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Original Article

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ABSTRACT

Using high-resolution positron emission tomography (PET), we have recently described the normal pattern of glucose utilization in 11 anatomical regions of the human cerebellum. In the present study, we evaluated the phenomenon of crossed cerebellar diaschisis in 40 patients (mostly children) with unilateral cerebral injury sustained at various periods of brain development. Diaschisis refers to a functional impairment at a *remote* site following injury to an anatomically connected area of brain and, presumably due to a loss of afferent input to the remote site. Of the 40 patients, 11 had sustained their cerebral injury prenatally, 7 in the perinatal period (± 24 hours of birth), and 22 postnatally (1 day to 15 years). Crossed cerebellar hypometabolism was seen in 22 patients; symmetric cerebellar metabolism was found in 16 subjects. The presence of crossed cerebellar hypometabolism was typically associated (75% of cases) with a postnatal injury, while symmetric cerebellar metabolism was seen only in patients with injury occurring prior to 4 weeks of age (13 of the 16 had prenatal or perinatal insults). A third pattern of cerebellar metabolism, consisting of paradoxical crossed cerebellar *hypermetabolism*, was seen in two patients; both had sustained their cerebral injury at 4 months of age. These findings suggest the presence of considerable plasticity, which is dependent on age at injury, in the cerebrocerebellar pathway of developing brain. (*J Child Neurol* 1997;12:407–414).

In a recent study, we described the functional anatomy of the human cerebellum using high-resolution positron emission tomography (PET) of brain glucose utilization.[1] Our findings indicated that, in contrast to earlier studies with low-resolution PET that reliably identified only cerebellar hemispheres and vermis, technological advances in PET now allow the reliable identification of 11 anatomical regions in the cerebellum. Our description provided a guide for subsequent studies aimed at evaluating pediatric neurologic disorders affecting cerebellar function.

The present study was designed to evaluate the phenomenon of crossed cerebellar diaschisis in children with unilateral cerebral injury sustained at various periods of brain development. Diaschisis as defined by von Monakow refers to a *temporary* functional impairment at a *remote* site following injury to an anatomically connected area of brain and presumably due to a loss of afferent input to the remote site.[2] In functional neuroimaging studies either with PET or single photon emission computed tomography (SPECT), crossed cerebellar diaschisis consists of decreased glucose and oxygen metabolism or blood flow in the cerebellar hemisphere contralateral to the side of cerebral insult, and is well-described in adults who have suffered from cerebrovascular injury[3–7] or brain tumor.[5,8] Crossed cerebellar diaschisis is believed to result from a transneuronal disruption of the corticopontocerebellar pathway, the most important of cerebrocerebellar connections.[9] The term crossed cerebellar diaschisis was used by Baron et al[3] when they observed this phenomenon using PET, since their findings appeared to meet the strict definition of diaschisis. However, since their report, crossed cerebellar diaschisis determined with PET has been noted to be persistent in the vast majority of adults.[10–12]

There have been very few studies of crossed cerebellar diaschisis in children using PET scans. We reported previously that, of eight children with hemiplegic cerebral palsy due to prenatal or perinatal ischemic events resulting

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Table 1. Summary of Patient Data and Asymmetry Index (AI) in Transaxial Images

