

REVIEW ARTICLE

Apraxia in movement disorders

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The definition of apraxia specifies that the disturbance of performed skilled movements cannot be explained by the more elemental motor disorders typical of patients with movement disorders. Generally this does not present a significant diagnostic problem when dealing with 'higher-level' praxic disturbances (e.g. ideational apraxia), but it can be a major confound in establishing the presence of limb-kinetic apraxia. Most motor disturbances characteristic of extrapyramidal disorders, particularly bradykinesia and dystonia, will compromise the ability to establish the presence of loss of dexterity and deftness that constitutes this subtype. The term 'apraxia' has also been applied to other motor disturbances, such as 'gait apraxia' and 'apraxia of eyelid opening', that perhaps are misnomers, demonstrating the lack of a coherent nomenclature in this field. Apraxia is a hallmark of corticobasal degeneration (CBD) and historically this has received the most attention among the movement disorders. Corticobasal degeneration is characterized by various forms of apraxia affecting limb function, particularly ideomotor apraxia and limb-kinetic apraxia, although buccofacial and oculomotor apraxia can be present as well. The syndrome of parkinsonism and prominent apraxia, designated the 'corticobasal syndrome' (CBS), may be caused by a variety of other central nervous system pathologies including progressive supranuclear palsy (PSP), Alzheimer's disease, dementia with Lewy bodies and frontotemporal dementias. Distinct from the CBS, PSP and Parkinson's disease can demonstrate varying degrees of apraxia on selected tests, especially in those patients with more severe cognitive dysfunction. Diseases that cause the combination of apraxia and a primary movement disorder most often involve a variety of cerebral cortical sites as well as basal ganglia structures. Clinical-pathological correlates and functional imaging studies are compromised by both this diffuse involvement and the confusion experienced in the clinical evaluation of apraxia in the face of the additional elemental movement disorders. Finally, although apraxia results in clear disability in patients with the CBS, it is not clear how milder ideomotor apraxia found on specific testing contributes to patients' overall day-to-day motor disability.

Keywords: apraxia; corticobasal degeneration; Huntington's disease; movement disorders; Parkinson's disease; progressive supranuclear palsy

Abbreviations: ALO = apraxia of eyelid opening; CBD = corticobasal degeneration; CBS = corticobasal syndrome; DLB = dementia with Lewy bodies; IMA = ideomotor apraxia; LKA = limb-kinetic apraxia; MSA = multiple system atrophy; OFA = orofacial apraxia; PSP = progressive supranuclear palsy

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Introduction

Apraxia covers a wide spectrum of disorders that have in common the inability to perform a skilled or learned act that cannot be explained by an elementary motor or sensory deficit or language comprehension disorder. Praxis errors have been well defined clinically and kinematically and can

be superimposed on elementary motor disorders such as weakness, bradykinesia, rigidity, tremor, dystonia and ataxia (Heilman, 1985; Roy and Square, 1985; Poizner *et al.*, 1990, 1995). In many higher order apraxic disorders, such as ideational apraxia, this does not usually pose a diagnostic

dilemma. Although bradykinesia and other extrapyramidal signs (e.g. rigidity or dystonia) might cause a delay in initiation or performance of a gesture, the quality of the gesture should not be affected by these and so gestural impairment could not be explained by their presence alone. However, in some cases, such as those with limb-kinetic apraxia (LKA), bradykinesia and rigidity could readily compromise the ability to distinguish the loss of dexterity and coarseness of movement that characterize this subtype. In this review we will begin with a summary of the basic types of apraxia and the underlying neuroanatomical and physiological mechanisms thought to play a role, particularly as they relate to diseases of the basal ganglia. We will then discuss the different movement disorder syndromes commonly, and not so commonly, associated with apraxia. The neurological diseases chosen are based largely on descriptions of apraxia in those conditions in the literature as well as clinical experience. Certain disorders that are called ‘apraxia’, such as eyelid opening apraxia (ALO), but are probably better classified separately from apraxia, are also addressed.

Overview of apraxia

The first contemporary ideas of apraxia stem from the work of Liepmann, who proposed that in order to perform an action, the motor engram (or ‘space–time plan’) has to be conveyed from the left parietal lobe via association fibres to the ‘Central region’, in which Liepmann included the precentral and postcentral gyri, the middle and superior frontal gyri and their underlying white matter tracts. The Central region effected the action through the primary motor cortex, i.e. through the final common pathway of the pyramidal tract. If the left limb is to perform a task, then the information needed to be transmitted through the corpus callosum to the Central region on the right in order to activate the right pyramidal tract to carry out the action (Liepmann, 1908, 1920). Since that time, many other studies have confirmed the dominance of the left hemisphere in praxis (Basso *et al.*, 1980; De Renzi *et al.*, 1980, 1982). Apraxia, as tested by imitation and object use pantomime, has been found in ~50% of patients with left hemisphere damage and in <10% with right hemisphere damage. This suggests that many patients have bilateral representation of praxis functions (De Renzi, 1989). Even Liepmann pointed out that the right hemisphere probably has some praxis skills, and this has been used to explain why there is sparing of certain left-hand praxis functions after callosal or left hemisphere lesions (Geschwind and Kaplan, 1962; Graff-Radford *et al.*, 1987).

