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Hemispheric disconnection syndrome with a 'crossed avoiding' reaction in a case of Marchiafava-Bignami disease

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SUMMARY A clinicopathological study is presented of a case of Marchiafava-Bignami disease with a hemispheric disconnection syndrome, an association that does not appear to have been reported previously. Gross and microscopic examination of the brain revealed necrosis of the corpus callosum (sparing a small area in front of the splenium) and of the anterior commissure, cortical and subcortical infarction of the right lingual gyrus, diffuse cortical lesions of the laminar sclerosis type, and lacunae in the basal ganglia and the pons. The patient was unable to grasp objects presented to the right visual half-field with the left hand, or to respond to contralateral somaesthetic stimuli with either of the upper limbs. This motor inhibition, with the associated extended posture, is described as a 'crossed avoiding reaction', and attributed to the inability of one hemisphere to respond to visual or somaesthetic stimuli projected to the other hemisphere. Clinicopathological correlations and visuomotor co-ordination mechanisms are discussed in the light of previous clinical and experimental studies. Anomia to pictures projected tachistoscopically to the left visual field, disturbances in the transfer of somaesthetic information, left sided ideomotor apraxia with agraphia, right sided dyscopia, and ideational apraxia especially marked in the right visual field were observed.

In 1903, Marchiafava and Bignami reported six cases of alteration of the corpus callosum in alcoholic subjects. Since then, several studies of this disease have been published. Rancurel (1966) analysed 99 of these cases and added four of his own; Castaigne *et al.* (1971) reviewed the literature and added a further six cases. These authors distinguished two forms of the disease, an acute form, characterised by sudden onset, coma, epileptic seizures, ending in stupor and rapid death, and a chronic form, characterised by dementia and dysarthria, and sometimes lasting for several years. Publications by Leventhal *et al.* (1965), Pons-Tortella and Pou-Seradell (1965), Cozzo (1967), Ishizaki *et al.* (1970), Constantinidis and Tissot (1971), and Hathaway and Chi'en (1973) bring the number of reported cases to 117.

In 1962, Gazzaniga *et al.* showed that surgical section of the corpus callosum caused hemispheric disconnection; they have subsequently published numerous accounts of this syndrome. In the same year, Geschwind and Kaplan reported the inability to name objects placed in the left hand, in association with left sided agraphia and alexia, in a patient with callosal infarction. Colour anomia with alexia in the left visual field due to an infarct in the splenium and an occipital lesion was previously reported by Geschwind and Fusillo (1966). Schott *et al.* (1959), Rubens and Benson (1971), and Barbizet *et al.* (1974) gave detailed clinical descriptions of impairment in inter-hemispheric transfer, which they attributed to callosal infarction. Thirteen cases of callosal lesions of vascular, tumoural or post-traumatic origin, with confirmation by necropsy in seven, have been presented in a work by Brion and Jedynak (1975), who also reviewed the early literature. We wish to present a case of cerebral hemispheric disconnection in Marchiafava-Bignami disease. To our knowledge, this is the first time that such an association has been reported.

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Case report

On 3 May 1971, HV, a 46 year old, right handed examiner, suddenly lost consciousness at his home. He recovered within seconds, but was unable to speak or walk, and failed to recognise his family. He was

immediately taken to the Caen University Hospital and admitted to a medical ward.

There was a previous history of tuberculous lymphadenopathy at 19 years of age, and of a gastric ulcer diagnosed in 1967. The patient was known to consume several litres of red wine daily and was a confirmed alcoholic, frequently becoming inebriated and sometimes being brought home in a state of coma. In 1969, he developed polyneuritis of the lower limbs. From 1970, he had reduced his consumption of alcohol and no longer became drunk. Though his behaviour was normal, his family noted memory disturbances. On examination, the patient was found to be confused, disoriented as to time and place, with unintelligible speech. He could not understand simple orders. Generalised oppositional muscular hypertonia and paresis of the lower limbs were noted. Plantar responses were flexor. The rest of the physical examination was negative. Blood pressure was 90/50 mmHg.

The blood pyruvic acid level was 7 mg/l. The EEG revealed a dominant rhythm of 8 Hz. This was symmetrical and blocked on eye opening. There was some irregular theta activity which increased on hyperventilation over the left fronto-temporal area. The brain scan revealed no abnormality.

Despite intramuscular administration of thiamine and pyridoxine, the patient's condition declined. He no longer recognised his wife, thought that he was at home, and tried to leave his room through the window. Thus, on 3 June 1971, he was transferred to a psychiatric hospital. Here he was found to be in a state of extreme mental confusion. He wandered undressed through the wards, was unable to control defaecation, and covered his face with his excrement. Severe dysarthria was present, and ideation was slow.

His mental state improved progressively, so that by the end of September 1971, he was able, although only very slowly, to read and write. Incoordinated meaningless movements of the upper limbs and constructional apraxia were noted at this point.

On 4 November 1971, he was transferred back to the Caen Hospital to the Department of Neuropsychiatry. Alertness, comprehension of orders, spatial and temporal orientation were all satisfactory. No deficit in muscular power was found, nor any cerebellar disorder, and the cranial nerves appeared intact. There was no grasp reflex. Ankle and knee reflexes were absent, plantar reflexes were flexor. Tactile and thermalgesic sensation of the distal extremities of both lower limbs was diminished, but arthrokinetic sensitivity was unimpaired. A sensory extinction phenomenon to touch and pinprick was noted in the upper left limb. The visual field was normal; visual acuity was 8/10 in each eye without correction and 10/10 after correction.

Demonstration of the disconnection syndrome

MOTILITY DISORDER OF THE LEFT LIMBS IN THE RIGHT VISUAL FIELD

The patient was able to grasp an object, the examiner's hand or his own right hand presented to his left visual field, with his left hand. However, when he was asked to grasp the examiner's hand or an object presented to his right visual field, his left arm would stiffen, stretch out slightly behind his body, his shoulder would lift and his head turn towards the right with the neck extended. His left leg would also stretch out, thus lifting the trunk and causing lordosis. During this phenomenon of 'crossed avoiding', if seated, he would rise involuntarily, and his face would become red and wet with perspiration due to obvious great physical effort (Fig. 1). Frequently, a few drops of urine were passed.

