Apraxia in Parkinson’s disease, progressive supranuclear palsy, multiple system atrophy and neuroleptic-induced parkinsonism

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Summary
We studied 45 non-demented patients with Parkinson’s disease (PD), 12 with progressive supranuclear palsy (PSP), 10 with multiple system atrophy (MSA) and 12 with neuroleptic-induced parkinsonism (NIP) for the presence of apraxia. Our aim was to determine whether a standard comprehensive assessment of different praxic functions would demonstrate specific types of errors not attributable to bradykinesia, rigidity, tremor or any other abnormal elementary motor deficit. PD patients on chronic levodopa treatment were examined in the ‘on’ and ‘off’ (treatment) states. Based on apraxia assessment scores, bilateral ideomotor apraxia for transitive movements was found in the ‘on’ (75%) and 12 (27%) of PSP and PD patients, respectively. Ideomotor apraxia was mainly characterized by spatial errors (i.e. external and internal configuration, body-part-as-object and trajectory). Four PSP but no PD patients exhibited ideomotor apraxia for intransitive movements. PSP as well as PD patients with ideomotor apraxia also had difficulties in imitating hand and finger postures, but none of them failed on pantomime comprehension and pantomime recognition/discrimination. Some PSP patients exhibited, in addition, a limbkinetic type of apraxia and a minority of them displayed deficits on tasks involving multiple steps. Neither MSA nor NIP patients showed any disturbance of praxic functions. There were no differences in age, disease duration, Mini Mental State Examination (MMSE), Unified Parkinson’s Disease Rating Scale and Hoehn–Yahr scores between apraxic and non-apraxic PD patients, and ideomotor apraxia scores were similar in the ‘on’ and ‘off’ states. A correlation was found between ideomotor apraxia scores in PD patients and deficits in frontal lobe-related neuropsychological tasks such as the Tower of Hanoi, verbal fluency and the Trail Making Test. Furthermore, PD patients with apraxia showed higher Hamilton depression scores than non-apraxic PD patients. The presence or absence of cortical involvement, and its severity and distribution might determine the presence and type of apraxia in PD and PSP. Apraxia in these conditions would therefore reflect combined cortico-striatal dysfunction.

Keywords: apraxia; Parkinson’s disease; progressive supranuclear palsy; multiple system atrophy; neuroleptic-induced parkinsonism

Abbreviations: FAS = Controlled (Fast) Oral Word Association Test; MIT = Movement Imitation Test; MMSE = Mini Mental State Examination; MSA = multiple system atrophy; NIP = neuroleptic-induced parkinsonism; PD = Parkinson’s disease; PSP = progressive supranuclear palsy; UPDRS = Unified Parkinson’s Disease Rating Scale; WCST = Wisconsin Card Sorting Test

Introduction
Patients with ideomotor apraxia display ‘an impairment in the timing, sequencing and spatial organization of gestural movements’ (Rothi et al., 1991). Praxic functions traditionally have been thought to be the province of the cortex, and ideomotor apraxia usually has been reported in patients with damage to the dominant parietal association area.
(particularly the inferior parietal lobe), the premotor cortex (mainly the supplementary motor area), the corpus callosum or the intrahemispheric white matter bundles such as the arcuate and superior occipito-frontal fasciculus which reciprocally connect frontal and parietal association areas (Faglioni and Basso, 1985; Heilman and Rothi, 1985). While patients with lesions in the dominant premotor cortex may develop bilateral ideomotor apraxia for transitive rather than intransitive movements, they usually show normal comprehension and discrimination of gestures (Watson et al., 1986). On the other hand, patients with left parietal lesions may show ideomotor apraxia together with deficits in the comprehension and discrimination of gestures (Heilman and Rothi, 1985).

Most authors are reluctant to include the basal ganglia in the modular neural network which mediates the production of learned skilled movements (praxis) (for reviews, see Della Sala et al., 1992; Pramstaller and Marsden, 1996), despite the fact that several cases of apraxia with CT scanning or MRI documentation of damage restricted to the dominant grey structures (basal ganglia and thalamus) have been described (Agostini et al., 1983; Basso and Della Sala, 1986; De Renzi et al., 1986; Mozaz et al., 1991; Shuren et al., 1994).

Few studies of apraxia in Parkinson’s disease (PD) have been published (Sharpe et al., 1983; Goldenberg et al., 1986; Grossman et al., 1991). Sharpe et al. (1983) evaluated 14 patients with PD with a gestural test which involved the representation of implement usage (representational task) and the imitation of non-representational gestures (non-representational task). PD patients performed at a lower gestural level on the representational tasks and made significantly more spatial errors on the non-representational task than the normal controls. Goldenberg et al. (1986) studied the ability of 42 patients with mostly moderate to severe PD to copy single or sequential finger hand and arm movements, as well as their abilities to execute symbolic gesture and pantomime object use to verbal command. Execution of movement sequence and a ‘total apraxia score’ were worse in patients than in controls, and such deficits appeared to correlate with visuospatial disabilities. Grossman et al. (1991) studied the ability of 22 non-demented patients with PD to execute two gestural tasks from the praxis battery of the Boston Diagnostic Aphasia Examination; PD patients made more errors than controls on both types of tasks, and such errors were not explained convincingly by bradykinesia.

Conversely, no single study has specifically addressed higher motor behaviour or praxis in progressive supranuclear palsy (PSP) and multiple system atrophy (MSA), although the presence of ‘dynamic’ apraxia and ideomotor apraxia in patients with PSP has been briefly described by Cambier et al. (1985) and Collins et al. (1995), respectively.

Cambier et al. (1985) described the presence of ‘dynamic’ apraxia, but not ideomotor or ideational apraxia in 10 patients with PSP. However, these patients were tested only on three representational and three non-representational intransitive movements. Collins et al. (1995) described upper limb ideomotor apraxia in two out of 12 neuropathologically proven PSP cases, but neither the quality of praxic errors nor the assessment of apraxia was specified. Thus, there is some evidence for apraxia in PD and PSP, but its exact nature and mechanism have not been explored.

The problem of motor behaviour, elementary or complex, is central to contemporary neurology. Akinesia (subsuming hypokinesia and bradykinesia) and rigidity, which are hallmarks of basal ganglia disorders such as PD, PSP and MSA, may not be sufficient to explain the full motor deficits present in these conditions. The breakdown of movement seen in PD, PSP and MSA may have an additional component due to a higher order motor disorder or apraxia. Another parkinsonism-plus syndrome, corticobasal degeneration (Rebeiz et al., 1967, 1968; Gibb et al., 1989; Rinne et al., 1994) classically causes ideomotor apraxia (Leiguarda et al., 1994).

