

# Cerebral blood flow SPECT may be helpful in establishing the diagnosis of progressive supranuclear palsy and corticobasal degeneration

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## Abstract

**BACKGROUND:** We present 4 cases, which illustrate the usefulness of neuroimaging studies in atypical forms of Parkinsonism. Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) are rare neurodegenerative progressive disorders of the central nervous system of unknown cause. The clinical accuracy in this diagnosis is not very high even in centres specialising in movement disorders. Functional imaging can be helpful in diagnosing PSP and CBD.

**MATERIAL AND METHODS:** We present the results of cerebral blood flow (CBF) SPECT scanning in 2 patients with PSP and 2 patients with CBD. This was performed using a triple-head gammacamera and <sup>99m</sup>Tc-HMPAO.

**RESULTS:** In PSP patients a diffuse frontal perfusion deficit was seen, eventually with striatal and occipital hypoperfusion. CT/MRI was either normal or showed a diffuse cortical-subcortical atrophy. In CBD patients left fronto-parieto-temporal cortex and a striatal hypoperfusion were shown. CT scanning was normal in one case and showed an asymmetrical temporo-parietal atrophy in second one.

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**CONCLUSIONS:** The pattern of diffuse frontal perfusions deficit in PSP and asymmetrical, contralateral to symptoms of CBD, cortico-subcortical hypoperfusion may be helpful in establishing the correct diagnosis.

**Key words:** cerebral blood flow, SPECT, progressive supranuclear palsy, corticobasal degeneration

## Introduction

Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) are neurodegenerative disorders of the central nervous system of unknown cause. They are progressive, usually begin in middle to late years of life and occur sporadically, although familial occurrence has been reported [1–4]. The pathological features comprise neurofibrillary tau positive tangles in many cerebral regions within PSP and tau positive immunohistochemistry within neurones of the cortex, subcortical and brain stem nuclei in CBD, making them (along with Alzheimer's and Pick's diseases or inherited frontotemporal dementia with Parkinsonism) one of a number of so-called "taupathies" [1, 2]. Clinical diagnosis of Parkinsonian syndromes in most disorders is based on clinical history and established clinical criteria, which do not include neuroimaging. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) in nondegenerative movement disorders, like Tourette's syndrome or dystonia, tend to be normal. In neurodegenerative disorders, like Parkinson's Disease (PD), Multiple System Atrophy (MSA) or PSP, some changes (like brain stem and cerebellar atrophy, e.g. in MSA) are present, but they are unreliable and do not have a clinical value [5]. Clinical accuracy in diagnosing PD, astonishingly, is not very high, even in centres specialising in movement disorders. Two separate clinical-pathological series of observations concluded that only 76% of patients with a clinical diagnosis of PD actually met the pathological criteria; the remaining 24% had evidence of other causes of Parkinsonism [6, 7]. There is a problem with the accuracy of clinical diagnosis of other Parkinsonism-plus syndromes, not so