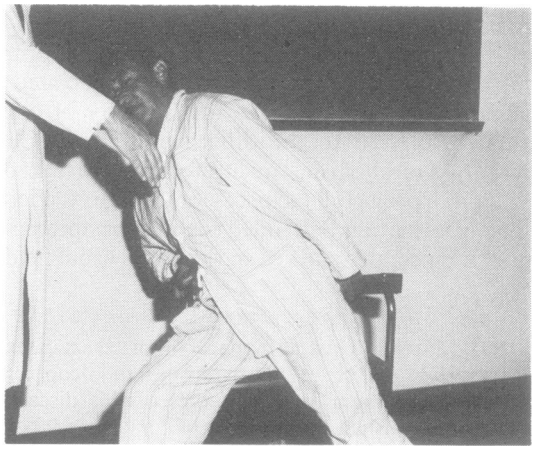

Fig. 1 *Patient is unable to grasp examiner's hand presented to his right visual field with his left hand*

The patient's awareness remained normal, and he declared that he was trying to seize the object presented to him, but that he was unable to do so. When his head was passively turned to the right before the test, he would sometimes succeed. It is presumed that in these instances he was using the left visual field. When the patient was asked to touch his right hand with his left, the former being in his right field of vision, the 'crossed avoiding' reaction would occur 50 per cent of the time; however, there was total success when he guided his left hand towards his right hand by feeling his way across his body, or when an object was moved progressively from the left half of his visual field to the right half, and he would grasp it with his left hand in each of its successive positions. The patient was also able to touch his right shoulder

with his left hand; when asked to do so, he would fling this hand onto its target in a succession of increasingly rapid movements.

When there was no specific target, the movement of projecting the left hand to the right of the meridian was normal, with eyes open or closed. If the patient was asked to pick up an object in his right visual field with his eyes closed, the 'crossed avoiding' phenomenon would occur if he had been shown the object in its place before closing his eyes. However, if the object had not been presented beforehand, he would hesitantly explore the area with his left hand, eyes closed, but there was no 'crossed avoiding'. The patient did not complain spontaneously of his motor disorders, but he used his left hand less than his right in habitual gestures.

With his left foot in dorsiflexion, he was able to lift the handle of a small bucket placed in the left visual field. When the bucket was placed in the right half of his visual field, a little less than half the time, the left leg would stretch out but would not begin the required movement, and at the same time, his head would turn to the right, his neck extended, and the left arm would extend slightly backwards.

The right arm moved normally in both the left and right visual fields, as did the right leg.

DISTURBANCES IN THE INTERHEMISPHERIC TRANSFER OF SOMAESTHETIC INFORMATION, AND IN THE CROSSED MOTILITY OF THE LIMBS

Arthrokinetic sensitivity

When the patient was asked to *grasp the right thumb with the left hand*, with his eyes closed, the crossed avoiding reaction occurred consistently in the left arm; when he was asked to grasp the left thumb with the right hand, the reaction appeared one out of three times.

When the patient was asked to *imitate a pose* held by the right hand (wrist in flexion or extension), with vision excluded, he would raise his left forearm, and the hand would straighten out, fingers spread apart. The same test with the right hand produced with equal frequency, perfect success, partial success or the same extended movement as with the left hand. With eyes open, the test was always carried out successfully by the right hand; the left arm would begin the movement of crossed avoiding 50 per cent of the time, and would not be able to mimic the pose of the right wrist despite intense effort.

The patient was able to *imitate different positions of the fingers* of one hand with the other, with his eyes closed, one out of two times, demonstrating no significant difference between the two hands. During the test, the hand and fingers moved constantly, and on the left side, the patient would raise his hand, spread out his fingers and slightly extend the whole arm.

The *left leg* (patient supine, eyes closed) a little more than half the time, was unable to mimic the position impressed on the right leg by the examiner, but remained extended and motionless. The pose of the left leg was correctly imitated by the right leg.

Topagnosis: localisation of nociceptive stimuli

The finger of one hand was pricked and the patient was asked to move, eyes closed, the corresponding finger of the other hand. No errors were made when the stimulus was given to the left hand. However, when the right hand was pricked, the left hand would remain motionless, the fingers extended, although the patient declared that he knew which finger had been pricked and what he was supposed to do. In a second series of tests, also with vision excluded, the patient was asked to indicate, with the hand that had been pricked, the corresponding point on the other hand. He succeeded in doing so when the right hand was stimulated, but when the left hand was pricked, it straightened out and the crossed avoiding reaction occurred, even when the two hands were only a few centimetres apart. The patient did not demonstrate finger agnosia, autotopagnosia, or right–left confusion.

Stereognosis

With his eyes closed, the patient correctly named objects placed in each hand, but took seven seconds longer to identify a series of 14 different items when they were placed in the left hand. There was little difference in his ability to recognise by touch, from among a collection of other items, an object identical to the one placed in the opposite hand (three to four failures out of 10). When the object was named verbally by the examiner, recognition by touch, with the eyes closed, was very similar for both hands (correct 9/10 times), although the test was performed more quickly by the right hand.

TACHISTOSCOPIC TESTING

Visual acuity was 8/10 for each eye, and 10/10 after correction. The visual field measured by the Goldman technique was normal. Ocular motility and the fundi were normal, as were vestibular tests.

Methods

The patient was tested twice weekly from 4 November to 24 December 1971. The testing unit was adapted from that described by R. W. Sperry. The patient was seated behind a vertical transparent screen 1×0.6 m placed facing him on a table. The screen was divided into two by a vertical meridian with a fixation point at its centre. A projector placed behind it and equipped with a roller-blind shutter flashed pictures selectively to one or both visual fields, at 1/5 or 1/10

second. The patient could slide his hand under the screen to retrieve objects hidden from his view on an insulating cloth that covered the table. The patient's head was held stationary, and all tests were monocular, the eyes being studied in turn. The patient was made to fix his gaze on the central point of the screen before each projection. The pictures of the letters and objects presented were all more than 10 cm high. Three series of tests were carried out: verbal identification of the pictures; recognition by touch of the object projected, from among a collection of different items; and imitation of pictured hand poses.

Results

Naming tests

Pictures of 20 *common objects* were projected at 1/5 second to the left visual field. The patient could name none of these, saying only that he saw a square, a shape, or nothing at all. However, 11 out of 20 pictures projected to the right visual field were named correctly, or almost correctly for some items—for example, round for button, pencil for fountain pen.

Pictures of capital letters flashed to the right visual field at 1/5 second were all identified correctly, but the patient was unable to name them when they were projected at the same speed to the left visual field.

Words of four or five letters projected to the right visual field at 1/5 second were all read correctly, but when these were projected at the same speed to the left visual field, the patient said that 'he had seen something, it was neither an object nor a letter, but he did not know what it was'.

Colours projected to the left visual field at 1/10 second were all named incorrectly. No errors were made in the right visual field.

When two pictures were projected simultaneously, one to each visual field, the picture appearing in the right visual field was named correctly, but he would declare that he had seen nothing in the other field; only the right hand part of composite words was read when these were projected half to one side of the meridian and half to the other, and he was only able to read the two final syllables of four syllable words projected in the same way.

Finally, if two different coloured spots were projected simultaneously, one to each visual half-field, all but one of those presented to the right half were recognised without error, but none of those on the left were named correctly.