In the present study we examined a consecutive series of patients with PD on chronic levodopa treatment and a series of patients with PSP, MSA and neuroleptic-induced parkinsonism (NIP) for the presence of apraxia. Our main goal was to determine whether a standard comprehensive assessment of different praxic functions would reveal specific types of errors not attributable to bradykinesia, rigidity, tremor or any other abnormal elementary motor behaviour.

Patients and methods

Forty-five patients meeting strict clinical criteria for idiopathic PD (Hughes et al., 1992) without clinical evidence of dementia, 12 PSP patients diagnosed according to the criteria set out by Lees (1987), 10 patients with MSA diagnosed according to the criteria proposed by Quinn (1989, 1994), and 12 schizophrenic patients with NIP were included in the study.

Parkinson’s disease

The PD sample consisted of consecutive patients on chronic levodopa treatment examined in the neurology clinic as part of regular follow-up visits. Only patients with a Mini Mental State Examination (MMSE) (Folstein et al., 1975) score of $>24$ were included (Table 1).

The mean age of patients with PD was 62.6±8.9 years and the mean duration of disease was 5.4±3.7 years; 26 were men and 19 were women (unless stated otherwise data are presented as mean ± SD throughout this paper). Mean Unified Parkinson’s Disease Rating Scale (UPDRS) scores and Hoehn and Yahr stages in ‘off’ and ‘on’ (medication) states were, respectively, 17.4±8.6, 7.9±5.1 and 2.6±0.8, 2.0±1. Mean MMSE score was 26.4±2.9. Memory and language scores were within the normal range. In 23 out of 45 patients, the onset of symptoms and the most severe extrapyramidal signs were on the right side, while in the remaining 22 patients the onset and greater severity of...
extrapyramidal signs were on the left side. All 45 patients were studied in the ‘off’ state 12 h after withdrawal of levodopa therapy and in the ‘on’ state following administration of 200/50 mg of levodopa/carbidopa.

Neuroleptic-induced parkinsonism (NIP)
The NIP sample consisted of consecutive admissions to a disinhibition signs were present in 10 and seven of the 12 patients, respectively. Ocular signs other than supranuclear gaze palsy were levator palpebrae inhibition (n = 4) and inhibition of eye closure (n = 1), blepharospasm (n = 3), and lid retraction (n = 1). Three of the 12 patients showed some fine postural tremor. None had a classical rest tremor. The MMSE score was $\geq 24$ in five patients and $> 24$ in the remaining seven (mean $23.8 \pm 5.7$). Of particular note were the symmetry of clinical signs and the absence of cortical sensory loss, alien hand sign and myoclonus. Long-term response to levodopa treatment was poor or absent in all 12 patients.

Multiple system atrophy (MSA)
A consecutive series of 10 patients (three female, seven male) with a mean age of 61.7 $\pm$ 5.85 years were studied. All of them fulfilled the clinical diagnostic criteria of clinically probable MSA (striatonigral-type, n = 8; olivopontocerebellar-type, n = 2). Mean age at disease onset was 54.9 $\pm$ 5.36 years. Mean duration (+ SD) of illness at the time of entry into the study was 6.8 $\pm$ 4.07 years. Presenting features were mainly motor; one patient presented with parasomnia (Table 3).

All patients had some signs of autonomic dysfunction. Parkinsonism was present in all cases, to a lesser degree in the two olivopontocerebellar-type cases. Cerebellar and pyramidal signs were found in four of the 10 cases. Two patients had a symmetrical axonal sensorimotor poly-
Table 2 Summary of clinical features of 12 PSP patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
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<th>Disease duration (years)</th>
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<th>Pseudo bulbar palsy</th>
<th>Neuro-behavioural changes</th>
<th>Postural instability</th>
<th>Akinesia</th>
<th>Rigidity</th>
<th>Tremor</th>
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+++ = severe; ++ = moderate; + = mild; 0 = none.

Table 3 Summary of clinical features of 10 MSA patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Disease duration (years)</th>
<th>MSA type</th>
<th>Autonomic signs</th>
<th>Parkinsonism</th>
<th>Cerebellar signs</th>
<th>Pyramidal signs</th>
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<tr>
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OPCA = olivopontocerebellar atrophy; SND = striatonigral degeneration; +++ = severe; ++ = moderate; + = mild; 0 = none.

neuropathy. Irregular postural tremor was found in four patients, two of whom also showed intermittent myoclonic finger jerks. Respiratory stridor, excessive snoring and hypophonic dysarthria were detected in half of the patients. Severe anterocollis was present in one patient. The MMSE score was >24 in every patient (mean 28.0 ± 2.1). All 10 patients were receiving levodopa preparations or bromocriptine at some stage but without definite benefit.

A group of 50 normal controls, 29 men and 21 women; mean age 58.6 ± 10.8, without a history of head injury, or physical or neurological illness were also tested. Informed consent was obtained from all patients and control subjects prior to testing. The study was approved by the local ethical committees of the two institutes.

Apraxia assessment

Patients were tested with a comprehensive apraxia battery which is described below. Gestures were scored as apraxic whenever (i) no abnormal involuntary movements (e.g.: tremor, dystonia, myoclonus) interfered with the motor response; (ii) comprehension of the command was normal and (iii) the abnormal response was not corrected after verbal instructions were repeated once. Patients were allowed to use their preferred hand. Whenever the dominant hand was the most affected by the disease or showed apraxia, the contralateral hand was also examined.

Scores were considered abnormal when they were <2 SD from the mean values in control subjects. These lower limits are referred to below as ‘cut-off scores’.

Orofacial and respiratory apraxia

Patients were asked to perform five non-representational (e.g. ‘stick out your tongue, purse your lips, blow up your cheeks’) and five representational orofacial gestures (e.g. ‘whistle, lick lips, yawn as if asleep’); and three non-representational (‘take a deep breath, breathe out fully and breathe quickly’) and three representational respiratory gestures (‘suck on a straw, blow out a match and smell a flower’). Patients were given three points when the movement was accurately performed; two points when correct only after imitation; one point when the correct performance was preceded by pauses, or the overall gesture was acceptable though defective in
terms of amplitude, force or speed; and zero points when the gesture was incomplete or irrelevant, there was perseveration, or no oral movements were carried out. Total scores and cutoff scores for oro-facial apraxia were 30 and 28 and for respiratory apraxia were 18 and 17, respectively.