Patient No.	*Sex*	*Injury Side*	*Age at Insult*	*CT/MRI Findings (Location)*	*PET Findings*	*Age at PET*	*CD*	*HP*	*AI*
1	F	L	10 mo	Ventriculomegaly, parenchymal atrophy(FL, P,T)	FL, P,T	10.08	+	+	24.24*
2	F	R	15 yr	Ventriculomegaly, porencephalic cyst (FL,T), encephalomalacia (FL)	FL,T	19.08	+	+	−36.18*
3	M	L	4 yr	Hemiatrophy, ventriculomegaly, porencephalic cyst (FL, P,T)	FL, P,T	13.05	+	+	14.08*
4	F	L	Prenatal	Porencephalic cyst (FL, P,T)	FL, P,T, O	4.10	+	+	5.32*
5	M	R	8 mo	Hemiatrophy, ventriculomegaly, porencephalic cyst (FL, P), encephalomalacia (FL)	FL, P	16	+	+	−14.48*
6	M	L	Perinatal	Hemiatrophy, microcephaly	FL, P,T, O	8.02	+	+	8.82*
7	M	R	Perinatal	Hemiatrophy, ventriculomegaly, porencephaly (FL, P, O)	FL, P,T, O	1.09	+	+	−41.80*
8	F	R	Prenatal	Hemiatrophy, ventriculomegaly	FL, P,T, O	10.09	+	+	−34.64*
9	M	L	1 yr	Report not available	FL, P,T, O	4.09	+	−	7.26*
10	M	L	2 yr	Hemiatrophy, ventriculomegaly, cerebellar atrophy (right side)	FL, P,T, O	30.03	+	+	8.00*
11	F	R	1 yr	Hemiatrophy	FL, P,T, O	9.05	+	+	−10.21*
12	F	L	Perinatal	Porencephalic cyst (FL, P,T)	FL, P,T	9.04	+	+	26.46*
13	F	L	4 mo	Hemiatrophy, porencephalic cyst (FL, P,T)	FL, P,T	3.01	+	+	7.35*
14	F	R	5 yr	Report not available	FL, P,T	16.03	+	+	−43.53*
15	F	L	9 yr	Hemiatrophy, ventriculomegaly	FL, P,T, O	13.11	+	+	10.86*
16	M	L	15 yr	Encephalomalacia (hemisphere), ventriculomegaly	FL, P,T, O	32.11	+	+	23.03*
17	F	R	4 yr	Porencephalic cyst (FL,T), degenerative change (motor cortex)	FL, P,T	18.01	+	+	−7.19*
18	F	L	9 yr	Encephalomalacia (FL)	FL,T	16.09	+	+	13.79*
19	F	R	4 mo	Encephalomalacia (hemisphere)	FL, P,T, O	1.04	(+)	+	12.53*
20	F	L	4 mo	Hemiatrophy	FL, P,T, O	9.04	(+)	+	−13.00*
21	M	R	2 wk	Encephalomalacia (FL)	FL, P,T	2	±	+	−3.95
22	M	R	3 d	Porencephalic cyst (FL, P,T, O)	P,T, O	7.06	±	+	−0.91
23	F	L	1 d	Encephalomalacia (FL, P,T)	FL, P,T, O	6.06	±	+	1.34
24	M	L	2 yr	Encephalomalacia (FL, P, O)	FL, P,T	7.11	±	+	3.27
25	F	L	Perinatal	Parenchymal atrophy (P,T), ventriculomegaly	FL, P,T	20.02	−	+	0.94
26	F	R	Prenatal	Hemiatrophy, porencephalic cyst (P, O)	P,T	13.02	−	−	3.19
27	M	L	Prenatal	Hemiatrophy, ventriculomegaly, encephalomalacia (FL, P,T), porencephalic cyst (P,T)	FL, P,T	16.03	−	+	−0.27
28	F	L	3 wk	Hemiatrophy, ventriculomegaly	FL, P,T, O	11	−	+	−1.91
29	M	L	Prenatal	Porencephalic cyst (FL, P,T)	FL, P,T	8.02	−	+	0.08
30	M	R	Prenatal	Porencephalic cyst (FL, P)	FL, P	9	−	+	−0.77
31	F	R	Perinatal	Porencephalic cyst (FL, P,T)	FL, P,T, O	5.04	−	+	−2.14
32	F	L	3 d	Porencephalic cyst (P)	P,T	0.08	−	−	2.59
33	F	L	Prenatal	Hemiatrophy, porencephalic cyst (FL, P,T)	FL, P,T	2.08	−	+	0.00
34	M	L	Prenatal	Hemiatrophy, porencephalic cyst (P), ventriculomegaly	FL, P,T, O	1.09	−	+	−0.70
35	M	L	1 mo	Porencephaly (FL, P, O)	P,T	13.06	−	+	0.47
36	F	L	Prenatal	Encephalomalacia (FL, P, O)	P,T, O	14.04	−	+	0.49
37	M	L	Perinatal	Hemiatrophy, encephalomalacia (P, O)	FL, P,T, O	16.05	−	+	0.59
38	F	L	Prenatal	Hemiatrophy, ventriculomegaly, porencephaly (P)	FL,T, O	0.05	−	−	1.23
39	M	L	Perinatal	Hemiatrophy	FL,T, O	15.03	−	+	1.65
40	M	R	Prenatal	Hemiatrophy	FL, P,T, O	17.11	−	+	1.03

*±2 SD of normal value.
CD = cerebellar diaschisis; HP = hemiplegia; F = frontal lobe; P = parietal lobe; O = occipital lobe; T = temporal lobe; (+) = paradoxical CD; ±CD = CD is detected in visual inspection.

in unilateral porencephaly, none appeared to have significant crossed cerebellar diaschisis on PET scanning with 2-deoxy-2[^{18}F]fluoro-D-glucose (FDG) performed later in childhood.[13] Subsequently, we observed that crossed cerebellar diaschisis does indeed occur in children and, in the present study, we examined whether there is any relationship between the *timing* of unilateral cerebral injury (ie, age when the patient sustained lesion) and the presence of crossed cerebellar diaschisis on FDG-PET performed in the chronic state. Since some of the patients were studied on a high-resolution PET system, we also examined the topographic relationship between cerebral lesion and cerebellar function.

