

Abnormal MRI signal in the rigid form of Huntington's disease

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Abstract

Eighteen patients with Huntington's disease (HD) were examined with MRI. Eleven had the common hyperkinetic form, seven had the rigid variant. All seven patients with rigid HD had increased signal intensity in the neostriatum in intermediate and T2-weighted images. Only one hyperkinetic HD had similar findings. In all the other cases, signal abnormalities were questionable or absent. Histological differences that account for differences in signal intensity may therefore lie in the caudate nucleus and putamen. Age of onset may be important, since the rigid patients were younger. Follow up studies may help in understanding these signal differences.

Huntington's disease (HD) is a disabling degenerative disease with autosomal dominant inheritance, clinically characterised by involuntary hyperkinesia, affective-emotional disturbances and intellectual deterioration, usually beginning between 35 and 45 years of age. HD clinical features may be variable and an atypical form mainly characterised by plastic rigidity and a Parkinsonian-like posture has been described.¹ This "rigid" variant of HD is more common in young patients, but similar cases have also been observed in adults. The classic hyperkinetic HD may often evolve toward an akinetic state.¹

Gross pathological changes include diffuse cerebral atrophy and, more characteristically, atrophy of the striatum. The head of the caudate nucleus shrinks considerably and the profile of the frontal horn of the lateral ventricle therefore becomes flattened. The putamen is also reduced in size, and, less commonly and to a lesser degree, the pallidum may be affected.²

Atrophy of the head of the caudate nucleus with enlargement of the frontal horn, the most characteristic aspect of HD, was demonstrated in vivo even by pneumoencephalography. It is demonstrated by CT and MRI. Density changes have not been reported on CT, nor has abnormal increased signal intensity been reported on MRI studies.^{3,4} MRI is better for demonstrating, in transverse and in coronal sections, the atrophy of the head of the caudate nucleus. No signal abnormalities are mentioned in a series of 12 patients with HD by Kido *et al*;³ decreased signal intensity in

the neostriatum in T2-weighted images at 1.5 T was described by Rutledge *et al* in four cases, consistent with increased iron content.⁴

We have recently observed high signal intensity in T2-weighted images in cases with the rigid variant of HD. We report a series of patients with HD, in which we compare the signal abnormalities of the cases with the rigid variant versus the cases with the classic hyperkinetic form.

Methods

We reviewed a series of 18 patients with HD. Eleven patients had the typical hyperkinetic form and seven had the rigid variant. All the patients had a family history of HD, as proved by examination of other affected members of the family and a review of medical records. Diagnosis of rigid HD was made according to Bruyn and Went's criteria, when a definite rigidity was observed. To our knowledge, no necropsy had been performed on other members of the affected families.

Of the 11 hyperkinetic HD patients, seven were males, and four females. Age ranged from 17 to 63 years (mean 45.2 years); disease duration ranged from one to 14 years (mean 5.1 years).

Of the seven rigid HD patients, three were males, four females. Age ranged from 14 to 47 years (mean 28.8 years). Disease duration ranged from three to nine years (mean 5.7 years). These patients presented rigidity and bradykinesia. In three subjects, postural tremor was observed; in four cases, mild hyperkinesia involved face and distal segments of the limbs.

Physical disability was estimated by the Shoulson and Fahn rating scale.⁵ Mean (SD) disability rating was 6.42 (3.55) for the rigid form, and 7.09 (3.20) for the hyperkinetic form.

All patients were studied with MRI 0.5 T. One patient with the rigid form was also examined with a 1.5 T unit. All the examinations included sagittal T1-weighted images and transverse SE intermediate and T2-weighted images. Occasionally T1-weighted images in coronal or transverse planes were available.

Results

All patients presented with atrophy, both diffuse and focal, particularly involving the head of the caudate nucleus (fig 1). No differences

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Received 16 July 1990
and in final revised form
20 December 1990.
Accepted 9 January 1991

Figure 1 HD, hyperkinetic form. (A) Severe atrophy of the head of the caudate nucleus (arrowheads) in coronal section in a 42 year old male. (B) Atrophy of the putamen (arrowheads) in transverse section in a 57 year old female. No signal abnormalities in both cases (SE 2100/50); compare the signal intensity of the neostriatum with that of the insular cortex.