Damasio and Geschwind (1985) defined apraxia as demonstrating varying combinations of the following disturbances in order of progressive dysfunction: the failure to produce the correct movement in response to a verbal command, the failure to correctly imitate a movement performed by the examiner, the failure to perform a movement correctly in response to a seen object and the failure to handle an object

correctly. It is classified by both the nature of the errors made and the means by which they are elicited. For instance, abnormal performance can be due to ‘temporal errors’ (such as impaired timing and poor sequencing of a movement that requires multiple positionings, as long as the overall content of the movement remains recognizable), ‘spatial errors’ (such as abnormal amplitude, internal or external configuration orientation and body-part-as-object substitution), ‘content errors’ (such as perseveration) or ‘other errors’ (such as lack of response or an entirely unrecognizable response) (Rothi *et al.*, 1988). Since Liepmann’s original description, others have tried to advance his model in order to account for different types of praxis errors. Roy and Square (1985) proposed a two-part model in which a conceptual component encodes an abstract knowledge base for actions, including information about tool use and sequencing a series of single actions, and a production component provides sensorimotor information on how to perform an action ‘programme’ and then translates these programmes into actions. Much of our understanding of apraxia is based on lesioning studies and yet no single area alone has consistently been involved in the production of apraxia. This suggests that praxis functions are distributed through different neural networks working together. Depending on the neural network involved, the types of errors will differ. For example, as pointed out by Leiguarda and Marsden (2000), there is a parietofrontal system that encodes reaching and grasping mechanisms, and a frontostriatal system that encodes sequential motor events. Moreover, the extent to which these systems are affected depends on the context of the movement and the cognitive demand of the action (Leiguarda and Marsden, 2000). Table 1, which summarizes the major classification of motor limb apraxias (Rothi and Ochipa, 1991), will serve as a background to the types of apraxia found in movement disorders discussed below.

Role of the basal ganglia and apraxia

The motor and premotor areas of the cortex send projections to the basal ganglia (Alexander *et al.*, 1986), as do areas of the parietal cortex that are interconnected with those areas of the motor cortex, making up the parietofrontal circuits. These circuits act in parallel. Each one is involved in sensorimotor integration or in the translation of specific sensory data into information for movement production (e.g. visual and somatosensory transformation for reaching and body part location data for control of body part movements). There are also distinct frontostriatal circuits that play a role in action sequencing. The circuit activated depends on whether the action to be performed is prelearned or new, and on the complexity of the cognitive demands of the task (Grafton *et al.*, 1995; Catalan *et al.*, 1998). Apraxia can be found in diseases of the basal ganglia, including Parkinson’s disease, progressive supranuclear palsy (PSP) and Huntington’s disease, and reportedly in isolated lesions of the basal ganglia.

Table 1 Summary of apraxia types

Apraxia type	Definition	Clinical testing	Localization
Limb-kinetic	Loss of hand and finger dexterity resulting from inability to connect or isolate individual movements (Kleist, 1907)	All movements are affected—symbolic, non-symbolic, transitive (i.e. using tools and instruments, e.g. a hammer or a hairbrush) and intransitive (i.e. communicative gestures, e.g. representational tasks such as waving goodbye and non-representational tasks such as touch your nose and wiggle your fingers) Mainly distal in finger and hand Movements are coarse and mutilated No voluntary automatic dissociation:	All pathologically confirmed cases have shown a degenerative process involving frontal and parietal cortices (Fukui <i>et al.</i> , 1996) or primary motor cortex (Tsuchiya <i>et al.</i> , 1997)
Ideomotor	Disorder of goal-directed movement. Patient knows what to do but not how to do it. Disturbance of timing, sequencing and spatial organization of gestural movement (Rothi and Ochipa, 1991)	Impairment of pantomiming ability to use tool. Movement is incorrectly produced but the goal of the action can usually be recognized. Abnormal errors include spatial errors [i.e. (i) abnormal amplitude; (ii) body-part-as-object substitution, e.g. the patient uses his own finger to represent a toothbrush when asked to brush his teeth; (iii) abnormal orientation of body part performing the action, e.g. when the patient is asked to pantomime brushing his teeth he closes his fist tightly with no space for the imagined toothbrush handle or he may hold his hand right next to his mouth without demonstrating the distance necessary to accommodate the imagined toothbrush] and temporal errors (i.e. irregular timing, which can be either an increased or decreased rate of production of a pantomime and sequencing abnormalities, e.g. an addition, deletion, or transposition of movement parts as long as the overall movement structure remains recognizable) (Rothi <i>et al.</i> , 1988). Improves on imitation and with use of actual tool. Transitive more affected than intransitive. Voluntary automatic dissociation is present, so that deficit is more apparent in clinical setting than in everyday life.	Anatomically diverse lesions mainly in left hemisphere; typically involve parietal association areas and white matter bundles connecting frontal and parietal association areas. Less commonly premotor and supplementary motor cortex are involved as well as basal ganglia and thalamus. Unilateral lesions of the left hemisphere in right-handed patients produce bilateral deficits, usually less severe in the left than in the right limb
Ideational/ conceptual	Patient does not know what to do. Content errors. This terminology can be confusing not only because definitions of ideational and conceptual apraxia vary among authors (Ochipa <i>et al.</i> , 1992; DeRenzi and Lucchelli, 1988) but also because a distinction between the two is debated by some. Error types include, impairment in carrying out sequences of actions requiring the use of various objects in the correct order so as to achieve an intended purpose (Liepmann, 1920), and loss of tool action knowledge	Inability to perform a multiple-step task (e.g. prepare a letter to mail) owing to errors such as perseveration. Disturbance of single tool use—cannot associate tool and object with the corresponding action (e.g. unable to choose a hammer to drive a nail or correctly pantomimes an action when requested to perform a very different one) (Roth <i>et al.</i> , 1988; Leiguarda <i>et al.</i> , 2000a; Ochipa <i>et al.</i> , 1992)	No one anatomical area has been identified, although in focal hemispheric lesions, most have damage to left hemisphere. Damage typically thought to involve left parieto-occipital and parietotemporal regions (Liepmann, 1920) but can also involve left frontal, frontotemporal and temporal regions with or without subcortical involvement (Heilman <i>et al.</i> , 1997)

Thus it seems likely that the basal ganglia are involved in the transformation of action plans, or movement formulas, to motor acts and, therefore, that dysfunction of the basal ganglia itself could lead to errors of praxis.