MATERIALS AND METHODS

Patients Studied

The study population consisted of 40 patients (mostly children) with predominantly unilateral brain injury as shown by structural imaging (Table 1), some of whom also had ipsilateral basal ganglia damage. Eleven patients were examined with PET at Children's Hospital of Michigan, and 29 patients at the University of California, Los Angeles Medical Center (UCLA). The subjects ranged in age from 5 months to 32 years (mean, 11.01 years) when studied with PET; 22 patients were female and 18 were male. In 11 patients, the injury had probably occurred prenatally based on clinical history and findings. Seven patients sustained brain injury in the perinatal

Table 2. Asymmetry Index of Cerebellar Lobe and Lobules

	Patient No.									Control (n = 22)
	17	18	24	19	20	35	36	39	40	Mean ± SD
Anterior lobe	−2.49	−1.88	−1.08	13.13*	−8.51*	−4.18	−2.92	−4.78	0.73	−0.75 ± 2.44
Posterior quadrangular lobule	−3.99	−0.17	5.78*	35.19*	−12.46*	0.78	−1.99	−4.70	1.68	−1.38 ± 2.66
Superior semilunar lobule	−2.83	8.13*	8.36*	24.93*	−9.52*	0.87	3.09	2.37	−0.56	1.58 ± 2.22
Inferior semilunar lobule	−10.24*	5.65*	2.94	15.50*	−7.66*	0.48	0.18	3.49	0.81	−0.14 ± 2.29
Gracile lobule	−3.02	−0.44	2.70	24.20*	−1.12	−4.70	−1.06	−2.90	2.71	−1.19 ± 2.73
Biventer lobule	−2.12	−0.42	3.29	17.75*	−16.60*	−2.53	0.65	0.27	1.99	0.21 ± 3.33
Tonsil	−12.01*	−1.14	2.28	−1.29	−8.73*	−1.43	0.29	−0.08	−1.30	−1.25 ± 3.33
Dentate nuclei	−10.23*	4.40	0.89	4.62	−17.00*	−1.15	0.47	−0.50	−12.78*	0.18 ± 3.05

*±2 SD.

period, defined here as between 24 hours prior to and 24 hours after delivery. The remaining 22 patients suffered postnatal injuries between 1 day and 15 years. Patients with progressive neurologic diseases were not included in this study. Computed tomography (CT) scans or magnetic resonance imaging (MRI), or both, were reviewed in all cases and confirmed the presence of unilateral supratentorial injury. One patient (case 10) had cerebellar hemiatrophy contralateral to the side of supratentorial injury. Patients whose cerebral injury did not include at least frontal or parietal cortex on CT, MRI, or PET were excluded from this study, since these cortical regions are the sites of origin of the corticopontocerebellar pathway.[6,10,14,15] The primary sensorimotor region was included in the area of injury in all subjects. Thirty-six of the 40 patients had hemiplegia contralateral to the side of brain injury. Clinical data of these patients are presented in Table 1. In many cases, the etiology of brain injury could not be determined with confidence to allow analysis of this as a variable. Twenty-two subjects (14 male and 8 female), age ranging from 2 months to 16 years, served as a control group; the strategies used in collecting normative data in PET have been described previously.[1]

PET Procedures

All PET studies of brain glucose utilization using FDG were performed in the chronic state at least 5 months after brain injury. The dose of FDG injected intravenously was 0.143 mCi/kg. Dosimetric considerations and the FDG-PET procedure, as applied to children, have been described previously.[16–18] The patients were kept awake during the first 30 minutes (uptake period) following FDG administration. In patients with epilepsy, the electroencephalogram was monitored during the uptake period in order to determine the presence of subclinical seizures. During the FDG uptake period, external stimuli were minimized by dimming the lights and by discouraging speech and other forms of interaction. A head holder was used to minimize movement during scanning. Approximately 30 minutes after injection, tomographic scanning of the brain was performed during either natural sleep or sedation with chloral hydrate, midazolam hydrochloride, or pentobarbital sodium. Patients were scanned at UCLA with either a NeuroECAT positron tomograph (Siemens, Knoxville, TN) or a CTI 831 positron tomograph (Siemens), or scanned at Children's Hospital of Michigan with an ECAT-EXACT/HR positron tomograph (Siemens). All tomographic images obtained were oriented parallel to the canthomeatal plane. For further analysis of cerebellar lobes and lobules, images at Children's Hospital of Michigan were reconstructed to display the data in coronal planes to optimally display cerebellar structures in 9 patients (cases 17–20, 24, 35, 36, 39, and 40).

