

LEFT AND RIGHT HEMISPHERE CONTRIBUTION TO RECOVERY FROM NEGLECT AFTER RIGHT HEMISPHERE DAMAGE—AN [^{18}F]FDG PET STUDY OF TWO CASES

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Abstract—A 2- ^{18}F -Fluoro-2-Deoxy-D-Glucose (^{18}F)FDG and positron emission tomography (PET) study was performed in the acute and chronic phase of stroke in one patient with unilateral neglect due to a right hemispheric lesion. In the acute phase, severe neglect, as well as hypometabolism in both the right and in the left unaffected cerebral hemisphere, was demonstrated. At follow-up evaluation the patient showed an almost complete recovery from unilateral neglect. This was associated with a return of left hemisphere metabolism to normal values and partial metabolic recovery in the right hemisphere, where frontal and parietal areas remained functionally impaired. Another patient with an extensive right cerebral ischaemic lesion on CT and severe unilateral neglect was studied by PET in chronic phase. A severe metabolic depression in the left unaffected hemisphere and in the right cerebral areas spared by the lesion, was found. These data suggest that the remission of unilateral neglect might be associated to a functional metabolic recovery in both the undamaged left hemisphere and the unaffected regions of the right hemisphere.

INTRODUCTION

UNILATERAL SPATIAL neglect is typically produced by damage of the right cerebral hemisphere. The lesions, as assessed by pathological examination or CT scan, most frequently involve the inferior parietal lobe, but neglect may also occur after frontal or subcortical damage [33]. In most stroke patients neglect recovers over time. The size of the right-sided lesion is the main anatomical predictor of improvement: the smaller is the right-sided lesion, the better is recovery [16, 21]. A few studies using functional imaging methods for measurement of cerebral blood flow and metabolism have been recently performed in neglect patients with subcortical vascular lesions [2, 7, 27]. In these reports, the main finding, by means of a semiquantitative right/left hemispheric assessment, was a functional derangement (reduced blood flow or metabolism) in the cortex ipsilateral to the lesion, which appeared normal on CT. The follow-up study of VALLAR *et al.* [34] has shown that in patients with vascular right subcortical lesions, spontaneous recovery from neglect parallels the reduction of hypoperfusion, measured by SPECT, in the undamaged cortical regions of the right hemisphere. These few available data from neglect patients suggest, therefore, that a possible neural mechanism of recovery involves restoration of function in the undamaged regions of the right hemisphere. Studies in the monkey have shown that also the hemisphere contralateral to the lesion which has produced neglect

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may be involved in the recovery processes [11, 19, 36]. However, no quantitative data on regional cerebral function of the left hemisphere in behavioural recovery are available in man.

We measured glucose metabolism by 2-[^{18}F]-Fluoro-2-Deoxy-D-Glucose ([^{18}F]FDG) and positron emission tomography (PET) in two patients with unilateral neglect due to a right cerebrovascular lesion. One patient was studied longitudinally, in the acute and chronic phase, the other 4 months after the onset of stroke.

MATERIAL AND METHODS

Neuropsychological assessment

Visuo-spatial neglect was assessed by the following tasks: (1) circle cancellation [5]; (2) letter cancellation [13]; (3) sentence reading; (4) Wundt Jastrow illusion test [22]. In the cancellation tasks the patients were required to cross-out left- and right-sided targets by making use of the right hand. In the reading task the patients had to read aloud 10 newspaper headlines. Normal subjects have an errorless performance in the circle cancellation and reading tasks, while neglect patients typically make left-sided omission errors. In the letter cancellation task the maximum difference between left- and right-sided omission errors is 4 [22]. In the illusion test the patients were required to judge whether two black fans are or are not equal in length. The illusional effect, whereby one fan appears longer, is produced by either the left or the right half of the fan. Neglect patients fail to show the normal left-sided illusion effect.

PET method

[^{18}F]FDG PET studies were performed in resting state using a four ring whole-body positron emission tomograph (Siemens/CPS, 931-04/12). The scanner allows the simultaneous acquisition of data from seven axial planes (four direct and three cross planes), slice thickness 6.75 mm, covering an axial field of view (FOV) of 5.4 cm. The image spatial resolution for a line source in air, positioned in the centre of the field of view, was 6.1 Full Width at Half Maximum (FWHM) [31]. A transmission scan was taken, using ring sources of ^{68}Ge , to measure attenuation in the scanned cross-sections for later use in attenuation correction. Patients were positioned on the scanning bed, with the head symmetrically aligned along the orbitomeatal line, resting in an individually-made rigid polyurethane foam head mould. Patients were studied with open eyes, in a darkened, quiet room. Acquisition protocol consisted of blank and transmission scans for attenuation correction, tracer injection, and emission scan in the steady state condition. 250–300 MBq of [^{18}F]FDG were injected as a bolus, followed by a rapid arterial blood sampling to obtain the arterial input function. Arterial blood samples were collected every 2–3 sec in the first minute, then at 1.5, 3.0, 5.0, 7.5, 10, 15, 25, 35, 45 and 65 min from the injection time. Forty-five minutes from the tracer injection (steady state), two spatially consecutive emission scans (10 min each), needed to cover the whole brain, were acquired by an automatic software control of the bed position. Fourteen axial slices, parallel to the orbito-meatal line, were thus obtained. The blood samples were centrifuged for plasma separation and the radioactivity in the plasma was measured using a sodium iodide well counter. Images were reconstructed using a filtered back-projection algorithm with a Hann filter (cut-off frequency 0.5 cycles/pixel). The images were zoomed by a factor 3, resulting in an effective pixel size of 1.57 mm. Values of local cerebral metabolic rate of glucose (LCMRGlc) were calculated according to a model based upon the autoradiographic technique proposed by SOKOLOFF *et al.* [30] and revised by REIVICH *et al.* [29] for human PET studies.