Recognition by touch of objects and letters corresponding to pictures projected to one visual half-field

All but one of the *objects* corresponding to the pictures presented to the right visual field were retrieved rapidly by the right hand from a collection of 10 items. The left hand was only able to pick out two objects after lengthy exploration; several times, the patient picked up the correct object, felt it for a long time, but after looking at it, declared it to be the wrong one.

Recognition by touch of objects corresponding to pictures projected to the left visual field was as poor for the right hand as for the left (only two correct answers, after much hesitation). The patient made errors constantly, and wept in despair.

The *10 letters* projected to the right visual field were all identified correctly by the right hand. When the letters were projected to the left visual field, seven out of 10 correct replies were given by the left hand. The patient consistently refused to perform tests with the contralateral hand.

Imitation of hand poses

The left hand did not move at all when a picture was projected to the left visual field. The right hand only succeeded in copying the pose presented to the right visual field once out of 20 times, although each projection provoked an attempt at imitation.

APRAXIA TESTING

Ideomotor apraxia

Left sided ideomotor apraxia was demonstrated in imitated movements with no specific meaning (forming a ring with the thumb and index finger, with one hand alone or both hands interlocking), in symbolic gestures carried out to verbal command (military salute, sign of the cross, V for victory, shaking the fist), and especially in the miming of movements to verbal instruction (taking a cigarette, catching a fly, using a large pair of cutting shears with both hands). In each of these situations, the patient would begin the movement, but the left hand, slow and clumsy, would lag behind, sometimes completely out of synchronisation with the right (especially in the miming of cutting with the shears).

Ideational apraxia

This was clearly demonstrated when the patient was asked to light a candle. He either stuck the extinguished match into the candle, or tried to light the wick with the side of the matchbox.

In order to show up any differences in the manipulation of objects in the right and left halves of the visual field, we asked the patient to hammer a nail into a small wooden board which was placed first at the right then at the left end of the table. The patient was seated in the middle, and made to look straight ahead. The action was always carried out correctly in the left visual field (the hammer in the right hand and the nail in the left). However, in the right visual field (nail in left hand and hammer in right), the left hand tried

to drive the nail into the hammer or scratched it against the hammer. The right hand waved the hammer about in the air, or hit the left hand with it, but was never able to carry out the action required.

Constructional apraxia

Graphic representation The patient was able to draw simple geometric figures correctly to verbal command with the right hand, and outlines of objects showed a fair resemblance but no perspective. The plan of the room was extremely poor. With the left hand, he drew all the geometric figures as a square (except the circle, which was drawn correctly), and drawings of common objects showed no resemblance to them at all.

When asked to copy simple designs with the right hand, instead of drawing in the space next to the model, the patient would keep going over the model itself (closing in). If, however, his hand was first placed over the blank part of the page, he was able to copy a rectangle, circle, or triangle correctly, but failed to copy drawings with perspective. With the left hand, 'closing in' did not occur, and he was able to copy only a rectangle or circle correctly.

Two things must be emphasised—the extreme slowness in the execution of the drawings (30 minutes for 12 figures), with the patient's sharp awareness of his failure, and the fact that the left side of the sheet of paper was never neglected.

In three-dimensional constructions (with building blocks), failure was total when there was no model to copy. With a model, the results were markedly better for the left hand than for the right; when both hands were used together, performance was the same as for the left hand alone.

The patient did not demonstrate bucco-facial apraxia, nor did he have difficulty in dressing himself. There was no visual agnosia. Topographic memory was good. The patient did not neglect the space to his left in his general behaviour. He could cut a thread into two equal parts.

LANGUAGE TESTS

These tests were administered by Mrs Bonner.

Spontaneous speech and naming of objects showed no abnormality.

Reading was slow and laboured, and the patient was only able to read large printed letters. When sentences exceeded four words, he would try to fabricate the rest. Apart from three letters (c for o, y for v, d for b), letter alexia was not observed.

Writing to dictation was poor but possible. In November 1971, the patient took down dictated sentences satisfactorily, but the same test in March 1972, produced unintelligible results. The patient was able to take down dictated letters, except for those difficult to write (R, K, G). He wrote down numbers correctly six out of ten times.

Copying of separate letters was faulty. His attempts to copy a text were slavish and unfruitful; although he spent 10 minutes copying out two lines, his copy made no sense, and bore little resemblance to the original. When he was asked to write with his left hand, he would attempt a few letters and then refuse to continue.

Calculation. The patient's ability to carry out mental calculations corresponded to his educational level. When written down, single figure multiplication and division were carried out correctly: in two figure transactions, the patient used the right method but wrote the figures in the wrong place, thus giving incorrect answers.

INTELLECTUAL LEVEL

The patient's verbal IQ was 87 (Wechsler Bellevue), but he was unable to carry out the performance test. No behavioural disorders were observed by the department staff. The patient was aware of his disorders and this upset him greatly. His memory was good except for lacunar amnesia covering the period at the psychiatric hospital.

FURTHER COURSE OF ILLNESS

Physical examination showed signs of ischaemia in both left limbs with a lowering of the oscillometric index. The clinical diagnosis, given by one of us (Andersson, 1973) in a doctoral thesis, was: 'hemispheric disconnection syndrome; lesions of the corpus callosum and of the right area 18, of vascular origin, or due to the known heavy intake of alcohol'.

The patient was discharged on 24 December 1971. We learnt from his family that when he sat in his usual armchair to the left of the sideboard, he could not pick up his cigarette lighter, which was always kept there, with his left hand. On 14 April 1972, the patient was readmitted for intermittent claudication in the left leg. The visual field was normal (Fig. 2). During the following three weeks, the crossed avoiding reaction occurred with the left arm only, and after that, could not be induced at all. Left sided ideomotor apraxia persisted, however. Brion personally conducted tests for the 'sign of the foreign hand'. In these tests, the patient holds his hands behind his back. One of his hands is then placed in the other by the examiner. 'The patient is unable to tell who the hand belongs to, although he is perfectly aware of the presence of another hand in his own' (Brion, 1972, 1975). The patient would sometimes mistake the examiner's hand for his own left hand, but he always recognised his left hand when it was placed in his right. On 30 April, he went into a delirium which lasted several days and included a fit of jealousy about

