Crossed cerebellar diaschisis accompanied by hemiataxia: a PET study

Makoto Tanaka, Susumu Kondo, Shunsaku Hirai, Koji Ishiguro, Tomio Ishihara, Mitsunori Morimatsu

Abstract

To study crossed cerebellar diaschisis (CCD), cerebellar blood flow and oxygen metabolism were measured with positron emission tomography (PET) in 12 patients who showed a minimal degree of hemiparesis due to single unilateral supratentorial lesion. Six patients presenting with mild to moderate cerebellar type hemiataxia showed CCD, that is, decreased blood flow and oxygen metabolism in the cerebellar hemisphere contralateral to the side of supratentorial lesion. Hemiataxia and reduced cerebellar blood flow and metabolism occurred in the ipsilateral side. Lesions were located in the thalamus in four patients and the parietal lobe and internal capsule in one each. The other six patients did not exhibit ataxia, and oxygen metabolism was not reduced in the contralateral cerebellar hemisphere. In two of these cases, however, reduced cerebellar perfusion was observed in the contralateral cerebellar hemisphere. These findings indicate that CCD occurs with hemiataxia and suggest that it results not only from disruption of the corticopontocerebellar pathway but also of the dentatorubrothalamic pathway. CCD associated with hemiataxia, demonstrated in patients with thalamic lesions, was presumed to result from retrograde deactivation of the cerebellar hemisphere via the dentatorubrothalamic pathway.

Diaschisis is a concept developed by von Monakow¹ to explain temporary deactivation in an undamaged area of the brain after injury to a remote site. A good example is crossed cerebellar diaschisis (CCD), wherein damage in one cerebral hemisphere produces a functional depression in the contralateral cerebellar hemisphere.² Loss of cerebellar excitatory afferent input is presumed to cause CCD primarily through disruption of the corticopontocerebellar tract.²⁻⁴ The clinical importance of CCD, however, is not understood despite repeated demonstration with positron emission tomography (PET) and single photon emission tomography.

Patients with cerebrovascular disorders often show CCD, but cerebellar manifestations are rarely detected on neurological examination. Only a few case reports exist.^{5,6} This may imply that the depression of the cerebellar function seen in CCD has no or little relation to

the clinical presentation of ataxia, a major manifestation of cerebellar dysfunction. An alternative interpretation is that the motor weakness and hypertonicity usually occurring with CCD mask additional motor deficits, including ataxia.

Thalamic injury, especially to the ventrolateral portion, is a well known cause of contralateral hemiataxia.⁷ Although this is explained as being due to destruction of major projections from the cerebellum via the dentato(rubro)thalamic pathway⁸ at the terminal, cerebellar efferent pathways have not been investigated with reference to CCD. We therefore initiated the present study in patients without hemiparesis, which can mask ataxia, and with single lesions in various supratentorial regions.

Materials and methods

Twelve patients with cerebral infarction or haemorrhage presenting minimal hemiparesis were studied by PET (table 1). They were selected from a consecutive series of patients studied since March 1986 at the Gunma University Hospital Cyclotron Center for PET Diagnosis. All were examined neurologically to ensure the absence of motor impairment due to muscle weakness or hypertonicity, which can mask ataxia. Clinical diagnosis and lesion site were also confirmed by neuroradiological evaluation including brain CT in all patients, angiography in five (cases 1, 8, 9, 11, 12) and magnetic resonance imaging (MRI) in six (cases 1, 2, 7, 8, 9, 12), and by clinical course and neurological findings. All but one patient (case 3) had a single supratentorial lesion without clinical or radiological evidence of cerebellar or brain stem involvement. Of these, six (cases 1 to 6) showed mild to moderate cerebellar ataxia with preserved deep sensation (vibration, proprioception, and kinesthesia), while the remaining patients (cases 7 to 12) had no ataxia. A clinical history of cases 1 and 5 has been reported in detail previously.⁹ Four hemiataxic patients had a history of old thalamic haemorrhage or infarction, and one patient (case 1) had infarction in the parietal lobe. Case 3 showed pure motor hemiplegia on examination at the time of onset, which had improved to mild hemiataxia 48 hours later. Although a small capsular or pontine lacune not revealed by x ray CT was suspected as the cause of these transient symptoms,¹⁰ hypoperfusion and oxygen hypometabolism on the left cerebral hemisphere later revealed by PET favoured a capsular lacune. Thirteen healthy

Gunma University
School of Medicine,
Maebashi, Japan

Department of
Neurology
Makoto Tanaka
Susumu Kondo
Shunsaku Hirai
Koji Ishiguro

Department of
Radiology
Tomio Ishihara

Department of
Neurology, Yamaguchi
University School of
Medicine, Japan
Mitsunori Morimatsu

Correspondence to: Dr
Tanaka, Department of
Neurology, Gunma
University School of
Medicine, Showa-machi,
Maebashi 371, Japan.