Data analysis

Reconstructed images were analysed on SUN (SPARC) work stations. Image processing was performed with Analyze software (BRU/Mayo Clinic). Numerical data were obtained using circular regions of interest with a diameter corresponding to 1.5 FWHM (9.6 mm), manually drawn on all cortical and subcortical structures. Average values of LCMRGlc were calculated from the multiple ROIs included within the major anatomical subdivisions, which were identified making reference to an anatomical atlas [12]. These average values, corresponding to the 34 anatomical regions listed in Table 2 were used for statistical analysis. The same atlas was used to identify on the CT scans the damaged areas. These were excluded from the PET data analysis since reliable measures of glucose consumption are prevented by methodological problems related to LCMRGlc modelling in structurally damaged areas, such as in the case of infarction [3].

The LCMRGlc values of patients in acute and follow-up stages were compared with control values in seven normal subjects (age 51.28 ± 12.53). For each anatomical region, averaged LCMRGlc in neglect patients were considered pathological when outside 2 S.D. from averaged LCMRGlc of normal controls. The LCMRGlc values of Case 1 were submitted to an analysis of variance with two within-subject factors: time of assessment (initial and follow-up PET study) and hemisphere (right and left). In Case 1 the putamen and caudate structures were excluded from the analysis due to the presence of a right hemisphere haematoma. The cerebellum was not included due to the presence of

contralateral diaschisis. In Case 2, the amount of cerebral metabolic involvement was evaluated according to the number of regions of interest with LCMRGlc outside 2 S.D. from normal values.

Case reports

Case 1. A 65-year-old woman, with a long-lasting medical history of hypertension, was admitted to hospital on 4 March 1990, after the sudden onset of weakness of the left limbs. She was alert and co-operative. A neurological examination showed a left hemiplegia with increased deep tendon reflexes, left hemianaesthesia for touch and pain, and left homonymous hemianopia. The patient had 5 years of schooling, was right-handed on the Oldfield questionnaire (12/12), [25], and had no family history of left-handedness. A CT scan performed on the day of admission revealed a hyperdense lesion involving the right basal ganglia and internal capsule, interpreted as a cerebral haematoma (Fig. 1). No abnormalities were detected on doppler sonography. The patient was not aware of her neurological deficits and showed mild personal neglect. When tested for hemispatial neglect, 2 days later, she showed extrapersonal neglect in a number of visuo-spatial tasks (Table 1). The same day she underwent a [^{18}F]FDG PET study for the evaluation of regional cerebral metabolic rate of glucose (LCMRGlc). In this acute stage, an extensive reduction of metabolism in both cerebral hemispheres, more severe in the right affected side (with values below 2 S.D. the mean normal average of LCMRGlc) was demonstrated (Table 2; Fig. 2A).

A follow-up examination was performed 8 months later. The patient completely recovered from hemianaesthesia; hemianopia was no longer present, but visual extinction to double simultaneous stimulation was found. The motor deficit improved both in the upper and the lower limbs. Recovery from visuo-spatial neglect was virtually complete, with a minor residual deficit in the letter cancellation test (Table 1). Personal neglect and anosognosia were no longer present. A control CT scan showed a hypodense lesion in the right basal ganglia, corresponding to the outcome of the haematoma. Recovery of the bilateral cerebral metabolic depression was demonstrated on the second PET study (Table 2; Fig. 2B). LCMRGlc values below the cut-off score were still present in the right fronto-temporo-parietal areas, while an almost complete recovery of hypometabolism was demonstrated in the left, unaffected hemisphere. The analysis of variance showed significant main effects of hemisphere [$F=104.15$, d.f. = 1, 30, $P<0.0001$] and of time of assessment [$F=39.98$, d.f. = 1, 30, $P<0.0001$]. The interaction was also significant [$F=21.13$, d.f. = 1, 30, $P<0.0001$]. This was explored by a test of simple main effects. The difference between the two hemispheres was significant both at the first [$F=150.42$, d.f. = 1, 30, $P<0.0001$] and the second [$F=71.32$, d.f. = 1, 30, $P<0.0001$] PET study. The difference between the two assessments was significant both in the right [$F=6.41$, d.f. = 1, 30, $P<0.017$] and in the left [$F=69.50$, d.f. = 1, 30, $P<0.0001$] cerebral hemisphere. In right hemisphere the regions with LCMRGlc values (ml/100 g/min) below the 2 S.D. cut-off score were 32/32 in the first and 25/32 in the second PET examination [$\chi^2=7.86$, d.f. = 1, $P=0.005$]. In the left hemisphere, the regions with LCMRGlc values below the cut-off were 26/34 in the first and 7/34 in the second PET study [$\chi^2=21.25$; d.f. = 1; $P=0.001$].