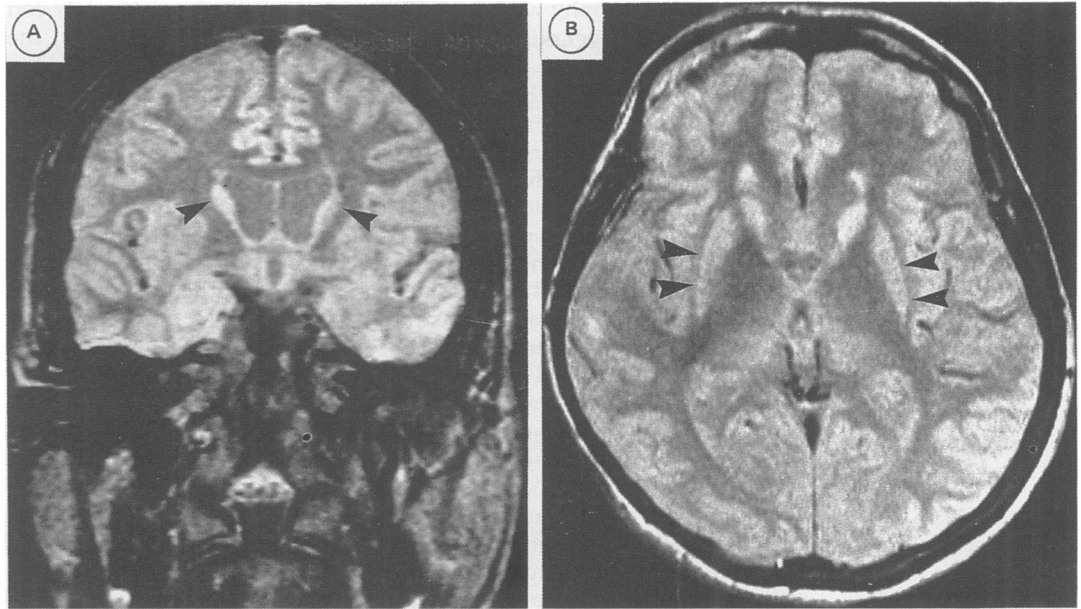
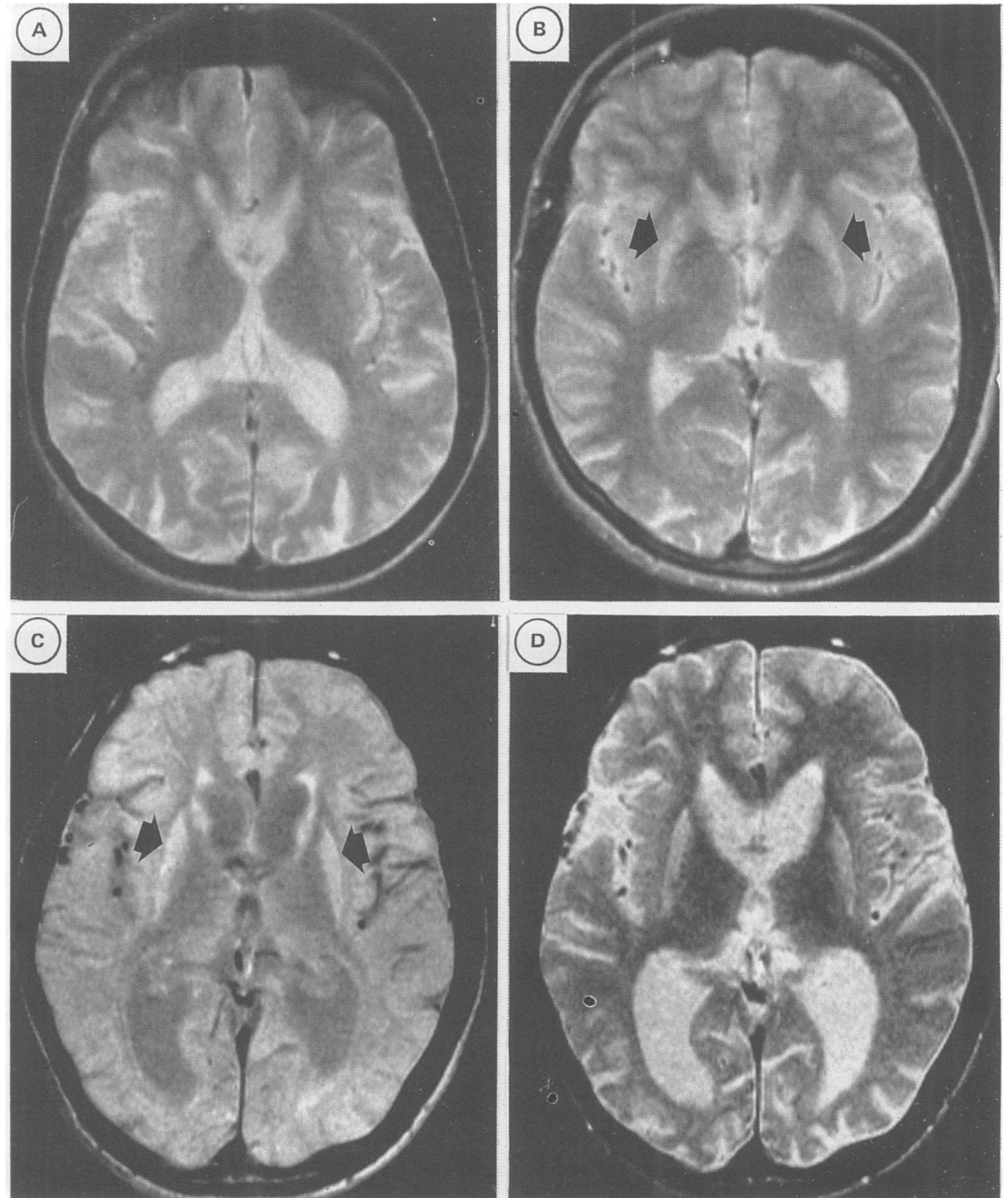


