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Cortico-basal ganglionic degeneration: radiological and functional features

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Background. *Cortico-basal ganglionic degeneration is a rare degenerative pathology that involves parietal areas and gradually determines frontal involvement. The aim of our work was to describe the main radiological findings in this pathology and to evaluate the cortical activation in these patients by f-MRI during simple and complex movements.*

Patients and methods. *We have evaluated eight patients with morphological and functional magnetic resonance by using a 1.5 T imager.*

Results. *Morphological evaluation: We found an asymmetric perirolandic cortical atrophy in seven patients, a mild hyperintensity in the perirolandic cortex in five patients, a mild atrophy of the basal ganglia in seven patients and, in one, a hypointensity in the lenticular nuclei. In one patient the morphological aspect was normal. Functional evaluation: The most important aspect was the hypoactivation of the parietal areas during the movement with the affected hand in all the patients.*

Conclusions. *We consider f-MRI a helpful tool for the diagnosis and follow-up of this pathology.*

Key words: basal ganglia diseases, cortico-basal degeneration; magnetic resonance imaging; fluorine radioisotopes, f-MRI; movement, apraxia, parietal lobe

Introduction

Cortico-basal ganglionic degeneration (CBGD) has become a more widely recognized entity: it has been considered as a degenerative movement disorder since its first description by Rebeiz thirty years ago.[1] Since then, one hundred cases have been reported,[2] but it remains a rare disease of unknown incidence and prevalence.[3,4]

CBGD usually presents after the fifth decade of life, with a varied combination of symptoms including stiffness, clumsiness, jerking, segmental dystonia, bradykinesia and usually ideomotor apraxia which can progress to the complete development of an »alien hand syndrome«. Other symptoms, such as action-induced and stimulus sensitive

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focal reflex myoclonus may precede or accompany the development of dystonic postures.[5] Invariably, it leads to a progressive disability (both motor and cognitive) which gradually leads to immobilization and institutionalisation.

Logistic regression analysis identified two models that contributed to distinguish these disorders and predicted the diagnosis of CBGD. The first one included asymmetric Parkinsonism as symptom onset and instability and falls at first clinic visit. The other one included cognitive disturbances, asymmetric parkinsonism within the first year of symptom onset and speech disturbances at the first clinic visit.[6] A recent evaluation[7] suggests that cognitive signs of disruption, which comprise a marked impairment of daily living functions, may be the commonest presentation of CBGD, rather than the better recognised perceptual-motor syndrome, described previously.

Radiological evaluation seems to be important as a diagnostic and clinical follow-up instrument. The most constant expression of the pathological features are: an important atrophy of the perirolandic gyri, particularly in the postrolandic cortex, associated with a mild atrophy of the basal ganglia,[8-10] and an almost evident, though not constant hypointensity of the lenticular nuclei.[8-10]

The possibility of a direct and functional evaluation of cortical activation during hand motion, registered in CBGD patients, seems to us very interesting. This was the aim of our study: we discussed the results with an overview of literature.

Patients and methods

During the period between 1st January 1997 and 1st January 2002, eight patients (three males and five females) were included into our observation. Their mean age was 62.1 years old (SD + 6.9), all of them were right-handed (average score at Briggs and Nebes Test: + 22.56).[11]

The past history of all the patients was completely mute for cerebrovascular disease, hypertension and metabolic disorders. No signs of addiction could be found. Their most common complain was the relatively recent development of an asymmetric akinetic syndrome (55% of cases), affecting in all the eight patients their left superior limb, ideomotor apraxia (43% of cases), bradykinesia (36% of cases), alien-limb syndrome (16% of cases), slurred speech (5% of cases) and gait difficulty (5% of cases). Only two of the subjects (35% of cases) showed action tremor and one of them (13% of cases) supranuclear gaze palsy affecting vertical and horizontal gazes (evidenced at oculomotor evaluation). All the patients underwent a complete oculomotor evaluation: a normal saccadic velocity (considering anti-saccades, reflexive saccades and voluntary saccades), with increased latency of saccades (especially of voluntary saccades) and preserved pursuit and optokinetic nystagmus were globally evidenced.

