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The Functional Nature of Cerebellar Diaschisis

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We report a patient who presented with transient clumsiness of his right hand due to a small hemorrhage in the left globus pallidus. Ten days later, positron emission tomography performed at rest showed decreased oxygen metabolism and blood flow at the site of the anatomic lesion and in remote areas such as the ipsilateral frontotemporoparietal cortex and the contralateral cerebellar hemisphere. Cerebellar hypometabolism has been ascribed to functional disconnection of the contralateral hemisphere from the cerebral cortex and has been termed crossed cerebellar diaschisis. One month later, positron emission tomography performed during unilateral motor activation (finger opposition) showed increased blood flow in the sensorimotor and supplementary motor areas contralateral to the hand engaged in the motor task. An at-rest study at this time showed resolution of the crossed cerebellar diaschisis observed acutely, but cerebellar asymmetry was demonstrated during performance of the motor task with the normal as well as with the previously paretic hand. Our activation study demonstrated cerebellar asymmetry in the chronic phase during a motor task, even though resting cerebellar blood flow was symmetrical. This observation reveals the dynamic, functional nature of crossed cerebellar diaschisis and may partially explain the lack of any clinical counterpart in functional studies of the cerebellum performed with the patient at rest. (*Stroke* 1990;21:1365–1369)

Cerebellar diaschisis contralateral to a supratentorial lesion was first described by Baron et al[1] in 1980 using positron emission tomography (PET) in a stroke patient. Interruption of cerebrocerebellar pathways, probably due to damage of the predominantly excitatory corticopontine projections, is considered to be the principal mechanism of this transneuronal cerebellar metabolic depression, although interruption of spinocerebellar pathways has also been implicated.[2]

Despite its name, crossed cerebellar diaschisis has characteristics that do not fit with the classical definition of diaschisis, which implies a functional phenomenon without structural change and which is reversible.[3] Crossed cerebellar diaschisis has been observed in diseases of slow onset, such as progressively enlarging tumors, or may persist or even worsen with time.[4] In this regard, it has been suggested that anterograde transneuronal degeneration is responsible for the irreversible component of the phenomenon, which then reflects secondary morphologic change. Nevertheless, recovery from crossed cerebellar diaschisis has been described in patients with cerebrovascular diseases, and the relative contributions of the two components, functional and structural, are not always obvious from static imaging. There are no clinical clues to the presence of secondary, irreversible cerebellar atrophy following cerebral hemispheric infarction.

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Case Report

We studied a 52-year-old man who presented with clumsiness of his right hand, followed by complete recovery the next day. Magnetic resonance imaging showed a small hemorrhagic lesion of the left globus pallidus (Figure 1). Cerebral angiography was normal. To evaluate the cerebral metabolic rate for oxygen ($CMRO_2$) and the cerebral blood flow (CBF), a dynamic PET oxygen-15 steady-state study[5,6] was performed 10 days after the onset of symptoms. The study was carried out with an ECAT 931/8/12 PET

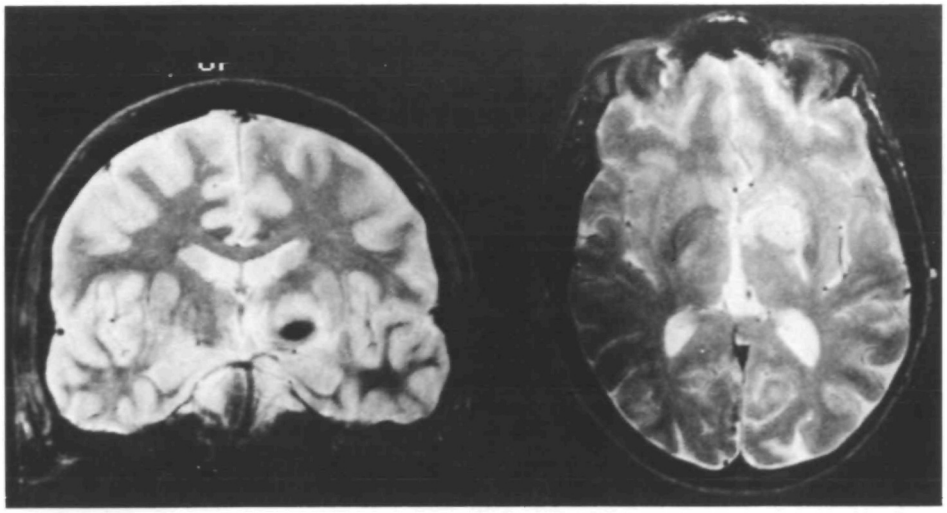

FIGURE 1. *Magnetic resonance images, coronal and transverse sections showing low T1 signal in left globus pallidus. Left side of body appears on right side of figure.*