Figure 2 (A) Hyperkinetic HD in a 43 year old female. No abnormal signal intensity in T2-weighted image (SE 1933/100). (B) Rigid HD in a 23 year old female. Slightly increased signal intensity in T2-weighted image (SE 2100/100), (arrows). (C) and (D) Intermediate and T2-weighted images (SE 2100/50, 100) in a 28 year old male with rigid HD; increased signal intensity in the neostriatum (arrows) is more evident.



in severity of atrophy were found between the two groups of hyperkinetic versus rigid HD patients.

All patients with the rigid form of HD presented signal abnormalities consisting of mild to moderate hyperintensity in the caudate nucleus and putamen in intermediate weighted images and, all but one, also in T2-weighted images. The single study performed at 1.5 T showed signal hyperintensity in the neostriatum, more marked in the putamen, as the 0.5 T examination had demonstrated. In the group of typical hyperkinetic HD, only one patient, a 17 year old man with a two year history of the disease, presented signal hyperintensity in the neostriatum similar to that demonstrated in the patients with the rigid variant. Two other patients presented a milder hyperintensity in the neostriatum. The other eight patients had normal signal intensity except for occasional, questionable hyperintensity in the neostriatum only in intermediate weighted images but normal signal intensity in T2-weighted images (figs 2 and 3).

Discussion

There are various observations about the histological differences between rigid and hyperkinetic HD.

Dom *et al*⁶ reported an almost complete loss of the smaller small cell population and an outfall of large neurons of the striatum in the rigid form. Conversely, Bugiani *et al*,⁷ emphasised the survival of large striatal neurons in the rigid variant; this form could be the expression of the inhibition of the substantia nigra resulting from an unbalanced striatal output. The importance of pallidal lesions have also been advocated to explain rigidity in HD.^{8,9} It is generally accepted, however, that the neuronal loss is more marked in the putamen in the patients with the rigid form, in whom a global putaminal volume loss is more evident.^{2,8,10} The presence of more extensive damage in rigid HD

has been recently confirmed by immunohistochemical studies; these studies demonstrated that, in the rigid variant, striatal neurons projecting both to the lateral and medial segments of the pallidum are lost, while in the hyperkinetic form the projections to the medial globus pallidus are preserved.¹⁰ In our series of patients, MRI constantly demonstrated increased signal intensity in intermediate and T2-weighted images in the caudate nucleus and in the putamen in the patients affected by the rigid form of HD. With one exception, this signal abnormality was not seen or was very mild or questionable in the hyperkinetic HD patients.

