Role of the basal ganglia and cerebral cortex in tardive dyskinesia: evidence from cerebrovascular accident

Sir: Animal models have elucidated the role of both the basal ganglia and cortico-spinal tracts in tardive dyskinesia. Confirmation in humans could be obtained by examining the effect of accidental brain lesions on the development and clinical course of tardive dyskinesia. To our knowledge no such cases have been reported. We now report such a case.

In 1972, a 48 year old non-hypertensive man with a 12 year history of schizophrenia and neuroleptic exposure (haloperidol, thioridazine, chlorpromazine, etc) had a sudden onset of weakness in the left arm and leg. Two years later at age 50 he gradually developed involuntary movements of the right arm and leg. At this time the patient had recovered substantially from his left hemiparesis and was able to ambulate and use the left arm without much difficulty. He continued on treatment with various neuroleptics through 1985 when he was readmitted to the hospital for control of his involuntary movements, having been tried on several medications without success. Neurological examination at that time revealed a very mild left hemiparesis with minimal left sided hyper-reflexia and hypertonicity. The patient postured the left arm in a flexed position and was able to ambulate normally. There was no sensory deficit to pin, vibration or position. There were no involuntary movements of the left arm and leg. Marked stereotypic and continuous semirhythmic involuntary movements of both the right upper and lower extremities were present on sitting and standing. Minimal stereotypic mouthing movements were also present. An asymptomatic left systolic carotid bruit was heard and occasional premature ventricular contractions were noted on examining the heart.

A CT scan showed a radiolucent area involving the right caudate (fig a). Doppler studies revealed extensive atherosclerosis and stenosis of the left carotid artery. Neuroleptic treatment was gradually discontinued over a few days. The involuntary movements were almost completely suppressed over a period of 6 weeks with gradual increments of reserpine up to 2.25 mg/day in divided doses. No recorded episodes of hypotension nor side effects were encountered.

Seven weeks after admission, while awaiting consultation on his vascular disease, the patient had a sudden onset of weakness in the right arm and leg. Reserpine was discontinued. Examination revealed a right hemiparesis involving the arm more than the leg and an expressive dysphasia. There was no sensory deficit. Right sided involuntary movements were no longer present. The left carotid bruit and left hemiparesis remained unchanged. The vascular disease consultant determined that the patient was not a surgical candidate. The patient was placed on aspirin 650 mg bid and dipyridamole 50 mg tid. During the next month there was a marked improvement in the dysphasia and right hemiparesis and the patient was again able to ambulate. However, there was a gradual but not total return of his right sided involuntary movements affecting the

Fig (a) CT scan showing area of involvement of first cerebrovascular accident: right caudate. (b) CT scan showing area of involvement of second cerebrovascular accident: left frontal lesion. Right sided lesion as in (a).
leg more than the arm.

Repeat CT scan revealed the aforementioned findings and evidence of a large left frontal infarction (fig b). Echocardiogram was normal. Holter monitor revealed occasional runs of unifocal premature ventricular contractions and he was started on procainamide 250 mg qid.

This case illustrates how a lesion to the basal ganglia can prevent the onset of tardive dyskinesia (the first CVA) and how a lesion to the upper motor neuron pathways can suppress an already existing tardive dyskinesia (the second CVA). Prior to the second cerebrovascular accident our patient had marked tardive dyskinesia in the right arm and leg and none in the left arm and leg. It is thus virtually certain that the first cerebrovascular accident did, in fact, prevent the onset of the left hemi-tardive dyskinesia since patients with asymptomatic tardive dyskinesia always have at least some dyskinesia on the less affected side. 2

The basal ganglia sends fibres to the ipsilateral cortex to modulate voluntary motor activity of the contralateral limbs. The fibres to the cortex and the returning corticospinal tracts both pass through the internal capsule which, in turn, is close to the caudate nucleus. We cannot exclude the possibility that involvement of either of these fibre pathways is responsible for the prevention of the tardive dyskinesia. However, we consider these possibilities to be far less likely since there was no sensory deficit and the left hemiparesis was minimal. We consider the prevention of tardive dyskinesia to be more likely due to the caudate infarction visible on CT scan (fig). Tardive dyskinesia is thought to be caused by hypersensitive postsynaptic dopaminergic receptors on the neurostriate (caudate and putamen) portion of the basal ganglia. 3 Eliminating the receptors before they have a chance to become hypersensitive would be expected to prevent tardive dyskinesia.