scanner (CTI Inc., Knoxville, Tenn.) with an intrinsic spatial resolution of 6.5×6.5×7.0 mm full width at half-maximum (FWHM),[7] which allowed simultaneous collection of 15 contiguous transaxial planes. Reconstruction, attenuation correction (by measurement), and filtering resulted in an image with a resolution of 8.5×8.5×7.0 mm FWHM. The data set was then expanded by linear interpolation in the axial dimension to produce 43 transaxial slices with cubic voxels allowing three-dimensional visual inspection of the scans. The scans were analyzed on a computer (SUN 3/60, Mountain View, Calif.) with image analysis software (ANALYZE; Biodynamic Research Unit, Mayo Clinic, Rochester, Minn.) that allowed them to be scaled to standard stereotactic coordinates based on the atlas of Talairach et al[8] and to be displayed relative to the intercommisural line for precise anatomic localization.[9] At the cerebellar level, two irregular regions of interest comprising the entire cerebellar hemisphere were chosen. At the cerebral level, irregular regions of interest were drawn interactively on the areas of visually observed marked reductions of regional CBF. Values averaged from all planes were assigned to lobes and expressed relative to the global CBF obtained at each brain level from the remaining, normal brain areas to normalize the values and to allow comparison with subsequent measurements of CBF.

Performed with the patient at rest in a quiet, dimmed room, the dynamic PET study showed reduced $CMRO_2$ and CBF at the site of the anatomic lesion, in the ipsilateral frontotemporoparietal cortex, and in the contralateral cerebellar hemisphere (Figure 2). The asymmetries of CBF and $CMRO_2$ between the affected region and the homologous region in the unaffected hemisphere were −38% and −35% in the frontal cortex, −25% and −20% in the temporal cortex, and −30% and −20% in the parietal cortex, respectively. Our mean±SD values for right/left asymmetries in six normal volunteers in these three regions are −2.3±4.3%, 0±4.4%, and −2.3±3.9% for CBF and −1.9±3.6%, 0±3.2%, and −1.5±2.4% for $CMRO_2$, respectively. In the cerebellum, the left/right asymmetry was 27% for CBF and 19% for $CMRO_2$, well outside our normal range (0.3±4.6% and 0.1±3.5%, respectively).

After a month, the PET study was repeated during the performance of several motor tasks using $C^{15}O_2$ as a CBF marker in an attempt to elucidate the functional significance of the previously observed cerebellar asymmetry. CBF was measured using an integral/dynamic technique described elsewhere.[10,11] The study included acquisition of data at six 10-minute intervals during various states of physiological activation: A) at rest, B) during opposition of the right (recovered) fingers, and C) during opposition of the left (normal) fingers. The tasks were performed in the order ABCCBA to control for habituation and time-dependent effects. Thus, we compared the average of the two CBF measurements during each physiological state. During motor performance, CBF increased an average of 11.3% over that during the resting state in the sensorimotor and supplementary motor areas contralateral to the hand engaged in the motor task (Figure 3). The two at-rest measurements showed no significant cerebellar CBF asymmetry (5.8%). The cerebral cortical asymmetries seen in the 10-day study were also no longer apparent, with right/left ratios of −2.7%, −4.1%, and −3.3% in the frontal, temporal, and parietal cortices, respectively. However, a marked left/right cerebellar asymmetry, characterized by an increase in CBF in the left hemisphere, was revealed during the performance of the motor task with the normal (left, 19%) as well as with the previously paretic (right, 14%) hand (Figure 4).

Discussion

Our results suggest that crossed cerebellar diaschisis is a complex phenomenon. At rest, it frequently occurs during the early phase of stroke, probably due to acute cerebrocerebellar disconnection. The functional nature of crossed cerebellar diaschisis is underlined by its occurrence in patients with transient ischemic attacks, without any evident supraten-