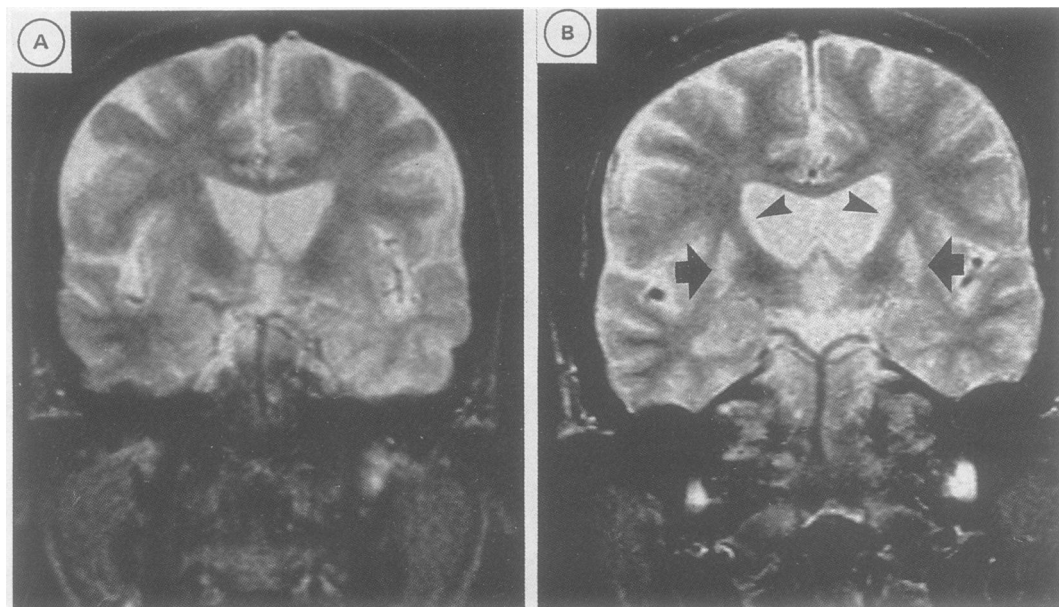
Signal hyperintensity in intermediate and T2-weighted images is consistent with increased amounts of water, therefore compatible with cell loss or gliosis. In the only rigid case studied with 1.5 T magnet, hyperintensity was seen, just as in the 0.5 T study. No hypointensity in T2-weighted images consistent with increased iron content was demonstrated in this patient, as reported by Rutledge *et al* in four cases.⁴

According to our data, it seems that the histological differences between rigid and hyperkinetic HD lie in the neostriatum and that the importance of changes in the pallidum or other locations should probably be excluded. There are no differences in disease duration and disability scale between the two different forms that account for the signal abnormalities.

It will be extremely interesting to observe follow up MRI studies for the possible development of signal abnormalities in the hyperkinetic patients, if some of them become akinetic.

The younger age of the patients with the rigid variant might also have some importance in determining the high signal intensity, since the only patient with equal hyperintensity in the hyperkinetic group was the youngest subject of this latter group. In fact, it has been

Figure 3 Coronal sections in a 43 year old female with hyperkinetic HD (A), and in a 24 year old male with rigid HD (B), (SE 1933/100). Signal hyperintensity is present in the putamen (arrows) and caudate nucleus (arrowheads) only in the rigid patient.



reported that the forms of HD with juvenile onset are associated with a more marked cell loss and atrophy of the neostriatum.¹¹

In conclusion, the signal hyperintensity in the neostriatum described here is not exclusively observed in the rigid form of HD, but seems to be a characteristic of this variant; it is very rare in the classic hyperkinetic form.

We thank Dr F Tagliavini, neuropathologist, for his helpful comments. This study was partly supported by a grant of the Associazione Italiana Corea di Huntington. Presented in part at the 42nd annual meeting of the American Academy of Neurology, Miami Beach, Florida USA, May 1990.

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