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Table 1 Details of patients with cerebral infarction or haemorrhage presenting minimal hemiparesis

Case number	Age (years)	Sex	Neuroimaging findings	Presenting signs and symptoms	Neurological findings on PET study	Time from onset to PET study
1	34	F	Infarction in left parietal cortex and subcortical white matter	Dysesthesia and clumsiness of right hand	Right sided hemiataxia, mildly disturbed combined sensations	13 Months
2	56	M	Old haemorrhage localised in left thalamus (ventrolateral nucleus)	Sensorimotor disturbance	Right sided hemiataxia, dys- and hyperesthesia	18 Months
3	71	M	No abnormal findings on repeated CT	Pure motor hemiplegia in right side	Right sided hemiataxia without motor weakness	24 Hours
4	47	F	Small localised haemorrhage in right lateral thalamus at onset, no abnormalities on follow up CT	Sensorimotor disturbances	Left sided hemiataxia, dys- and hyperesthesia, hyperalgesia	2 Years
5	70	F	Old haemorrhage localised in left thalamus	Severe sensory and mild motor disturbances	Right sided hemiataxia, dys- and hyperesthesia, hyperalgesia	4 Years
6	77	F	Small infarction in left thalamus (ventrolateral nucleus), periventricular lucency	Sensorimotor disturbances	Right side hemiataxia, hand tremor, dys- and hypesthesia, hypalgesia	7 Years
7	58	M	Infarction in right centrum semiovale and mild cortical involvement	Sensorimotor disturbances	Left sided minimal hemisensory disturbance	8 Years
8	37	M	Right temporoparietoccipital infarction due to Moyamoya disease	Subjective hemisensory disturbances	Left-sided hemispatial neglect, disturbed combined sensations	1 Month
9	49	M	Infarction in right temporoparietal cortex and subcortex due to obstruction of middle cerebral artery	Sensorimotor disturbances	Left sided disturbed combined sensations	1 Month
10	82	F	Infarction in left posterior inferior frontal lobe	Speech disturbance	Motor aphasia	1 Month
11	72	M	Infarction in subcortex of left temporoparietal junction	Speech disturbance	Conduction aphasia	3 Months
12	61	M	Small infarction in anterior medial portion of left thalamus	Mental deterioration	Amnesic syndrome	7 Months

volunteers were subjected to PET study as control subjects.

PET was performed with a PCT-H1 (Hitachi, Japan) with four rings with 128 bismuth germanate oxide detectors providing seven views per scan cycle. The best spatial resolution was 7.4 mm full width at half maximum (FWHM) at the centre of the scan field, and axial resolution at the centre was 16 mm (slice thickness). Before PET study, x ray CT (CT-HSF, Hitachi) images were obtained to identify anatomical structures in the PET views. PET and x ray CT scanners were located side by side and joined by rails on which the bed moved with the patient's position fixed, thus providing identical tomographic planes. The patient's head was fixed to the headrest to obtain a tomographic plane parallel to the orbitomeatal line. The initial positioning and the absence of head tilt during the scan were ensured by crossed beams projected on ink marks drawn on the patient's face. A transmission scan with Germanium-68 and gallium-68 was performed for 10 minutes for attenuation collection. Calibration factors between the PET scanner and well counter were obtained in each study. The oxygen-15 steady state technique¹¹ was used to measure regional cerebral blood flow (rCBF) and regional cerebral oxygen metabolic rate (rCMRO₂). Oxygen-15 gas (750–1,100 MBq per minute) then oxygen-15 labelled carbon dioxide (350–550 MBq per minute) were inhaled continuously. Scan data

were collected for 5 to 8 minutes. The blood was sampled three times during each scan process from a cannulated radial artery and subjected to determinations of oxygen-15 radioactivity in whole blood and plasma as well as blood cell count and blood gas analysis. No correction was performed for intravascular oxygen-15 labelled oxyhaemoglobin.

