

SHORT REPORT

Parkinson's syndrome after closed head injury: a single case report

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Abstract

A 36 year old man, who sustained a skull fracture in 1984, was unconscious for 24 hours, and developed signs of Parkinson's syndrome 6 weeks after the injury. When assessed in 1995, neuroimaging disclosed a cerebral infarction due to trauma involving the left caudate and lenticular nucleus. Parkinson's syndrome was predominantly right sided, slowly progressive, and unresponsive to levodopa therapy. Reaction time tests showed slowness of movement initiation and execution with both hands, particularly the right. Recording of movement related cortical potentials suggested bilateral deficits in movement preparation. Neuropsychological assessment disclosed no evidence of major deficits on tests assessing executive function or working memory, with the exception of selective impairments on the Stroop and on a test of self ordered random number sequences. There was evidence of abulia. The results are discussed in relation to previous literature on basal ganglia lesions and the effects of damage to different points of the fronto-striatal circuits.

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Parkinson's syndrome as a component of post-traumatic encephalopathy in boxers and National Hunt steeple chase jockeys is well recognised.¹ A relatively pure "striatal" variant of the punch drunk syndrome has also been occasionally described.² However, very few convincing cases have been described after a single closed head injury. More than 50 years ago, Crouzon and Justin-Besancon³ proposed a set of minimum operational criteria for the diagnosis of Parkinson's syndrome secondary to acute head injury. They considered that the trauma should be severe and have led to concussion or unconsciousness, that there should be a close temporal relation between the acute trauma and the onset of parkinsonian features, and that the course of the subsequent Parkinson's syndrome should be uninterrupted. Factor *et al* increased the stringency of these criteria by insisting that there should also

be evidence of midbrain damage or compression established at necropsy or by neuroimaging.⁴

The only convincing examples of post-traumatic parkinsonism after acute closed head trauma that we have found in the literature are the cases reported by Lindenberg⁵ and the report by Nayernouri.⁶ The first case of parkinsonism after an acute spontaneous intracranial haematoma, after rupture of a right middle cerebral artery aneurism, has recently been described.⁷ Well documented cases of parkinsonism after a contralateral ischaemic lesion of the striatum are rare. Fenelon and Houeto reported a case of non-progressive unilateral parkinsonism occurring a few months after an ischaemic stroke.⁸ Brain MRI was suggestive of an ischaemic lesion in the territory of the left lenticulostriate arteries involving the entire striatum, apart from the fundus striati, and probably most of the lateral pallidum.

We now report a further case of Parkinson's syndrome, which we consider to have occurred probably as a direct consequence of closed head trauma.

Case report

A 24 year old barman was involved in a road traffic accident in 1984. He sustained a skull fracture and a fractured right arm, and was unconscious for 24 hours with post-traumatic amnesia lasting several weeks. According to the patient and accessible medical notes he was in hospital for 1 month, during which time he received no neuroleptic drugs. Six weeks after the head injury, the patient noticed a coarse resting tremor, marked loss of dexterity, and slowness in his right hand, and complained of forgetfulness. Over the next 3 years there was little change in his symptoms, but in 1989 he started to drag his right foot and noticed a mild additional shaking of his right leg. Seven years after the accident, a mild resting tremor of his left hand appeared and his speech was increasingly slurred. Over the next few years a slow progression of his parkinsonism occurred, with no response to levodopa or anticholinergic therapy.

In June 1995, he was seen at the National Hospital for Neurology and Neurosurgery. There was no history of previous exposure to dopamine antagonists. He smoked 10 cigarettes