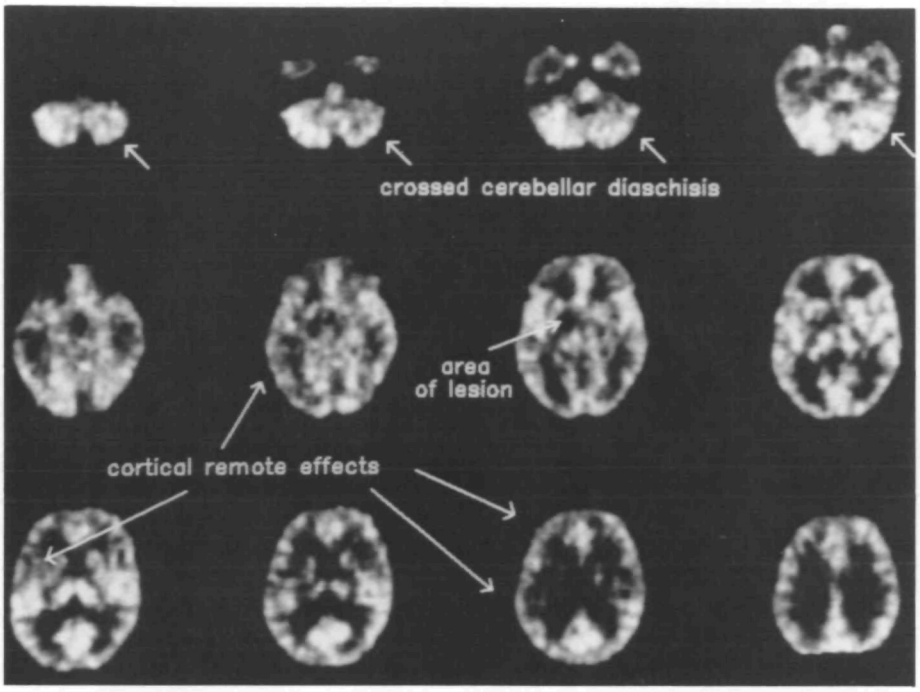

FIGURE 2. *Positron emission tomographic oxygen-15 steady-state study, showing reduced cerebral blood flow (CBF) at site of structural lesion and in remote regions such as ipsilateral frontotemporoparietal cortex and contralateral cerebellum (crossed cerebellar diaschisis). Cortex of normal cerebral hemisphere had CBF of 39.3 ml/100 ml/min and cerebral metabolic rate for oxygen of 3.5 ml O_2/100 ml/min. Values for lesion and left and right cerebellum were 24.0 and 1.6, 46.2 and 3.6, and 36.3 ml/100 ml/min and 3.1 ml O_2/100 ml/min, respectively.*

torial morphologic change.[12,13] Crossed cerebellar diaschisis often resolves with time, but the mechanisms of returning cerebellar metabolism to normal are still unknown.

Our activation study revealed the presence of cerebellar asymmetry of regional CBF during later stages when resting cerebellar CBF was symmetrical. This may partially explain reported findings of the lack of a clinical counterpart or an association with abnormal function in the cerebellum when the patient is studied at rest.

Our patient raises questions about the nature of "transient" crossed cerebellar diaschisis, which could merely reflect the lack of cerebellar hemispheric