Data Analysis

Analysis of PET data was performed independent of information concerning timing of brain injury. The tomographic images of cerebral glucose utilization were initially analyzed by visual inspection. Subsequently, the images were displayed on a monitor and regions of interest were drawn for the cerebellar cortex in the transaxial plane, and for the cerebellar lobes and lobules of each hemisphere in the coronal plane with the guide of an atlas generated in our laboratory.[1] Local tissue concentrations of radioactivity were calculated for each region. Whenever the cerebellar structures appeared on more than one tomographic slice, which was typically the case, the radioactivity concentration represented an average (weighted by area) of the values for each plane in which the structure appeared. An index of cerebellar asymmetry was calculated for each brain region of interest as follows:

$$\text{Asymmetry index (\%)} = (L-R) \times 200/(L+R)$$

where L and R are the left and right cerebellar radioactivity concentrations, respectively.

RESULTS

Table 1 summarizes the findings of the PET studies. The asymmetry index values of cerebellar hemisphere, as a whole, and each cerebellar lobe or lobule from the patients and control subjects are shown in Table 2. The mean asymmetry index values of the cerebellar hemispheres in normal subjects were 0.21 ± 2.3% (mean ± SD, $n = 22$; range, −4.7% to 3.5%). The mean asymmetry index values of each cerebellar region are presented in Table 2. The presence of crossed cerebellar diaschisis was defined as an asymmetry index greater than 2 SD from the normal mean asymmetry index.

Crossed cerebellar diaschisis was present in 24 of the 40 patients from visual inspection of transaxial images (Figure 1). In 20 of these 24 patients, the asymmetry index values were greater than 2 SD below or above the mean of the controls (−43.5% to 26.5%). These 20 subjects included 15 with postnatal, 2 with prenatal, and 3 with perinatal brain injuries. The two patients (cases 4 and 8) with prenatal brain injury demonstrated diffuse ischemic insult in nearly the entire hemisphere, including subcortical regions. The three patients with perinatal brain injury (cases 6, 7, and 12)

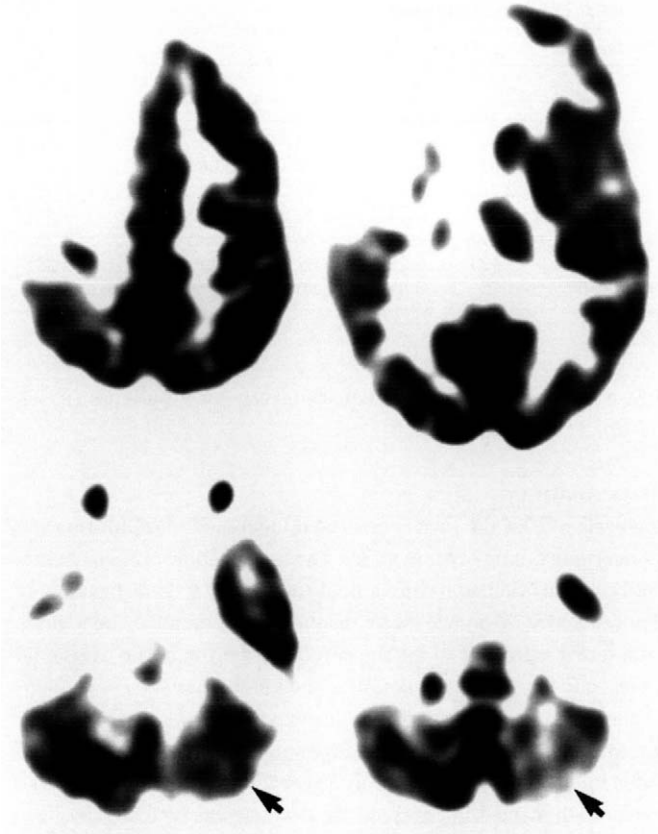

Figure 1. MRI scans of an 18-year-old female with traumatic brain injury at 4 years of age show a large porencephalic cyst in the right frontotemporal region. The PET study showed absence of glucose metabolism in the right frontal and parietal cortex, with hypometabolism in the right temporal lobe, basal ganglia, and thalamus. Decreased glucose metabolism was observed in the left cerebellar hemisphere (arrows), representing crossed cerebellar diaschisis.