Animal and human studies, using both electrophysiology and functional imaging, have tried to define the role of the basal ganglia in producing apraxia. Experimental studies in monkeys have shown that putaminal lesions cause inaccurate reaching (Kendall *et al.*, 2000) and globus pallidus internus lesions cause impaired reaching and grasping (Wenger *et al.*, 1999). Furthermore, positron emission tomography studies in humans have found activation of the caudate/anterior putamen during the performance of new or complex learned sequences and activation of the middle putamen during the performance of automatic sequences (Jueptner and Weiller, 1998). Electrophysiological studies have shown that there are subsets of neurones in the external and internal segments of the globus pallidus and substantia nigra pars reticulata that increase their discharge frequency in relation to the amplitude and velocity of movements (Georgopoulos *et al.*, 1983) whereas other pallidal neurones fire in relation to the direction of arm movement (Mitchell *et al.*, 1987). Moreover, there are yet other pallidal neurones that change activity in remembered sequential tasks and are influenced by the contextual setting of the movement. This suggests that the basal ganglia are involved in the production of both new and learned movement sequences.

Using three-dimensional analysis, Leiguarda and colleagues (2000*b*) studied the kinematic properties of a bread-slicing movement in patients with Parkinson's disease, PSP and multiple system atrophy (MSA). This task was chosen in part because of the repetitive, precise spatial movements required to successfully complete it, recognizing that the basal ganglia play a part in such movements. As will be discussed below, two of the five patients with PSP, two of the eight with Parkinson's disease, and none of the five MSA patients were felt to have ideomotor apraxia (IMA) clinically. Subjects in all groups made some spatial errors, although the errors made by the apraxic patients were more severe. The authors felt that the milder errors in movement trajectory and external configuration found in their patients supported the role of the basal ganglia as an integral component of a brain network for praxis. Additional damage to this network by extension of pathology beyond the basal ganglia might then result in clinically overt IMA, as seen in a subgroup of their patients.

Mink (1996) described the role of the basal ganglia in terms of a gate that moderates response choice by selectively inhibiting competing input from the cortex. As such, basal ganglia lesions could disrupt the organized production of purposeful movement by flooding the system with competing response options (Mink, 1996). Supporting this notion is a study on apraxia in Huntington's disease, which found that apraxia was related to disease severity. The authors postulated that apraxia in this situation was due to an inability to effectively gate competing motor programmes. If this was due to caudate damage alone, which is typically seen early in the course of the

disease, then all patients with Huntington's disease should exhibit apraxia. Rather, those with longer disease duration exhibited apraxia, again suggesting that apraxia is secondary to damage to the basal ganglia plus other structures such as surrounding white matter (Hamilton *et al.*, 2003).

The suggestion that dysfunction of the basal ganglia alone is insufficient to cause apraxia is further supported by the work of Pramstaller and Marsden (1996), who reviewed 82 cases of 'deep' apraxia as a result of defined lesions, using imaging (CT, and MRI if available) in 73 and neuropathological correlation in 9. They found that most had lesions in the left hemisphere, that isolated lesions of the putamen, thalamus, or lenticular nucleus were uncommon (8 out of 82) and that most patients actually had larger lesions involving damage to the basal ganglia and/or thalamus as well as to the periventricular and peristriatal white matter, disrupting association fibres. In fact no cases of pallidal lesions alone caused apraxia, and lesions of the caudate which caused apraxia ($n = 3$) all had white matter involvement. Limb IMA was the most common type of apraxia described (72/82), followed by orofacial apraxia (OFA) in association with IMA ($n = 37$) (Pramstaller and Marsden, 1996). Thus, as stated above, although the basal ganglia may be involved in the production of learned, skilled motor acts, it seems unlikely that isolated lesions in the basal ganglia are capable of producing the disturbances of motor performance subsumed under the concept of apraxia. Rather, the basal ganglia alters the expression of apraxia based on the context of movement required.

Disorders possibly misdesignated as apraxia

Since the term apraxia was first coined, many conditions have been called 'apraxia'. If the current definition of apraxia is applied, some conditions have probably been erroneously designated as apraxias. Based on the literature, varying theories can be advanced as to the pathophysiology underlying these, although more work is needed to better classify them. Two—apraxia of eyelid opening and apraxia of gait—are commonly seen in movement disorder patients and will be discussed below. Limb-kinetic apraxia, which to some represents an elemental motor disturbance rather than a true apraxia, will be discussed in the section on corticobasal degeneration (CBD).

'Apraxia' of eyelid opening

Apraxia of eyelid opening is a syndrome characterized by the inability to voluntarily open the eyes. The underlying pathophysiology of ALO is not well understood, as evidenced by the numerous other proposed designations, including inhibition of levator palpebrae (Lepore and Duvoisin, 1985; Fahn, 1988), akinesia of lid opening (Fahn, 1988) and lid freezing (Jankovic *et al.*, 1990). Goldstein and Cogan (1965) described the difficulty in initiating the act of lid elevation in four patients with basal ganglia disease and subsequent reports emphasized the presence of this syndrome in extrapyramidal disorders, in

particular PSP (Lepore and Duvoisin, 1985; Krack and Marion, 1994; Boghen, 1997). There is considerable support for the classification of many cases as a form of focal eyelid dystonia. It is frequently found in association with blepharospasm, and rarely occurs as an isolated entity (Elston, 1992). In one population study ALO coexisted with adult-onset blepharospasm in 75% of cases and with atypical parkinsonism in 25% (Lamberti *et al.*, 2002). Among the overall patient population seen in the authors' movement disorders clinic, it was isolated in 10 patients, associated with adult-onset dystonia in 13 (10% of all of their patients) and with parkinsonian syndromes in 9 patients (2% of their parkinsonian patients; a third of these had PSP). Recently ALO has been reported in up to 31% of patients undergoing subthalamic nucleus deep brain stimulation for Parkinson's disease (Krack *et al.*, 2003).

