et al.*, 1989), regional cerebral blood flow (rCBF) changes using PET (Petersen *et al.*, 1988; Posner *et al.*, 1988), and more recently with functional MRI (fMRI) during sensory activation and cognitive tasks (Belliveau *et al.*, 1991; Le Bihan *et al.*, 1993; McCarthy *et al.*, 1993). A certain level of functional hemispheric asymmetry is also detectable at rest by measuring both phase coherence in the EEG and rCBF with single photon emission computed tomography (SPECT), measures that reflect corticocortical connectivity and local neuronal activity, respectively. In right-handed adults and school-age children, the left hemisphere reveales higher phase coherence and higher blood flow than the right (Gur *et al.*, 1982; Thatcher *et al.*, 1987).

During brain development, rCBF values exhibit dramatic changes, similar to those reported for local cerebral glucose utilization measured by PET (Chugani *et al.*, 1987; Chiron *et al.*, 1992). The rCBF rises higher in the first decade than that in the adult, and then declines to reach adult values at the end of the second decade. Because this time course matches that of initial overproduction and subsequent elimination of excessive axons, dendrites and synapses known to occur during cerebral maturation, rCBF is considered an appropriate parameter for study of the developing human brain (Chugani *et al.*, 1987; Chiron *et al.*, 1992).

To study the hypothesis of 'differential rates of hemispheric maturation', we measured the functional development of the left and right cerebral hemispheres in children from birth to adulthood by measuring absolute values of rCBF at rest using SPECT.

Patients and methods

Recruitment of the subjects

Data on rCBF were collected in children suffering from transient abnormal symptoms in which cerebral imaging was needed in order to confirm the integrity of the brain (Table 1). All subjects had a normal neurological examination, EEG and CT scan at the time of the investigation; children with any evidence of cerebral lesion, epilepsy, or abnormal brain development were excluded from the study. SPECT examination was considered as part of their clinical evaluation. In all cases informed consent was obtained from either the parent or guardian following a full explanation of the investigative procedures. The study was also approved by the Ethical Committee of The Cochin Hospital and was designed according to the guidelines set by the French Atomic Energy Commission.

Among these children, we selected those who were further proved to be right-handed and were subsequently found to have normal neurological examination and normal psychomotor development on at least 2 years follow-up.

Subjects

A total of 39 subjects, reasonably representative of normal children, (19 males and 20 females) were recruited for this study. Clinical signs at the time of SPECT investigation are shown in Table 1. They all had normal EEG and cerebral CT, had exhibited no epileptic seizure and were free of any medication. Ages ranged from 18 days to 19 years. Twenty-seven have previously been described in a paper reporting normal age-related CBF values, but these were expressed in terms of pooled data from left and right hemispheres without any details about the absolute values on each side (Chiron *et al.*, 1992).

Handedness assessment

Handedness was assessed according to the inventory of Dellatolas *et al.* (1988). Parents were asked to indicate the hand preference of their child for each of the 10 items of the questionaire as 'right' (R), 'left' (L) or 'either hand' (E). A score of 0, 1 or 2, respectively was given for each right, either hand, or left-hand answer, respectively. A handedness score was obtained for each individual by adding these item scores together. The subjects were classified as right-handed or left-handed, taking the mid-point of the population handedness scores as cut-off.

SPECT investigation

SPECT was performed using a highly sensitive tomographic system specifically dedicated to the brain, TOMOMATIC 564 (Medimatic), which provides five contiguous axial slices, 20 mm thick, from level OM (orbitomeatal) +20 to +100 mm (Fig. 1), with a spatial resolution of 12 mm. The rCBF was assessed by the dynamic SPECT technique using ^{133}Xe as the tracr (Lassen, 1985). In this technique tomographic imaging is performed during the washout of ^{133}Xe. Because ^{133}Xe is metabolically inert and freely diffusable, its disappearance from a brain region is a function of blood flow to that region. Absolute values can be measured by using the Celsis algorithm (Celsis *et al.*, 1981) The children under 5 years received premedication of 4 mg/kg of rectal pentobarbital and of 0.5