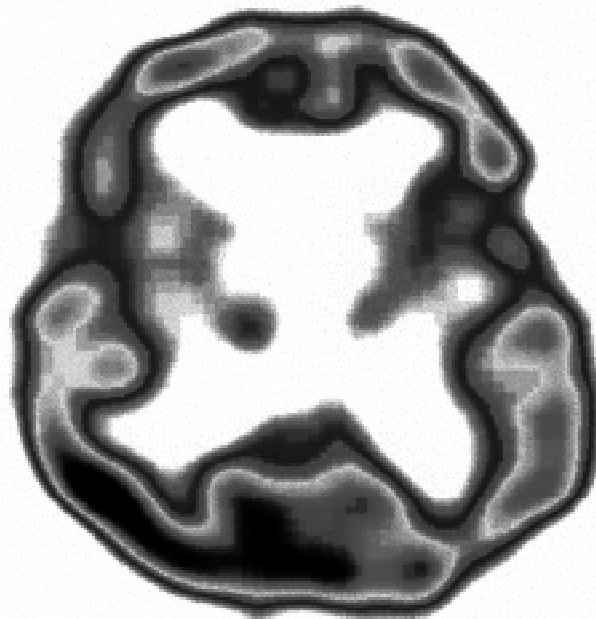
frequent as PD. According to the combined database of two American centres (Movement Disorders Clinic at Baylor College of Medicine and Houston and Columbia-Presbyterian Medical Center, New York), PSP and CBD were found in respectively 5% and 2% (381 and 143 among all 7,564) cases of Parkinsonism [8]. There is a question as to whether those entities are so rare or so underdiagnosed. Although the diagnostic criteria for both disorders are established [1, 2, 9], in many cases the clinical diagnosis may be difficult — in CBD unilateral rigidity and apraxia at onset and in PSP the akinetic-rigid syndrome with initial moderate response to L-dopa make a distinction from idiopathic PD and other Parkinsonian disorders difficult. It seems to be important from the clinical point of view that not all the clinical features appear at the same time and in many cases the final diagnosis is established (according to criteria) after a few years from the onset of first symptoms. Some characteristic features even will not appear at all. The well known and recognised as an almost pathognomonic symptom of CBD — “alien limb phenomenon” — was present in only 42% of cases, when Parkinsonism (100%), higher cortical dysfunction (93%), dyspraxia (82%), gait disorder (80%) and dystonia (71%) were more frequently observed in a large group of 147 patients from 8 centres (10). Functional imaging provides a sensitive means of detecting changes in cerebral blood flow, brain metabolism and receptor binding. Positron emission tomography (PET) and single photon emission computed tomography (SPECT), utilising different radionuclide tracers for special subtypes of receptors or transport systems within basal ganglia, are not widely used in everyday clinical practice, but more available regional cerebral blood flow SPECT (rCBF SPECT) may help in the clinical diagnosis of PSP and especially of CBD. In PSP the clinical diagnosis of probable PSP, with typical presentation on rCBF SPECT, was confirmed at autopsy in a few cases [5]. Cortical metabolism tends to be globally depressed, but particularly affected are frontal areas presenting the picture of so-called “hypofrontality” [11]. However, this is not specific for PSP and can also be found in Huntington’s or Pick’s disease, but with other clinical features of possible or probable PSP it may be helpful in establishing the final diagnosis. In CBD rCBF SPECT scanning shows the characteristic blood flow changes: asymmetric cortico-subcortical flow deficit, contralateral to clinical signs (fronto-parietal, medial temporal and thalamic areas).

## Material and methods

We present 4 cases (two of PSP and two of CBD), which illustrate the usefulness of neuroimaging studies in atypical forms of Parkinsonism. rCBF SPECT scanning was performed using three-head gammacamera Multispect-3 (Siemens, Erlangen, Germany) 1 hr post i.v. injection of 740MBq of  $^{99m}\text{Tc}$ -HMPAO (Amersham, Amersham, United Kingdom) using a low energy, ultra-high resolution collimator. The images were reoriented in the axial, coronal and sagittal planes and displayed on a 10-grade colour scale. Focal perfusion abnormalities were read twice by two independent observers.

## Case descriptions

**Case 1.** Male, 65 years old. In 1994 — first symptoms were: gait disturbances (short steps and propulsion and falls), micrographia, dysarthria and stuttering. CT was normal. Moderate im-



**Figure 1.** rCBF SPECT scan of case 1.

provement was observed after L-dopa started in 1995. In 1997 the loss of postural stability, resulting in frequent falls (mostly backwards) and speech disturbances (palilalia and palilogia) were observed. Next year rigidity, apraxia and hypometric eye saccades, with minimal restriction of down and up gaze, were noticed. MRI scans were normal and rCBF SPECT scan revealed diffused deficit of perfusion, predominantly within both frontal lobes and striatum, but also within left parietal and temporal lobes (Fig. 1). In 2000 the final diagnosis of PSP was established due to very pronounced restriction of vertical eye movements and dysphagia, fulfilling the clinical criteria for PSP. At that time the constantly increased L-dopa dosages were ineffective and after cessation there was no deterioration.

**Case 2.** Female, 60 years old. The first symptoms appeared at the end of the 1980s: depression and bradykinesia, which was related probably to reactive depression after her husband’s death. But in the following years dysarthria and progressive akinetic-rigid syndrome became progressive. At the beginning moderate response to L-dopa was observed. In 1996 besides rigidity, hypomimia and the most dangerous complication — unsteadiness with frequent falls — occurred. The typical supranuclear palsy with complete lack of vertical eye movements (up and down) was diagnosed in 2000. At the same time she had problems with swallowing, monotonous (almost impossible to understand) speech, very marked rigidity and unsteadiness. The memory deficits (exact testing difficult due to restricted executive functions) progressing in the last few years were noticed. CT scans at that time revealed cortical-subcortical, cerebellar and truncal symmetrical atrophy and rCBF SPECT scanning showed symmetrical hypoperfusion within both frontal lobes. Increased dosages of L-dopa were ineffective and retrospectively she did not find such responsiveness for many years.