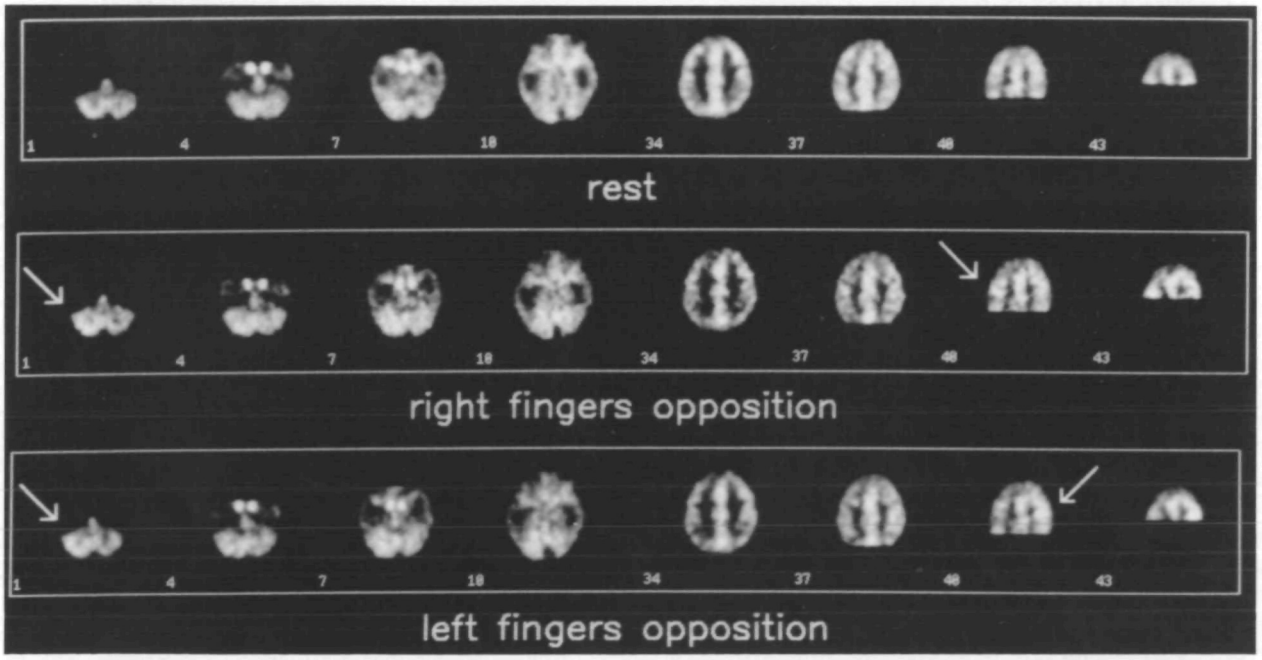

FIGURE 3. *Positron emission tomographic $C^{15}O_2$ dynamic study* (top row) *at rest showing absence of cerebellar blood flow asymmetry,* (middle row) *during right (previously paretic hand) finger opposition showing increase of cerebral blood flow in left sensorimotor and supplementary motor areas and in left cerebellar hemisphere (14%), and* (bottom row) *during left (normal hand) finger opposition showing increase of cerebral blood flow in right sensorimotor and supplementary motor areas and in left cerebellar hemisphere (19%).*

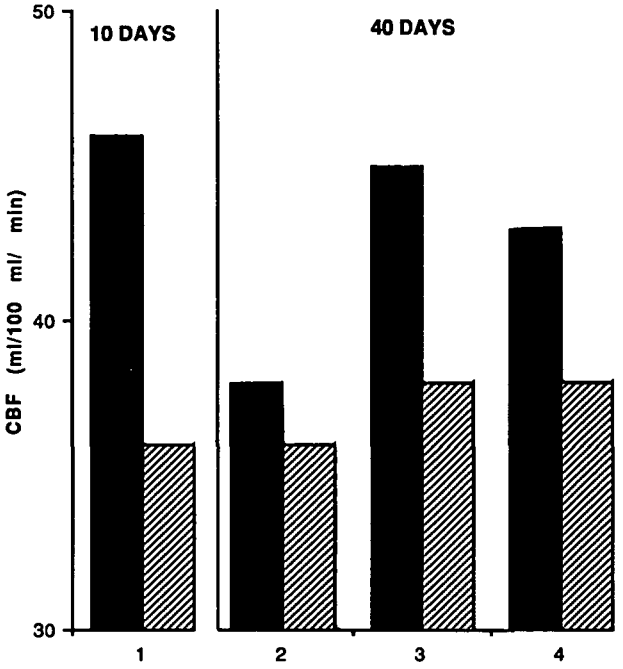

FIGURE 4. *Bar graph summarizing cerebral blood flow (CBF) asymmetries (filled bars, left; shaded bars, right) at cerebellar level in first positron emission tomographic study at rest (1) and in three physiological states during activation study (at rest, 2; with movement of normal left fingers, 3; and with the movement of recovered previously paretic right fingers, 4).*

asymmetry since the functional studies were performed at rest. We show that cerebellar asymmetry can be demonstrated in patients with lesions of the motor pathways by engaging the patient in motor tasks.

Hand movement increases regional CBF in the ipsilateral cerebellar hemisphere.[14-16] During focal ictal activity, there is transient cerebellar hyperperfusion contralateral to the cerebral epileptic focus.[17] Studies in normal and diseased humans indicate that the cerebellum responds to activation of the motor cortex in a very precise lateralized manner. In our patient, cerebellar asymmetry was elicited on the same side of the cerebellum (the left) by motor activity in the previously paretic, as well as in the contralateral unaffected, hand. Our findings suggest bilateral activation of the cerebellum during a lateralized motor task. The occurrence of reversed cerebellar asymmetry during performance of the task with the previously paretic, now recovered, hand indicates that the phenomenon might reflect the emergence of new, functional neuronal connections and/or cross-talk between the affected and unaffected cerebral hemispheres (at whatever anatomic level), causing bilateral cerebellar activation. Such a mechanism would result in a relative state of unbalanced afferent input to the cerebellar hemispheres, thus revealing the functional incompetence of cerebral efferent projections to the contralateral cerebellar hemisphere.