The upper motor neurons comprise the final common pathway for all motor movement. The second cerebrovascular accident shows that their destruction can suppress an already existing tardive dyskinesia. While all the right hemi-tardive dyskinesic movements were orginally suppressed by the CVA, they returned with greater severity in the leg as it was least affected by the stroke. We thank Lena DiMauro for typing this manuscript.

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Chorea and the lupus anticoagulant

Sirs: Chorea is a well recognised but rare accompaniment of systemic lupus erythematosus (SLE) and may occasionally be the only neurological feature.1–3 The pathogenesis is obscure but recently an association with the lupus anticoagulant has been suggested. 2 I report the case of a young woman with acute chorea in whom the presence of the lupus anticoagulant was the only serological abnormality. She had the other complications commonly associated with the anticoagulant: recurrent spontaneous abortion, thromboses and mild thrombocytopenia,6 but had none of the classic features of SLE. Her chorea stopped after the introduction of low dose aspirin.

A 22 year old white Caucasian was admitted to the Radcliffe Infirmary, Oxford, on 2 September 1985 for investigation of chorea. One month prior to admission she had developed right-sided involuntary movements which started in the hand but rapidly progressed to involve the whole of the right side. Her speech had become slurred. One week prior to admission, her mother had noted left-sided involuntary movements of which the patient was unaware. There were no other neurological or psychiatric symptoms.

In November 1983, she had an incomplete abortion at 12 weeks gestation and in December 1984 a missed abortion at 22 weeks. In January 1985, she had been admitted to another hospital with an acute anterior myocardial infarction. This was complicated by a life threatening pulmonary embolus. A coronary angiogram 6 months later showed stenosis of the left anterior descending artery, thought to be the result of a recanalised thrombus.

There was no family history of chorea, psychiatric, rheumatological or vascular disease. She smoked 20 cigarettes per day. She was on no medication and had never received an oral contraceptive pill.

On examination, she was generally fit and well. There were no rashes, arthropathy or lymphadenopathy. She was in sinus rhythm, all peripheral pulses were normal and her blood pressure was 110/55 mm Hg. Her heart was not enlarged, but there was a soft systolic murmur compatible with mild mitral regurgitation secondary to papillary muscle dysfunction. Bed-side testing of higher mental function was normal. She was mildly dysarthric. Her gait was steady, but on walking she had wild gyrations of the arms. Choreiform movements of all the limbs, head and face were present at rest, more marked on the right side. She was unable to maintain tongue protrusion. Eye movements and the remainder of the cranial nerves were unremarkable. Power, tone and sensation in the limbs were normal, all deep tendon reflexes were present and the plantar responses were flexor.

The following investigations were all normal: urea and electrolytes, creatinine, liver function tests, calcium and phosphate, blood glucose, thyroid function tests, cerebroplasmin, serum and urinary copper, fasting cholesterol and triglycerides. Haemoglobin 11·7 g/dl. White cell count 6·3 × 109/l with a normal differential. Platelets 117 × 109/l, ESR 30 mm/hour. Prothrombin ratio (PTR) 1·2, kaolin clotting time (KCT) 83 seconds (normal 64 seconds). Kaolin cephalin clotting time 52 seconds, (normal less than 40 seconds); attempted correction with 1:1 patient and normal serum only reduced the kaolin cephalin clotting time to 50 seconds, indicating the presence of an inhibitor rather than clotting factor deficiency. The thrombin time, antithrombin III and factor VIII levels, and fibrinogen titre were normal. Anti-nuclear and double stranded DNA antibodies negative. Cardiolipin antibody (VDRL) positive but specific syphilis tests negative. Complement levels C3 92 mg/dl (69–130), C4 17 (12–27). Creative protein <0·6 mg/dl (<0·8). Chest radiographs and CT scan of the brain were normal. Electrocardiogram showed evidence of an old full thickness
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