Table 1 *Individual characteristics and CBF-values*

Age	Sex	Clinical signs	mCBF		Frontal		SM		Broca's		Auditory		PPT		UPTO	
			L	R	L	R	L	R	L	R	L	R	L	R	L	R
18 days	F	Sleep myoclonia	37	35	29	31	42	39	36	32	49	45	38	35	33	32
1.5 months	F	Cutaneous angioma	40	41	30	34	41	49	50	49	44	50	35	40	59	52
1.5 months	M	Sleep myoclonia	46	48	40	39	48	51	51	47	49	50	41	46	46	48
2 months	M	Cutaneous angioma	51	49	41	40	61	59	49	45	62	55	53	50	56	52
2 months	F	Cutaneous angioma	58	58	47	41	73	78	70	61	66	72	62	60	60	64
3 months	M	Cutaneous angioma	54	50	51	45	66	62	61	53	62	49	55	52	52	51
3 months	F	Cutaneous angioma	42	42	35	35	46	47	42	43	50	46	42	38	44	41
4 months	M	Cutaneous angioma	60	68	57	53	69	83	62	74	60	74	65	66	62	72
4.5 months	F	Cutaneous angioma	53	43	49	38	60	48	57	44	56	43	55	44	52	44
6 months	M	Cutaneous angioma	52	54	43	42	61	61	56	62	62	72	59	63	50	56
7 months	F	Oesophagitis	53	52	47	55	63	55	55	45	62	58	56	53	53	55
9 months	M	Febrile convulsion	58	54	51	47	59	54	53	48	62	63	64	60	56	61
10 months	F	Cutaneous angioma	66	63	57	55	78	73	75	71	73	61	65	63	65	52
12 months	M	Cutaneous angioma	61	64	54	51	67	70	65	59	67	64	66	68	60	66
13 months	F	Cutaneous angioma	56	58	52	52	63	64	62	60	55	50	58	62	51	54
14 months	F	Cutaneous angioma	69	82	53	62	72	79	78	72	81	87	78	100	73	92
14.5 months	M	Cutaneous angioma	68	72	62	56	75	80	77	57	66	85	68	81	69	79
16 months	M	Febrile convulsion	56	55	46	45	64	62	63	69	57	60	56	58	55	54
17.5 months	F	Febrile convulsion	74	73	63	64	74	76	66	76	91	78	82	81	71	71
20 months	F	Cutaneous angioma	67	67	56	57	72	68	73	75	71	71	65	70	68	67
20 months	F	Opso-myoclonic syndrome	66	70	53	58	75	80	66	63	80	84	68	77	70	74
22 months	F	Opso-myoclonic syndrome	47	49	47	47	53	56	65	55	60	50	43	49	45	47
26 months	M	Opso-myoclonic syndrome	73	74	58	61	83	81	70	73	83	89	81	82	75	74
28 months	F	Cutaneous angioma	73	72	55	59	78	81	77	61	74	65	84	88	78	76
29 months	M	Febrile convulsion	55	60	53	51	60	61	55	59	54	65	55	62	51	59
31 months	F	Benign paroxysmal vertigo	63	68	55	55	65	70	66	64	68	74	63	76	61	61
3 years	M	Opso-myoclonic syndrome	69	66	60	63	70	66	68	70	79	75	68	48	58	59
3 years	M	Cerebellar cavernous angioma	72	74	61	61	78	72	76	67	76	86	74	70	66	69
3.7 years	F	Syncope	82	85	66	69	84	80	84	82	89	97	87	94	82	80
5 years	F	Cutaneous angioma	82	76	77	72	89	83	95	80	94	96	78	77	75	71
6 years	M	Benign choreo-athetosis	75	67	65	59	87	79	72	68	77	62	87	78	68	63
8 years	F	Syncope	77	72	65	62	81	72	82	70	83	78	76	75	68	66
10 years	M	Paroxystic dystonia	71	66	71	64	77	70	73	71	80	65	65	64	61	60
11 years	M	Syncope	66	65	62	62	65	69	88	59	63	65	64	63	61	62
11 years	F	Benign choreo-athetosis	65	66	59	60	70	67	78	76	73	73	63	66	59	56
12 years	M	Headache	64	62	59	59	74	70	76	73	64	58	63	59	60	57
12 years	M	Benign choreo-athetosis	75	70	66	56	87	75	81	75	74	74	78	71	76	70
16 years	F	Arachnoid cyst	51	48	44	45	49	47	54	48	52	51	55	46	50	47
19 years	M	Benign choreo-athetosis	50	52	47	48	52	53	55	52	48	52	53	55	49	51