In patients with isolated ALO, the complaint is generally the inability to open the eyes and not the forceful closure of the eyes that constitutes blepharospasm. In one series (Krack and Marion, 1994), apraxia of eyelid opening, referred to as 'focal eye dystonia' by the authors, was seen in two patients with parkinsonism responsive to levodopa but in whom focal dystonia (spasmodic torticollis and blepharospasm) preceded the onset of parkinsonism. No ALO was seen in over 200 patients with idiopathic Parkinson's disease without preceding dystonia. Further support for considering it a form of dystonia is the fact that some patients can use sensory tricks, such as touching the sides of their eyes, to help initiate eyelid opening and that many of the same triggers that aggravate typical blepharospasm, such as bright light and looking up, are also present in ALO. The response of ALO to treatment with botulinum toxin in many patients also favours the consideration of dystonia rather than a form of apraxia. Excessive activity isolated to the pretarsal component of orbicularis oculi probably accounts for both the absence of forced eyelid closure in many and the response to botulinum toxin (Jankovic, 1996; Defazio *et al.*, 1998).

However, dystonia is unlikely to account for all cases of ALO. Inappropriate inhibition of the levator palpebrae muscle also seems to play an important role in the inability to initiate eye opening in some patients with ALO. In a study (Aramideh *et al.*, 1994) of five patients referred for botulinum toxin injections for 'blepharospasm' (four with blepharospasm and levator inhibition and one with isolated levator inhibition), the patient with isolated levator inhibition did not have ongoing spasms of the eyelids but frequently experienced involuntary drooping of the lids. No overt abnormal contractions of the orbicularis oculi were noted in this patient; electromyography showed no dystonic activity of the orbicularis oculi, but frequent episodes of inhibition of levator palpebrae activity were present. Here, as opposed to cases with overactivity of pretarsal orbicularis oculi, botulinum toxin failed to improve ALO.

Neither of these causes of eyelid opening dysfunction is consistent with current concepts of the various types of limb apraxia. Furthermore, when apraxia is evident in orolingual muscles, eyelid opening difficulties are not an

associated or accompanying feature. Although tradition will continue to encourage the use of the term 'apraxia of eyelid opening', the weight of evidence supports not classifying this as a form of apraxia.

'Apraxia' of gait

'Apraxia of gait' is another term that perhaps is a misnomer. It is distinct from 'leg apraxia', and often the two do not coexist. Leg apraxia can be tested using similar concepts to those that guide examination of the upper limb. The patient can be asked to pantomime tasks such as kicking a ball or stubbing a cigarette out with a foot. However, leg apraxia has not been routinely well studied in the assessment of praxis, and most of the literature on apraxia concentrates exclusively on the upper limb. This is in part because there is no standardized testing of the lower limb and in part because there are fewer movements (especially complex tasks) that can be tested in the lower limb.

In contrast to the infrequent mention of leg apraxia, 'apraxia of gait' has garnered considerable attention; however, the literature on this topic is quite complex, with various examples of lumping and splitting 'higher order' gait disorders (commonly with overlapping features using different, often confusing, terminology). For instance, whereas some assume that the terms 'marche a petit pas', 'lower body parkinsonism', 'vascular parkinsonism', 'Bruns' ataxia' and 'gait apraxia' all represent a similar gait subsumed under the umbrella term 'frontal gait disorders' (Geschwind, 1975; FitzGerald and Jankovic, 1989; Schiller, 1995; Elble *et al.*, 1996), others have used this term to refer to different gait patterns including frontal disequilibrium, isolated gait ignition failure and freezing of gait (Geschwind, 1975; Nutt *et al.*, 1993; Poizner *et al.*, 1995). Nutt *et al.* (1993) referred to all of these gait disturbances as 'higher level gait disorders' to signify dysfunction of the highest integrative sensorimotor systems with intact basic motor and sensory functions. In classifying these disorders they mixed clinical phenomenology (gait ignition failure) with anatomical location ('frontal gait disorder'). In contrast, Liston *et al.* (2003) tried to avoid this potential confound by simply classifying all 'higher level gait disorders' (they limited their discussion to vascular causes) as apraxic gaits and naming them according to the primary problem seen, namely, 'ignition apraxia', 'equilibrium apraxia' or 'mixed gait apraxia'. This assumes that all higher level gait disorders can be considered forms of apraxia; however, this may not be appropriate. It has been postulated that gait ignition failure (Freeman *et al.*, 1993; Georgiou *et al.*, 1993) in Binswanger's disease and lower body parkinsonism owing to vascular disease occurs when damage to white matter tracts alters communication between the basal ganglia and the supplementary motor area, which may be involved in the internal cueing and guidance of learned, skilled, motor acts of the limbs (Chang *et al.*, 1992; Hennerici *et al.*, 1994). However, 'gait apraxia' typically exists without any evidence of other forms of apraxia and patients with bilateral limb apraxia

can have a normal gait (Geschwind, 1975; Thompson and Marsden, 1987). Furthermore, in the strictest of definitions, apraxia is the inability to perform ‘skilled or learned motor acts’. However, locomotion is not a consciously learned motor act but rather a repetitive motor pattern generated by spinal mechanisms and modified by brainstem structures (Shik and Orlovsky, 1976; Armstrong, 1988; Grillner *et al.*, 1995). One could argue that since walking is more ‘hard wired’ there can be no such thing as an apraxic gait. With a better understanding of the underlying anatomical and functional pathology resulting in the clinical phenomenology, perhaps a more uniformly acceptable nomenclature could be devised and current confusion eliminated.