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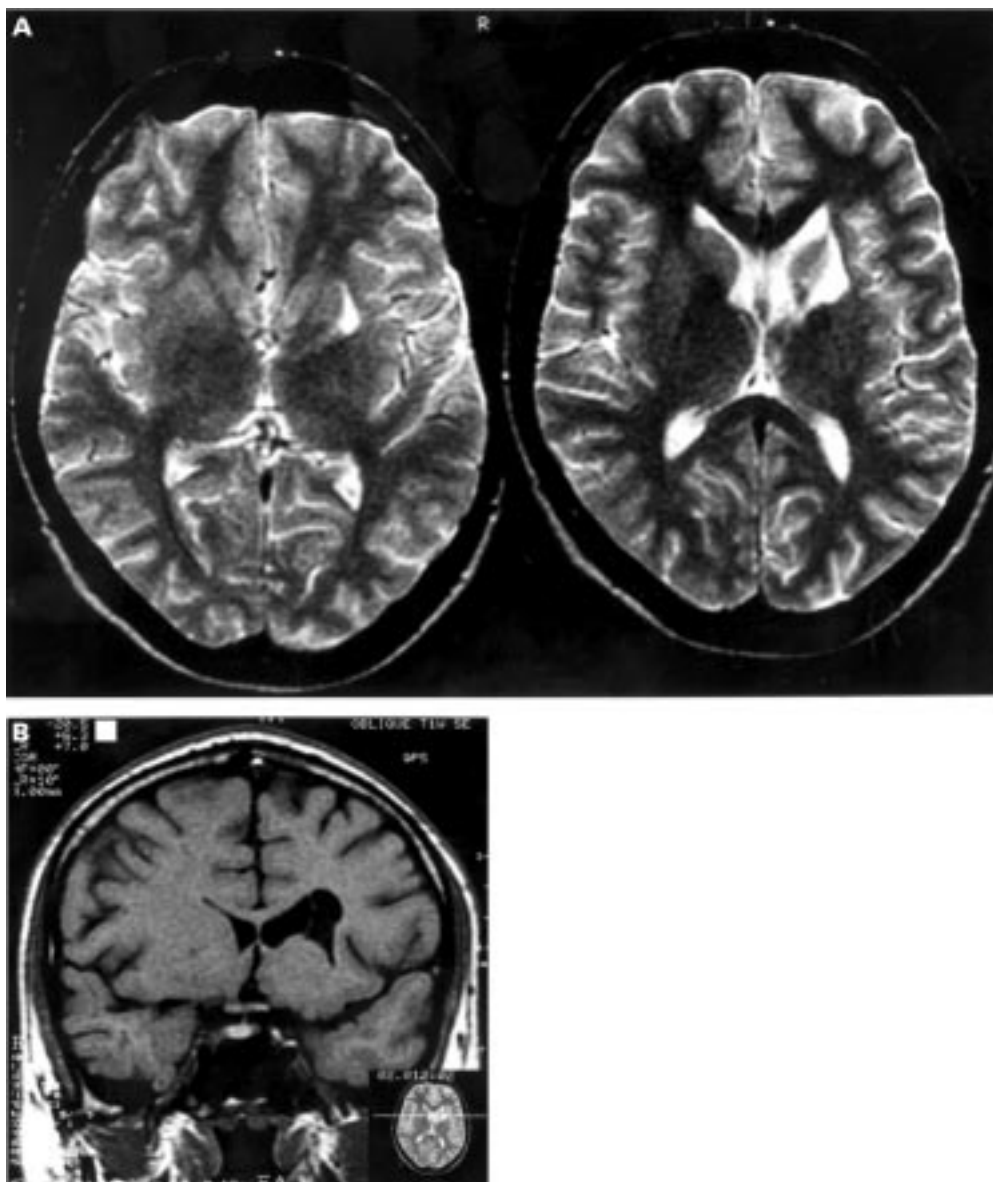


Figure 1 (A and B) MRI showing a well defined area of abnormal signal adjacent to the frontal horn and anterior part of the body of a slightly enlarged left lateral ventricle, most probably a post-traumatic infarct.

a day and had drunk 30 units of alcohol a week for the past 10 years. He was developmentally dyslexic, and had attended a special school up to the age of 15, after which he had worked as a steeplejack and later as a storeman and then as a barman. He had been right handed before the accident, but had subsequently switched to using his left hand for many dexterous activities. There was no family history of Parkinson's syndrome or essential tremor.