mCBF = mean CBF across hemisphere; SM = sensorimotor; PPT = plurimodal parieto-temporal; UPTO = unimodal parieto-temporo-occipital; L = left; R = right.

mg/kg of intramuscular droperidol in order to avoid head movement during data acquisition, that is immediately following the injection in dynamic SPECT. Data acquisition lasted 5 min and was performed, at rest, according to a preestablished non-invasive procedure, with eyes closed and without any external stimulation (Chiron *et al.*, 1992). Radiation dose to the lung (the target organ for ^{133}Xe) was 2.5–4.5 mGy.

Definition of the studied regions

Images of rCBF were obtained on which a measure of CBF expressed in ml/min/100 g was performed in 20 circular cortical regions of interest per slice, including nine left, nine right and two median regions of interest (Fig. 1). The two median regions of interest were excluded from further calculations. The left and right cortical rCBF values were calculated in each hemisphere. Hemispheric mean CBF (mCBF) was taken as the mean value of the regions of interest localized on the three slices OM + 40, + 60 and + 80 mm, in the left and the right hemisphere. rCBFs were calculated on each side in six large cerebral regions defined according to Brodmann's areas and corresponding to frontal, sensorimotor, Broca's area, auditory area including Wernicke's area, plurimodal parieto-temporal and unimodal parieto-temporo-occipital cortex (Fig. 2).

Statistical analysis

The visual analysis of the curves representing left and right CBF values according to age suggests that the difference