Apraxia in corticobasal degeneration

Clinical features

Apraxia has been described in a number of diseases of the basal ganglia, such as Parkinson’s disease, PSP and Huntington’s disease. Corticobasal degeneration is the disorder most commonly associated with apraxia, which is present in up to 70% of patients with clinically diagnosed CBD (Leiguarda *et al.*, 1994). Corticobasal degeneration is characterized by an akinetic-rigid syndrome combined with asymmetric, lateralizing cortical signs including sensory loss, alien limb behaviour and apraxia. In fact, apraxia is considered a hallmark of CBD and is an important component of all proposed diagnostic criteria (Litvan *et al.*, 2003). However, this then serves as an important source of clinical bias: a very high proportion of patients with the clinical diagnosis of CBD have apraxia because apraxia is believed to be a distinguishing factor. Of equal importance, it is a source of misdiagnosis: patients with parkinsonism plus apraxia are typically diagnosed as having CBD rather than the more appropriate designation of ‘cortical-basal syndrome’ (CBS) (Boeve *et al.*, 2003; Lang, 2003). The CBS may be caused by a variety of underlying central nervous system pathologies, including PSP, Alzheimer’s disease, dementia with Lewy bodies (DLB) and frontotemporal dementias (see below).

In ‘classic’ CBD two types of apraxias have been emphasized: ideomotor and LKA. Ideational apraxia has not been discussed in detail. It has been suggested that this was a late feature related to more severe dementia (Gibb *et al.*, 1990). However, since then it has been recognized that dementia may be a common presenting feature of this disorder (Grimes *et al.*, 1998). Because this subgroup of patients are rarely given the clinical diagnosis of CBD, the nature of apraxia seen with this presentation has not been routinely evaluated. One study that compared features associated with a cognitive presentation with features associated with an extrapyramidal presentation found that ideational apraxia was present in both groups and, although less common, could occur in the absence of IMA (Kertesz *et al.*, 2000).

In patients with clinically diagnosed CBD, perhaps the most commonly recognized type of apraxia—and the one that has received the most attention—is ideomotor limb apraxia

(Table 1) (Leiguarda *et al.*, 2000a). This is commonly bilateral but typically asymmetrical, especially early in the disease course (Rothi *et al.*, 1985). The majority of errors made by CBD patients with IMA consist of spatial, temporal and sequencing errors, reflecting disruption of the ‘action production system’ (Leiguarda *et al.*, 2000a). As is also to be expected, the errors are more frequently observed when performing transitive than intransitive tasks and often improve when the subject is given an object to use (Table 1). A number of different studies (Pillon *et al.*, 1995; Blondel *et al.*, 1997; Jacobs *et al.*, 1999) have found that, although patients with CBD make errors on gesture to command as well as imitation, most have relative preservation of gesture recognition. Studying a group of healthy volunteers using H₂¹⁵O positron emission tomography, Peigneux *et al.* (2004) showed that regional cerebral blood flow increases in the medial frontal gyrus (supplementary motor area) in the left hemisphere during pantomime to command versus gesture recognition. This conforms to anatomical divisions of praxis and the sites of most profound pathological involvement in classical CBD, in which the brunt of cortical pathology is in the superior frontal and precentral and postcentral gyri (Dickson *et al.*, 2000). For example, in a study of patients with IMA resulting from anterior and posterior lesions in the left hemisphere, only those patients with a damaged parietal lobe had impairment in the recognition of gestures (Heilman *et al.*, 1982; Rothi *et al.*, 1985). The authors concluded that there are anterior and posterior forms of IMA and that in the former gesture recognition is preserved, whereas in the latter it is not. This is because the visuokinaesthetic motor engrams are stored in the parietal lobe and project to the supplementary motor area. They proposed that the supplementary motor area transcodes the space–time representation into an innervation pattern and then projects this information to the primary motor cortex, which directs the movement. In parietal lobe damage the visuokinaesthetic information is disturbed and gesture comprehension is impaired. In the anterior type of IMA, in which there is damage to the supplementary motor area or to subcortical white matter which disconnects motor areas from the intact parietal lobe, the ‘praxicon’ (visuokinaesthetic engram) is still intact and so patients can recognize gestures easily; however, the information on how to perform the gesture is lost (Heilman, 1985). Now there is evidence from brain imaging studies in man (Steinmetz *et al.*, 1989; Martin *et al.*, 1995) that, in fact, action recognition relies more on temporal lobe structures than on the parietal lobe. In a study comparing gesture recognition in patients with parietal lobe damage to patients with premotor/supplementary motor area damage and normal controls, minimal deficits in gesture comprehension were found in the group with parietal lobe damage and no deficits were present in the other two groups (Halsband, 2001). The preservation of gesture recognition in CBD implies frontal rather than parietal or temporal lobe damage.

