

Acute Frontal Lobe Syndrome and Dyscontrol Associated with Bilateral Caudate Nucleus Infarctions

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Background. A 67-year-old man presented with acute onset of spatial and temporal disorientation, memory loss and associated episodic dyscontrol. Investigations showed infarctions of both caudate nuclei. This patient presented a unique opportunity to study the relationship between the lesions, his behaviour, and neuropsychological testing.

Method. Single case report. Investigations included interviews to determine cognitive impairment, i.e. WAIS-R, MMSE, and neurological examination.

Results. Extensive neuropsychological testing revealed severe impairment on tasks requiring planning, memory or abstract thought. These findings are very similar to those seen in Huntington's disease.

Conclusions. A neurobiological hypothesis is proposed to account for his symptoms, and recent discoveries in the basic sciences used to inform his management.

Case report

Mr C, a 67-year-old man, with a 13 year history of type 2 diabetes mellitus complicated by peripheral vasculopathy, was found late one night wandering beside the electrified track between two stations on the London Underground system. When found by police, he appeared confused and stated that he was walking through the tunnel to get to Portsmouth *en route* to France. A former policeman and well respected company worker, he was described by informants as a hard-working man with a normal premorbid personality. There was a six year history of minor cognitive decline. During this time he had become gradually less interested in social activities and his previously high standards of personal hygiene, although he had been able to live independently and to care for himself until the day prior to admission.

On admission he was alert and in clear consciousness. He was elated, jocular and disinhibited. His speech was loud, pressured and difficult to interrupt. There was severe confabulation, perseveration, and circumstantiality, but no evidence of grandiosity, delusional beliefs, hallucinatory experiences or of a change in appetite or sleep patterns. He was grossly disoriented in time, place and person. It was difficult to engage and maintain his attention. He had very poor concentration and severely impaired short-term memory. Initial Mini Mental

State Examination (MMSE) score was 22/30. Neurological examination revealed a prominent pout reflex, but no other neurological abnormalities, and in particular no other frontal lobe signs or movement disorders. He was normotensive and apart from an elevated plasma glucose, blood chemistry and haematology were normal. During the first interview and subsequently, until treatment was started, he had repeated, severe, catastrophic rage reactions which were usually precipitated by minor frustrations, and would be associated with violent and aggressive outbursts which would cease only very gradually. On some occasions he absconded from the ward and would immediately become lost. His subsequent rage reactions constituted a very real danger to the public. A full psychometric assessment was clearly impossible at this stage. A CT brain scan was performed (Fig. 1) which showed infarctions in the heads of both caudate nuclei and the thalamus; large cerebral ventricles, and periventricular lucencies consistent with vascular disease within the white matter. Treatment was successfully instituted initially using haloperidol to achieve some behavioural control, which was gradually phased out as carbamazepine was introduced. A full psychological assessment was then carried out.

He had an average premorbid intellectual capacity, as indicated by his educational and employment history. The Wechsler Adult



Fig. 1 Computerised tomographic scan showing infarctions in the central portion of the heads of both caudate nuclei (arrows). A small area of infarction can also be seen inferiorly in the thalamus.

Intelligence Scale Revised (WAIS-R) revealed: full scale IQ = 80, performance IQ = 72, and verbal IQ = 86. Analysis of the various sub-tests of the WAIS-R showed a very good performance on tests of information and digit span, while he did moderately well on tests of vocabulary, arithmetic, similarities, picture completion, and block design. However, he did very poorly on tests of comprehension, picture arrangement and digit symbol. There was poverty on tests of verbal fluency and marked concreteness when asked to explain proverbs. On the short Wisconsin Card Sorting Test (WCST) he made 48 errors, and no correct categories.

Discussion

Clinical findings

The initial clinical picture was suggestive of an acute dementia of the frontal lobe type. However, while *chronic* frontal lobe lesions are notorious for not having any neurological localising signs, this neurological 'silence' is more unusual in acute frontal lobe lesions, and here there was only a

pout reflex. In addition it was established that the onset had been extremely rapid, indicating a catastrophic event. It is of interest that the results of the neuropsychological testing were not only indicative of a subcortical type of dementia, but were virtually identical to those observed in Huntington's disease (HD), in which degeneration of the caudate nuclei (CN) is a prominent feature (Jacobs & Huber, 1992).

The caudate nucleus and behaviour

Increasing evidence supports the notion that subcortical structures are involved in many behavioural and psychological activities (Cummings, 1993). One of the most studied of these structures is the CN, which has attracted particular attention because of its association with HD. The involvement of the CN in psychological and behavioural activity is not surprising since it receives projections from higher order association cortex, as well as the hippocampus and amygdala (Parent, 1990).

Acquired lesions of the CN are quite rare: there are fewer than 50 cases in the world literature, and ours is only the second bilateral case. Sporadic case reports (e.g. Pozzilli *et al*, 1987) have indicated that lesions of the CN may be associated with apathy and with disturbances of memory, language, praxis and gnosis. Impaired problem solving abilities and disinhibition have also been described (Richfield *et al*, 1987). Two series have attempted a more systematic delineation of the neurobehavioural associations of caudate lesions. Mendez *et al* (1989) described 12 patients with lesions in the CN, in only one of whom was the damage bilateral. Two also had other neurological lesions, and the patient with bilateral lesions was described as having dementia (MMSE score of 18/30). These patients displayed acute behavioural changes characterised by apathy, disinhibition or disturbances of mood. Interestingly hallucinations also occurred in two patients: auditory in one and visual in another. Seven of these patients (excluding the individual with bilateral CN lesions) underwent neuropsychological testing, which indicated impairment of tasks requiring planning and sequencing.