Case 2. A 67-year-old man, with 17 years of schooling and a medical history of heavy smoking and untreated hypertension, suddenly developed a left-sided hemiparesis in September 1990 and was admitted to hospital. The patient was right-handed (12/12) at the Oldfield questionnaire [21]. A neurological examination revealed a left homonymous hemianopia, left supranuclear facial palsy and left hemiplegia. Touch and pain sensation were abolished on the left side and a steady right-sided deviation of the head and gaze was

also present. A large hypodense lesion corresponding to a cerebral infarct involving the right middle and posterior cerebral artery territory was found on CT scan. A neuropsychological evaluation revealed a severe extrapersonal visual neglect (Table 1). A mild anosognosia for hemiplegia was present.

At a 4-month follow-up examination the neurological deficits were unchanged. A large right cerebral hemispheric lesion, sparing the anterior cerebral artery territory, was confirmed on a control CT scan (Fig. 3). A neuropsychological evaluation showed the persistence of severe visuo-spatial neglect (Table 1). The patient was submitted to a [^{18}F]FDG PET study, which revealed a severe and widespread metabolic reduction in the left hemisphere and in the right frontal, unaffected regions: the left hemisphere regions with metabolic values below the cut-off score were 32/34 (Table 2).

DISCUSSION

Studies using PET and SPECT in patients with cerebrovascular disease have revealed a reduction of cerebral perfusion or metabolism in undamaged cerebral regions remote from the structural lesion [3]. The term "diaschisis", originally proposed by VON MONAKOW [24] on a clinical basis, is currently used to describe these distant effects attributed to neural deafferentation [15]. A few studies also investigated the relationships of this functional cerebral involvement with neurological and neuropsychological deficits [9, 23, 26–28].

The present cases show different metabolic patterns associated with different courses of spatial neglect. Case 1, who has a comparatively small subcortical lesion, displays a substantial, albeit not complete, recovery from neglect and neurological deficits. These behavioural changes were paralleled by an almost complete normalization of the severe hypometabolism, which, in the acute phase, was present both in the left and right hemisphere. The second PET study showed, however, a persistent hypometabolism in areas which belong to networks involved in spatial representation, such as the right fronto-parietal and thalamic regions [32]. A parallel between behavioural recovery and reduction of hypometabolism in the hemisphere contralateral to the lesion has not been reported so far. On the other hand, the observation of a reduction of diaschisis in the unaffected right occipital and temporal areas in Case 1 is consistent with previous findings, which have suggested a role of the undamaged regions of the right hemisphere in the recovery processes [34]. The complete recovery of glucose metabolism in the right primary visual areas parallels regression of hemianopia (see comparable data in Ref. [8]). Case 2, who has an extensive cortico-subcortical lesion, associated with persistent neurological deficits and severe neglect, showed a profound metabolic depression, involving not only the right cerebral areas spared by the lesion [27, 34], but also the whole of the left hemisphere.

The results in our patients suggest, therefore, that restoration of metabolism not only in the undamaged regions in the right hemisphere, but also in the left hemisphere, may contribute to recovery from spatial neglect.

Animal experiments provide support for the view that both the contralateral and the ipsilateral damaged hemisphere are involved in the recovery processes. CROWNE *et al.* [11] found that lesions of the frontal eye field produce a contralateral visuo-motor deficit, which recovers over time. A successive callosal section brings about a worsening of the deficit, suggesting a role of the undamaged hemisphere, via the callosal commissures, in the recovery process. However, the deficit produced by the callosal section also lessens over time. This suggests that the integrity of the callosal pathways is not crucial for recovery, which is likely to