Limb-kinetic apraxia is one of the most striking features of CBD, although it is not exclusive to this disorder (Leiguarda

et al., 1997). It was first described by Kleist in 1907 as an ‘innervatory apraxia’ (Kleist, 1907), and then Liepmann advanced the term ‘limb-kinetic apraxia’ (Liepmann, 1920). He considered it the ‘most motor’ apraxia. Its existence as an actual apraxia, rather than a consequence of more elemental motor deficits, was largely ignored until its occurrence in CBD was recognized (Geschwind, 1965; Heilman, 1985; Okuda *et al.*, 1992; Denes *et al.*, 1998; Leiguarda *et al.*, 2000a). This has brought renewed interest in this type of apraxia. Unlike IMA, which is typically bilateral, LKA is usually unilateral and involves the most affected limb. Ideomotor apraxia and LKA may be combined in the same limb. As outlined in Table 1, LKA consists of impaired, coarse, ‘mutilated’ execution of simple movements of the hand contralateral to the cortical lesion. This is more evident distally than proximally and is most notable for incoordination between fingers, as seen in object manipulation tasks and fine finger movements. This makes it the most difficult praxis disorder to distinguish from bradykinesia, rigidity and dystonia—three movement deficits commonly seen in CBD. Leiguarda *et al.* (2003) studied the clinical and kinematic features of LKA in five patients with clinically diagnosed CBD compared with five patients with Parkinson’s disease and ten controls using a comprehensive apraxic battery, three-dimensional motion analysis of manipulative movements and motor evoked potentials. They found that all five CBD patients demonstrated a unilateral praxic deficit characterized by chaotic movement with marked interfinger incoordination. Using a measure of movement quality (QMC) they showed that the QMC was significantly different in the CBD patients compared with controls and most notably patients with Parkinson’s disease, suggesting that neurological abnormalities such as bradykinesia and rigidity alone are not able to explain LKA. They hypothesized that dysfunction in the premotor cortex accounts for LKA. The results of a study to assess processes underlying apraxic disorders in CBD, using a cognitive model based on work by Roy and Square (1985), also supported dysfunction of the premotor cortex in LKA (Blondel *et al.*, 1997). Finally, clinicopathological evidence in five patients also supports the role of damage to the premotor cortex underlying LKA in CBD (Tsuchiya *et al.*, 1997).

There is some debate, however, as to whether ‘limb-kinetic apraxia’ is a misnomer as well. As mentioned previously, initially Liepmann did refer to it as a true apraxia, yet others disagreed and felt it was a primary motor deficit. With its more recent recognition in CBD, it has generally been considered an apraxia again; however, there are reasons to question this classification. For example, damage to the pyramidal tracts in primates is recognized to result in clumsy movements characterized by an isolated deficit in independent finger movements (Tower, 1940; Lawrence and Kuypers, 1968). Furthermore in amyotrophic lateral sclerosis, often ‘loss of fractionated movement is an early characteristic of hand dysfunction’ (Weber *et al.*, 2000), typically long before the occurrence of other cognitive disturbances that might suggest more widespread cortical involvement (Lomen-Hoerth *et al.*,

2003). These deficits are reminiscent of those considered typical of LKA. Perhaps, then, LKA is better classified as a primary or elemental motor dysfunction, with variable presentation based on the extent of pathological changes, rather than a type of apraxia.

The features of apraxia, including buccofacial apraxia, were evaluated in 10 patients with clinically diagnosed CBD (Leiguarda *et al.*, 1994). Although seven patients had IMA and three had both IMA and ideational apraxia, no patient demonstrated buccofacial apraxia. In contrast to the lack of OFA in this study, others have found this to be a common feature in patients with CBD. Ozsancak *et al.* (2000) evaluated dysarthria and OFA in 10 patients with clinically diagnosed CBD: 9 patients had dysarthria, and voluntary movements of the tongue and lips were impaired in all 10. Orofacial apraxia for simple gestures was present in only four patients, whereas impairment of sequential gestures was present in nine patients. A rare presentation for CBD is the combination of profound dysarthria and OFA (Lippa *et al.*, 1991; Lang, 1992; Tanaka *et al.*, 2001). One of our patients first noted difficulties pronouncing words. He ultimately became anarthric and exhibited apraxia of all facial movements at a time when he had no other clinical deficits. Subsequent post-mortem study demonstrated a predominance of cortical pathology in the region of Broca’s area in the dominant left hemisphere in contrast to the more typical mesial predominance of cortical pathology in CBD (Bergeron *et al.*, 1996).

Eye movement abnormalities that perhaps represent a type of oculomotor apraxia can be seen in CBD as well. Cogan first used the term ‘oculomotor apraxia’ to refer to ‘the inability to initiate horizontal saccades in the head-fixed condition’. The oculographic pattern is characterized by increased latencies and decreased amplitude of horizontal saccades. In his series, vertical saccades were normal (Cogan, 1953; Cogan and Adams, 1953). Oculomotor apraxia is characteristic of two diseases (both of which may demonstrate prominent movement disorders): ataxia telangiectasia and ataxia oculomotor apraxia. In the former, reflexive and voluntary saccade latencies are prolonged, saccades are hypometric, velocities are normal and head movements are used to initiate gaze shifts (Stell *et al.*, 1989; Lewis *et al.*, 1999). This is quite typical of Cogan’s initial description. In ataxia oculomotor apraxia, on the other hand, latencies are said to be normal but saccades are extremely hypometric (mimicking slow eye movements), square wave jerks are present and synkinetic blinking is used to compensate for lack of vestibulo-ocular reflex cancellation. There is also a dissociation of eye–head movements in which the head reaches the target before the eyes (Le Ber *et al.*, 2003, 2004). Although not well recognized at first, eye movement abnormalities are a common manifestation of CBD with characteristics reminiscent of the original description by Cogan. Horizontal and vertical eye movements are equally affected. Typically, the latency of saccades and not their velocity is impaired. Initiation of horizontal saccades can be delayed and some patients are unable to produce