**Ideomotor apraxia**

Patients were asked to perform 10 intransitive movements, five non-representational (e.g. ‘touch your nose, make a fist, wiggle your fingers’) and five representational (e.g. ‘wave good-bye, salute like a soldier, hitchhike’); and 10 transitive movements (e.g. ‘use a hammer, use a screwdriver, use a key’) in verbal, visual and tactile modalities, as well as on imitation. For intransitive movements, two points were scored for a correct performance; one point when the correct performance was preceded by hesitation or a repeated trial; and no points when the gesture was partially or not performed (maximum score = 20 points).

For transitive movements, patients were given three points whenever the performance was appropriate for the object; two points when the performance resembled the correct one but included temporal or spatial errors; one point when the movement had a weak resemblance to the appropriate gesture; and no points when the gesture was so wrong or incomplete as to be unrecognizable, or there was a complete failure to carry out the command (maximum score for each modality of transitive movements was 30 points).

Four types of errors were considered, namely, content, temporal, spatial and other (Rothi et al., 1988). Delay in the initiation and timing, and amplitude errors were not considered as apraxic in our present series of patients. Content errors, lack of response, and unrecognizable movements were not scored as ideomotor apraxia errors. Ideomotor apraxia was diagnosed whenever patients made >1 error on intransitive movements and >4 errors on transitive movements (cut-off scores for intransitive and transitive movements were 19 and 26, respectively; combined cut-off score = 45). Based on the final score on this task, the severity of apraxia was rated as mild (41–45 points), moderate (25–40 points), or severe (<25 points).

Patients were also asked to recognize gestures. In the pantomime comprehension (non-verbal) task, patients watched an actress performing a pantomime. The patient was presented with a response page containing five pictures (a comb, matches, a nail, an envelope, a musical instrument) and was asked to indicate which of the five pictures ‘went with the gestures’. The actress pantomimed each transitive gesture in two different ways. More than one error on this test was considered abnormal. In the recognition/discrimination task an actress pantomimmed five acts: hammering, toothbrushing, sawing, screwdriving and combing. Each act was performed in three different ways: a well-executed movement, a clumsily executed movement and using a body part as an object. The patient had to recognize the act and discriminate well from badly performed movements. More than one error on the gesture recognition task, and >2 errors on the gesture discrimination task were considered abnormal.

**Movement imitation test (MIT)**

The MIT consisted of four subtests of three gestures each, and evaluated the ability to imitate different positions and sequences of fingers and hands (e.g. making a circle with the thumb and index fingers). Scores for each gesture ranged from zero to three, the maximum score was 36, and the cut-off score was 33.

**Multiple step tasks**

Patients were asked to carry out three multiple step tasks. For the first task, patients were given a flashlight and two batteries, and were asked to take the proper steps to turn on the bulb. Thus, they had to unscrew the bottom of the flashlight (Step 1), introduce the batteries (Step 2) and turn on the light (Step 3). In the second task, patients were given a closed padlock and the corresponding key, and were asked to open the padlock and close it again. The steps were: to introduce the key in the padlock and open it (Step 1), to take out the key (Step 2) and to close the padlock (Step 3; the padlock would not close with the key in). Finally, patients were given a piece of paper, an open envelope and a stamp, and were asked to mail the letter. The steps were: to fold the paper (Step 1), to put the paper into the envelope and close the envelope (Step 2) and to glue the stamp to the envelope (Step 3). The alternative sequences of gluing the stamp before folding the paper or putting the paper into the envelope were also considered as correct. Scoring was based on the number of errors, which included lack of response, a verbal response instead of the actual movement, perplexity, omission, mislocation of steps, misuse of objects and sequence errors. More than one error in each task was scored as abnormal.

All movements were videotaped. The videotapes were subsequently assessed by three investigators who were unaware of the patients’ diagnoses and were asked to judge the presence of apraxia and the types of errors. A task was considered abnormal when at least two of the three investigators independently agreed on the presence and type of error.

**Neuropsychological and neuropsychiatric examination**

Patients with PD in the ‘on’ medication state were examined by a neuropsychologist who was blind to the neurological and praxis findings, with a comprehensive neuropsychological and neuropsychiatric evaluation which included the following task:

**Wisconsin Card Sorting Test (WCST).** This test
measures the ability to develop new concepts and shift sets, and it also requires the subject to suppress a previously correct response and produce a new one. Overall proficiency on the test was scored on the basis of the number of categories achieved (Nelson, 1976).

**Trail Making Test.** This test examines visual, conceptual and visuomotor tracking (Reitan, 1958).

**Raven’s Progressive Matrices.** This test measures visuospatial reasoning (Raven et al., 1986).

**Buschke Selective Reminding Test.** This test measures verbal learning and memory during a multiple trial list-learning task. The outcome measures were the long-term retrieval and delayed-recall scores (Buschke and Fuld, 1974).

**Benton Visual Retention Test—Revised.** This test assesses visual perception and nonverbal memory (Benton, 1974).

**Digit Span subtest of the Wechsler Adult Intelligence Scale.** This test measures auditory attention (Wechsler, 1955).

**Boston Naming Test.** This test examines the ability to name pictured objects.

**Controlled Oral Word Association Test (FAS).** This test examines access to semantic information with time constraint (Benton and Hamsher, 1978).

**Tower of Hanoi.** This test assesses strategy and visual planning (Simon, 1975).

**Hamilton Depression Scale.** This is a 17-item interviewer-rated scale that measures psychological and autonomic symptoms of depression (Hamilton, 1960).

**Statistical analysis**
Statistical analysis was carried out using means and SDs, analysis of variance (ANOVA), and post hoc Student’s *t* test when required. Regressions were calculated with a stepwise forward regression analysis and Spearman *r*. Frequency distributions were calculated with contingency tables, Fisher’s exact texts and *χ*² tests with a Yates’ correction for cell sizes <1. All *P* values are two-tailed.

**Results**
The results of apraxia assessment, MIT, multiple step tasks and MMSE in patients with PD, PSP, MSA and NIP are shown in Table 4.