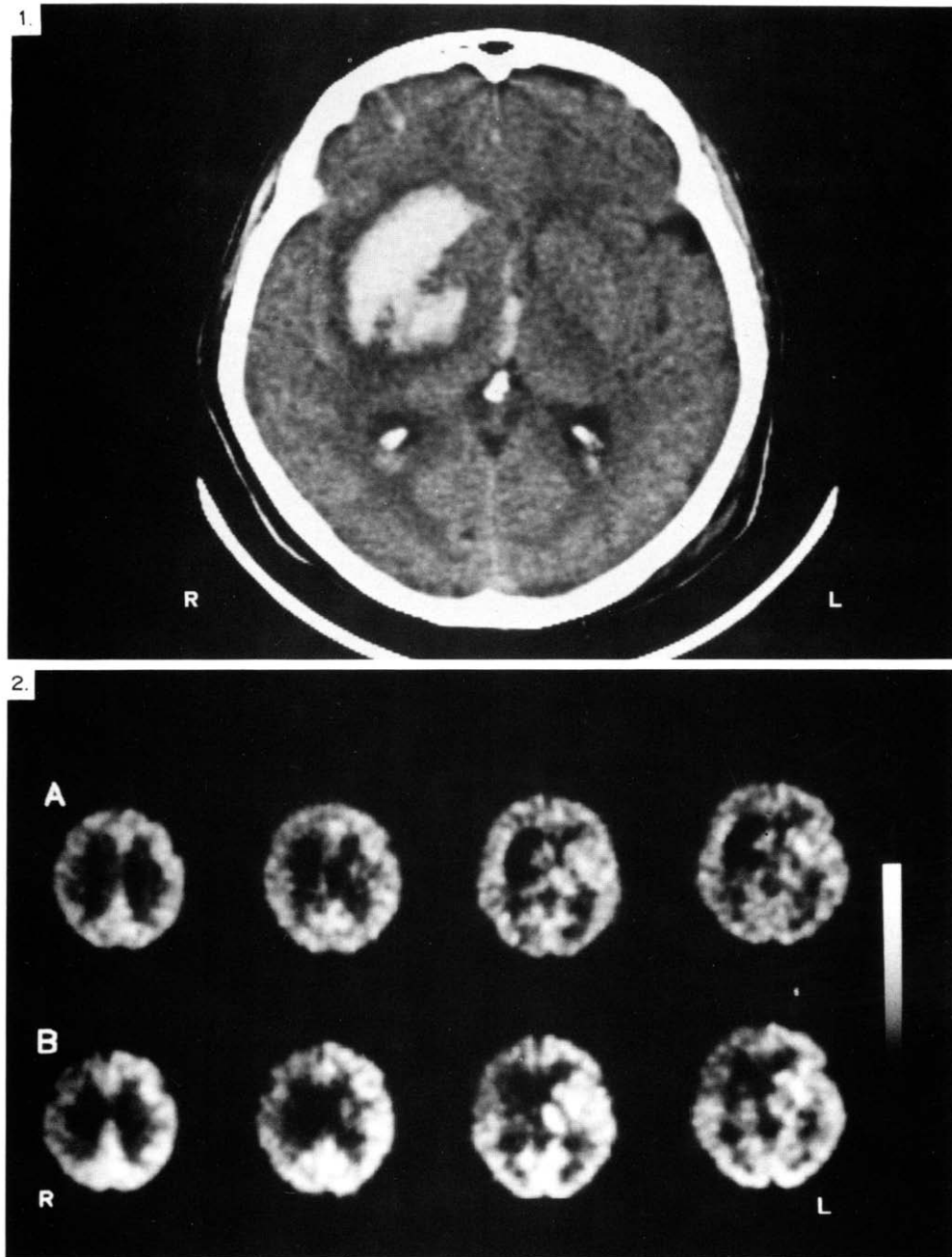


Fig. 1. Case 1. CT images showing a capsulo-lenticular haematoma.

Fig. 2. Case 1. (A) [^{18}F]FDG PET (axial slices) in acute phase showing bilateral cerebral hypometabolism, more severe in the right affected hemisphere. (B) [^{18}F]FDG PET in chronic phase showing the complete metabolic recovery in the left hemisphere and in the posterior cortical areas of the right hemisphere, where residual hypometabolism is present in the frontal and parietal regions.

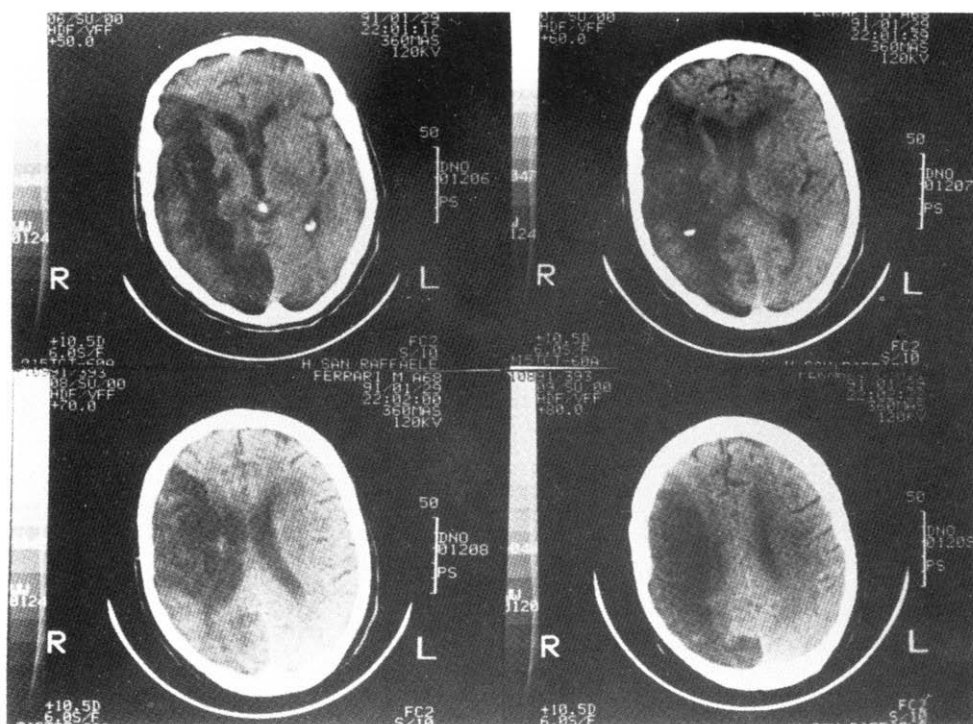


Fig. 3. Case 2. CT images showing a large ischaemic lesion involving the right middle cerebral artery territory and the right occipital lobe.