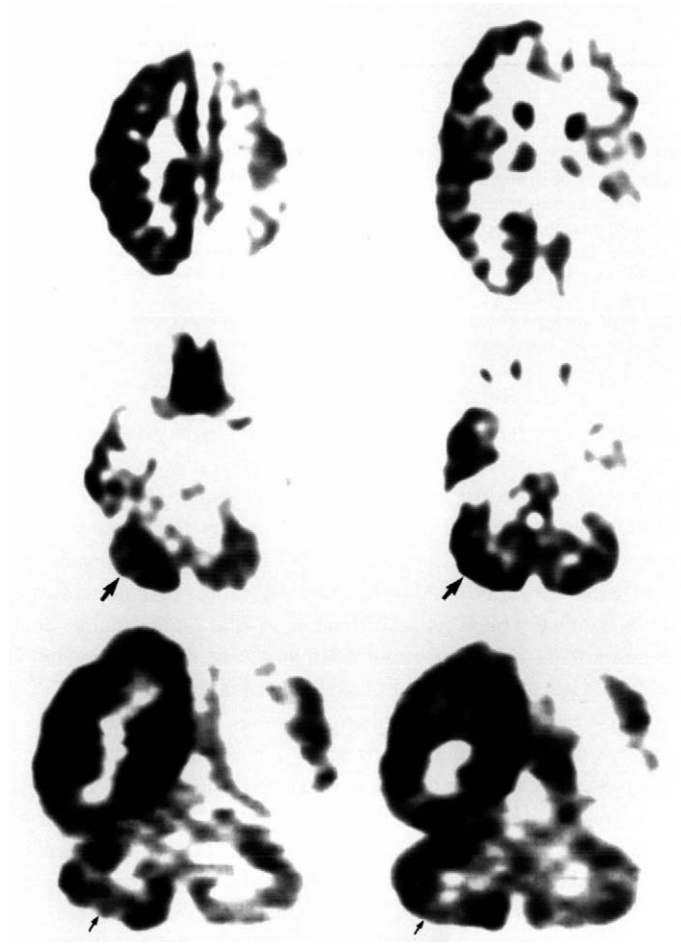

Figure 2. PET images of a 9-year-old girl, who had a stroke at 4 months of age. MRI showed left cerebral hemiatrophy. Severe glucose hypometabolism affecting nearly the entire left hemisphere is seen. Although the left caudate and putamen (not shown) showed preservation of glucose utilization, the left thalamus showed mild hypometabolism. The right cerebellar hemisphere showed a paradoxical pattern of increased glucose metabolism relative to the left side (thick arrows). The coronal images of cerebellar hemisphere showed glucose hypermetabolism in nearly all right cerebellar regions, including the dentate nuclei, but not the gracile lobule (thin arrows).

showed *bilateral* but asymmetric supratentorial abnormalities on PET. Therefore, in fact, neither cerebral hemisphere could be considered normal, despite the suggestion of strictly unilateral damage on CT or MRI.

Four patients (cases 21–24) with a suggestion of crossed cerebellar diaschisis from visual analysis did not have abnormal asymmetry index values in transaxial images. In these four cases, cerebellar hypometabolism were seen in relatively focal areas (patients 21, 22, and 23) as compared to other patients showing a more diffuse pattern of crossed cerebellar diaschisis, or was detected only on coronal images (patient 24).

An unexpected finding was the presence of a "paradoxical cerebellar diaschisis" in which cases a relative cerebellar *hypermetabolism* (rather than hypometabolism) was present contralateral to the side of cerebral injury; this phenomenon was seen in 2 subjects (cases 19 and 20; Figure 2). Both of these patients had suffered their brain insult at 4 months of age.

In 16 patients, there was no evidence of cerebellar metabolic asymmetry based on visual inspection and quantitative analysis of PET data (Table 1; Figure 3); cerebellar asymmetry index values in this group ranged from –2.14% to 3.19%. Of these 16 patients, there were 13 with either prenatal or perinatal injury. The remaining 3 patients had postnatal injury; however, it was noted that in all 3, the injury had occurred at 4 weeks of age or earlier.

The asymmetry index of eight cerebellar regions, including the dentate nuclei, in nine patients studied on high-resolution PET at Children's Hospital of Michigan are presented in Table 2. Two of these (patients 19 and 20) had the paradoxical pattern of cerebellar diaschisis (Figure 2); patient 19 showed left cerebellar hypermetabolism involving the entire hemisphere except for the tonsil and the dentate nuclei. Patient 20 showed hypermetabolism of the whole right cerebellar hemisphere except for the gracile lobule. Three other patients (cases 17, 18, and 24) showed focal asymmetries of the cerebellar hemispheres (Table 2). Patient 17 showed decreased glucose metabolism in the left