**Parkinson disease**
Twelve of the 45 PD patients (27%) had bilateral ideomotor apraxia for transitive movements (defined as making 4 or more errors), which improved on imitation and became almost normal with the use of objects. Mean ideomotor apraxia scores for transitive movements in the 12 apraxic patients were 23.4±2.0; the non-apraxic patients scored 29.2±1 \[F(1,43) = 127.7, \quad P = 0.0001\]. Spatial errors (i.e. external configuration orientation, body-part-as-object, internal configuration and movement or trajectory errors) were the most frequently found. Hesitation, occurrence and sequence errors were unusual while content errors were not observed. Although abnormal, the intended gesture was always easily recognizable to the examiner.

Ideomotor apraxia scores for intransitive movements in patients with apraxia were 19.5±0.7; non-apraxic patients scored 19.8±0.4 \[F(1,38) = 2.42, \quad P < 0.1\]. No patient made >1 error on intransitive movement. None of the PD patients had orofacial or respiratory apraxia and none showed deficits on the multiple step tasks or discrimination/comprehension abnormalities.

The mean scores for movement imitation (MIT) in PD patients with and without ideomotor apraxia were 32.8±0.6 and 35.7±0.5, respectively \[F(1,38) = 282.4, \quad P < 0.0001\]. None of the patients without ideomotor apraxia for transitive movements performed below the cut-off score on the MIT whereas three of the patients with apraxia had a clearly abnormal score, and eight scored just in the lower limit. The prevailing types of errors were spatial, sequence and omissions.

There were no significant differences in age, disease duration, education, MMSE, UPDRS or Hoehn–Yahr scores between apraxic and non-apraxic patients \[F(6,16) = 1.62, \quad P < 0.20\]. The frequency of ideomotor apraxia in patients with onset of symptoms on either the right or left sides was not significantly different \[χ²(1) = 0.34, \quad P = 0.55\]. Furthermore, no significant differences in ideomotor apraxia scores were found in the ‘on’ as compared with the ‘off’ states in the PD apraxic group \[F(1,13) = 2.1, \quad P = 0.13\] (see Table 5).

A stepwise multiple regression analysis was carried out using ideomotor apraxia scores as the dependent variable and UPDRS items (rigidity, finger tap, hand movements and alternating movements) as independent variables. No significant correlation was found \[r^2 = 0.18; \quad F(4,40) = 2.24, \quad P = 0.15\]. A stepwise multiple regression was also performed using ideomotor apraxia scores as the dependent variable and UPDRS items (posture, arising from a chair, body bradykinesia, masked face and stability) as independent variables. A significant correlation was found \[r^2 = 0.27; \quad F(6,38) = 2.44, \quad P = 0.04\], with body bradykinesia being responsible for the majority of the variance \((\hat{\beta} = 1.1, \quad P = 0.001)\).

There were no significant correlations between MIT and UPDRS variables \[r^2 = 0.20; \quad F(1,25) = 0.5, \quad P = 0.4\].
more errors (expressed in mean ± SD). Patients with PD and PSP were divided into those exhibiting ideomotor apraxia, defined as those making five or more errors ($n = 12$ and $8$, respectively) and those who did not. $P < 0.0001$; **$P < 0.0001$; ***$P < 0.006$ (all ANOVA).

Table 5 Relationship between motor UPDRS and ideomotor apraxia scores in PD patients with apraxia when they are on and off medication

<table>
<thead>
<tr>
<th>Scores</th>
<th>Off medication</th>
<th>On medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS</td>
<td>20.2 ± 6.7</td>
<td>8.6 ± 5.8*</td>
</tr>
<tr>
<td>IMA</td>
<td>23.4 ± 1.9</td>
<td>23.6 ± 2.0</td>
</tr>
</tbody>
</table>

Data shown as mean ± SD. IMA = ideomotor apraxia. *$P = 0.0008$ (ANOVA).

Moreover, MIT scores in the ‘on’ and ‘off’ states were not significantly different ($P = 0.9$).

To correlate ideomotor apraxia scores with frontal lobe functions a Spearman correlation test was performed using apraxia scores as the dependent variable and WCST, FAS and the Trial Making Test (difference B–A) as independent variables. Significant correlations were found for the FAS ($r = 0.37$, $P = 0.02$) and the Trial Making Tests (difference B–A) ($r = 0.43$, $P = 0.03$), but not for the WCST ($r = 0.15$, $P = 0.3$).

Twelve of the 33 non-apraxic PD patients and one out of 12 apraxic PD patients were able to complete the Tower of Hanoi ($\chi^2(1) = 2.09$, $P = 0.14$). Apraxic PD patients made significantly more errors than non-apraxic PD patients ($F(4,44) = 5.20$, $P = 0.011$).

There was only a trend towards statistically significant differences between apraxic and non-apraxic PD patients in the performance of the Raven Progressive Matrices ($F(1,10) = 4.05$, $P < 0.08$).

MIT scores correlated significantly (by multiple regression analysis) with Tower of Hanoi ($r^2 = 0.26$; $F(2,23) = 4.2$, $P < 0.02$) and with the Raven Progressive Matrices ($r^2 = 0.19$; $F(2,27) = 3.2$, $P < 0.05$).

PD patients with apraxia showed significantly higher Hamilton depression scores than non-apraxic patients [$F(1,31) = 11.61$, $P < 0.002$]. There were no statistically significant between-group differences in any of the remaining neuropsychological tests.

Progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome)

Using a cut-off score of 26, eight out of the 12 patients revealed features of bilateral ideomotor apraxia for transitive movements. Mean ideomotor apraxia score for transitive movements in the eight apraxic patients was $18.2 ± 5.9$; the non-apraxic patients scored $28.7 ± 0.3$ [$F(1,10) = 11.95$, $P < 0.006$]. Patients clearly improved on imitation and with tactile cues provided by object use. Five of the patients with ideomotor apraxia for transitive movements also had ideomotor apraxia for intransitive movements. Mean ideomotor apraxia scores for intransitive movements in patients with and without ideomotor apraxia for transitive movements were $17.2 ± 2.7$ and $20.0 ± 0.0$, respectively [$F(1,10) = 4.02$, $P < 0.07$]. In decreasing order of frequency the most prominent error types were spatial (i.e. the use of body-part-as-object, internal and external configuration and trajectory).

Temporal errors, such as hesitation, were frequent, but sequencing errors occurred rarely. Content errors, related and/or non-related, were not found. Although the execution of the requested motor act was abnormal, the errors seen were embedded in a conceptually correct motor performance.