In a second series, Caplan *et al* (1990) described 18 patients with unilateral lesions of the CN. This study is more difficult to interpret since lesions extended into the internal capsule in nine of the patients, and into the putamen in five. There were variable abnormalities, including disturbances of language and speech, apathy, agitation and

hyperactivity. Clearly in none of these subjects was the behavioural disturbance as profound as in the patient described here.

Dysfunction within the caudate nucleus has been implicated in depressive illness (Krishnan *et al*, 1992) and perhaps in schizophrenia (Buchsbbaum, 1990). Our patient showed no evidence of either of these disorders. While one could speculate that this was attributable to the 'protective' effect of a normal premorbid personality, it must be recognised that the CN is a large volume of tissue, and it is highly likely that it contains many functional domains. Specific psychiatric symptoms may be a consequence of lesions within specific—and as yet poorly-defined—regions in the CN.

Evidence from patients and from animal work indicates a series of five frontal-subcortical circuits, all of which run from specific regions in the frontal lobes to the thalamus via the CN (Cummings, 1993). Lesions in the CN have the effect of disconnecting frontal cortex from subcortical and perhaps limbic structures. The first is a motor circuit originating in the supplementary motor area, which runs through the ventral caudate to the globus pallidus and finally the thalamus. Lesions in this circuit appear not to have behavioural consequences. The second is an oculomotor circuit which originates in the frontal eye fields and passes through the central body of the CN. The third circuit passes from the dorsolateral prefrontal cortex through the dorsolateral head of the CN. Deficits in this circuit lead to difficulties in 'executive function' and motor programming. Particular deficits occur on the Wisconsin Card Sorting Test, and on tests of verbal and design fluency. These problems were clearly present in this patient, indicating that this circuit was interrupted, which is confirmed by the position of the lesions on CT scan.

The fourth circuit begins in the lateral orbitofrontal cortex and passes through the ventromedial cortex. Lesions in this circuit lead to marked changes in personality, with disinhibition, inappropriate behaviour, irritability, imitation and utilisation—an enslavement to environmental cues. Clearly all were present in this patient, and the site of the lesion is shown on the CT scan. A final circuit runs from the anterior cingulate gyrus through the ventral portions of the CN. Lesions here can result in akinetic mutism. This portion of the CN appears to have been spared, judging by the clinical picture and the imaging studies. Consideration of what is now known of the connections of the CN, and the site

of the lesions in this case, provides a clear explanation for the behavioural and neuropsychological findings.

While it is quite clear that the observed behavioural changes were superimposed upon a picture of a very gradual cognitive decline over the preceding years, it is also apparent that there was a sudden catastrophic change in this man. He changed, in a matter of hours, from being a self-caring individual to one who was seriously incapacitated, and a danger both to himself and to others. Over the subsequent two months his behaviour gradually normalised as treatment was instituted, although there was presumably also improvement as the acute effects of the cerebrovascular accident receded. Unfortunately his severe cognitive impairment remained entirely unchanged.

Management

Initially he presented a serious problem because of his highly aggressive behaviour and rage reactions. Benzodiazepines may be associated with paradoxical effects, particularly in brain damaged individuals. Haloperidol was selected partly for its sedative effects, but mainly because of its high affinity for dopamine receptors, which appear to have a 'permissive' effect for aggressive behaviour: in mice aggression can be ameliorated by blockade of dopamine-D₂ receptors (Nikulina & Kapravola, 1992). His catastrophic reactions began to respond to this treatment in three days, allowing titration of the dosage against his response. The speed of this response suggests, but does not prove, that it was due to dopaminergic blockade, which has normally been attained in this period, rather than just sedation. Carbamazepine is frequently used to treat victims of head injuries who exhibit catastrophic reactions, and it appears to help episodic dyscontrol (Lewin & Summers, 1992).

The dosage was adjusted according to plasma levels, which were maintained within the anticonvulsant range. Because of the risks of antipsychotic agents in the elderly, and the consideration that haloperidol might, by lowering the seizure threshold, antagonise the effects of carbamazepine, its dosage was rapidly reduced, and he was ultimately maintained on 1.5mg/day, until further medical complications supervened. In view of his severe vasculopathy and accompanying complications, his long-term prognosis is unfortunately very poor, and despite

the behavioural control he remains severely incapacitated, requiring long-term residential care.

Implications

- The caudate nucleus has important roles in human behaviour.
- Lesions at this site should be considered in patients with acute onset of confusion, disorientation, catastrophic reactions or frontal lobe signs.
- Unless contraindicated, conventional antipsychotic agents and carbamazepine may be of value in cases marked by catastrophic reactions or dyscontrol.

Limitations

- A single case report.
- The dramatic findings were superimposed on a previous, gradual cognitive decline.
- The lesions probably involved several of the discrete pathways of the caudate nucleus, preventing a more detailed cognitive and behavioural dissection.

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