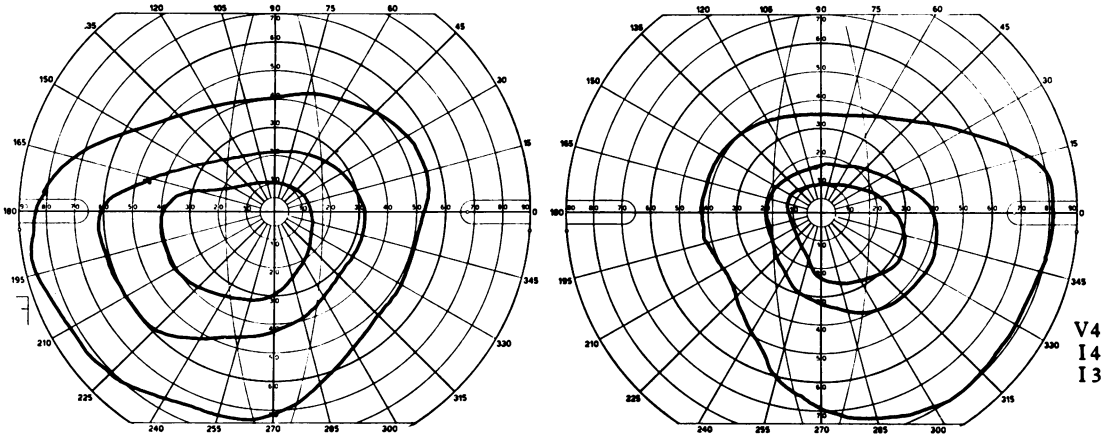

Fig. 2 *Visual fields*

his wife. From June 1972, intellectual deterioration was noted. The patient began to have difficulty in recognising his family and familiar staff, and became withdrawn. He then began losing his way in the wards.

From July 1972 to November 1974, he underwent several thrombectomies on both lower limbs. In March and May 1974, his visual field was tested and left lateral hemianopsia was reported, but the patient was in such a weakened state that it was difficult to conduct the tests satisfactorily. The right limb was finally amputated at the thigh, and he died on 18 November 1975 as a result of postoperative infection.

Neuropathological examination

Macroscopic examination of the brain revealed bilateral frontal atrophy and ochre-coloured infarction of the posterior part of the right lingual gyrus. Coronal sections of the encephalon revealed two cavities in the corpus callosum, the one, anterior, extending from the genu to the level of the section through the hippocampi, the other, posterior, necrosing the entire splenium.

Numerous atheromatous plaques were present, causing a 30% stenosis at the periphery of the right vertebral artery, a 50% stenosis of the left internal carotid, and a 25% stenosis at the origin of the right posterior cerebral artery.

Microscopic examination was made of sections embedded in paraffin and celloidin and then stained with haematoxylin and eosin, PAS, Mallory's phosphotungstic acid, and by the methods of Loyez, Nissl, Bodian, Holzer, and Weil-Davenport.

CORPUS CALLOSUM

The left anterior forceps was demyelinated except in its internal fifth. In the right anterior forceps, a zone of necrosis prolonged the cavity located in the genu; a vast demyelinated zone surrounded this necrosis and extended to the frontal pole, more anteriorly than in the left forceps.

The genu of the corpus callosum was hollow in the centre (Fig. 3B), but the cavity spared two thin strips of healthy tissue ventrally and dorsally, which were separated from it by a 'transitional zone'. However, the most anterior fibres of the corpus callosum were normally myelinated, so that at the anterior extremity of the genu, only two symmetrical lateral cavities were seen at the junction of the corpus callosum and its radiations (Fig. 3A).

On the left, the central cavity was separated from a second, more lateral cavity by an island of demyelinated white matter. The radiations of the corpus callosum were demyelinated. On the right, the cavity did not reach the level of the internal wall of the lateral ventricle, but was separated from it by a zone of slightly demyelinated white matter and a strip of normal periventricular tissue. The demyelination extended into the corpus callosum radiations overhanging the anterior cornu (Fig. 3B).

The appearance of the corpus callosum on the section through the anterior part of the basal ganglia was similar (Fig. 3C).

No necrosis of the corpus callosum was found on the coronal section through the hippocampi, the red nucleus and the thalamus, but there was a central demyelinated zone which diminished progressively, above and below, towards the dorsal and ventral strips of normal tissue, and was prolonged laterally in a thin band which widened in the radiations of the corpus callosum (Fig. 3E).

On the section through the anterior part of the pulvinar and the posterior commissure, the central part of the corpus callosum appeared slightly paler

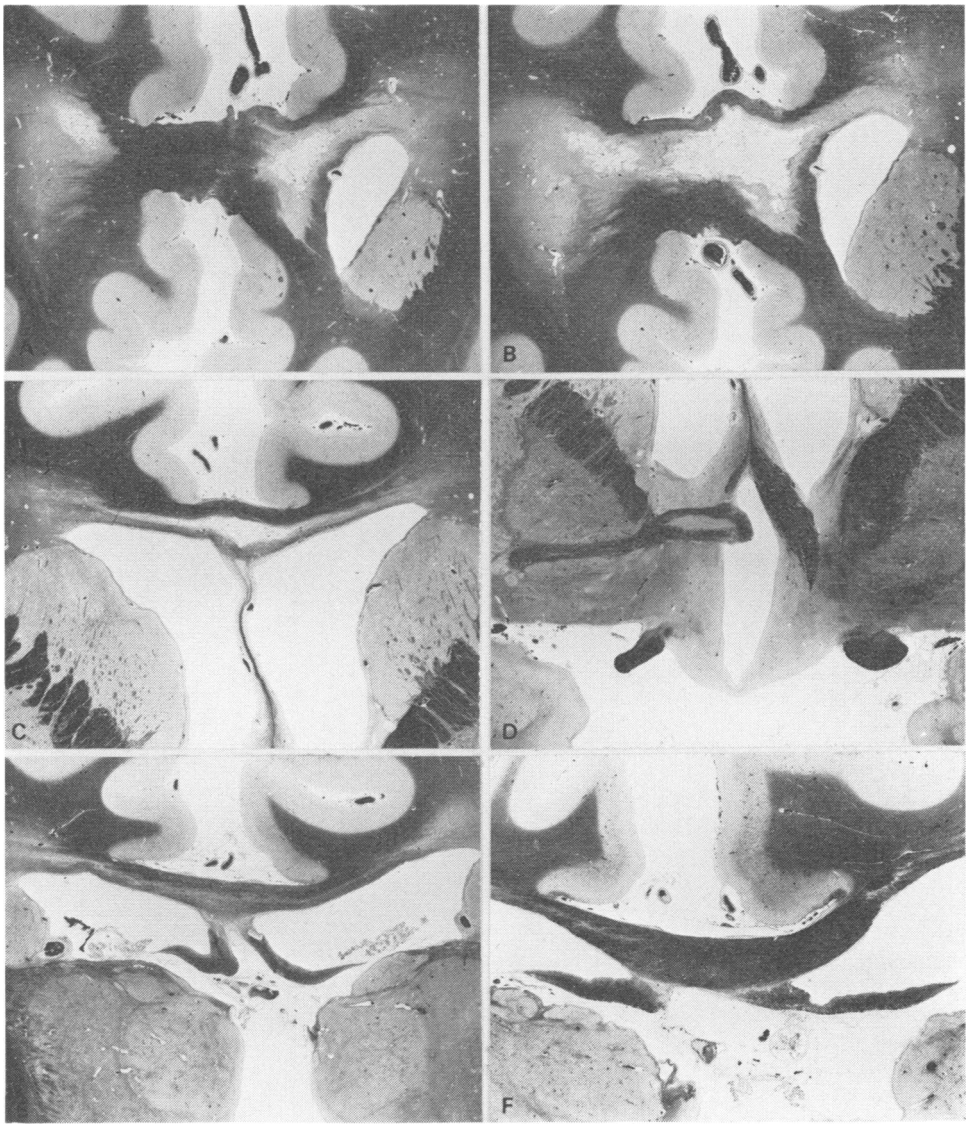

Fig. 3 (A, B, C, E, F) *Coronal sections of corpus callosum showing central necrosis and demyelinisation.* (D) *Necrosis and demyelinisation of the anterior commissure (Loyez)*

than normal; there was a thin bilateral demyelinated band at the junctions of the corpus callosum and its radiations (Fig. 3F).