The mean duration of symptoms dated from 7.62 + 5.32 months prior to their admission.

From the cognitive perspective, intelligence performances were within normal ranges (111 + 2.34) as stated by the average score obtained in Raven Standard Progressive Matrices;[12] the patients recognised right/left personal and extrapersonal hemispace, and no signs of tactile agnosia and of bucco-facial apraxia were found. Wechsler Adult Intelligence Scale (WAIS) average results demonstrated a mild general tendency to global deterioration (21.1% SD + 2.34%).[13] All the patients could reproduce Koh's Block quite well, by copy and by memory. Wechsler Memory Scale (WMS)[14] put in evidence an MQ average score of 56.35 (SD + 5. 41), underlying a mild deterioration of logical, procedural and verbal memory strategies. All the subjects could not pantomime to

verbal command of the examiner: all together showed signs of ideomotor apraxia with the left, affected hand. On the contrary, they did not show signs of ideational apraxia. All the patients showed moderate insight into their general situation, but principally into their motion disruption.

All the patients underwent brain-MRI, performed by a 1.5 T magnet. For the morphological evaluation an axial SE PD/T2 (TR/TE=2709/20-80) and a turbo-FLAIR (TR/TE/TI=9832/150/2000) sequences were performed.

In order to obtain a dynamic acquisition of cortical activation during complex and acquired motor process, we decided to study our patients with f-MRI. After training, subjects had to oppose the thumb to the other fingers in a sequential task, in a 2, 3, 4, 5 sequence and in a complex, alternating sequence, 1-2, 1-4, 1-3 and 1-5 sequence.

The total acquisition time was equally divided into three-motor task periods, alternated with a three-rest period. Seven images per period were collected; so, in each measurement, 42 images were acquired. The images were oriented transversally. The major parameters of the 2D gradient-echo MR pulse sequence were the following: TR=60 ms, TE=40ms, Flip Angle=25, FOV=160x144 mm^2, Slice Thickness=4 mm, Scan Matrix=128x 128. The T1 contrast enhancement option was activated.[15]

An MR angiography acquisition was performed per each T1-GRE f-MRI acquisition. The major parameters of the angiographic sequence were the following: TR=shortest, Flip Angle=20, FOV=the same of the T1-gre, Slice Thickness=1 mm, Scan Matrix=256x256, Slices=12, Slice Thickness=1 mm, Phase Contrast Technique.

The image analysis is performed by a program developed in IDL environment (Interactive Data Language, Research System Inc., USA). The basic analysis consists of the calculation of the correlation coefficient between the time-intensity behavior of each pixel and the square wave model function.

In order to exclude transient hemodynamic responses, 5 images per block (from the 3rd to the 7th of each block) are included in the analysis. A raw activation map was obtained by applying a correlation analysis ($p<0.001$) and a cluster filtering (at least 5 pixels). The raw map was affected by flow artefacts; to eliminate these artefacts, activation map and MR angiography were compared and activation clusters related to the vessels were rejected. Whole-head high-resolution T1-weighted images (TR/TE=500/15) were then acquired to be used as an anatomical reference for the transformations into the Talairach space.[16]

Results

In seven patients, the morphological examination showed an important, asymmetric perirolandic and postrolandic cortical atrophy (Figure 1) associated to a mild atrophy of the basal ganglia. Subtle MRI T2 hyperin-

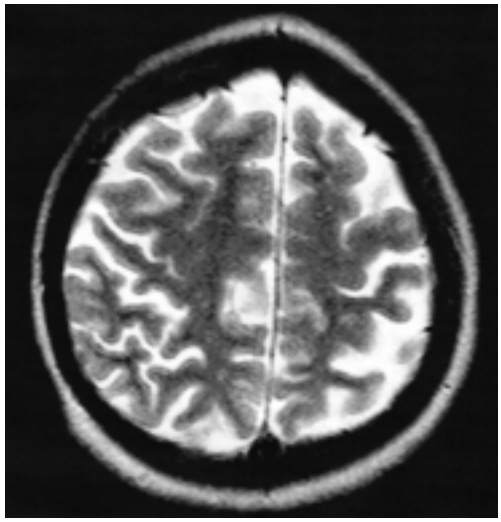

Figure 1. Axial SE T2 image: Diffuse brain atrophy particularly marked at the level of the right perirolandic cortex.

tense lesions in the primary motor cortex, compatible with underlying gliosis, were found in five patients (Figures 2a, 2b), hypointensity in the lenticular nuclei in one case only. In one patient the morphological aspect was normal.