In addition to the spatial and temporal errors characteristic of ideomotor apraxia, five patients also showed very awkward and clumsy movements preceeded by hesitation and unsuccessful attempts when pantomimining any movement, irrespective of the type of the gesture and the modality for evoking them. This abnormal motor behaviour exceeded the observed
bradykinesia and/or rigidity and it was more obvious in the more affected hand.

None of the PSP patients failed on pantomime comprehension. Pantomime recognition/discrimination was normal in all patients. Two patients performed below normal on the multiple step tasks; the apraxia errors seen were perplexity, omission, sequence and mislocation. Both patients also had ideomotor apraxia and showed the lowest MMSE scores.

Mean values of MIT in PSP patients with and without ideomotor apraxia were 29.5±5.0 and 33.2±1.7, respectively \(F(1,10) = 1.99, P < 0.1\). Using a cut-off value of 33, movement imitation abnormalities were seen in six PSP patients; all but one had also ideomotor apraxia.

The mean orofacial and respiratory apraxia scores for the whole PSP patient group (apraxic and non-apraxic) were 22.3±7.2 and 14.2±4.2, respectively. Using cut-off scores of 28 for orofacial and 17 for respiratory apraxia, 10 and eight PSP patients, respectively, showed some apraxic behaviour in executing the requested motor acts. The most striking and frequent feature observed on testing orofacial and respiratory praxis in these patients was that of an overall final correct motor performance which was preceded by variably long pauses during which unsuccessful movements occurred. At all times and in all movements, however, the correct intent or concept of the motor action was identifiable.

The impression was that the patients knew exactly what to do, but could not do it flawlessly. Irrelevant or complete failure on orofacial/respiratory motor performance was found in only one patient who also had ideomotor apraxia. Another feature observed was perseveration (\(n = 3\)). However, it was often difficult to interpret the exact nature of the apraxic orofacial/respiratory behaviour seen, because of the unique facial appearance usually present in PSP patients (Jackson et al., 1983), sometimes referred to as ‘spastic’ (Richardson, 1963) or dystonic in the sense of a sustained abnormal posture.

The mean MMSE score of apraxic PSP patients was 21.9±6.2; while non-apraxic PSP patients scored 27.5±1.9 \(F(1,10) = 2.89, P < 0.1\). Five of the eight PSP patients who exhibited ideomotor apraxia performed below normal (<24) on MMSE while none of the non-apraxic PSP patients showed an abnormal score. Thus, ideomotor apraxia scores correlated significantly with MMSE scores (\(r^2 = 0.57, P = 0.002\)).

Multiple system atrophy (MSA)

None of the MSA patients revealed signs of any praxis disturbance. The mean scores were 29.6±0.7 and 17.7±0.6 for orofacial and respiratory apraxia, respectively. Mean ideomotor apraxia score for intransitive movements was 19.8±0.6; mean ideomotor apraxia score for transitive movements was 29.6±0.6. None of the scores for individual patients fell below the cut-off point for ideomotor apraxia. All patients had normal gestural recognition and discrimination. The mean for movement imitation was 34.1±1.2 and all patients performed normally on the multiple step tasks.

The mean MMSE score of MSA patients was 28.0±2.1; there was a significant difference between the MMSE scores of MSA patients and those of apraxic PSP patients \(F(1.16) = 8.31, P < 0.01\) but no significant difference was found between non-apraxic PSP patients and MSA patients \(F(1.12) = 17, P < 0.6\).

Neuroleptic-induced Parkinsonism

None of the 12 patients with NIP showed apraxia. Mean ideomotor apraxia scores for intransitive and transitive movements were 20.0 and 29.1±8, respectively, while mean scores for orofacial and respiratory apraxia were 29.8±0.4 and 17.9±0.2, respectively. All patients performed normally on the MIT and no errors were detected on the multiple step tasks. Pantomime comprehension and recognition/discrimination were normal in all patients.

Discussion

We investigated the presence of apraxia in a consecutive series of non-demented patients with PD on levodopa treatment and in patients with PSP, MSA and NIP, and there were several important findings. Some 25% of PD and 75% of PSP patients showed ideomotor apraxia for transitive movements, which tended to be more severe in PSP patients. Ideomotor apraxia in PSP and PD was mainly characterized by spatial errors, followed by hesitations, occurrence and sequence errors. Some PSP cases but none of the PD patients exhibited ideomotor apraxia for intransitive movements; both groups, however, had difficulties in imitating hand and finger postures. Neither PSP nor PD patients showed abnormalities in recognition/discrimination and comprehension of pantomimes. In addition to ideomotor apraxia, some PSP patients also showed a more ‘simple’ breakdown of motor behaviour which might be called limb-kinetic apraxia, and a minority displayed deficits on tasks involving multiple steps, suggestive of a more conceptual component in their apraxic behaviour. Neither MSA nor NIP patients showed ideomotor apraxia, abnormalities in movements imitation or deficits on tasks with multiple steps. Among PD patients, ideomotor apraxia significantly correlated with body bradykinesia, deficits on frontal lobe-related neuropsychological tasks and higher depression scores; it failed to improve with dopaminergic therapy. In PD patients there was a positive correlation and a clear trend towards significance between deficits in visuospatial cognition and MIT scores, and visuospatial cognition and apraxia severity, respectively. Ideomotor apraxia in PSP patients correlated with cognitive impairment; when the cognitive deficit was severe, a mild conceptual apraxic deficit also became evident.

Before further discussion, one crucial limitation of our study should be pointed out. The apraxia was scored on the basis of the raters’ subjective judgement. While this may
result in some arbitrary decisions, apraxia was diagnosed only when at least two of the three raters independently agreed on the presence and type of errors. In future studies, the presence of apraxia should be examined using more objective techniques.