On the section through the posterior part of the pulvinar, the corpus callosum was hollowed out by a necrotic zone filled with fatty macrophages.

In the splenium, there was a central necrotic cavity which ended in a point in the radiations on the right side. To the left of the cavity there was a small necrotic zone lined with abundant macrophages. At the left extremity of the splenium, extensive necrosis spared only a thin central strip of healthy tissue (Fig. 4A).

Generally, the wall of the callosal cavity was irregular, its tissue spotted with fatty macrophages filled with scattered or clustered haemosiderin. Inside the cavity, there were fragments of fibres of the corpus callosum and glial cells with large, clear oblong nuclei. This appearance was found in both the genu and the splenium.

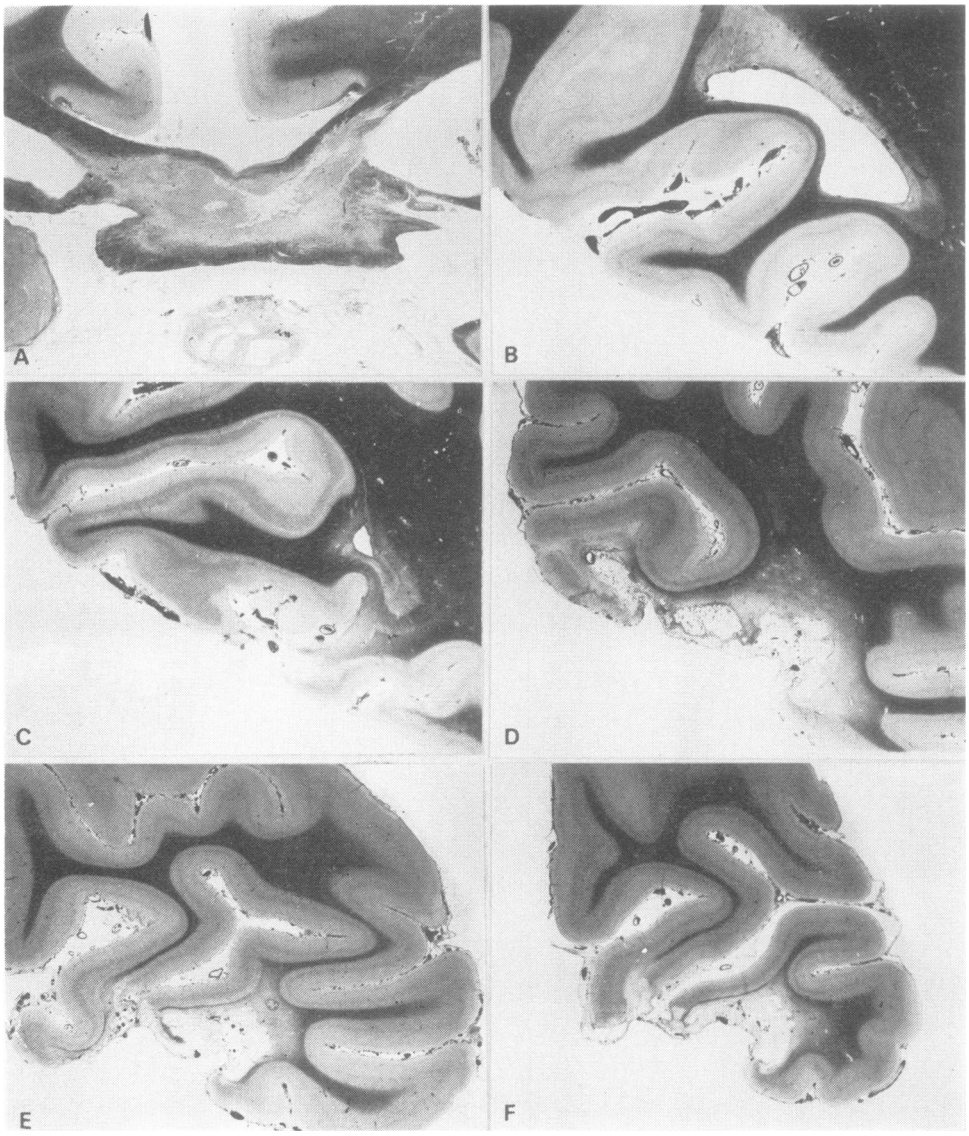

Fig. 4 (A) *Necrosis of splenium of corpus callosum (Loyez).* (B–F) *Section of right occipital lobe showing infarcted lingual gyrus (Mallory)*

In the demyelinated zone, the axons were preserved to differing degrees. Silver impregnation revealed axonal swelling. The myelin at the edge of the zone of normal fibres of the corpus callosum showed chainlike fragmentation. The neurites in proximity to the cavity were destroyed.

In the slightly demyelinated white matter, the arterioles were altered, the media thickened, and the intima hypertrophic; numerous periarteriolar cuffs consisting of a few fatty macrophages and mononuclear cells were present.

The distribution of gliosis in the demyelinated regions was complex. Astrocytic gliosis was present in the entire demyelinated area. In the corpus callosum, it consisted of big oblong astrocytes with large, clear spindle- or kidney-shaped nuclei with one or two pseudonuclei, the cytoplasm sometimes containing granulations which stained bright pink with PAS. On the edge of the necrotic areas, there was no gliosis, but occasional astrocytes with scattered spindle-

shaped nuclei were present; extensive gliosis, however, was present in the demyelinated zone surrounding the necrotic cavity, especially in the genu (Holzer stain was positive), and the splenium. A decreased number of oligodendrocytes was noted in the demyelinated zones, but in the central part of the corpus callosum, where the myelin appeared pale, they were present normally. In proximity to the necrotic regions, especially in the splenium, abundant vascularisation was found.