Table 1. Case 1. (A) Performance in tasks assessing visuo-spatial neglect in the first (I) and follow-up (II) assessments. The scores are left-sided errors. The patient did not make right-sided errors. (B) Contralateral (left) neurological deficits on a standard neurological examination [4]. Score: 0 (normal), 1/2/3 (mild, moderate, severe deficit). In the case of somatosensory and visual half-field deficits score 1 indicates contralateral extinction to double simultaneous stimulation. (C) Anosognosia for motor and visual half-field deficits; score 0-3 (absent-to-severe) [6]; n.c.: not examined due to recovery from the neurological deficit

Case 1. Test	I	II
(A) Visuo-spatial neglect		
Circle cancellation	3/6	0/6
Letter cancellation	31/53	7/53
Sentence reading	3/10	0/10
Wundt-Jastrow illusion test	6/20	0/20
(B) Neurological deficit		
Motor		
Upper limb	3	2
Lower limb	3	2
Somatosensory		
Upper limb	3	0
Lower limb	3	0
Visual half field		
Upper quadrant	2	1
Lower quadrant	3	1
(C) Anosognosia		
Motor deficit		
Upper limb	3	0
Lower limb	3	0
Somatosensory deficit		
Upper limb	3	n.c.
Lower limb	3	n.c.
Case 2. Test	I	II
(A) Visuo-spatial neglect		
Circle cancellation	6/6	6/6
Letter cancellation*	91/104	64/104
Sentence reading	3/10	10/10
Wundt-Jastrow illusion test	20/20	20/20
(B) Neurological deficit		
Motor		
Upper limb	3	3
Lower limb	3	3
Somatosensory		
Upper limb	3	3
Lower limb	3	3
Visual half field		
Upper quadrant	3	3
Lower quadrant	3	3
(C) Anosognosia		
Motor deficit		
Upper limb	1	0
Lower limb	1	0
Somatosensory deficit		
Upper limb	1	0
Lower limb	1	0

*In this task the patient failed to cross out letters in the left half of the sheet and in the left portion of the right half of the sheet.

Table 2. Local cerebral metabolic rate of glucose consumption (LCMRGlc) is expressed in ml/100g/min. The cerebral regions are labelled according to the atlas of DAMASIO and DAMASIO [12], with the corresponding Brodmann's areas in brackets

Regions	Normal controls		Case 1				Case 2	
	LH	RH	1st study		2nd study		PET study	
			LH	RH	LH	RH	LH	RH
F1	6.06 (0.80)	5.98 (0.63)	4.67*	3.82*	4.74*	3.97*	3.18*	2.80*
F2	7.22 (0.94)	7.31 (1.03)	5.08*	4.32*	4.36*	4.26*	4.44*	2.79*
F3	6.43 (0.71)	6.28 (0.60)	5.27	4.13*	5.65	4.14*	3.71*	3.09*
F4	6.21 (0.66)	6.10 (0.88)	4.37*	3.43*	5.00	3.46*	3.55*	2.76*
F5	6.57 (0.91)	6.54 (1.02)	4.86	4.18*	5.07	4.85	4.27*	3.50*
F6	6.37 (0.70)	6.51 (0.64)	4.44*	3.66*	5.31	2.70*	4.03*	#
F7	6.63 (0.60)	6.56 (0.71)	4.33*	3.43*	5.27*	2.82*	4.14*	2.46*
F8	6.57 (0.66)	6.59 (0.67)	4.66*	3.52*	5.77	2.95*	4.43*	#
F11	5.93 (0.62)	5.89 (0.67)	3.88*	3.02*	4.09*	2.96*	3.73*	2.85*
F12	5.96 (0.46)	5.88 (0.45)	4.30*	3.32*	4.47*	3.31*	3.63*	2.71*
P1	6.14 (0.44)	6.33 (0.61)	4.38*	3.42*	5.45	3.06*	3.98*	#
P2	6.48 (0.58)	6.59 (0.65)	4.81*	3.74*	6.04	3.63*	4.29*	#
P3	6.84 (0.89)	6.92 (0.62)	4.18*	3.85*	5.37	4.02*	4.79*	#
P4	7.61 (1.10)	7.54 (0.94)	5.15*	4.45*	5.93	5.28*	4.64*	3.45*
T3	5.70 (0.55)	5.69 (0.56)	4.10*	3.14*	4.95	3.41*	3.66*	#
T4	6.37 (0.63)	6.19 (0.60)	4.10*	3.16*	5.20	3.60*	3.88*	#
T5	5.10 (0.62)	5.06 (0.58)	4.25	3.36*	4.66	3.90*	3.43*	#
T6	5.90 (0.50)	5.78 (0.52)	4.38*	3.59*	5.68	4.58*	4.16*	#
T7	6.53 (0.42)	6.47 (0.71)	5.52*	4.35*	6.39	4.05*	4.99	#
T8	5.34 (0.46)	5.45 (0.49)	4.51	3.60*	4.80	3.81*	3.98*	#
T9	6.24 (0.57)	6.32 (0.53)	4.99*	3.95*	6.11	4.32*	4.36*	#
T10	4.49 (0.40)	4.32 (0.43)	3.07*	2.68*	3.70	3.47*	2.98*	#
T11	5.23 (0.66)	5.31 (0.58)	3.80*	3.40*	5.54	3.81*	3.83*	#
T12	4.34 (0.57)	4.25 (0.23)	3.48	2.86*	4.03	3.24*	3.05*	#
O1	7.08 (0.41)	6.90 (0.33)	4.23*	4.34*	5.44*	5.28*	4.26*	#
O2	7.35 (0.92)	7.31 (0.89)	5.19*	4.40*	6.88	5.95	5.13*	#
O3	5.90 (0.69)	5.80 (0.69)	4.04*	4.03*	4.88	5.03	3.95*	#
O4	6.42 (1.02)	6.48 (0.80)	4.16*	3.98*	5.79	5.17	4.04*	#
O5	6.42 (0.97)	6.55 (1.13)	4.70	4.19#	6.30	5.16	4.63	#
O1/2	7.84 (1.32)	7.62 (1.28)	5.35	4.82*	7.29	6.22	5.74	#
CAU	6.37 (0.59)	6.38 (0.56)	4.95*	#	5.30	#	3.85*	#
PUT	6.70 (0.71)	6.70 (0.65)	6.36	#	6.59	#	4.84*	#
THAL	6.32 (0.73)	6.44 (0.77)	4.59*	3.20*	5.45	2.12*	4.86	#
CBL	5.56 (0.68)	5.56 (0.62)	3.35*	4.73*	3.62*	5.30	2.90*	4.69