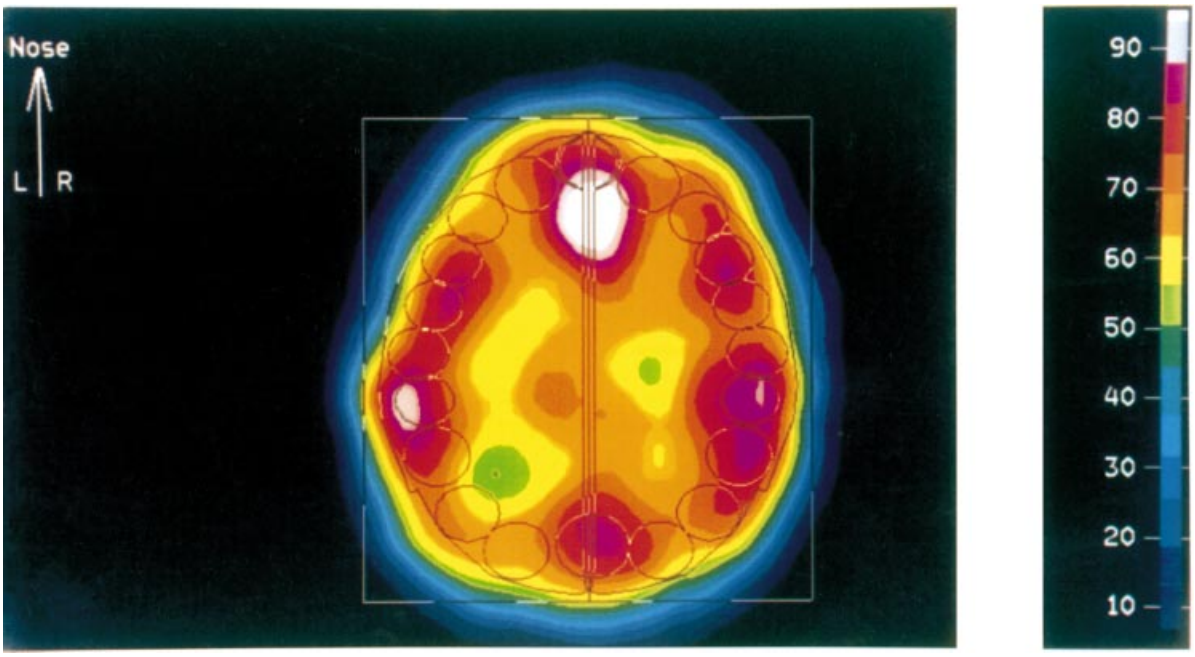

Fig. 1 Image of rCBF obtained at the level OM + 60 mm (60 mm over the orbitomeatal plane) using ^{133}Xe and dynamic SPECT. The colour scale represents the absolute values of rCBF expressed in ml/min/100 g. The circular regions of interest are symmetrically drawn by the computer on the cortical ribbon of each hemisphere.

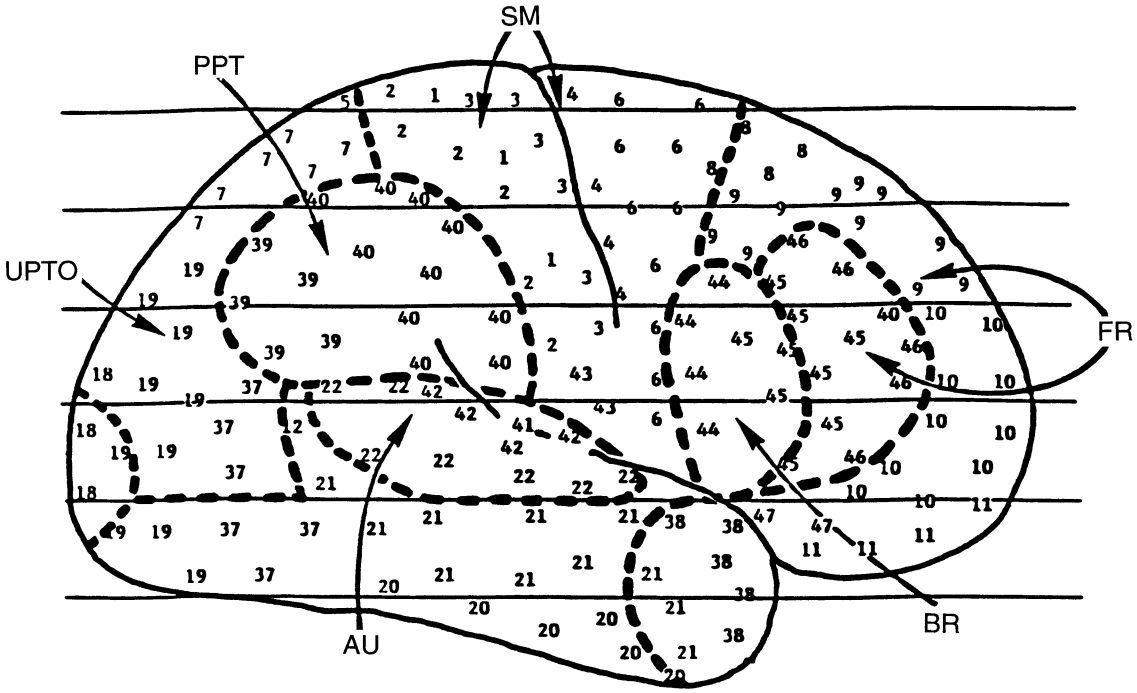

Fig. 2 Regions where the CBF was calculated. They were defined according to Brodmann's areas which are represented by numbers. FR = frontal; BR = Broca's area; SM = sensorimotor area; AU = auditory area; PPT = plurimodal parieto-temporal region; UPTO = unimodal parieto-temporo-occipital region.

between the two sides could change its sign during childhood (Fig. 3). In order to study such suspected age-related changes statistically, using the difference between left and right CBFs, we performed statistical analysis following three successive steps.