The nature of apraxia in PD and PSP

Apraxia in the traditional sense, as defined by Geschwind (1975), may not be the correct term to employ in patients with basal ganglia diseases, because they manifest elementary motor deficits such as akinesia, rigidity and tremor. Nevertheless, it is possible to distinguish between lower level deficits of motor control and higher level apraxic errors. Poceck (1982) concluded: ‘The diagnosis of ideomotor apraxia is not made if a patient fails to carry out a certain movement at all, nor is mere clumsiness of movements sufficient to consider a patient apraxic. The diagnosis is made when a patient is impaired in the proper execution of the motor elements which constitute a movement and in the correct ordering of these elements in a motor sequence’. The errors we have detected in our apraxic group of PSP and PD patients fit the concept and definition of ideomotor apraxia proposed by Poceck (1982) and by Rothi et al. (1991). Spatial errors, such as internal and external configuration and movement trajectories, were among those most frequently observed in our patients, and could not be explained by the elementary motor deficits of parkinsonism. Moreover, three additional findings argue against the suggestion that lower level deficits of motor control explain the findings of apraxia in PSP and PD. First, with the exception of bradykinesia there was no significant correlation between the severity of apraxia and the cardinal signs of PD. Secondly, none of the patients with MSA and NIP, even those with severe motor manifestations, had any deficit on praxic functions. Thirdly, no significant differences in apraxia scores were recorded when PD patients were examined in their ’on’ and ’off’ states.

Spatial errors produced by our apraxic PD and PSP patients may reflect an overall deficit in visuospatial functions. Certain visuospatial deficits have been reported frequently in PD (Cummings and Huber, 1992), as well as in PSP (Fisk et al., 1982; Maher et al., 1985; Dubois et al., 1988; Pillon et al., 1991). In the present study, in PD patients, we found a clear trend towards statistically significant correlations between apraxia severity and MIT scores with deficits on a visuospatial task (Raven’s Progressive Matrices). Goldberg et al. (1986) have also described a significant association between spatial errors on a motor task and disturbance of visuospatial functions. The initial stage of motor programming may depend partially on visuospatial abilities, which are complex and multifaceted in nature (Harrington and Hasland, 1991), requiring the functional integration of activity in occipital, parietal and frontal cortices as well as the contribution of subcortical structures. PD and PSP patients have been found to have deficits in several domains of visuospatial performance. Deficits in visuomotor abilities (Villardita et al., 1982; Maher et al., 1985; Brown and Marsden, 1988; Levin, 1990) and visuospatial cognition (Asso, 1969; Stern et al., 1984; Maher et al., 1985; Dubois et al., 1988; Beatty and Monson, 1990; Dubois et al., 1990; Pillon et al., 1991) may reflect poor strategy and planning, psychomotor retardation and working memory abnormalities, so they have been ascribed to frontal lobe disturbances. Others, such as deficits in visual discrimination abilities (Boller et al., 1984; Hovestadt et al., 1987; Dubois et al., 1988), clearly point to a visuo perceptual dysfunction.

Though less frequent, temporal errors were also present in our apraxic PD patients. One explanation for the lower prevalence of temporal as compared with spatial errors is that the apraxia assessment may not have been sensitive enough to detect motor sequencing and timing abnormalities. Deficits in the performance of sequential movement are well documented in PD (Benecke et al., 1987), and have been demonstrated to correlate with abnormal visuospatial processing but not with disease severity (Harrington and Hasland, 1991). Furthermore, the significant role of the basal ganglia in motor timing as well as in temporal perception has been addressed by several authors who demonstrated that PD patients are impaired on a variety of tasks which require the production of appropriately timed movements (Nakamura et al., 1975; Artieda et al., 1992; Pastor et al., 1992; Freeman et al., 1993; O’Boyle et al., 1995). Whether the abnormalities of temporal processing observed in PD patients primarily reflect dysfunction of the basal ganglia themselves, or an interference with the normal functions subserved by those cortical regions to which the damaged basal ganglia project, has yet to be established. A role of the supplementary motor area and premotor cortex in motor timing function has been well documented (Freund, 1989; Lang et al., 1990; Halsband et al., 1993).

The spectrum of apraxic disturbances in PSP was wider and more complex than in PD patients. Eight of the 12 patients with PSP exhibited ideomotor apraxia for transitive movements and five of these also for intransitive movements. The pattern of apraxic errors was qualitatively similar although more severe than that seen in PD patients. Moreover, two PSP patients with significant cognitive impairment also showed a poor performance in the multiple step tasks, which suggests dysfunction of the conceptual praxis system in addition to the production praxis system (Roy and Square, 1985). Furthermore, superimposed on the characteristic ideomotor apraxia errors, five PSP patients also showed a different, more ‘simple’ breakdown of movements. The patient seemed to know what to do and always tried to carry out the movement requested, but there was marked hesitation, unsuccessful movement or fruitless attempts preceding the requested motor act. The correct intent of the motor act itself, however, was always recognizable against this background of hesitation, clumsiness and unsuccessful attempts.

It is difficult to define exactly the nature of this underlying ‘simple’ apraxic motor behaviour in PSP. The hesitation, clumsiness and unsuccessful attempts at moving cannot easily
be explained by akinesia and rigidity, for it was not evident in equally disabled patients with MSA or in patients with drug-induced parkinsonism. These components of the overall motor performance, on top of which spatial ideomotor praxic errors were evident, might be interpreted as limb-kinetic apraxia, in which case the overall motor performance of apraxic PSP patients could be viewed as a combination of ideomotor and limb-kinetic apraxia.

The usefulness of the term limb-kinetic apraxia has been debated for decades, and is still not generally accepted. Liepmann (1920) considered limb- or melo-kinetic apraxia as possibly distinct from ideomotor apraxia. He viewed limb-kinetic apraxia as loss of ‘kinaesthetic motor engrams’, due to damage to the contralateral ‘sensomotorium’. By contrast, he conceived ideomotor apraxia as due to disconnection between the (left) posterior areas (auditory, visual and tactile cortical areas) and the (left) ‘sensomotorium’; the limb kinetics were maintained but detached from the ideation of movement. While limb-kinetic apraxia occurs unilaterally in the limbs opposite to the lesion, ideomotor apraxia due to a unilateral lesion in the dominant (left) hemisphere is invariably bilateral although usually more severe in the right hand. Liepmann (1920) postulated that motor apraxia (subsuming limb-kinetic and ideomotor apraxia) would hardly ever be seen in a pure ‘limb-kinetic’ or pure ‘ideomotor’ form; a mixture of both would be much more likely.