F1: anterior cingulate gyrus [24]; F2: posterior cingulate gyrus [23, 31]; F3: mesial supplementary motor area [6]; F4: pre-frontal regions [8–10]; F5: mesial rolandic regions [1–4]; F6: frontal operculum [44, 45]; F7: pre-frontal regions [8, 9, 46]; F8: lateral pre-motor [6] and rolandic [1–4] regions; F11: anterior orbital frontal region [10]; F12: posterior orbital frontal regions [11–13, 47]; P1: supramarginal gyrus [40]; P2: angular gyrus [39]; P3, P4: lateral and mesial superior parietal lobule [5, 7]; T3: anterior part of middle temporal gyrus [21]; T4: posterior part of middle temporal gyrus [37]; T5: anterior part of inferior temporal gyrus [20]; T6: posterior part of inferior temporal gyrus [37]; T7: auditory region [41, 42]; T8, T9: superior temporal gyrus anterior and posterior to auditory region [22]; T10, T11: mesial temporal regions [28, 36]; T12: polar temporal area [38]; O1/2: calcarine cortex [17]; O1, O2: infra and supra calcarine mesial occipital areas [18, 19]; O3: temporo-occipital junction [37, 36]; O4, O5: inferior and superior lateral occipital regions [18, 19]; CAU: caudate nucleus; PUT: putamen; THAL: thalamus; CBL: cerebellum; #: structural lesion.

be mediated by the undamaged regions of the lesioned hemisphere. In line with these findings, in monkeys with a partially recovered contralateral visual deficit produced by a lesion in the frontal eye fields, a second lesion in the contralateral frontal eye fields yields a worsening of the visual disorder [19].

The present observation of a reduced metabolism in the hemisphere contralateral to the

lesion is consistent with findings in patients with unilateral vascular lesions examined by PET in an early phase after stroke [1, 14, 17, 18, 20]. In the absence of other variables such as multiple bilateral lesions, large vessel occlusion, transtentorial herniation or drug effects, the contralateral functional depression associated with a unilateral lesion has been explained in terms of transhemispheric neuronal diaschisis [14, 18, 20]. This interpretation is supported by the observation that in baboons the anterior section of the corpus callosum produces a bilateral depression of cortical metabolism, mainly in the anterior regions [37]. The extent of transhemispheric diaschisis may in turn be related to the size of the contralateral lesion: larger lesions are more likely to disrupt interhemispheric callosal connection, therefore producing a more severe metabolic depression. In line with this view, Case 2, who had an extensive right cortico-subcortical lesion, showed a major hypometabolism in the left hemisphere, which did not recover over time. By contrast, in Case 1, who had a right subcortical haematoma, the cortex was undamaged on CT scan, but a severe reduction of metabolism was shown by PET. This right cortical metabolic depression may in turn have produced, through callosal connections, a comparatively minor left hemispheric diaschisis, which recovered over time. Also the site of the cerebral damage may be relevant: small lesions, if strategically located to disrupt the interhemispheric connections, may bring about a severe contralateral hypometabolism (see the experimental callosal sections of YAMAGUCHI *et al.*) [37].

The present study has shown a correlation between clinical and functional parameters: recovery from hemineglect and neurological deficits parallels the reduction of hypometabolism in both cerebral hemispheres. In the follow-up study, Case 1 showed neurological recovery and has a mild residual visuo-spatial neglect. The latter may be related to the persistent hypometabolism in the fronto-parietal and thalamic regions of the right hemisphere, which are known to be involved in visuo-spatial functions [27, 33]. These findings suggest that the regression of functional impairment in the left hemisphere contributes to the amelioration of neglect. However, a complete behavioural recovery requires a total regression of diaschisis in the undamaged regions of the right hemisphere. Accordingly, in Case 2 the severe diaschisis in the left cerebral areas, contralateral to a large right-sided lesion, may have prevented the takeover of neuropsychological functions by the left hemisphere.