On examination, he had an oblique scar in the medial region of his forehead about 9 cm long. He was alert and oriented, but was slow to respond to questions. He had facial hypomimia, a markedly reduced blink rate with a positive glabellar tap sign and occasional blepharoclonus. Eye movements were full in range, but he had diminished convergence and fine horizontal gaze evoked nystagmus to the left. His tongue was tremulous and his speech quiet and monotonous. There was a coarse pill rolling, 5 cycles/second, resting tremor of the

right hand with an associated postural tremor, and a mild resting tremor of his right leg and left hand. He had severe right sided lead pipe rigidity with cogwheeling at the right wrist and mild left sided stiffness. There was moderate bilateral bradykinesia and hypokinesia, worse on the right than the left, with striking micrographia. He had absent right arm swing and a slightly diminished left arm swing.

The fractured right arm was well healed by the time of our assessment and there was no residual loss of function.

There were no cerebellar signs, the plantar responses were downgoing, and there was no evidence of autonomic failure.

Normal investigations included a full blood count, urea and electrolytes, fasting blood glucose, lipids, serum B₁₂, thyroid function, routine liver function tests, serum copper, and caeruloplasmin. Wet blood film screening for acanthocytes was negative and treponemal serological tests were also negative. His eryth-

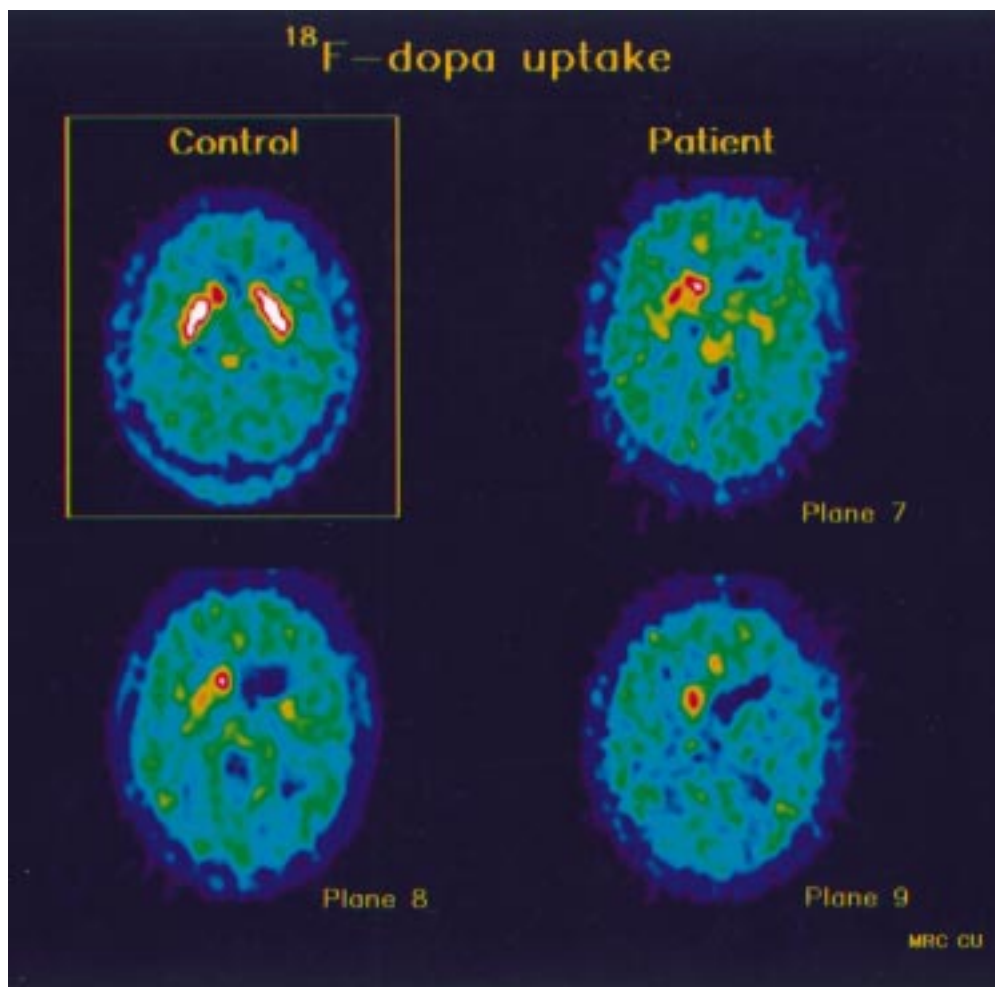


Figure 2 Positron emission tomography using ^{18}F -dopa showing bilateral reduction of putamen uptake.

rocyte sedimentation rate was 12 ml/hour and chest radiography, ECG, and EEG were normal. Slit lamp examination showed no Kayser-Fleischer rings.