**Case 3.** Female, 59 years old with onset of disease in 1999 — she noticed the loss of dexterity of the right hand and she started falling, due to gait apraxia rather than unsteadiness. At the

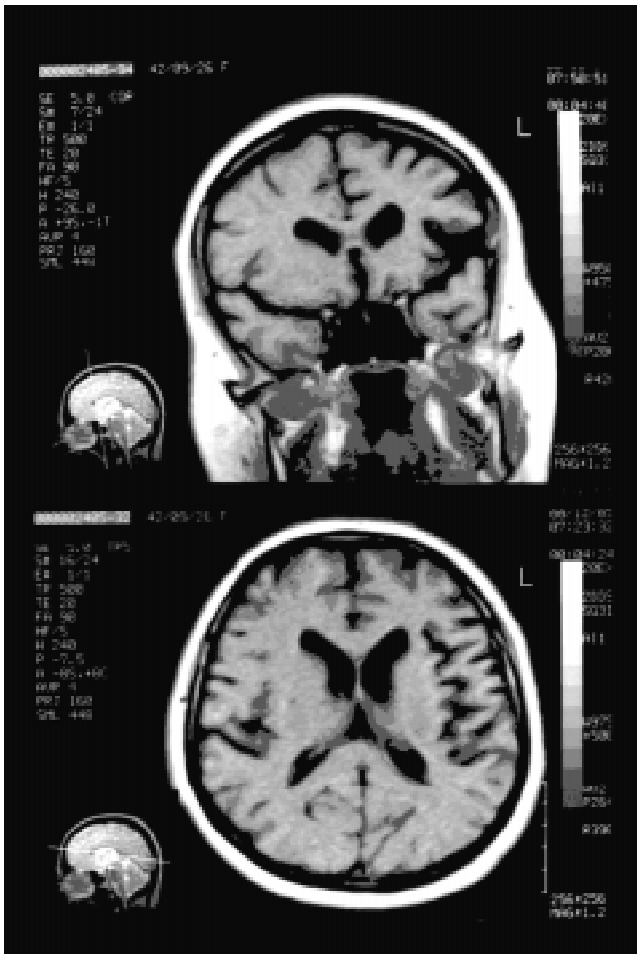


Figure 2. CT scan of case 3.

beginning of 2000 gait disturbances were prominent and 3 months later the family noticed the inability to find the proper names (amnesic aphasia), dysarthria, marked bradykinesia and temporary right hemidysaesthesia. On admission to the hospital (at the end of 2000) the upper motor neurone signs (bilateral Babinski's sign, hyperreflexia and clonus), and progressive rigidity, tactile facial myoclonus, motor and amnesic aphasia, with dystonic posture of right hand and both feet in following months, were noticed. L-dopa (800 mg per day with benserazide for 3 months) therapy was completely ineffective. Cerebro-spinal fluid, neuroelectrophysiology tests (evoked potentials) and memory testing were normal. MRI scans revealed characteristic asymmetrical cortical atrophy (temporal and parietal lobe) with enlarged lateral ventricle on the left (contralaterally to initial symptoms at onset) (Fig. 2). rCBF SPECT at the same time showed the diffused areas of hypoperfusion within left fronto-parieto-temporal cortex (asymmetry index — AI = 12–32%) and left striatum (AI = 13%).

**Case 4.** Female, 51 years old. In 1992 presented for the first time right hand tremor with loss of dexterity, followed after few months by gait disturbances with propulsion and inability to stop, dysarthria, hypomimia, bradykinesia and rigidity. During the next two years disease progressed - gait apraxia, speech difficulties (dysarthria) and bilateral Babinski sign were pronounced. In 1997 the patient showed complete inability to stand and walk (without paresis), anarthria, tactile myoclonus of limbs, dystonic posture

of upper extremities (flexion), severe rigidity, positive Marinesco-Radovici reflex, Babinski sign and oculomotor apraxia. From the beginning she did not response to L-dopa (800mg per day with benserazide), anticholinergics, amantadine, and clonazepam. There was no dementia. CT scanning performed in 1992 and 1994 and MRI in 1996 did not reveal any significant changes. There was a slight enlargement of left lateral ventricle and mild atrophy of left parietal and temporal cortex, but these changes were noticed retrospectively, were not severe and resembled mild asymmetries seen in other cases without such pathology as in CBD (Fig. 3). rCBF SPECT scanning performed a few months later showed a diffuse perfusion deficit of lower part of left frontal lobe (AI = 11%), fronto-lower part of the left temporal lobe (AI = 16%) and left basal ganglia (AI = 16%) (Fig. 4).