The present suggestion of a bi-hemispheric contribution to recovery from neglect and neurological deficits is in line with recent PET findings in patients with hemispheric vascular lesions, who recovered from hemiplegia. Finger movements of the contralateral recovered hand activate a number of *bilateral* regions (sensorimotor, premotor, and inferior parietal cortex, cerebellum, etc.). By contrast, movements of the unaffected fingers activate mainly the contralateral hemisphere [10] (see also Ref. [35]). This suggests that recovery of motor function is mediated by a bilateral neural network.

Finally, the relative contribution of the two hemispheres may not be fixed, but vary over time. For instance, the role of the undamaged left hemisphere may be more important in an early phase after stroke, when the right hemisphere dysfunction is maximal. In a later recovery stage the role of the undamaged regions of the right hemisphere may become more and more relevant.

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REFERENCES

1. ANDREWS, R. J. Transhemispheric diaschisis: A review and comment. *Stroke* **22**, 943–949, 1991.
2. BARON, J. C., D'ANTONA, R., PANTANO, P., SERDARU, M., SAMSON, Y. and BOUSSER, M. G. Effects of thalamic stroke on energy metabolism of the cerebral cortex. *Brain* **109**, 1243–1259, 1986.

3. BARON, J. C., FRACKOWIAK, R. S. J., HERHOLZ, K., JONES, T., LAMMERTSMA, A. A., MAZOWER, B. and WIENHARD, K. Use of PET methods for measurement of cerebral energy metabolism and hemodynamics in cerebrovascular disease. *J. cereb. Blood Flow Metab.* **9**, 723–742, 1989.
4. BISIACH, E., CAPPA, S. F. and VALLAR, G. *Guida all'Esame Neuropsicologico*. Cortina, Milano, 1983.
5. BISIACH, E., LUZZATTI, C. and PERANI, D. Unilateral neglect, representational schema and consciousness. *Brain* **102**, 609–618, 1979.
6. BISIACH, E., VALLAR, G., PERANI, D., PAPAGNO, C. and BERTI, A. Unawareness of disease following lesions of the right hemisphere: anosognosia for hemiplegia and anosognosia for hemianopia. *Neuropsychologia* **24**, 471–482, 1986.
7. BOGOUSLAVSKY, J., MIKLOSSY, J., REGLI, F., DERUAZ, J.-P., ASSAL, G. and DELALOYE, B. Subcortical neglect: Neuropsychological, SPECT, and neuropathological correlations with anterior choroidal artery territory infarction. *Ann. Neurol.* **23**, 448–452, 1988.
8. BOSLEY, T. M., DANN, R., SILVER, F. L., ALAVI, A., KUSHNER, M., CHAWLUK, J. B., SAVINO, P. J., SERGOTT, R. C., SCHATZ, N. J. and REIVICH, M. Recovery of vision after ischemic lesions: Positron Emission Tomography. *Ann. Neurol.* **21**, 444–450, 1987.
9. BOSLEY, T. M., ROSENQUIST, A. C., KUSHNER, M., BURKE, A., STEIN, A., DANN, R., COBBS, W., SAVINO, P. J., SCHATZ, N. J., ALAVI, A. and REIVICH, M. Ischemic lesions of the occipital cortex and optic radiations: Positron Emission Tomography. *Neurology* **35**, 470–484, 1985.
10. CHOLLET, F., DI PIERO, V., WISE, R. J. S., BROOKS, D. J., DOLAN, R. J. and FRACKOWIAK, R. S. J. The functional anatomy of motor recovery after stroke in humans: A study with Positron Emission Tomography. *Ann. Neurol.* **29**, 63–71, 1991.
11. CROWNE, D. P., YEO, C. H. and STEELE RUSSEL, I. The effects of unilateral frontal eye field lesions in the monkey: Visual-motor guidance and avoidance behaviour. *Behav. Brain Res.* **2**, 165–187, 1981.
12. DAMASIO, H. and DAMASIO, A. *Lesion Analysis in Neuropsychology*. Oxford University Press, New York, 1989.
13. DILLER, L. and WEINBERG, J. Hemi-inattention in rehabilitation. The evolution of a rational remediation program. In *Advances in Neurology*, Vol. 18. Hemi-inattention and hemisphere specialization, E. A. WEINSTEIN and R. P. FRIEDLAND (Editors), pp. 63–82. Raven Press, New York, 1977.
14. DOBKIN, J. A., LEVINE, R. L., LAGREZE, H. L., DULLI, A. D., NICKLES, R. J. and ROWE, B. R. Evidence for transhemispheric diaschisis in unilateral stroke. *Arch. Neurol.* **46**, 1331–1336, 1989.
15. FEENEY, D. M. and BARON, J.-C. Diaschisis. *Stroke* **17**, 817–830, 1986.
16. HIER, D. B., MONDLOCK, J. and CAPLAN, L. R. Recovery of behavioral abnormalities after right hemisphere stroke. *Neurology* **33**, 345–350, 1983.
17. KUHL, D. E., PHELPS, M. E., KOWELL, A. P., METTER, E. J., SELIN, C. and WINTER, J. Effects of stroke on local cerebral metabolism and perfusion: Mapping by emission computed tomography of ¹⁸F-FDG and ¹³NH₃. *Ann. Neurol.* **8**, 47–60, 1980.
18. LAGREZE, H. L., LEVINE, R. L., PHDULA, K. J., NICKLES, R. J., SUNDERLAND, J. S. and ROWE, B. R. Contralateral flow reduction in unilateral stroke: Evidence for transhemispheric diaschisis. *Stroke* **18**, 882–886, 1987.
19. LATTO, R. and COWEY, A. Visual field defects after frontal-eye fields lesions in monkeys. *Brain Res.* **30**, 1–24, 1971.
20. LENZI, G. L., FRACKOWIAK, R. S. J. and JONES, T. Cerebral oxygen metabolism and blood flow in human cerebral ischemic infarction. *J. Cereb. Blood Flow Metab.* **2**, 321–335, 1982.
21. LEVINE, D. N., WARACH, J. D., BENOWITZ, I. and CALVANO, R. Left spatial neglect: effects of lesion size and premorbid brain atrophy on severity and recovery following right cerebral infarction. *Neurology* **36**, 362–366, 1986.
22. MASSIRONI, M., ANTONUCCI, G., PIZZAMIGLIO, L., VITALE, M. V. and ZOCCOLOTTI, P. The Wundt Jastrow illusion in the study of spatial hemi-inattention. *Neuropsychologia* **26**, 161–166, 1988.
23. METTER, J. F. Neuroanatomy and physiology of aphasia: evidence from positron emission tomography. *Aphasiology* **1**, 3–33, 1987.
24. MONAKOW, C. VON. Die Lokalisation im Grosshirn und der Abbau der Funktion durch kortikale Herde. *Wiesbaden: Bernmann*, 1914.
25. OLDFIELD, R. C. The assessment and analysis of handedness. *Neuropsychologia* **9**, 97–113, 1971.
26. OLSEN, T. S., BRUHN, P. and OBERG, R. G. E. Cortical hypoperfusion as a possible cause of subcortical aphasia. *Brain* **109**, 393–410, 1986.
27. PERANI, D., VALLAR, G., CAPPA, S. F., MESSA, C. and FAZIO, F. Aphasia and neglect after subcortical stroke. A clinical/cerebral perfusion correlation study. *Brain* **110**, 1211–1229, 1987.
28. PERANI, D., DI PIERO, V., LUCIGNANI, G., GILARDI, M. C., PANTANO, P., ROSSETTI, C., POZZILLI, C., GERUNDINI, P., FAZIO, F. and LENZI, G. L. Remote effects of subcortical cerebrovascular lesions: a SPECT cerebral perfusion study. *J. cereb. Blood Flow Metab.* **8**, 560–567, 1988.
29. REIVICH, M., ALAVI, A., WOLF, A., FOWLER, J., ARNETT, C., MACGREGOR, R. R., SHIUE, C. Y., ATKINS, H., ANAND, A., DANN, R. and GREENBERG, J. H. Glucose metabolic rate kinetic model parameter determination in humans: The lumped constants and rate constants for ¹⁸F-fluorodeoxyglucose and ¹¹C-deoxyglucose. *J. cereb. Blood Flow Metab.* **5**, 179–192, 1985.