During simple motor task carried out with the non-affected hand, we could observe a good activation of the contralateral rolandic cortex, associated with a discrete activation of the supplementary motor area (SMA) and of the parietal regions, as well as with a discrete activation of the right prefrontal region, but without significant difference from those in healthy population.

On the contrary, during a simple task of opposing the fingers executed with the affected hand, an evident hypo-activation of the homolateral and contralateral perirolandic cortex, associated with an evident hypo-activation of the contralateral SMA and with the affected parietal region, was observed. It was significantly different from the healthy control subjects.

During the complex sequence execution by the non-affected hand, an obvious bilateral activation of rolandic areas, of the parietal areas, of the SMA, and of the contralateral frontal region could be seen. These observations are similar to those in healthy controls.

When the complex sequence was executed by the affected hand, the observed activation was limited to the bilateral rolandic region, to SMA, and to a very modest activation of the parietal regions. Quantitatively, hypoactivation was significantly different from that in healthy population.

Qualitatively, the movement of the affected hand was impaired and not fluent at all despite more training exercises. Moreover, it was obvious that the patients had to see the entire procedure when they were performing the exercise with the affected hand. Without receiving the visual input that controlled the motor act the movement was even more impaired.

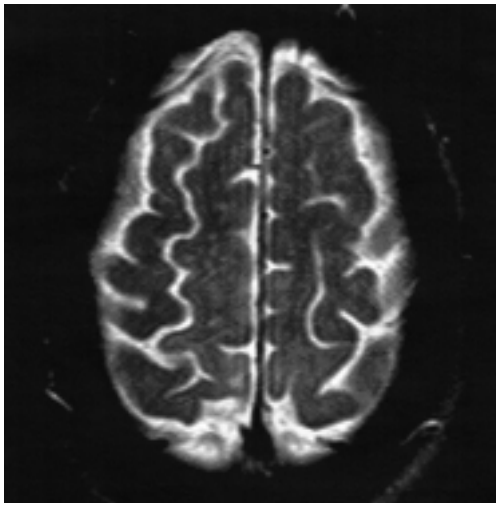

Figure 2a. Slight hyperintensity at the level of the right perirolandic cortex shown on the T2 weighted image.

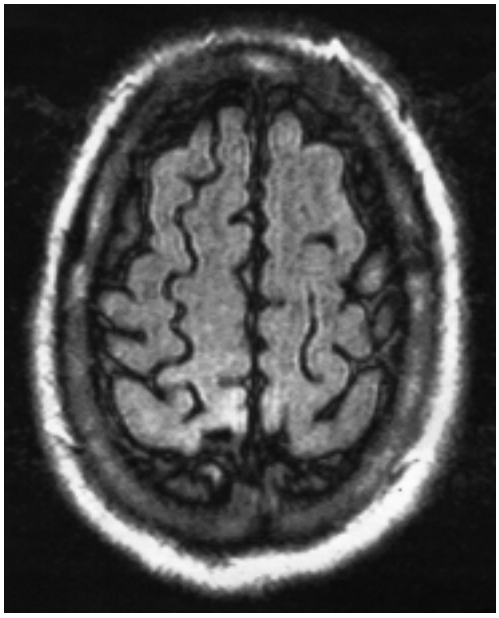

Figure 2b. Slight hyperintensity at the level of the right perirolandic cortex better shown on the FLAIR image.