(i) The mean CBF values on the left were compared with those on the right in the overall population using a Wilcoxon test.

(ii) Because the difference between left and right CBF values seemed to change from birth to adulthood, we used a 'mean change-point test' (Hawkins, 1977) in order to determine at what ages these changes appear. The 'mean

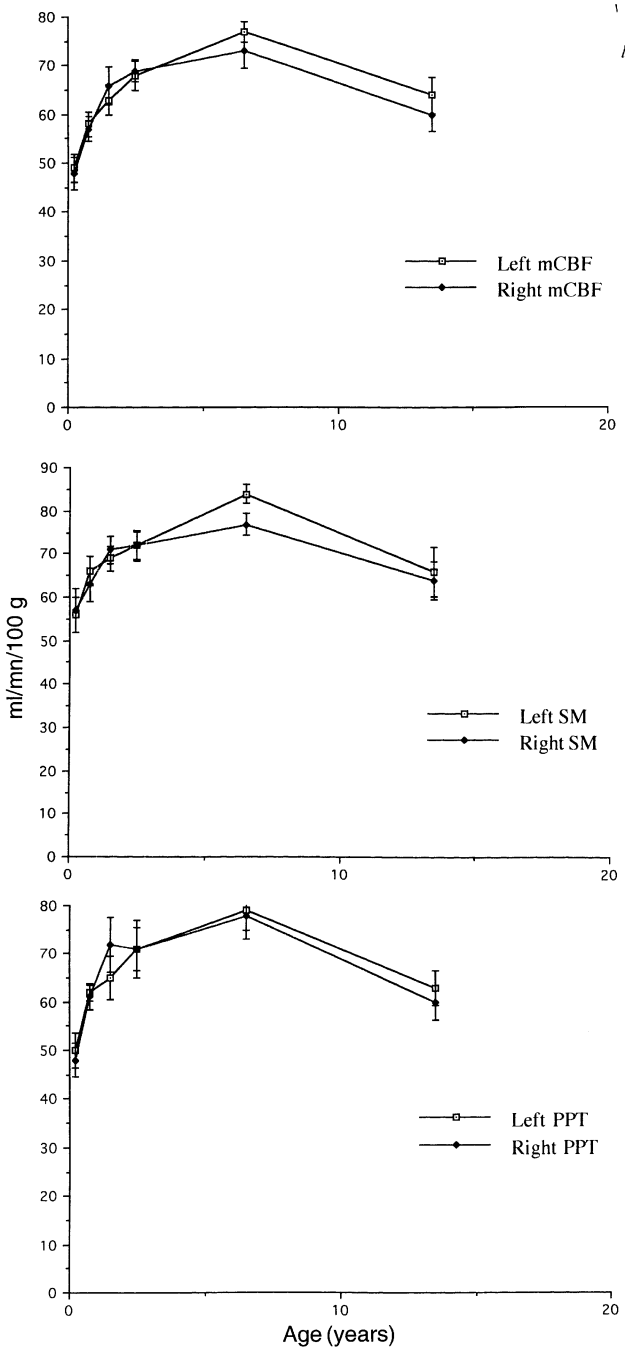

Fig. 3 Changes of the left and right CBF values with age in the whole hemisphere (mCBF), in the sensorimotor (SM) and the plurimodal parieto-temporal (PPT) regions. Two change-points had been found for mCBF, at 10 and 44 months, also two for PPT, at 12 and 31 months, and one for SM, at 31 months. In order to obtain visual evidence of such changes in the left–right differences of CBF values with age, curves of left and right CBF in the hemisphere, the PPT and the SM have been drawn here, using the mean of left and right CBF values, in age-groups as follows: patients from 15 days to 4.5 months (mean 2.4 months, $n = 9$); patients from 6 months to 1 year (mean 8.8 months, $n = 5$); patients from 1 to 2 years (mean 17 months, $n = 8$); patients from 2 to 3 years (mean 31 months, $n = 6$); patients from 3 to 10 years (mean 6.5 years, $n = 5$); patients from 10 to 19 years (mean 13.5 years, $n = 6$).