voluntary horizontal saccades, but this improves when something is given to them to look at. Eye blinking and head movements may be used to initiate voluntary saccades (Rebeiz *et al.*, 1967; Gibb *et al.*, 1989; Lang *et al.*, 1994b). In support of considering this a manifestation of apraxia, one study found a relationship between the apraxia score and the saccade latency (Vidailhet and Rivaud-Péchoux, 2000). The characteristics of the eye movement abnormalities have been used to distinguish CBD from PSP, where vertical saccade impairment is an early feature, saccadic velocity (but not latency) is impaired, the presence of square wave jerks is almost a uniform feature and more errors are found on an antisaccade task (Vidailhet and Rivaud-Péchoux, 2000). In addition to characterizing patients with the classical presentations of CBD or PSP, these eye movement differences may also be useful in distinguishing patients with more atypical presentations. Rivaud-Péchoux *et al.* (2000) followed a group of 16 patients (9 diagnosed with CBD and 7 with PSP), longitudinally with electro-oculography and clinical exams 6 months apart, for a mean of 37 months. They divided the CBD group into 'probable' (six out of nine) and 'atypical CBD' (three out of nine) because the latter group did not fit all diagnostic criteria for CBD (Litvan *et al.*, 1997). In the probable CBD group they found that horizontal saccades remained impaired, characterized by increase in saccade latency of reflexive visually guided saccades over time, and this was more marked ipsilateral to the side in which apraxia predominated. Horizontal saccade velocity did not decrease and square wave jerks were infrequently present. However, in the atypical CBD group, early square wave jerks, decreased saccade velocity and a high percentage of errors in the antisaccade test were more suggestive of PSP, and 4–6 months following the electro-oculography recordings, the early clinical diagnosis of CBD was revised to a diagnosis of PSP (Rivaud-Péchoux *et al.*, 2000) (Table 2).

Imaging and electrophysiology in corticobasal degeneration and apraxia

Imaging studies have been used to support the diagnosis of CBD. One of the most striking features, when clinical asymmetry is evident, is the asymmetry of frontoparietal cortical atrophy on MRI and CT, which is most notable contralateral to the most severely affected side. In one series this asymmetry was an almost constant feature with mild signal changes seen in the atrophic cortex (mainly on fluid-attenuated inversion recovery and proton density sequences) but minimal or no abnormalities evident in the basal ganglia (Savoirdo *et al.*, 2000). Early in the disease the asymmetric changes may be subtle, and late in the course bilateral abnormalities may be evident. Recently volumetric imaging has been used to try to differentiate between CBD and other parkinsonian syndromes (Groschel *et al.*, 2004), although none to our knowledge has specifically studied apraxia. On the other hand, several functional imaging studies have attempted to evaluate the pathophysiological mechanisms underlying apraxia. In one study

that examined six patients with clinically diagnosed CBD (all of whom had limb apraxia), regional cortical oxygen metabolism was globally reduced, but more significantly so in the superior prefrontal cortex, both lateral and mesial premotor areas and in the sensorimotor, inferior parietal and superior temporal cortices (Sawle *et al.*, 1991). Striatal 18F-6-fluorodopa uptake was reduced in an asymmetric pattern as well, with the caudate and putamen being involved in all cases. Using a voxel-based approach and ¹⁸fluorodeoxyglucose (¹⁸FDG) positron emission tomography, another study found a similar metabolic profile when 22 patients with clinically diagnosed CBD were studied (Garraux *et al.*, 2000). Other positron emission tomography studies have shown similar patterns of reductions in regional oxygen consumption and glucose metabolism (Blin *et al.*, 1992; Eidelberg *et al.*, 1991). The changes in regional cerebral blood flow have also been studied using ^{99m}Tc-HMPAO SPECT (Frasson *et al.*, 1998; Markus *et al.*, 1995; Morimatsu and Negoro, 1995). These studies also showed significant reductions of regional cerebral blood flow in the more affected hemisphere, with the posterior frontal cortex, parietal lobe, caudate, thalamus and putamen being most commonly affected. Okuda *et al.* (1995) used *N*-isopropyl-*p*[¹²³I]-iodoamphetamine in two patients with CBD. Both had LKA and one had constructional apraxia. Both showed asymmetrical cortical hypoperfusion in the perirolandic area, supporting the importance of dysfunction of this area to LKA, and the patient with constructional apraxia had unilateral hypoperfusion in the left posterior parietal area. In an attempt to further refine our understanding of the neural networks involved in IMA in CBD, attempts to correlate ¹⁸FDG positron emission tomography data with a cognitive neuropsychiatric assessment of apraxia have been made. In one such study that evaluated 18 patients with CBD, two complementary measures of apraxia were used. First, a performance score measured error frequency during gesture execution and, second, a correction score measured the patient's ability to correct initial errors on a second attempt. The authors found that anterior cingulate hypometabolism predominated in patients with CBD who performed below the cutoff performance score for apraxia (14/18) and that in those (7 out of 18) who could not correct their errors (which occurred mainly in gesture imitation), hypometabolism in the contralateral superior parietal lobe and supplementary motor area predominated, although there was also a deficit noted in the ipsilateral precentral gyrus (Peigneux *et al.*, 2001).