Cerebellar asymmetry during motor performance by the affected limb supports the notion that spinocerebellar input to the ipsilateral cerebellum plays a minor, if any, role in evoking a cerebellar functional response.

In conclusion, our observation confirms that crossed cerebellar diaschisis is mainly due to a disturbance of corticocerebellar input,[4] that spinocerebellar input is of little significance in the mechanisms underlying the phenomenon, and that recovery following stroke may be accompanied by functional rearrangements of neuronal connectivity that may compensate more or less adequately for the motor deficit. The correlation between crossed cerebellar diaschisis and clinical prognosis has been very poor; we suggest that PET scanning during motor activation will result in a better understanding of the significance of the phenomenon in relation to clinical outcome.

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References

1. Baron JC, Bousser MG, Comar D, Castaigne P: "Crossed cerebellar diaschisis" in human supratentorial infarction (abstract). *Ann Neurol* 1980;8:128
2. Biersack HJ, Grunwald F, Linke DB: Transient cerebellar diaschisis (letter). *Lancet* 1988;1:825
3. von Monakow C: Diaschisis (1914 article, Harris G [trans], in Pribram KH (ed): *Brain and Behaviour I: Mood States and Mind.* Baltimore, Penguin, 1969, pp 27–36
4. Feeney DM, Baron J-C: Diaschisis. *Stroke* 1986;17:817–830
5. Frackowiak RSJ, Lenzi GL, Jones T, Heather JD: Quantitative measurement of regional cerebral blood flow and oxygen metabolism in man using ^{15}O and positron emission tomography: Theory, procedure and normal values. *J Comput Assist Tomogr* 1980;4:727–736
6. Lammertsma AA, Jones T: Correction for the presence of intravascular oxygen-15 in the steady-state technique for measuring regional oxygen extraction ratio in the brain: 1. Description of the method. *J Cereb Blood Flow Metab* 1983;3:416–424
7. Spinks T, Guzzardi R, Bellina CR: Performance characteristics of a whole body positron tomograph. *J Nucl Med* 1988; 29:1833–1841
8. Talairach J, Szikla G, Tournoux P, Prossalentis A, Bordas-Ferrer M, Covello L, Iacob M, Mempel E: *Atlas d'anatomie stereotaxique du telencephale.* Paris, Masson et Cie, 1967
9. Friston KJ, Passingham RE, Nutt JG, Heather JD, Sawle GV, Frackowiak RSJ: Localisation in PET images: Direct fitting of the intercommisural (AC–PC) line. *J Cereb Blood Flow Metab* 1989;9:690–695
10. Lammertsma AA, Cunningham VJ, Heather JD, Nutt J, Frackowiak RSJ, Jones T: A combination of dynamic and integral analyses to obtain accurate functional images of rCBF (abstract). *J Cereb Blood Flow Metab* 1989;9(suppl 1):S582
11. Lueck CJ, Zeki S, Friston KJ, Deiber MP, Cope P, Cunningham VJ, Lammertsma AA, Kennard C, Frackowiak RSJ: The colour centre in the cerebral cortex of man. *Nature* 1989; 340:386–389
12. Pantano P, Lenzi GL, Guidetti B, Di Piero V, Gerundini P, Savi AR, Fazio F, Fieschi C: Crossed cerebellar diaschisis in patient with cerebral ischemia assessed by SPECT and ^{123}I-HIPDM. *Eur Neurol* 1987;27:142–148

13. Perani D, Gerundini P, Lenzi GL: Cerebral hemispheric and contralateral cerebellar hypoperfusion during a transient ischemic attack. *J Cereb Blood Flow Metab* 1987;7:507–509
14. Schwartzman RJ, Yu Y, Alexander GM, Greenberg J, Reivich M, Klose J: Quantitative 2-deoxyglucose mapping of the cerebellum. *Ann Neurol* 1979;6:165–166
15. Colebatch JG, Cunningham VJ, Deiber M-P, Friston KJ, Frackowiak RSJ, Passingham RE: Regional cerebral blood flow during unilateral arm and hand movements in human volunteers (abstract). *J Physiol* 1990;423:9P
16. Ginsberg MD, Chang JY, Kelley RE, Yoshii F, Barker WW, Ingenito G, Boothe TE: Increases in both cerebral glucose utilisation and blood flow during execution of a somatosensory task. *Ann Neurol* 1988;23:152–160
17. Duncan R, Patterson J, Bone I, Wyper DJ: Reversible cerebellar diaschisis in focal epilepsy. *Lancet* 1987;2:625–626

KEY WORDS • cerebral blood flow • diaschisis • tomography, emission computed