Finally, an acute subcutaneous apomorphine challenge and oral levodopa challenge tests were negative, confirming dopaminergic unresponsiveness. However, he developed choreiform peak dose dyskinesia in his right arm on increasing the dose of sinemet to 1000 mg daily in January 1998.

Results

NEUROIMAGING

Brain CT showed an area of low density, interpreted as focal brain damage, in the left caudate nucleus, extending into the lentiform nucleus, with ex vacuo enlargement of the adjacent frontal horn.

On brain MRI this area was seen as a well defined area of non-specifically altered signal, slightly higher than that of CSF on all sequences; it was concluded that this was most probably a post-traumatic infarct. The lesion involved the head and the anterior part of the body of the caudate nucleus, extending laterally into the anterior limb of the internal capsule, reaching as far as the genu, and across to the anterior third of the putamen. It extended superolaterally into the centrum semiovale and

inferiorly to the anterior part of the globus pallidus. There was in addition a small focus of similarly non-specific abnormal signal in the white matter of the anterior right temporal lobe, associated with minor shrinkage, presumed to represent postcontusional encephalomalacia. The remainder of the cerebral hemispheres seemed normal, as did the midbrain and infratentorial structures (fig 1A and B).

A brain perfusion SPECT study showed a single abnormality seen as an area of focal reduction in perfusion to the white matter close to the left basal ganglia. The perfusion ratios to the grey matter of the cortex and to the basal ganglia on the right hemisphere were within normal limits.

Positron emission tomography using ^{18}F -dopa showed a reduced uptake in the right putamen ($0.0055 \text{ Ki min}^{-1}$) and normal caudate ($0.0091 \text{ Ki min}^{-1}$) compared with control values (caudate 0.0106 ± 0.0019 , putamen $0.0098 \pm 0.0011 \text{ Ki min}^{-1}$). The ^{18}F -dopa uptake on the left side was also markedly reduced, however, the anatomical distortion, induced by the lesion made this result uninterpretable (fig 2).

NEUROPSYCHOLOGICAL ASSESSMENT

Our patient had undergone neuropsychological assessment on two previous occasions: the

first in 1994, 10 years after the head injury, and the second 9 months after the first. The current assessment was performed 3 months after this second assessment and included neuropsychological tests, of which we summarise only the most relevant results.

The Wechsler adult intelligence scale-revised⁹ indicated functioning at a low average to borderline level, reflecting a pattern of ability which was longstanding and developmental in origin. Reading and spelling tests¹⁰ reflected dyslexic difficulties.

During the current assessment of memory functions, on the Rey auditory verbal learning test¹¹ his immediate span was low for his age, but probably in accord with his intellectual level. He showed some evidence of verbal learning, but also some loss of material after a delay of 45 minutes, with three false positives.

Performance was also assessed on some tests of executive function, such as the Wisconsin card sorting test, Weigl sorting task, verbal fluency, Reitan trail making, and Stroop test.¹²⁻¹⁶ With the exception of the Stroop colour word test¹⁶ there was little evidence of deficits on tests of executive function or behavioural regulation. On the Stroop test, interference was evident during colour naming of 32 colour words written in incongruent ink compared with naming the colour of 32 coloured rectangles.