Image data was processed with a Hitachi image processing computer with system subroutines to reconstruct functional images constituting 128 × 128 pixels. The region of interest was determined on both cerebellar hemispheres identified with x ray CT by track ball. The region was set as the x ray CT image on which the full width of both cerebellar hemispheres appeared. The outlines were traced by track ball, carefully avoiding the lateral sinuses and the fourth ventricles. The same region of interest was superimposed on cerebellar rCBF and rCMRO₂ tomographic planes identical to the x ray CT plane. The degree of asymmetry in rCBF and rCMRO₂ was expressed by the asymmetry index (AI) defined as follows;

$$AI (\%) = |lt - rt| \times 200 / (lt + rt)$$
lt and rt are the left and right cerebellar rCBF or CMRO₂, respectively.

We analysed cerebellar rCBF and rCMRO₂ with two way analysis of variance (ANOVA) with two fixed factors (a group factor with ataxic and non-ataxic and a side factor with ipsilateral and contralateral to the cerebral

Table 2 rCBF, rCMRO₂, and asymmetry indices (AI) in ataxic and non-ataxic patients and normal controls

Group	No. of Cases	Age		Mean (SD) rCBF† (ml/100 ml/min)	Mean (SD) AI (CBF)§ (%)	Mean (SD) rCMRO ₂ ‡ (ml/100 ml/min)	Mean (SD) AI (CMRO ₂)§ (%)
		Mean	S.D.				
Ataxic							
C*	6	59.2	16.5	38.57 (8.43)	14.01 (2.60)	2.56 (0.32)	12.00¶ (2.05)
I*	6			44.17 (10.47)		2.89 (0.32)	
Non-ataxic							
C*	6	59.8	16.0	32.97 (4.75)	6.44 (5.47)	2.90 (0.62)	3.05 (0.73)
I*	6			35.02 (6.41)		2.91 (0.57)	
Control†	13	51.3	12.5	38.93 (6.33)	2.13 (1.87)	3.10 (0.60)	2.88 (2.23)

*C and I refer to cerebellar hemisphere contralateral and ipsilateral to side of supratentorial lesion, respectively.

†Mean values of rCBF and rCMRO₂ in control group obtained from 26 cerebellar hemispheres in 13 subjects.

‡Not significant (two-way ANOVA). §p < 0.01 (one-way ANOVA). *p || 0.0001 and p < 0.05, compared with mean values of control and non-ataxic groups, respectively (t-test). ¶p < 0.0001, compared with mean values of other two groups (t-test).

Figure 1 Distribution of CBF and CMRO2 values in patients with hemiataxia (A) and without ataxia (B). ○ and ● indicate values for cerebellar hemispheres respectively contra- and ipsilateral cerebellar hemispheres to side of lesion. Hemispheres of each patient are connected by line.

damage). We used one-way ANOVA to compare AIs for cerebellar rCBF and rCMRO2 in the ataxic, non-ataxic, and control groups. If the ANOVA showed significant variation, student's *t* test was used to compare the group means.

Results

The rCBF and rCMRO2 values from the patients and control subjects are summarised in table 2. The patients were divided into two groups for data analysis as mentioned above, ataxic (cases 1 to 6, figure 1A) and non-ataxic (cases 7 to 12, figure 1B). There was no significant difference in time from clinical onset to PET study between the two groups. Crossed cerebellar diaschisis (CCD) was judged present in cases showing an AI higher than the control mean plus 2 SD. CCD was observed on functional images for rCBF and rCMRO2 in all patients with ataxia (Figures 2A and 2B). Of the patients without ataxia, cases 9 and 12 exhibited CCD in rCBF images but not in rCMRO2 images (figure 2C), while the other cases showed no CCD in either functional image.

Interhemispheric comparisons of mean values of patients with hemiataxia showed clear reductions of rCBF and rCMRO2 in the contralateral cerebellar hemisphere (table 2). In patients without ataxia there was little difference between ipsilateral and contralateral hemispheric rCBF or rCMRO2 values. No group showed significant variation by two-way ANOVA on cerebellar rCBF or rCMRO2. On the other hand one-way ANOVA on AIs showed significant group effects in both the rCBF and rCMRO2. Compared to the indices of the control and non-ataxic groups, the AIs for rCBF and rCMRO2 in patients with ataxia were significantly elevated, indicating a clear reduction in rCBF and rCMRO2 in the contralateral cerebellar hemisphere.