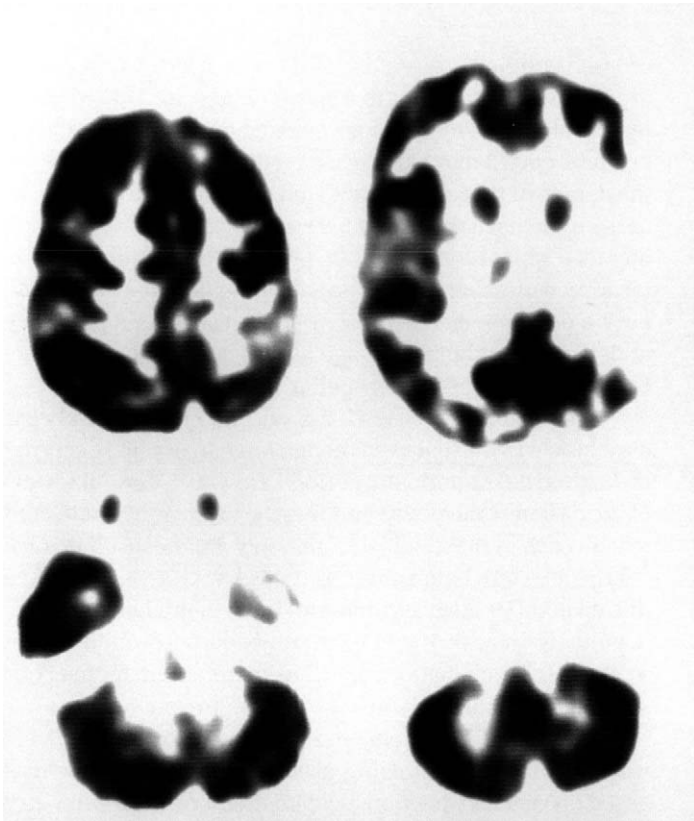

Figure 3. PET images of a 14-year-old girl with presumable stroke in the prenatal period. MRI demonstrated encephalomalacia in the left frontal, parietal, and occipital cortex. Although the PET scan revealed an extensive area of decreased glucose metabolism involving the left frontal, parietal, and temporal cortex and left thalamus, the cerebellar hemispheres showed normal symmetric glucose metabolism.

inferior semilunar lobule and tonsil (below 2 SD), and mild hypometabolism (almost < 2 SD) in the left superior semilunar lobule. This patient also showed significant asymmetry in the dentate nuclei. Patient 18 showed decreased glucose metabolism in the right superior semilunar and inferior semilunar lobule (> 2 SD). Another subject (case 24) showed abnormal asymmetry index in the posterior quadrangular and superior semilunar lobule (> 2 SD), though the transaxial images failed to show cerebellar hypometabolism. The asymmetry index of the regions of cerebellar hemisphere in the remaining four patients were within the normal range. However, the dentate nuclei in one of these patients (case 40) was beyond the normal range of asymmetry index in this structure.

DISCUSSION

The present study confirms our previous finding[13] that despite significant unilateral cerebral hemispheric injury occurring *early* in life (< 4 weeks), crossed cerebellar diaschisis is typically not present. However, the adult pattern of crossed cerebellar diaschisis can be seen in some pediatric brain injuries, particularly those occurring postnatally, and may persist years after the injury. We also describe an unusual pattern of a "paradoxical cerebellar diaschisis," which is characterized by relative *hypermetabolism* of the cerebellar cortex contralateral to the side of cerebral injury. Our findings suggest the presence of age-dependent plasticity of the corticopontocerebellar pathway in response to developmental brain injuries.

Ontogeny of Corticopontocerebellar Pathways

The fibers of the corticopontocerebellar system in humans have a protracted course of development. At around the second postnatal month, the corticopontine fibers in the internal capsule, cerebral peduncles, and pontine gray begin their myelination cycle that continues past the first year of life. The middle cerebellar peduncle, which is the major pathway of the pontocerebellar tract, also exhibits a protracted cycle of myelination, lasting at least until the fourth postnatal year.[19] Additionally, previous studies have demonstrated that the afferent fibers from the basilar pons projecting into the cerebellum are already in place prior to the maturation of their target neurons in the cerebellum in opossum,[20] and mouse.[21–23] This connection, terminating at the second order neurons of the corticopontocerebellar pathway, has been shown to be the last source of cerebellar afferents to mature in the opossum.[20] In addition, studies in mice have shown that during the second postnatal week of age, many single afferent axons in cerebellum had morphologic features of both climbing fibers and mossy fibers, and these premature axons formed connections not only with the granule cells, but also with Purkinje cells,[21,22] and these temporary connections may be functional.[24] Thus, special properties characteristic of the developing corticopontocerebellar tract may allow a greater degree of plasticity, following injury, as compared to the adult.