change-point test' aims to test the change in the mean of the differences between the left and the right CBFs (Table 1). The time intervals were determined by the ages of the children when they underwent CBF measures. For any one of the seven situations (mCBF and each rCBF), let X_i, ($i = 1$–39) be the difference and considered as independant gaussian variables. The test is based on the likelihood ratio. Depending on a fixed value of the change point, the '$2 \times \log_e$(likelihood ratio)' statistic is approximated by the law with two degrees of freedom, under the null hypothesis. We reject the null hypothesis (no change in the mean, this means that all variables X_i for any one of the seven situations have the same distribution) if the '$2 \times \log_e$(likelihood ratio)' is $\chi^2(0.05)$, i.e. >5.99 (*see* Table 2). When the test detected a change in mean, a second change-point test was performed on the two groups of variables X_i delineated under and over the change point, according to the same procedure (Table 3).

The test was completed by a non-parametric ANOVA (Kruskal–Wallis method; Hollander and Wolfe, 1973) to assess the significance of the changes in the mean left–right differences. The change-points detected represent, therefore, the ages at which the mean of the difference between left and right CBF values is significantly changing.

(iii) However, the 'change point' test does not indicate the sign of mean left–right difference. A Wilcoxon test was therefore performed again on the different groups delineated by the change points, in order to compare the mean of the left with the mean of the right CBF values in each group.

Results

In the overall population, there was no difference in CBF values between the two hemispheres, except for Broca's area where the mean value of rCBF on the left was significantly higher than that on the right ($P < 0.05$).

The change-point test showed the mean left–right CBF difference to be affected by age. The 'mean change point test' detected several change points in three regions, i.e. several ages at which the mean difference between the left and right CBF values are changing. Change points were found in hemispheric means at 10 and 44 months, in the sensorimotor area at 31 months and in the plurimodal parieto-temporal region at 12 and 31 months (Tables 2 and 3). Several time intervals were therefore delineated by the different change-points in these three regions. There were three time intervals for hemispheric means (18 days to 10 months, 12–44 months, 5–19 years), two time intervals for the sensorimotor area (18 days to 31 months, 3–19 years), and three time intervals for the plurimodal parieto-temporal region (18 days to 12 months, 13–31 months, 3–19 years). The left–right difference was statistically significant between all these groups ($P = 0.001$, Kruskal–Wallis test).

In order to determine which hemisphere showed the largest CBF in these different age-related groups, we compared the left and right CBF values (Table 1) using Wilcoxon test. Right CBF appeared to be higher than left earlier in life