This particular terminological dilemma in defining apraxia in basal ganglia disease has also been reflected in the most recent literature regarding the nature of apraxia in corticobasal degeneration (Okuda et al., 1992; Leiguarda et al., 1994; Okuda and Tachibana, 1994, 1995). Okuda and Tachibana (1994, 1995) took issue with Leiguarda et al.’s (1994) conclusion that ideomotor apraxia was the most frequent apraxia type in corticobasal degeneration. The former authors reported four corticobasal degeneration patients who presented with asymmetric, limb-kinetic apraxia but without signs of ideomotor or ideational apraxia. All four patients showed difficulties in making gestures and using objects, which could be attributed to limb-kinetic apraxia on the side of greater clumsiness, contralateral to the lesion. Leiguarda et al. (1994), however, stated that many of their corticobasal degeneration patients failed on tests for ideomotor apraxia, a failure that could not be explained by limb-kinetic apraxia alone. Okuda and Tachibana (1994) proposed two possibilities accounting for the discrepancy. First, limb-kinetic apraxia might induce a disorder of symbolic action which may mimic ideomotor apraxia and secondly, limb-kinetic apraxia and ideomotor apraxia might co-exist.

The relationship of frontal lobe dysfunction to apraxia in PD and PSP

The nature of the ideomotor apraxia found in PD and PSP patients was of the ‘anterior type’ (Heilman et al., 1982). Transitive movements were more affected than intransitive movements, and none of the patients failed on pantomime comprehension or pantomime recognition/discrimination. This anterior pattern of ideomotor apraxia suggests primary dysfunction of the frontal lobe praxis systems, or of association pathways from parietal to frontal lobe (Watson et al., 1986; Rothi et al., 1991). Alternatively, basal ganglia disease might disrupt the integration of cortico-striatal inputs carrying parietal cortex sensorimotor spatial information and frontal cortex action plans. As a result, there might be abnormal input from the basal ganglia to the premotor/ prefrontal cortex to which they project.

There were significant differences in performance of frontal lobe-related cognitive tasks and depression scores between apraxic and non-apraxic PD patients. A similar PD pattern of frontal lobe cognitive dysfunction also occurs in patients with PSP and to a lesser extent in MSA. Robbins et al. (1994) compared patients with PD, PSP and MSA on a variety of tests probing frontal lobe function. A distinctive pattern of cognitive deficits on tests of frontal lobe function was found in all three diseases, suggesting a common and fundamental cognitive syndrome that could be termed frontostriatal dementia. However, patients with PSP and PD were more impaired and also showed qualitative differences when compared with patients with MSA.

Frontal hypometabolism has also been reported in PD patients with depression (Mayberg et al., 1992). Functional imaging studies (PET and single photon emission tomography) have also consistently shown reduced frontal metabolism in PSP (D’Antona et al., 1985; Foster et al., 1988; Leenders et al., 1988; Goffinet et al., 1989; Blin et al., 1990; Bhatt et al., 1991; Brooks et al., 1992). Goffinet et al. (1989), for example, found that motor and premotor cortex and prefrontal glucose utilization may be reduced by >70% of normal in PSP. The usual explanation for such frontal hypometabolism in PSP is deafferentation due to loss of medial pallidal neurons projecting via ventrolateral thalamus to prefrontal areas, although cortical pathology (as discussed below) may play an important role.

On the other hand, frontal hypometabolism is not a consistent feature of MSA. While De Volder et al. (1989) did report reduced frontal glucose metabolism in MSA of striatonigral-type, Brooks et al. (1992) described normal frontal blood flow and oxygen metabolism in such patients.

The pathology responsible for apraxia in PD and PSP

Patients with PD and PSP who exhibit apraxia might do so because of the particular nature of the pathology in their basal ganglia, because of additional cerebral cortical pathology, or both.

It is difficult to attribute apraxia in PD and PSP to basal ganglia dysfunction alone. First, focal lesions confined to the basal ganglia rarely cause apraxia. Ideomotor apraxia, less frequently orofacial apraxia and exceptionally ideational
apraxia (always associated with ideomotor apraxia) is most commonly seen when the basal ganglia damage intrudes to the adjacent white matter to affect association fibres, in particular those of the superior longitudinal fasciculus and fronto-striatal connections (Della Sala et al., 1992; Pramstaller and Marsden, 1996). This additional involvement of periventricular, and especially peristriatal, white matter seems to play a crucial role in the development of apraxia in patients with such deep lesions.

Secondly, other conditions causing marked akinesia and rigidity due to basal ganglia dysfunction do not appear to produce apraxia. Striatal function is severely disrupted in PD due to massive degeneration of the nigrostriatal dopaminergic system (Hornykiewicz, 1982). However, striatal dopamine depletion does not seem to be responsible for the apraxic deficit in PD since apraxia scores did not differ in ‘off’ and ‘on’ states. In addition, none of the patients with drug-induced parkinsonism or MSA exhibited apraxia, yet neuroleptics block striatal dopamine receptors and MSA patients have severe dysfunction of the nigrostriatal dopaminergic system when studied by PET (Brooks et al., 1990). Some additional pathology must be invoked to explain the ideomotor apraxia seen in some patients with PD and PSP, but not in MSA and drug-induced parkinsonism.

We therefore conclude that basal ganglia damage by itself is unlikely to be responsible for the ideomotor apraxia seen in some patients with PD and PSP; most probably it is due to a combination of basal ganglia and cortical dysfunction.

Cortical dysfunction in PD and PSP might reflect damage to the ascending noradrenergic, serotonergic and cholinergic pathways known to occur in these diseases in addition to the pathology in the dopaminergic system, or it could be the direct result of associated local cortical pathology. We favour the second possibility. Cortical changes of the Alzheimer type (i.e. senile plaques and neurofibrillary tangles) and cortical Lewy bodies are frequently found in the cerebral cortex of PD patients, even in those without dementia (Boller et al., 1980; Hughes et al., 1992, 1993). Cerebral cortical pathology is now recognized to occur in PSP (Steele et al., 1964; David et al., 1968; Behrmann et al., 1969; Jellinger, 1971; Ishino et al., 1976; Bugiani et al., 1979; Davis et al., 1985; Ruberg et al., 1985; Mori et al., 1986; Sako et al., 1986; Hauw et al., 1990; Verny et al., 1994; Daniel et al., 1995). Daniel et al. (1995) reported neocortical neurofibrillary tangle pathology in all of their 17 pathologically proven PSP cases; tangles varied in number from being occasional to very frequent. Neurofibrillary tangles were identified in the cingulate, superior and medial frontal gyrus; when anterior (area 9) was compared with posterior (area 4) frontal cortex, the latter appeared most severely involved. The neocortical localization of neurofibrillary tangles in PSP seems distinct from that in Alzheimer’s disease. PSP shows more severe involvement of motor as opposed to association cortex. In addition, co-existence of PSP and Alzheimer’s disease pathology has been reported in a substantial number of cases (Gearing et al., 1994).