## Discussion

Although the clinical picture of the described cases allows us to make a diagnosis of CBD and PSP, the definite diagnosis was difficult in all patients at the onset of symptoms. Gaze palsy, characteristic and crucial for diagnosis of PSP, was a late symptom in both cases. In case no. 2 in the first year of disease there was no clear information about falls, which is characteristic for PSP, but the symptoms in the following years showed the typical clinical presentation for PSP. Another major clinical problem in the diag-

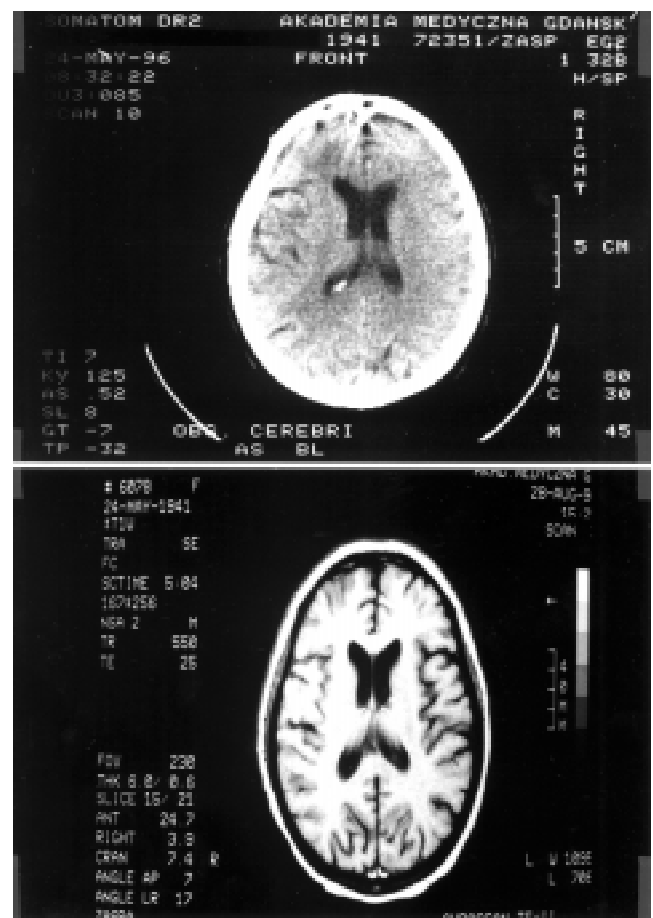
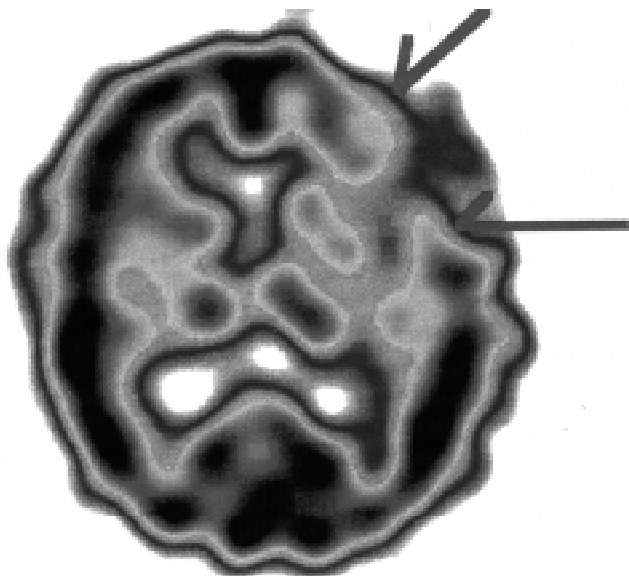


Figure 3. CT scan of case 4.