OTHER COMMISSURES

The entire length of the anterior commissure showed lack of myelin, but the fibres at the ventral and dorsal extremities were spared. The centre of the commissure (Fig. 3D) was necrotic, but there was no real cavity. In the demyelinated region, there were numerous astrocytes with reniform nuclei lying parallel to the nerve fibres. Occasional oligodendrocytes were present. The centre of the commissure contained clusters of fatty macrophages and showed abundant vascularisation. The posterior and habenular commissures were normal. The fornices did not show myelin loss, and the mamillary bodies appeared normal.

WHITE MATTER

A demyelinated zone surrounded the radiations of the corpus callosum, penetrating a short way into the centrum ovale. The occipito-frontal fasciculus, the white matter of the cingulum, and the corona radiata were intact. Numerous astrocytes with large round nuclei and scarcely visible cytoplasm were present in this region, but the gliosis was less abundant than in the corpus callosum. The media of the arterioles in the white matter appeared thick and the intima hypertrophic. Numerous small lacunae, lined with fatty macrophages filled with haemosiderin, were present in the deeper regions.

CEREBRAL CORTEX

Diffuse cortical lesions of varying severity were present in the different lobes. In addition to capillary vasodilatation, cortical atrophy was noted, predominantly in the frontal lobe. The leptomeninges contained fatty macrophages and histiocytic cells, and formed bridges over the deeply hollowed sulci. In the third layer, a clear band corresponding to a neuronal depopulation of varying intensity was seen, with proliferation of small astrocytes. The capillaries were dilated. These lesions were also present at places in the fourth and fifth layers. Spongiosis and neuronal swelling were not observed, nor was there any appearance of central chromatolysis. The lesions were present predominantly in the frontal cortex, at the convexity of the first and second frontal gyri, and in the precentral gyrus, where there was a loss of pyramidal cells. The cingulate cortex and the rest of the internal surface of the frontal lobe were only slightly affected. In the parietal, insular, and temporal cortex, only moderate gliosis was noted in the third layer. In the right second temporal gyrus, a small area of cortical and subcortical gliosis with capillary vasodilatation, probably of ischaemic origin, was present.

The hippocampi appeared normal.

The left occipital cortex was normal. In the right occipital cortex the lingual gyrus was infarcted. Anteriorly, the infarct extended to the coronal section passing through the extreme point of the occipital cornu; at this level, the inferior external cortex of the lingual gyrus was destroyed, and the subjacent white matter was pale and contained large astrocytes; the cortex of the collateral fissure presented only a band of necrosis with gliosis in the third layer; the calcarine area and the optic radiations were intact (Fig. 4C). On a more posterior section, behind the occipital cornu, the infarction extended to the cortex of the lingual gyrus and the subjacent white matter. The calcarine area and the optic radiations were normal (Fig. 4D). At the level of the occipital pole, the lingual gyrus showed cortical and subcortical infarction; the junction of the internal surface of the occipital lobe and the upper and lower lips of the calcarine sulcus were slightly infarcted (Fig. 4E, F).

VISUAL PATHWAY

On myelin staining, the centre of the optic tracts and the peripheral fibres of the chiasma appeared pale. The optic radiations were normal. (The optic nerves were not examined.) With haematoxylin and eosin staining, a few astrocytes with reniform nuclei were found in the central region of the optic tracts.

BASAL GANGLIA

The examination of the basal nuclei revealed numerous lacunae in the head of the caudate nuclei and the lower part of the putamen, where the vessels showed a ferro-calcium encrustation. In the lateral mass of the right thalamus, at the junction of the ventro-postero-lateral and the postero-dorsal nuclei, a small ischaemic zone containing fatty macrophages and bordered with large astrocytes was present.

BRAIN STEM

Small left para-median lacunae were present in the basal portion of the pons.

SPINAL CORD

The fasciculi graciles showed slight loss of myelin. In the grey matter there were numerous arterioles with thickened walls, packed with red blood cells. The

anterior horn of the spinal cord, especially at the cervical and thoracic levels, showed neuronal depopulation. At the lumbar level, fairly abundant central chromatolysis and large deposits of lipofuscin were found.

Discussion

NEUROPATHOLOGICAL STUDY

Extensive reviews of the literature on the subject of Marchiafava-Bignami disease have already been published (Jéquier and Wildi, 1956; Rancurel, 1966; Castaigne, 1971), and we shall thus limit ourselves to a discussion of the features specific to the present case.

In previous descriptions, the whole of the corpus callosum was affected, with the lesions predominating in the anterior third. In the case reported here, the corpus callosum presented the following appearance: anteriorly, a necrotic cavity, followed by a zone of demyelination, then a zone of almost normal tissue and finally, in the splenium, a second necrotic cavity. Only Bohrod and Beach (1942) have described a similar appearance. The slight asymmetry of the lesion is also an unusual feature. Marchiafava *et al.* (1911) reported on two such cases (cases 10, 12), and Constantinidis and Tissot (1971) on one. The absence of neuroglial proliferation observed by Marchiafava and Bignami was a factor of major importance for these authors, a notion that seems subsequently to have become established doctrine. However, numerous accounts of astrocytic gliosis are to be found (Guccione, 1929, case 2; Seitelberger and Brener, 1955; Jéquier and Wildi, 1956, case 2; Boudin *et al.*, 1957; Jellinger and Weingarten, 1961; Cozzo, 1963, 1967; Pons-Tortella and Pou-Seradell, 1965). In the present case, astrocytic gliosis was present in the demyelinated areas of the corpus callosum, staining positive with the Holzer stain (a fact also reported by Riesse *et al.* (1954); only scattered astrocytes were observed in the area immediately surrounding the necrosis. We were struck by the presence of numerous large astrocytes with reniform nuclei. These were also found by Orlando (1952) and Cozzo (1963, 1967), who described them as resembling fibroblasts. We consider that the elongated shape was due to the structure of the corpus callosum. These astrocytes were absent in the demyelinated regions of the hemispheres. Castaigne *et al.* (1971) reported loss of myelin in the anterior commissure in 25 per cent of the cases they reviewed. In our case, this demyelination predominated in the central regions of the anterior commissure and of the corpus callosum.

The cortical changes observed in the present case were described by Morel (1939) as 'alcoholic laminar cortical sclerosis'; a continuous sheet of macroglial cells in the third layer, predominantly in the frontal cortex, with neuronal loss and rarefaction of the myelin fibres outside the third layer. Jéquier and Wildi (1956) in a re-examination of Morel's case 4, found that necrosis of the corpus callosum was also present. Orlando (1952), although he made no reference to 'laminar sclerosis', described identical lesions, which he found in the fifth and sixth layers as well. Delay *et al.* (1959) added the presence of spongiosis in the third layer to this description, and suggested that laminar sclerosis might result from the interruption of the callosal fibres, which Karoll and Pandya (1971) demonstrated as ending in the third, fourth, and fifth layers. In his review of 103 cases of Marchiafava-Bignami disease, Rancurel (1966) noted 19 cases where the lesions fitted the description of laminar sclerosis, and observed that differing degrees of cortical changes, predominating in the external frontal cortex and the third layer, had been reported in 42 per cent of the cases.