The absence of apraxia in MSA would, according to this argument, be due to lack of pathology in those cortical regions responsible for praxis. It should be noted, however, that the cerebral cortex in MSA is not entirely normal. Argentophilic inclusions in glia and neurons (Papp et al., 1989; Papp and Lantos, 1994), so characteristic of MSA, are found not only in basal ganglia but also in cerebral cortex, particularly in motor cortical regions (supplementary motor area, cingulate motor area, primary motor and premotor cortical area). In contrast, the visual, auditory and primary somatosensory cortices as well as the prefrontal association and parietal areas contain no or only a few oligodendroglial cytoplasmic inclusions (Papp and Lantos, 1994). However, whether these inclusions are associated with neuronal loss or dysfunction is uncertain.

On balance, therefore, we suggest that ideomotor apraxia found in some patients with PSP and PD is due to the combination of pathological involvement of the cerebral cortex and basal ganglia/subcortical lesions. The presence or absence of cortical pathology, and its severity and distribution might determine the presence and type of apraxia encountered in these patients. Apraxia in this condition would therefore reflect combined cortico-striatal dysfunction. The association of cortical and basal ganglia pathology has been invoked to explain the apraxia so characteristic of cortico-basal degeneration (Leiguarda et al., 1994).

The interaction between cerebral cortex and basal ganglia in praxis

The cortical structures critical for gesture processing are the posterior parietal, the dorsolateral prefrontal and premotor cortices. These cortical regions project to different sectors of the striatum. Parietal area 7a and dorsolateral prefrontal cortex project to central striatum (Yeterian and Van Hoesen, 1978; Selemon and Goldman-Rakic, 1985; Yeterian and Pandya, 1991); parietal areas 5 and 7b and premotor, motor and somatosensory cortices project to lateral striatum (Kunzel, 1978; Percheron et al., 1984; Selemon and Goldman-Rakic, 1985); the medial striatal sector receives an input from the temporal lobe and the inferior prefrontal area (Van Hoesen et al., 1981; Selemon and Goldman-Rakic, 1985); the ventral striatum receives projection from some limbic and paralimbic areas (Baleydier and Mauguiere, 1980). The processed basal ganglia output returns mainly to the lateral prefrontal, premotor and motor cortices (Hoover and Strick, 1993) via topographically organized pathways that pass through the thalamus. These projections are organized in parallel basal ganglia–thalamo-cortical circuits (Alexander et al., 1990) whose strict anatomical and functional segregation have been recently questioned (Flaherty and Graybiel, 1994; Graybiel et al., 1994; Joel and Weiner, 1994; Inase and Tanji, 1995; Parent and Hazrati, 1995). The complex motor, cognitive...
and limbic informational processing in the whole cortico-basal ganglia system most likely depends on several mechanisms: (i) the convergence of cortical inputs on individual striatal projection neurons, where they are re-mapped systematically into convergent or divergent modules (Cowan and Wilson, 1994; Flaherty and Graybiel, 1994); (ii) the overlapping and integration of striatal projection on medial pallidal and nigral output neurons (Percheron et al., 1985, 1994; Filion et al., 1994); (iii) the interactions within nuclei in the basal ganglia circuits themselves (Flaherty and Graybiel, 1994; Graybiel et al., 1994; Parent and Hazrati, 1995a, b).

Medial premotor cortex, including supplementary motor area and cingulate premotor areas, is generally thought to be concerned with processes by means of which internal context implements action (Goldberg, 1985). Medial premotor cortex appears to play a role in movement selection when there are no external cues or when the act is to be performed from memory or is self-initiated. These regions are significantly activated when normal subjects perform a ‘free selection’ of hand movements (Deiber et al., 1991). On the other hand, the lateral premotor cortex is thought to be mainly involved in the selection of externally guided movements (Goldberg, 1985) and is highly activated when subjects learn new sequences (Jenkins et al., 1992). Unlike medial premotor cortex, lateral premotor cortex presumably supports neuronal programs required for the retrieval of movements appropriate to context. One of the difficulties experienced by ideomotor apraxia patients may be to select the appropriate movement (or action) given the context (Passingham, 1993).

The context-dependent role of the basal ganglia has been recently stressed by Marsden and Obeso (1994) and Houk and Wise (1995). Marsden and Obeso posit a dual function for the basal ganglia, a routine motor activity mainly concerned ‘with the execution of predictable and automatic cortically initiated movement’ and a context-dependent one when ‘novel external or internal events capture the attention of other striatal regions, to signify the need to change (or adapt) the course of the movement’. Most of the researchers who have studied striatal or pallidal modulation in awake monkeys have emphasized its context-dependent neuronal activity (Alexander and Crutcher, 1990; Kimura, 1992; Schultz and Romo, 1992), indicating that ‘discharge modulations do not obligatorily follow sensory events or accompany specific motor acts, but rather do so only under certain circumstances’ (Houk and Wise, 1995). Evarts and Wise (1984) and Alexander and Crutcher (1990) have identified a population of set-related putaminal neurons, whose activity changed in response to environmental cues, while neurons that respond to a novel stimuli of emotional significance have been found in the ventral striatum (Rolls and Williams, 1987).

Ideomotor apraxia of the type found in our PD and PSP patients usually is not apparent in every day behaviour. In a natural setting, learned, object-oriented actions are processed automatically. However, when praxis is tested in the laboratory, the subject has to adopt an unusual strategy because the content of the action has to be explicitly represented and the contextual cues are different. Thus, the motor response is triggered by external stimuli (auditory, visual, or somesthetic), the attentional load may be greatly enhanced, and emotional feedback is clearly present; new or non-routine decisions may have to be taken on different trials. A novel context for the motor behaviour is created and the lateral as well as the medial premotor striatal subchannel of the ‘motor’ circuit, the limbic circuit and the prefrontal circuit are all called into play. Therefore, we posit that ideomotor apraxia becomes clinically evident in PD and PSP when the neuronal imbalance caused by basal ganglia dysfunction is combined with disturbances of cortical function to affect the integration of those cortico-striatal circuits which process information about skilled, learned, object-oriented actions in a particular environmental setting and during specific attentional and motivational demands.

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