Table 2 *Results of the first 'mean change point' test*

i	Corresponding age	mCBF (L–R)	SM (L–R)	PPT (L–R)
2	1.5 months	0.0119	0.8680	0.0077
3	1.5 months	0.0470	1.4782	0.1973
4	2 months	0.0012	0.9481	0.0164
5	2 months	0.0001	2.0083	0.0030
6	3 months	0.1669	1.1428	0.0733
7	3 months	0.1343	1.3492	0.2707
8	4 months	0.1704	5.0032	0.2210
9	4.5 months	0.2308	1.8077	1.1432
10	6 months	0.0760	1.8712	0.7273
11	7 months	0.1129	0.7595	1.0133
12	9 months	0.4093	0.3610	1.4557
13	10 months	0.7281	0.1198	1.7047
14	12 months	0.3447	0.3412	1.4735
15	13 months	0.1681	0.4875	1.0722
16	14 months	0.3625	1.3680	0.0021
17	14.5 months	0.8412	2.3213	0.2636
18	16 months	0.7217	2.1261	0.3308
19	17.5 months	0.6160	2.6834	0.2536
20	20 months	0.6376	2.1326	0.4937
21	20 months	1.2567	3.3577	1.1824
22	22 months	1.6817	4.3931	1.8079
23	26 months	1.9623	4.2175	1.8939
24	28 months	1.8253	5.4710	2.4206
25	29 months	3.2260	6.3240	3.5925
26	31 months	5.1828	8.9506*	6.6508*
27	3 years	4.3131	8.1012	2.4245
28	3 years	5.4449	6.5622	1.8568
29	3 years 8 months	7.4021*	5.8916	3.0620
30	5 years	5.0304	4.6116	2.9873
31	6 years	2.4460	2.9331	1.5735
32	8 years	1.3422	1.4001	1.5071
33	10 years	0.5222	0.6020	1.4591
34	11 years	0.4723	1.6443	1.4358
35	11 years	0.8203	1.5010	2.2769
36	12 years	0.5964	1.1470	1.7597
37	12 years	0.0119	0.0207	0.6796
38	16 years	0.2688	1.1397	0.0410

Individual values of $2 \times \log_e$(likelihood ratio). *See* footnote to Table 1 for abbreviations. *Values correspond to the change-points.

whereas left CBF was higher in older children (Fig. 3). The right values were significantly greater than the left ones between 1 and 3.5 years for hemispheric means (means on the right and left, 68.2 and 65.7 ml/min/100 g, respectively, $P = 0.007$), and between 13 months and 3 years for the plurimodal parieto-temporal region (means on the right and left, 73.8 and 66.8 ml/min/100 g, respectively, $P = 0.0016$). In contrast, the left values were significantly higher than the right ones, after 5 years for hemispheric means (means on the left and right, 67.6 and 64.4 ml/min/100 g, respectively, $P = 0.0025$), after 3 years for the plurimodal parieto-temporal region (means on the left and right, 70 and 66.6 ml/min/100 g, respectively, $P = 0.040$) and for the sensorimotor area (means on the left and right, 74 and 69.4 ml/min/100 g, respectively, $P = 0.002$). No left–right difference was detectable in the youngest subjects, i.e. before 1 year for hemispheric means or the plurimodal parieto-temporal region, or before 3 years for the sensorimotor area.

Discussion

The present data show that functional brain activity measured by the rCBF is greater in the right hemisphere than the left in human infants and shifts from right-to-left predominance during the fourth year of life. This changing asymmetry is due to the shift of a single region, the posterior associative area.

SPECT using ^{133}Xe is a method sensitive enough to detect cerebral asymmetry at rest, not only in adults (Gur *et al.*, 1982) but also in children (Chiron *et al.*, 1995). However, the absence of any CBF asymmetry detectable during the first year of life in this series suggests that the sensitivity of this method may be low in young infants. The technique was adapted for the youngest subjects by adding sedation and administering ^{133}Xe intravenously, changes that do not induce significant changes in rCBF values (Chiron *et al.*, 1992). Barbiturates decrease global metabolism in adults but do not induce any changes in regional repartition (Theodore *et al*, 1986). It is therefore unlikely that left or right rCBFs could