Loss of myelin in the visual pathways, which Castaigne *et al.* (1971) noted in 18% of cases, has been known to be associated with intense astrocytic gliosis.

We would like to emphasise that the Marchiafava-Bignami disease in the present case was associated with extensive atheroma in the cerebral arteries, and ischaemic lesions in the basal ganglia, thalamus, pons, and occipital cortex. This is an important feature in the anatomo-clinical correlations that follow. The occipital infarct was old, but it was impossible to determine exactly when it occurred.

HEMISPHERIC DISCONNECTION SYNDROME

Visual symptoms

Our patient's inability to name pictures of objects, letters, or words flashed tachistoscopically to the left visual field can be attributed directly to the disconnection between the right striate cortex and the speech area. It must be remembered that the visual field was normal until one year before death. This syndrome has been described by Gazzaniga *et al.* (1962) after surgical section of the corpus callosum. Tresher and Ford (1937) reported that, after section of the posterior half of the corpus callosum to remove a cyst in the third ventricle, their patient was unable to name letters or objects presented to the left visual field, although she could write normally.

To these observations after surgery, must be added the report by Dejerine (1892) of alexia without agraphia in a case of infarction of the splenium and the left visual cortex, and the very similar case described by Geschwind and Fusillo (1966), who noted, moreover, that their patient was unable to name colours verbally although identical colours were correctly matched. Both these cases demon-

strated right lateral homonymous hemianopsia. Visual stimuli reaching the right hemisphere could not be transmitted to the left parieto-temporal cortex.

In the present case, pictures projected tachistoscopically to the right visual field were named immediately, and corresponding objects were easily recognised by touch with the right hand, but never with the left hand, a factor which can be attributed to the callosal necrosis. Normally, the patient should have been able to recognise by touch with his left hand, an object or letter corresponding to the picture flashed to the left visual field, but he was never able to do so. This failure suggests that the infarct in the lingual gyrus existed at the time of the tachistoscopic studies. Area 17 (in accordance with Fleschig's law) is connected to area 18 by short associational fibres only. It is linked to the motor cortex through the intermediary of area 18, which is the origin of other, longer association fibres to the sensory and motor cortex. Thus, in our patient, the right area 17 was disconnected both from the left hemisphere and from the right motor cortex because of the infarct in the right lingual gyrus which is located in area 18. The discovery of left hemianopsia one year before the death of our patient suggests that the small lesions in the calcarine sulcus may have developed at a relatively late date.

Disturbances in the transfer of somaesthetic stimuli

Our patient showed no evidence of left tactile anomia. Although Delay had discussed this disorder in his thesis in 1935, describing it as 'left sided astereognosis due to callosal lesions', it was through the observations presented by Geschwind and Kaplan (1962) that this inability to name objects held in the left hand really became known; their case presented infarction of the anterior two-thirds of the corpus callosum on pathological examination. In their review of the literature, Brion and Jedynak (1975) suggested that left tactile anomia could be attributed to a lesion located in the central region between the splenium and the anterior third of the corpus callosum. This area was only slightly damaged in the present case. Thus, left tactile anomia was not demonstrated in the splenium syndrome, which was, by contrast, characterised by visual anomia in the left visual field.

Section of the corpus callosum is known to cause disturbances in the transfer of nociceptive and arthrokinetic somaesthetic information, except for that coming from the head and neck region, which is under bilateral cortical control. Sperry *et al.* (1969) noted that after commissurotomy, crossed integration of stimuli to the hands was diminished but not altogether eliminated. Inability to imitate the position of one hand with the other has been demonstrated not only after section of the corpus callosum (Sperry *et al.*, 1969), but also in the case of infarction of the entire corpus callosum (Goldstein, 1908). The phenomenon of sensory extinction in the left arm may be attributed to callosal disconnection (Brion and Jedynack, 1975).

Behavioural disorder of the limbs in the contralateral field of action

The most striking feature of the present case is the behavioural disorder of the limbs in the contralateral field of action. This phenomenon cannot be described as a neglect of the left space, nor can it be attributed to optic ataxia, as it could be induced by contralateral somaesthetic stimuli. It was not dystonia of attitude as it occurred only during a movement triggered off by a contralateral stimulus, nor was it a dystonia associated with a specific action. A stereotyped response of the limbs to contralateral stimulus was observed, with only a few variations depending on the side stimulated and the stimulus itself—that is, inappropriate and ineffective proximal movement, extended proximal and distal posture, accompanied by considerable effort. Apraxia seemed far too general a term to describe this phenomenon, and we preferred to call it an 'avoiding reaction'—a term used by Denny-Brown who did not restrict its use to parietal lesions. The behavioural phenomenon which we have presented here may thus be described as a bilateral but asymmetrical 'crossed avoiding' reaction which can be triggered off by visual or somaesthetic stimuli.

This crossed avoiding reaction, when set off by visual stimuli, only occurred in the left limbs. By turning his head 45° to the right, we sometimes enabled the patient to carry out a movement with the left hand successfully, as this allowed him to use his left visual field. In this way, the right hemisphere received the visual stimulus and controlled the motor response. Right occipital infarction, which interrupted the transfer from the calcarine sulcus to the motor cortex, would account for the frequent failure, even in this position.

In numerous experimental studies attempts have been made to demonstrate the role of the corpus callosum in visually guided movement in animals, although Myers *et al.* (1962) have refuted this hypothesis. A 'split-brain' monkey with vision excluded in one eye by tarsorrhaphy will grasp an object with the hand contralateral to the stimulated eye (Downer, 1965; Lund and Downer, 1970; Trevarthen, 1965). If the side of the closed eye is changed, the monkey will immediately change hand preference (Downer, 1965).

When the animal is forced to use the hand ipsilateral to the eye stimulated, it is clumsy and

ineffective. Section of the optic tract or occipital lobectomy (Lehmann, 1968) has a similar effect to tarsorrhaphy. Thus, 'stimulation of one hemisphere of a split-brain favours orientation towards one particular side of the axis of the body and responsiveness by the forelimb of this side' (Trevarthen, 1965). Since publication of a review on this subject by one of the present authors (Lechevalier, 1973), Brinkman and Kuypers (1973) have demonstrated that, in the monkey, visuomotor coordination of the upper limb in the contralateral visual field can be controlled either by the crossed corticospinal pathway or by an ipsilateral pathway. Visually guided prehensile movements are possible only with the former. With ipsilateral control the limb is directed towards the object, but the extended fingers can only grasp it after previous palpation. These findings apparently contradict our own: in our case, there was no lesion in the left hemisphere to interfere with the operation of a possible ipsilateral system. The rotating movement of the body axis and the raising of the shoulder, however, would seem to be controlled by the ipsilateral pathway, which has perhaps a more limited function in man than in the monkey, the crossed corticospinal pathway being more developed in the former.