Discussion

The patients with progressive focal cortical syndromes are being recognized with increasing frequency. CBGD is a degenerative disor-

der, involving primarily parietal areas, and gradually extending to frontal areas. The patients with CBGD revealed a mild to moderate global deficits including a frontal dysexecutive syndrome, explicit learning deficits without retention difficulties and displayed prominent deficits on the tests of sustained attention/mental control and verbal fluency.[17]

Different neuroimaging studies have been conducted on CBGD, using conventional computed tomography (CT) and magnetic resonance imaging (MRI),[4,18] and demonstrating an asymmetric pericentral cortical atrophy in approximately 50% of cases. On the contrary, another recent MRI study, comparing clinically diagnosed cases of CBGD with progressive supranuclear palsy (PSP), found that 87.5% patients with CBGD (but none of the PSP group) had asymmetric fronto-parietal atrophy while midbrain atrophy was seen in 6.3% and 89.3% of the same cases respectively.[18]

Another radiological observation[4] revealed that pathologically proven PSP, frontal lobe dementia and AD with clinical features of CBGD had similar MRI cortical changes.

The only possible conclusion is that, due to the distribution of pathological changes, the static imaging simply correlates with the predominant clinical presentation and not with the specific underlying pathological substrate.

Functional imaging studies were done with positron emission tomography (PET), but results did not seem to be conclusive.[18]FDG-PET studies demonstrated a greater heterogeneity of the metabolic patterns including diffuse hypometabolism despite asymmetrical clinical features. F-Dopa PET demonstrated a severe asymmetric reduction in striatal F-Dopa uptake which tended to be equal in putamen and caudate consistent with widespread substantia nigra neuron loss.[19] From these studies, the general suggestion is that (18F)-fluorodeoxyglucose (FDG) and (^{18}F)-fluoro-dopa (F-Dopa)-PET must be utilized at the same time, in the same patient.[19,20]

Our study is the first one on f-MRI in CBGD: the most interesting part is the dynamic acquisition which gives information on how the cortex works when the affected arm is moving.

The results obtained from this selected group of eight patients confirmed the results, reported previously.[21-25]

Our f-MRI evaluation revealed, while the patients executed the simple task of opposing the fingers with the affected hand, a hypo-activation of the homolateral and contralateral perirolandic cortex, associated with an evident hypo-activation of the contralateral SMA and of the affected parietal region. During the complex motor skills with the affected hand, a drastic reduction of activation of premotor and motor areas (perirolandic region) of the contralateral cortex, associated with a very modest activation of the supplementary motor area of the same hemisphere were noted.

It is interesting to see a very modest activation of motor areas, associated with the reduced activity of the parietal area: the latter is largely preventable, but the former is rather unexpected.

The imaging studies on both monkeys and humans report of the activation in the region of the supplementary motor area, globus pallidus, and parietal cortex during the performance of sequential movements.[26] Neurons of the globus pallidus also discharge during specific phases of a sequential performance.[26] This does not involve uniquely motor speed and correct execution, but also attention, coordination and dynamic adjustment to the situation. The hypoactivity of the cortical areas we have reported does match with previous finding.

Nevertheless, there is an unresolved question: our patients indisputably presented with a parietal (postrolandic) atrophy: considering that the parietal damage is the cause, why should the pure motor areas should hy-

poactivated? We maintain that the brisk stop due to the disconnection of the parietal cortex and the SMA because of degenerative alteration of parietal areas causes an interruption of the neural net to putamen and pallidus, ending in frontal and prefrontal areas.

Therefore, f-MRI, with its constant demonstration of hypoactivity of motor cortical areas, SMA and parietal areas, while affected arm is moving, might be a valid supportive tool for the diagnosis of CBGD: a positive correlation with hypoactivation of motor areas could be found even in modest, and initial stages of disease.

Having assessed that the accuracy of neurologists' clinical diagnosis of CBGD is very low, even in specialized centers[2] (at first visit mean sensitivity for CBGD 35%, specificity 99.6% and at the last visit mean sensitivity 48.3% while specificity remained stable), then MRI and f-MRI might be suggested as an adjunctive tool of the diagnosis refinement.

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