Table 3 *Results of the second 'mean change point' test*

i	Corresponding age	mCBF (L–R)	SM (L–R)	PPT (L–R)
2	1.5 months	0.2342	0.2365	0.1225
3	1.5 months	0.0548	0.4449	0.0046
4	2 months	0.3378	0.0973	0.2680
5	2 months	0.4017	0.4680	0.6740
6	3 months	1.3016	0.0515	1.3670
7	3 months	1.3741	0.0565	2.4668
8	4 months	0.1538	1.6890	2.6078
9	4.5 months	2.1305	0.0692	6.3347
10	6 months	1.7067	0.0409	5.5317
11	7 months	2.1315	0.2002	7.3584
12	9 months	3.6664	0.7549	10.1471
13	10 months	6.1200*	1.6890	12.6027
14	12 months	4.2310	1.2769	13.0569*
15	13 months	3.7760	1.2540	12.4749
16	14 months	0.6380	0.4297	4.4262
17	14.5 months	0.2673	0.1156	2.0865
18	16 months	0.4885	0.3227	2.3417
19	17.5 months	0.7968	0.2360	3.4410
20	20 months	1.0064	0.8615	3.1413
21	20 months	0.5144	0.3484	1.9116
22	22 months	0.3949	0.1710	1.4883
23	26 months	0.1208	0.6133	2.3666
24	28 months	0.8487	0.3901	2.8594
25	29 months	0.3149	0.6664	2.6979
26	31 months	0.0075		
27	3 years	0.3303		
28	3 years	0.2781		

Individual values of $2\times\log_e$(likelihood ratio). *See* footnote to Table 1 for abbreviations. *Values correspond to the change-points.

have been selectively modified by the premedication in our series.

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 children so that a normal control population *stricto sensu* is unobtainable in this age range. The only means to assess control values is to collect data from a population of children 'a posteriori' considered normal, that means a series of patients exhibiting transient neurological or apparently neurological events but who proved to develop normally. Two such challenging studies were performed and provided the unique 'historical' reference values for metabolism and CBF using [^{18}F]fluorodoxyglucose-PET and ^{133}Xe-SPECT (Chugani *et al.*, 1987; Chiron *et al.*, 1992, respectively).

Two other issues follow from the very stringent ethical limits on performing SPECT in children. First, since the population we were able to study was relatively small, it was not possible to detect any sex effect on rCBF asymmetry, a factor which is known to be strongly linked to hemispheric specialization (Taylor, 1969; Geschwind and Galaburda, 1985; Shaywitz *et al.*, 1995). Secondly, the usual assumption that increase in rCBF and in regional metabolism do reflect a maturity issue in humans depends on data obtained in different subjects investigated at different ages (Chugani *et al.*, 1987; Chiron *et al.*, 1992). However, the only longitudinal study showed that rCBF values increased similarly to normal values during the first year of life in the non-lesioned hemisphere of a patient with a unilateral malformation (Chiron *et al.*, 1991). This provides a strong argument to interpretate rCBF changes in terms of development.

The present study shows a previously unreported strong regional component for CBF asymmetry. Significant left to right rCBF differences were detected at rest in sensorimotor cortex, Broca's area and the posterior highly associative regions, which, interestingly, are serving the most lateralized functions, handedness and language. The fact that these functions are localized in the left hemisphere and that language is associated with structural asymmetry in the planum temporale may explain the left CBF superiority at rest in older children. However, if CBF asymmetry does change with age in certain regions, structural asymmetry is probably not its only cause.

It has been claimed that asymmetries of brain growth serve as an important mechanism for functional hemispheric asymmetries in later life. Based on a higher responsiveness of the developing hemisphere to the incoming sensory information (Turkewitz, 1988; De Schonen and Mathivet, 1989), different scenarios have been considered to explain left-hemispheric dominance for speech and fine movements and right-hemispheric dominance for global visuospatial

processes. The left rCBF predominance in the sensorimotor region that emerges at ~2.5 years of age is concordant with the usual development of right-handedness and fine motor skills at this age. In the plurimodal parieto-temporal region, a right dominance preceeds the left and rCBF asymmetry switches from right to left during the third year of life. The right-to-left sequence of asymmetry seems to be related to the consecutive emergence of functions dedicated first to the right (visuospatial abilities), and then to the left posterior associative cortex (language abilities). The age at which these functions develop, the first and the third year of life, is concordant with the ages at which the right CBFs and then the left ones become predominant.

These results lead to a new view of hemispheric specialization during the first years of life in man. Longitudinal studies using non-invasive investigations without any ethical limits will probably provide further evidence for the importance of early surrounding interactions in establishing lateralized functions.

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