In the present study, 16 patients with prominent unilateral supratentorial lesions showed no evidence of crossed cerebellar diaschisis (Figure 3); of these, 13 sustained their lesions prenatally or perinatally, and the remaining 3 patients sustained unilateral cortical lesions postnatally but prior to 4 weeks of age. Thus, the absence of crossed cerebellar diaschisis in the presence of large unilateral cerebral injury sustained early in life is in sharp contrast to the typical finding of cerebellar diaschisis in adults sustaining the same degree of injury. These findings suggest that the corticopontocerebellar pathways may have undergone reorganization in response to injury, and are consistent with our earlier study that found no evidence of crossed cerebellar diaschisis in 8 children with congenital hemiplegia.[13]

The basis for absence of crossed cerebellar diaschisis in our subjects is not clear, but may involve anatomical reorganization resulting in an uncrossed or "recrossed" corticopontocerebellar pathway. Recrossing the midline of the corticospinal tract has been observed in both cats[25] and rats[26,27] following neonatal hemispherectomy, and may mediate motor recovery.[28] Alternatively, recovery may be mediated by strengthening of the ipsilateral connections. Deafferentation of elements of the crossed connection could result in an expansion of the territories of the remaining ipsilateral or contralateral connections. There have

been reports of the ability of cortical fibers to expand their territories and to adopt new functional roles in response to deafferentation.[29] In children, who have undergone cerebral hemispherectomy for the treatment of intractable epilepsy, PET studies performed longitudinally have also suggested functional reorganization of the corticostriatal pathways.[30] In the mouse, fibers of the corticopontocerebellar tract have the ability to innervate novel sites during development.[20,22] For these reasons, we suggest that novel Purkinje cell innervation by developing mossy fibers can at least be partially responsible for the ability of the developing cerebellum to strengthen these ipsilateral or remaining contralateral connections resulting in functional metabolic plasticity.

Topography of Supratentorial Lesion and Crossed Cerebellar Diaschisis

Although crossed cerebellar diaschisis in humans seemed to be most often associated with lesions around the central cortex,[10] Junck et al found that in normal adults, prefrontal and premotor regions of the frontal lobe exerted the strongest influence on contralateral cerebellar metabolism while parietal regions failed to show an effect.[31] However, crossed cerebellar diaschisis was highly correlated to parietal lobe hypometabolism, but not to frontal lobe hypometabolism in patients with either cerebral ischemia or tumor,[5] while Martin and Raichle demonstrated a significant correlation of crossed cerebellar diaschisis with frontal lobe abnormalities.[4] Anatomical studies in the monkey suggest sensory and motor cortical inputs to be the most important as they have the most dense connections to the cerebellum, with association areas having fewer connections.[32–34] Thus, areas 4, 3, 1, and 2 provide the majority of cortical input to the cerebellum with visual cortical areas also projecting heavily.[33]

Crossed cerebellar diaschisis has also been observed with putaminal,[35,36] capsular, or thalamic stroke.[7,37] Contralateral cerebellar diaschisis following putaminal and capsular stroke indicated a disruption of corticopontine pathways to be important in the diaschisis. Early PET studies suggested that the disruption of descending corticopontine fibers might functionally suppress the pontine nuclei and result in crossed cerebellar diaschisis.[38] Recently, high-resolution PET scanning has demonstrated pontine hypometabolism in patients with crossed cerebellar diaschisis resulting from unilateral supratentorial brain tumors, thus further supporting the involvement of corticopontocerebellar pathway in the phenomenon of crossed cerebellar diaschisis.[39] However, the occurrence of contralateral cerebellar diaschisis with thalamic lesions in a few studies suggested that crossed cerebellar diaschisis may also be induced by damage to the ascending cerebellothalamocortical system.[7]

When the results obtained with PET are interpreted in light of available anatomical data, several conclusions can be drawn: (1) the corticopontocerebellar pathway is substantially involved in most cases of crossed cerebellar diaschisis; (2) sensorimotor cortex is a major modulating component of the fiber system responsible for causing crossed cerebellar diaschisis; (3) cortical association areas are involved as well, but to a lesser degree; and (4) whereas temporal lesions never cause crossed cerebellar diaschisis, occipital cortex may also have a modulating effect; however, the degree of this effect is not well documented. Since most of the patients in the present series had large lesions, which included sensorimotor cortex, precise correlation of lesion location with severity of crossed cerebellar diaschisis could not be performed. The present study was aimed primarily at determining the role of age as a factor for the presence or absence of crossed cerebellar diaschisis.