Discussion

Only a few of the many reports on CCD refer to

accompanying ataxia.^{4,5} This may indicate that the clinical significance of CCD has not yet been recognised. The present PET study, however, revealed that CCD does appear in some cases in association with hemiataxia on the same side as the decreased cerebellar perfusion and oxygen metabolism. Thalamic lesions are well known causes of contralateral loss of limb coordination,⁷ as demonstrated in cases 2, 4, and 6 (figure 2B and 2C). Parietal lobe injury^{12,13} has also been reported to cause contralateral hemiataxia, as demonstrated in case 1. Ataxia due to injury in these regions is not always accompanied by disturbed deep or combined sensation.^{12,13} All cases in the present study showed hemiataxia essentially of the cerebellar type. To our knowledge, there have been no cases reported of hemiataxia after thalamic or parietal injury in which CCD was demonstrated by functional imaging of cerebrocerebellar perfusion and metabolism, other than our preliminary report⁹ (figure 2). Muscle weakness and spasticity in our patients were sufficiently moderate to permit unmasking of limb ataxia on neurological examination. This possibly explains the prevalence of hemiataxia with CCD in our series.

CCD is postulated to be a distant effect caused by disruption of the corticoponto-cerebellar pathway,² a principal cerebellar afferent connection.⁸ Although this mechanism explains cases 1 and 3, localised thalamic lesions in the other ataxic cases are unlikely to cause CCD via this afferent connection. Of the thalamic nuclei, the ventrolateral has been shown to have important connections with the contralateral cerebellar hemisphere via the dentato(rubro)thalamic pathway, a principal cerebellar efferent connection.⁸ On x ray CT, lesions involving the ventrolateral portion or adjacent regions were seen in all cases with hemiataxia after thalamic injury. We suggest that CCD with ataxia of thalamic origin is caused by disruption of cerebellar efferent fibres. Chung¹⁴ described four cases of retrograde crossed cerebellar atrophy confirmed by pathology in which the ventrolateral thalamus destroyed by brain tumour resulted in retrograde transneuronal atrophy of the contralateral cerebellar hemisphere. Case 12, in whom infarction in the left anterior medial thalamus which spared the lateral portion of the thalamus was noted, exhibited neither ataxia nor CCD on rCMRO2 imaging. This case also indicates the importance of localisation of intrathalamic damage in the development of CCD with ataxia.

There were two cases without ataxia in which CCD was observed on rCBF but not rCMRO2 imaging (figure 2C), while all cases with ataxia exhibited CCD on both images. This implies that cerebellar perfusion and metabolism in these two cases were uncoupled and that reduction of cerebellar metabolism rather than blood flow was an important causative factor. The cause of the uncoupling is not understood, but cerebral blood flow change has been shown to exceed cerebral metabolism change even under physiological conditions.^{15,16} Although the region of interest was defined carefully on the

Figure 2 X ray CT (or MRI) and functional images of patients. 1: x ray CT or MRI. 2 and 3: rCBF images at levels of lesion demonstrated by x ray CT or MRI (2) and of cerebellar hemispheres (3). 4 and 5: rCMRO2 images at same levels as rCBF images. The left side of the images corresponds with the left side of the brain. A: case 1 showed infarction of left parietal cortex and subcortical white matter on MRI. Crossed cerebellar diaschisis easily discernible in CBF and CMRO2 images. B: case 2 exhibited small low density area involving ventrolateral nucleus of left thalamus. Crossed cerebellar diaschisis was seen in both functional images. C: case 9 showed border zone infarction in right temporoparietal areas. Left cerebellar perfusion was reduced as shown in CBF image but oxygen consumption was preserved in both cerebellar hemispheres.

cerebellar hemisphere delineated by x ray CT, the possible presence of some artifacts should be taken into account. Radioactivity in the region was more or less influenced by that presenting in the lateral sinuses, as intravascular blood volume correction was not carried out in the present study.

Although CCD accompanied by ataxia was probably the result of damage to cerebellar afferent or efferent pathway, it is not necessarily linked to ataxia.¹⁷ Pappata *et al*¹⁷ reported that significant contralateral cerebellar hypometabolism was found in three of six patients with pure internal capsule infarction, suggesting a pathogenetic role for the corticopontocerebellar system. They also observed that contralateral hypometabolism occurred in two of six patients with thalamic lesions and made the assumption that this phenomenon also results either from damage to the ascending cerebellothalamocortical system or indirectly from hypometabolism of the cerebral cortex. Systemic association was not observed between crossed cerebellar hypometabolism and ipsilateral ataxia in their series.¹⁷ Their findings suggest that hypometabolism in the cerebral cortex, which is caused by transneuronal effect or by underlying cerebral ischaemia, also plays a pathophysiological role in CCD accompanied by ataxia. In our study, however, there seemed to be no association between ipsilateral hypometabolism in the cerebral cortex and CCD with ataxia (data not shown). A specifically designed study is required to reveal the pathogenesis producing CCD concurrent with ataxia.

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