We also evaluated our patient's performance on tests of working memory which require holding information "on line" and monitoring responses. He showed a selective impairment on the test of self ordered random number sequences¹⁷ and similar to that for patients with Parkinson's disease.¹⁸

On the Beck depression inventory (BDI) he obtained a score of 26.¹⁹

ASSESSMENT OF MOVEMENT PREPARATION, INITIATION, AND EXECUTION

Visual simple (SRT) and four choice (CRT) reaction time tasks were completed, as well as the Purdue pegboard and index finger tapping.^{18 20} On all these tests our patient performed worse than an age matched healthy normal subject and similar to previously published data^{18 20} for elderly patients with Parkinson's disease. For both the SRT and CRT tasks his initiation times were slightly slower and his movement times considerably slower with the right hand compared with the left. Movement related cortical potentials (MRCPs) in our patient were compared with a normal age matched subject, and the amplitude of all components was reduced.²¹ The MRCPs before left hand movements had a smaller amplitude and more delayed onset, with the early Bereitschaft Potential component possibly being absent, suggesting bilateral deficits in MRCPs.

Discussion

The association between acute head injury and the development of a Parkinson's syndrome has been an issue of controversial debate since James Parkinson's essay in 1817.²² Although authors reported Parkinson's syndrome after craniocerebral trauma,²³⁻²⁹ there have been only

a few cases with sufficient evidence to implicate closed head trauma as an aetiological factor. It is possible that the rarity of reported cases reflects the fact that head injuries severe enough to badly damage the basal ganglia often lead to death.^{29 30} Mechanisms which may be relevant to the development of Parkinson's syndrome after acute head injury include tearing of small brain stem vessels by shearing forces, direct traumatic injury to blood vessels leading to secondary thrombosis and infarction, and downward displacement of the brain stem leading to contusion or haemorrhage. Tears occurring between the substantia nigra and surrounding structures and the cerebral peduncle may also be important pathogenetic factors. It is also possible that morphological changes may not indicate the full extent of traumatic damage, but changes in neurotransmitter sensitivity and distal functional effects may also be important.

We think that acute head trauma is the likeliest aetiological cause for the Parkinson's syndrome in our patient. There was a close temporal relation between the onset of symptoms and the head injury which was severe enough to leave radiologically demonstrable focal brain injury in the left lenticular nucleus. The Parkinson's syndrome progressed much more slowly than expected for either Parkinson's disease or another neurodegenerative cause such as multiple system atrophy and there was no response to dopaminergic therapy. Functional imaging indicated that there was bilateral impairment of dopamine function in the nigrostriatal terminals, raising the possibility that the head injury had caused more substantial damage than was evident on anatomical imaging. Bilateral reduction in tracer uptake also raises the possibility that our patient's symptoms might be consistent with idiopathic Parkinson's disease, or that unilateral structural damage (left caudate and lenticular nucleus in our patient) can cause bilateral striatal dopaminergic dysfunction with retrograde degeneration of nigrostriatal terminals. Unilateral dopamine denervation models support the potential importance of dopaminergic interdependence between the two nigrostriatal systems.³¹⁻³⁵ For example, bilateral striatal dopamine depletion induced by unilateral lesion dorsal to substantia nigra was described in monkeys.³⁵ The nigral dopamine was severely reduced on both sides in the chronic experiments weeks after a unilateral caudate lesion in cats.³⁴

From a meta-analysis of the 240 cases with focal basal ganglia lesions reported in the literature, Bhatia and Marsden³⁶ concluded that Parkinson's syndrome was exceptionally rare, found only in 16 of the 240 cases (6%). Small (n=1) or large (n=4) lesions of the putamen, small (n=4) or large (n=1) lesion of the globus pallidus, or the lentiform nucleus (n=3), and in one case a large caudate lesion. In the patient studied by us, such a predominantly left sided subcortical damage was associated with a mainly right sided parkinsonism. There was also slowness of initiation of movement and particularly movement execution quanti-

fied on the reaction time tasks, and alterations of MRCPs. Such deficits have previously been reported for elderly patients with Parkinson's disease.¹⁸⁻²¹

There is evidence of an asymmetry of motor effects after cortical lesions. Wyke³⁷ reported that whereas dominant hemispheric lesions produced bilateral motor deficits, damage to the non-dominant hemisphere affected only contralateral limb movement. In our patient, the bilateral nature of the deficits shown by the reaction time tasks and MRCPs raises the possibility that subcortical motor structures show a hemispheric asymmetry—similar to that found after cortical damage.