In four subjects (cases 4, 7, 8, and 12) crossed cerebellar diaschisis was present even though brain injury had occurred in the prenatal or perinatal periods. However, careful review of the circumstances surrounding the brain injury indicated that, in each of these subjects, not only did the insult involve nearly the entire hemisphere, but there was strong evidence that bilateral (though asymmetric) brain injury had occurred. It is likely that, in these four subjects, an optimum substrate for reorganization resulting in metabolic recovery or sparing following early insult was not present.

Among the 40 patients in the present study, 4 subjects were classified as showing crossed cerebellar diaschisis based on visual inspection, despite their normal asymmetry index. Contralateral cerebellar hypometabolism in these patients were relatively mild and limited to focal regions of cerebellum. One of these subjects was studied on a high-resolution PET system, and quantitative analysis showed significantly abnormal asymmetry index in the posterior quadrangular and superior semilunar lobules. In addition, the present study provides topographic data on the anatomical and functional correlation between the human cerebrum and cerebellum. In 5 cases with crossed cerebellar diaschisis studied on high-resolution PET, the superior or inferior semilunar lobules were affected following cerebral injury. Although the number of patients showing such focal cerebellar hypometabolism was small in the present series, these findings suggest that cortical afferent fibers, especially from the frontoparietal area, might project predominantly into the lateral portions of the cerebellum. This is supported by electrophysiologic studies that, in monkeys, have shown that cerebral cortical regions, including premotor cortex (Brodmann area 6), frontal eye fields (area 8), precentral cortex (area 4), prefrontal cortex (areas 9 and 10), and postcentral cortex (areas 3, 1, and 2), most readily evoke potentials in the lateral portions of the cerebellar hemispheres.[14] Additionally, in the human brain, the lateral part of the cerebellar hemisphere is enormously enlarged, as compared to other species,[40] and may contribute not only to motor function but also to some sensory and cognitive functions.[40–42]

Paradoxical Cerebellar Diaschisis

The present study documents another form of diaschisis, consisting of relative glucose hypermetabolism contralateral to the side of cerebral injury. Several reports have described *ipsilateral* cerebellar hypoperfusion or hypometabolism, referred to as "ipsilateral cerebellar diaschisis."[8,43,44]

It is not clear whether "ipsilateral cerebellar diaschisis" and "paradoxical cerebellar diaschisis" reported in the present study are the same phenomenon. Based on the fact that the majority of corticocerebellar projections are crossed and our previous finding of a similar paradoxical increase in cerebellar metabolism contralateral to the side of cerebral hemispherectomy in some children,[45] we believe that "paradoxical cerebellar diaschisis" is a true phenomenon.

Both patients in our study who showed paradoxical cerebellar diaschisis had sustained their supratentorial injury in a relatively large area, and prior to 4 months of age. However, since only 2 among 40 subjects showed the paradoxical cerebellar diaschisis in the present series, further analysis is required in order to understand the pathophysiology of this phenomenon.

CONCLUSION

The present study has shown that age at the time of cerebral injury is an important factor in the pattern of reorganizational changes in cerebellum, and is consistent with the general concept that damage to the immature brain is less disruptive to the overall function of the individual than comparable lesions in adults. Anatomical studies tracing reorganization of corticopontocerebellar pathways in a suitable animal model of early unilateral cerebral injury would provide important insight into this form of developmental plasticity. In further studies, it will be important to relate sparing or recovery of metabolism in cerebellum to various clinical features, such as motor function and etiology of hemispheric injury. Thirty-six of 40 patients included in the present retrospective study were hemiplegic regardless of whether crossed cerebellar diaschisis was detected or not; of the 4 subjects without hemiplegia, 3 did not show any diaschisis. Although the association between crossed cerebellar diaschisis and the presence of hemiparesis is not consistent in both previous,[3,4,8,10] and present studies, further prospective studies that include comprehensive testing and description of the progression of motor coordination may lend insight into the existence and degree of motor recovery in relation to the phenomena of crossed cerebellar diaschisis, absence of crossed cerebellar diaschisis, and paradoxical cerebellar diaschisis.

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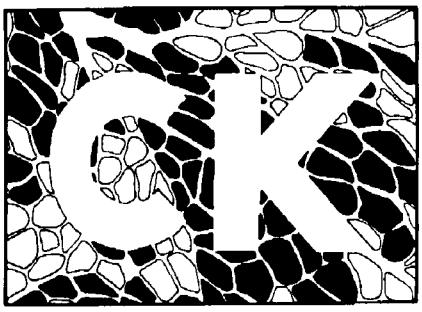

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