30. SOKOLOFF, L., REIVICH, M., KENNEDY, C., DES ROSIERS, M. H., PATLAK, C. S., PETTIGRE, K. D., SAKURADA, O. and SHINOARA, M. The ^{14}C -deoxyglucose method for the measurement of local cerebral glucose utilization: theory, procedure and normal values in the conscious and anesthetized albino rat. *J. Neurochem.* **28**, 897–916, 1977.
31. SPINKS, T. J., JONES, T., GILARDI, M. C. and HEATIER, J. D. Physical performance of the latest generation of commercial positron scanner. *IEEE Trans. Nucl. Sci.* **35**, 721–725, 1988.
32. VALLAR, G. The anatomical basis of spatial hemineglect in humans. In *Unilateral Neglect: Clinical and Experimental Studies*, I. H. ROBERTSON and J. C. MARSHALL (Editors). Lawrence Erlbaum, London, in press.
33. VALLAR, G. and PERANI, D. The anatomy of unilateral neglect after right hemisphere stroke lesions. A clinical CT/Scan correlation study in man. *Neuropsychologia* **24**, 609–622, 1986.
34. VALLAR, G., PERANI, D., CAPPAS, S. F., MESSA, C., LENZI, G. L. and FAZIO, F. Recovery from aphasia and neglect after subcortical stroke: Neuropsychological and cerebral perfusion study. *J. Neurol. Neurosurg. Psychiat.* **51**, 1269–1276, 1988.
35. WEILLER, C., CHOLLET, F., FRISTON, K. J., WISE, R. J. S. and FRACKOWIACK, R. S. J. Functional reorganization of the brain in recovery from striato-capsular infarction in man. *Ann. Neurol.* **31**, 463–472, 1992.
36. WATSON, R. T., VALENSTEIN, E., DAY, A. L. and HEILMAN, K. M. The effect of corpus callosum lesions on unilateral neglect in monkeys. *Neurology* **34**, 812–815, 1984.
37. YAMACUCHI, T., KUNIMOTO, M., PAPPATA, S., CHAVOIX, C., RICHE, D., CHEVALIER, L., MAZOYER, B., MAZIERE, M., NAQUET, R. and BARON, J. C. Effects of anterior corpus callosum section on cortical glucose utilization in baboons. *Brain* **113**, 937–951, 1990.