Abulia—that is, apathy with loss of initiative, spontaneous thought, and emotional responses—was found to be the commonest behavioural disturbance among 240 cases with focal lesions of the basal ganglia.³⁸

In light of this, our patient's slowness in responding to questions during the interview and the high score on BDI are of interest. He had endorsed items reflecting loss of interest, lack of enjoyment, difficulty in decision making, greater sense of fatigue, but absence of sadness. These suggest abulia rather than depression. Abulia is primarily a motivational deficit that can impair performance of willed actions. The surface manifestations of abulia can be similar to bradykinesia and akinesia, which are motoric deficits. Therefore, it is possible that the slowness of movement initiation and execution found in our patient by the reaction time tests, partly reflects the motivational deficits associated with abulia rather than the motor slowness associated with bradykinesia.

The current assessment suggested some loss of learnt material after a delay of 45 minutes. However, as impaired delayed recall was combined with correct delayed recognition of the 15 words, albeit with three false positives, this suggests mainly retrieval rather than retention deficits. The cause of the memory problems are difficult to determine. Focal lesions of the basal ganglia can be associated with retrieval deficits,³⁹ and presence of abulia can contribute to impairment of effortful retrieval. Additionally, in our patient MRI showed an abnormal signal in the anterior right temporal cortex, and on that basis impairment on tests of non-verbal memory would be expected. Memory for non-verbal material was not included in the current assessment and the results of the two prior assessments of cognitive function were inconsistent with regard to the presence or absence of such memory deficits.

Focal lesions of the basal ganglia do not result in uniform effects on cognitive function. Dubois *et al*³⁸ concluded that in terms of cognitive function, lesions of basal ganglia are associated with normal intellectual efficiency, preserved linguistic and spatial abilities, limited "frontal" dysfunction, memory retrieval deficit, and procedural learning disorders. They noted that the dysexecutive syndrome seen in patients with basal ganglia lesions was less severe than in patients with degenerative diseases of the basal ganglia such as Parkinson's disease.

This finding is borne out by the case studied by us. This patient was assessed on a range of tests considered to tap "frontal" executive function. With the exception of the Stroop test, there was little evidence of deficits on tests on which patients with idiopathic Parkinson's disease have been found to be significantly impaired.²⁰ Successful performance on the Stroop test requires development of a "perceptual set" for suppression of the dominant response of reading the words to name the colour of ink of the colour words printed in colour incongruent ink. Our patient had problems in developing or maintaining such a set. This was coupled with a selective impairment on a specific test of working memory, self ordered random number sequences, with relatively normal performance on other tests of working memory, such as self ordered pointing, random number generation, and missing digits. This selective impairment on a specific test of working memory is reminiscent of the results reported by Robbins *et al*,³⁹ who studied a young man with a left striatocapsular infarct, with a specific deficit when "carrying out a form of working memory task in which the subject has to 'self-order' a series of responses using a self-generated strategy". These same processes are also involved in the self ordered random number sequences on which our patient was impaired.

In monkeys, lesions of the dorsolateral prefrontal cortex have been shown to impair performance on tasks involving non-spatial working memory requiring monitoring and self ordered performance.⁴⁰ The test of self ordered random number sequences used in the current study has previously been shown to activate the dorsolateral prefrontal cortex in a PET study with healthy participants.⁴¹

The finding that our patient with damage predominantly to the left striatum showed a selective impairment on this test, suggests that as the effects of damage to the prefrontal cortex in the monkey,⁴² damage to the striatum can also produce deficits in self ordered working memory.

This is consistent with previous evidence that in the monkey, similar deficits are produced on tasks such as the delayed response or object reversal after lesioning the prefrontal cortex or the striatum—that is, at two different points in the frontostriatal loops.⁴²⁻⁴³ However, our patient and the case studied by Robbins *et al*,³⁹ showed a specific impairment of working memory in the absence of major deficits in other tests of executive function previously found to be impaired in patients with damage to the frontal cortex.⁴⁴ This suggests that despite similarities, in humans, the effects of striatal and prefrontal lesions are not quantitatively or qualitatively identical.⁴⁰⁻⁴⁴

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