**Figure 4.** CBF SPECT scan of case 4.

nostic process is the overlapping of characteristic symptoms which may appear in different disorders, e.g. oculomotor apraxia in the late stage of CBD (case no. 4) and gaze palsy seen in PSP (both cases), or rigidity, bradykinesia, gait disturbances in almost all Parkinsonian syndromes. "Alien limb" phenomenon, exceptional for clinical picture of CBD, was not noticed in either case (but in a large series of patients it was met only in 42% of cases) [10]. Unilateral tremor and loss of dexterity in both CBD patients, and initial moderate response to L-dopa in both PSP cases, might be the reason for misdiagnosis with idiopathic PD. The response to L-dopa in all cases of Parkinsonism has to be considered. It is initially minimal/moderate in PSP or MSA and by definition completely absent in CBD, which was observed in the above-presented cases. These diagnostic difficulties shown above are the reason for the exploration of new methods to make a diagnosis as accurate and as early as possible. The diagnostic value of external sphincter EMG abnormality (denervation) in PSP may point away from idiopathic PD due to Onuf's nucleus degeneration, but will not help differentiate between PSP and MSA [12]. The presented cases underline the usefulness of neuroimaging and especially rCBF SPECT scanning in diagnostic procedures in CBD and PSP. Hypofrontality in PSP (Fig. 1) and asymmetrical cortico-subcortical hypoperfusion, contralateral to onset of symptoms in CBD (Fig. 4), secondary to regional cerebral hypometabolism, may be helpful in establishing the correct diagnosis [13, 14]. This picture of regional, contralateral atrophy typical for CBD may be seen also in CT or MRI (case no. 3, Fig. 2), but rCBF SPECT chang-

es are more sensitive and may even precede the visible changes in CT and MRI [14]. In the presented cases CBF SPECT studies were performed either mid-way or in the late stage of a rather prolonged diagnostic process, but CBF scanning played its role in establishing the final diagnosis. In those disorders in fact there is no effective therapy, but a precise and fast diagnosis may give us the opportunity to investigate a pathogenesis and early markers of these disorders. It may prolong the period of potential neuroprotection or effective treatment which may emerge in following years.

## References

1. Watts RL, Brewer RP, Schneider JA, et al. Corticobasal degeneration. In: Watts RL, Koller WC (eds) *Movement Disorders*. McGraw Hill, New York 1997: 611–622.
2. Golbe LI. Progressive Supranuclear Palsy. In: Watts RL, Koller WC (eds) *Movement Disorders*. McGraw Hill, New York 1997: 279–296.
3. Verin M, Rancurel G, De Marco O, Edan G. First family cases of corticobasal degeneration *Mov Disord* 1997; 12 (suppl. 1): 55 (Abstract).
4. Rojo A, Pernaute RS, Fontan A, et al. Clinical genetics of familial progressive supranuclear palsy. *Brain* 1999; 122: 1233–1245.
5. Brooks DJ. Neuroimaging of movement disorders. In: Watts RL, Koller WC (eds) *Movement Disorders*. McGraw Hill, New York 1997: 31–50.
6. Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's Disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992; 55: 181–184.
7. Rajput AH, Rozdilsky B, Rajput A. Accuracy of clinical diagnosis in Parkinsonism — a prospective study. *Can J Neurol Sci* 1991; 18: 275–278.
8. Jankovic J. Atypical Parkinsonian syndromes. In: *A comprehensive review of movement disorders for the clinical practitioner — syllabus of 11<sup>th</sup> Annual Course of Columbia University College of Physicians and Surgeons*, New York 2001; 529–625.
9. Rinne JO, Lee MS, Thompson PD, Marsden CD. Corticobasal degeneration: a clinical study of 36 cases. *Brain* 1994; 117: 1183–1196.
10. Kompolitti K, Goetz CG, Boeve BF. Clinical presentation and pharmacologic therapy in corticobasal degeneration. *Arch Neurol* 1998; 55: 957–961.
11. Goffinet AM, De Volder AG, Gillain C, et al. Positron tomography demonstrates frontal lobe hypometabolism in progressive supranuclear palsy. *Ann Neurol* 1989; 25: 131–139.
12. Scaravilli T, Pramstaller PP, Salerno A, et al. Involvement of the Onuf nucleus in progressive supranuclear palsy. *Mov Disord* 2000; 15: (Suppl. 3): 225.
13. Gras P, Creisson E, Giroud M, et al. Degenerance cortico-basale: un nouvelle entite. *Presse Medicale* 1994; 23: 1772–1774.
14. Markus HS, Lees AJ, Lennox G, et al. Patterns of regional cerebral blood flow in corticobasal degeneration studied using HMPAO SPECT; comparison with Parkinson's Disease and normal controls. *Mov Disord* 1995; 10: 179–185.