Visuomotor disorders have not been mentioned often in the literature, especially after surgical section of the corpus callosum. Two patients observed by Gazzaniga *et al.* (1965) were only able to indicate points on tachistoscopically projected pictures with the hand ipsilateral to the stimulated visual field. In a later publication (1967), the same authors noted that the ipsilateral hand was, in fact, able to carry out very simple movements, as long as there was not any simultaneous projection of information to the other visual field. This success could be ascribed to ipsilateral corticospinal control. Stenvers (1961) described a patient (Case 34) with glioma of the corpus callosum and the right frontal lobe, who was unable to seize an object presented to the left visual field with the right hand, which remained motionless. In two cases of agenesis of the corpus callosum described by Rohmer *et al.* (1959) the patients were unable to pick up objects presented to one visual half-field with the contralateral hand, the disorders predominating in the left visual field.

Trevarthen and Sperry (1973) emphasised that after section of the corpus callosum in man, visual stimuli projected to the periphery of the visual half-field were perceived by both hemispheres. Peripheral vision would thus be projected mainly *via* 'extra-geniculo-striate' pathways. After relay and bilateralisation in the midbrain, the stimuli may be projected to the occipital cortex on both sides.

In our patient, the asymmetry of the crossed avoiding reaction triggered off by visual stimuli can be ascribed to the right occipital lesion. After section of the neocortical commissures, these 'extra-geniculo-striate' pathways probably serve as substitute pathways thus making ipsi- and contralateral visuomotor coordination possible, on condition that the occipital lobes are intact, which was not the case in our patient. Another explanation could be that through rapid scanning movements of the eye, afferent visual impulses could reach the left occipital lobe, setting off the motor response in the same hemisphere, and thus allowing the patient to pick up an object in the left visual field with his right hand. This transfer could not be made in the right hemisphere, however, as the afferent visual impulses reaching the right calcarine sulcus could not set off motor responses there, due to the infarct in the right lingual gyrus.

The crossed avoiding response cannot be considered only as a visuomotor disorder. In tests of interhemispheric transfer of nociceptive or arthrokinetic information, it occurred almost unfailingly in the left limbs, and once every two or three times in the right arm. What we have described here is, in fact, a behavioural disorder of the limbs in the contralateral 'field of action'. We have preferred this term to 'contralateral half space' as the disturbed movement is a motor response to a stimulus and not an exploratory movement in the contralateral half space. The asymmetry of the crossed avoiding reaction in response to arthrokinetic or nociceptive stimuli could perhaps be explained by the asymmetry of the hemispheric lesions: the callosal lesions were more marked on the right, and there was a small thalamic infarct in addition to the occipital infarction on the same side. Thus the right motor cortex was more deprived of sensory and visual afferent impulses than the cortex of the left hemisphere, from which, moreover, it was separated. Therefore, the crossed avoiding response can be ascribed to the absence of motor response in one hemisphere to the somaesthetic and visual stimuli received by the other hemisphere.

Apraxia and agraphia

The unilateral left sided ideomotor apraxia demonstrated by our patient was particularly apparent in intransitive movements. This cannot be attributed simply to a disconnection of the right motor cortex from the speech area. The disorder was not solely apraxia to verbal instruction, as in the case reported by Geschwind and Kaplan (1962), since even on imitation, the performance of the left hand remained poor. Although far less marked than the irrelevant movements of the right arm described by Liepmann (1900) in the case of the imperial counsellor, T . . . , the left sided apraxia demonstrated by our patient can

be explained using Liepmann's diagram. Liepmann placed the eupractic centre in the 'sensomotorium' located in the left parietal lobe; this lobe would then control the symmetrical right 'sensomotorium' through the intermediary of the corpus callosum. It must be remembered that although, in this study, a case of unilateral right sided apraxia was reported, it was specified in a later report (Liepmann and Maas, 1907) that this patient was, in fact, ambidextrous. In the case of the patient Ochs, described in the latter report, left sided apraxia was noted. In both cases, infarction of the corpus callosum in association with other ischaemic lesions was found.

In addition to cerebrovascular disease, callosal tumours have been reported as a cause of left sided apraxia (Hartmann, 1907; Hoff, 1931; Brion and Jedynak, case 2, 1975). Left sided apraxia has also been observed after surgical section of the corpus callosum (Gazzaniga *et al.*, 1965). In the present case, a distinction must be made between the left sided ideomotor apraxia and the crossed avoiding reaction, the latter being provoked by contralateral somaesthetic stimuli only. Ideational apraxia was demonstrated in both hands in the manipulation of objects. A most remarkable feature was the considerable intensification of the apraxia when both hands were used together in the right visual field. This was not only due to impaired visuomotor coordination, but also to the inappropriate movements shown by both hands. We believe this increased inability to be attributable to a combination of ideational apraxia and disturbed visuomotor coordination in the right visual field.

Left agraphia was suspected at the first test as the patient refused to write with the left hand. He could write correctly to dictation with the right hand, but was unable to copy a model. Left agraphia was confirmed at a later stage. Agraphia ipsilateral to the dominant hemisphere, first reported by Liepmann and Maas (1907), is not accompanied by aphasia and is demonstrated more in writing to dictation than in copying (including numbers). Brion and Jedynak (1975) who described four cases of left sided apraxia (two with callosal tumours, cases 2 and 6, and two with vascular malformation, cases R and C), listed the characteristics of this disorder and concluded that callosal apraxia cannot occur without agraphia, as both of these disorders are attributable to a callosal lesion situated just in front of the splenium.

The constructional apraxia demonstrated by our patient was more marked in the left hand than in the right in three-dimensional constructions to verbal command. With a model, the performance with the right hand was clearly poorer than with the left. This difference would seem to indicate the importance of minor hemisphere control in spatial representation. In two-dimensional drawings, the right hand consistently demonstrated 'closing in'. This never occurred with the left hand. Left dysgraphia with transitory right dyscopia was observed by Bogen and Gazzaniga (1965) and Bogen (1969) in eight commissurotomised epileptics who were given drawings of the Greek cross or a cube to copy. A similar disorder was reported by Brion and Jedynak in three of their patients, and Gazzaniga *et al.* (1965) described an epileptic who, after section of the interhemispheric commissures, showed a better left handed performance in copying simple figures with perspective.

Apraxia has been mentioned briefly in some of the accounts of Marchiafava-Bignami disease: marked ideomotor apraxia with agraphia was mentioned by Rancurel, (case 4, 1966) and Jéquier and Wildi (case 1, 1956) and meaningless and irrelevant movements by Cozzo (1963) and Bignami and Nazari (case 4, 1915), but it is difficult to assess in these last two cases whether the disorders were due to true apraxia or simply to mental confusion or dementia.

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