Other techniques that have been used to examine the central mechanisms underlying limb apraxia in CBD include somatosensory evoked potentials and transcranial magnetic stimulation. For example, somatosensory evoked potentials in five patients with CBD have been compared with those in 12 controls (Okuda *et al.*, 1998). This study found that all patients with limb apraxia, particularly LKA, had prolonged N20 latencies following median nerve stimulation on the more apraxic side, suggesting that somatosensory information processing involving the parietal cortex might be

Table 2 Apraxia in CBD

	No. of subjects	IMA	LKA	Ideational	Orobuccal
Jacobs <i>et al.</i> , 1999	6 CBD	+, spatial and temporal errors predominated	NA	NA	NA
Pillon <i>et al.</i> , 1995	15	+, inclusion criteria included presence of apraxia	+ 3/15	0	+
Blondel <i>et al.</i> , 1997	3	+	+	NA	NA
Okuda <i>et al.</i> , 1992	2	NA	2	NA	NA
Tsuchiya <i>et al.</i> , 1997	5	NA	2	NA	NA
Denes <i>et al.</i> , 1998	5	3	+, inclusion criteria included presence of LKA	NA	1
Martinez-Lage <i>et al.</i> , 1997	24	23	NA	23	NA
Ozsancak <i>et al.</i> , 2000	10	NA	NA	NA	9 dysarthria, simple gestures impaired in 5, sequential gestures impaired in 1
Leiguarda <i>et al.</i> , 2003	5	5	5	1	NA
Leiguarda <i>et al.</i> , 1994	10	7	NA	3	0
Frattali and Sonies 2000	13	NA	NA	NA	6 (46%) had oral apraxia 5 (38%) had oral apraxia and apraxia of speech

CBD = corticobasal degeneration; IMA = ideomotor apraxia; LKA = limb-kintetic apraxia; NA = not available; + = present in all subjects.

involved. The problem with all these studies is not only that most of the cases assessed were clinically diagnosed, and not autopsy confirmed, but also, and more importantly for the purposes of this discussion, that most patients studied had other deficits, including dystonia, rigidity and cortical sensory loss. Furthermore, many of the functional imaging studies were done in the resting state, and not while undergoing tests of praxis. Thus, it is impossible to be certain about the relationship between the metabolic or electrophysiological findings and the presence of apraxia.

Apraxia in other movement disorders

Other diseases can also give rise to the clinical picture typically ascribed to CBD, and so the approach to diagnosis is shifting from a single disease entity, CBD, to considering a number of different diseases capable of exhibiting a similar clinical phenotype, the CBS. This is comparable to the use of the term parkinsonism to describe a clinical syndrome and Parkinson's disease to refer to one distinct pathological cause of this syndrome. Several other pathological entities may present with the CBS including PSP (Boeve *et al.*, 1999; Saint-Hilaire *et al.*, 1996), Alzheimer's disease (Ball *et al.*, 1993; Eberhard *et al.*, 1996; Riley, 1996), Pick's disease (Lang *et al.*, 1994a; Fukui *et al.*, 1996; Boeve *et al.*, 1999), motoneuron inclusion disease with dementia (Grimes *et al.*, 1999), FTD-17 and Creutzfeldt–Jakob disease (Boeve *et al.*, 2003). These experiences suggest that it is the anatomical distribution of the pathological changes, and not the exact nature of this pathology, that results in the clinical phenotype. Increasingly, autopsy series of cases diagnosed as CBD in life are providing strong support for this concept. One of the

better examples of this is the experience reported from the Mayo Clinic in which 47% of cases (16/34) diagnosed as CBD in life had non-CBD pathology at autopsy. Almost without exception it is the occurrence of apraxia, especially if asymmetrical, associated with an akinetic-rigid syndrome, that encourages this misdiagnosis (Boeve *et al.*, 2003).

Progressive supranuclear palsy

Progressive supranuclear palsy deserves special mention as it is one of the most common disorders that is confused with CBD. In the absence of a vertical supranuclear palsy and early falls suggestive of PSP and lateralized motor and cognitive signs of CBD, clinical overlap including the presence of apraxia can pose a diagnostic dilemma (Litvan *et al.*, 1999). One study examined IMA in 14 patients with possible PSP using diagnostic criteria of Litvan *et al.* (1996) and 12 patients fulfilling modified criteria for CBD from Lang *et al.* (1994b) to determine whether there were any distinguishing features between the two groups that might be useful clinically (Pharr *et al.*, 2001). Not surprisingly, the study found that the overall praxis performance was worse in patients with CBD than in those with PSP, although the latter also scored lower than controls. Transitive tasks were more affected in PSP than intransitive tasks. In CBD, transitive tasks were also more affected than intransitive tasks, although both were affected, and distal movements were more affected than proximal movements. The authors concluded that intransitive tasks are the best apraxia measure to distinguish between PSP and CBD. Interestingly, in the CBD group distal movements were considered most affected, suggesting that at least some of the deficits in these patients could be accounted for by LKA in addition to or instead of IMA.

In a more recent study comparing only intransitive gestures in 24 patients with CBD, 25 with PSP and 19 controls, total apraxia scores were worse in both disease groups compared with controls but CBD patients were consistently more compromised than PSP patients in executing simple gestures. The CBD cohort committed more awkwardness and spatial errors than the PSP group, consistent with LKA, whereas sequencing errors were similar among the two groups (Soliveri *et al.*, 2005). However, as emphasized previously, these two studies suffer from lack of pathological proof of diagnosis and bias inherent in the evaluation of a clinical feature that is an important diagnostic criterion of one disorder (i.e. CBD) and often a source of diagnostic doubt or even an exclusionary criterion for the other (i.e. PSP).

In another study comparing the presence of apraxia in 45 non-demented Parkinson's disease patients, 12 with PSP, 10 with MSA and 12 patients with neuroleptic-induced parkinsonian, bilateral IMA for transitive movements was present in 8 (75%) of the PSP cases, and 5 of these also had abnormalities in intransitive movements (Leiguarda *et al.*, 1997). None showed errors of recognition of pantomimes and the total apraxia scores correlated with cognitive disturbances, most notably frontal lobe dysfunction. Of note, the authors described five patients who showed 'very awkward and clumsy movements preceded by hesitation and unsuccessful attempts when pantomiming any movement, irrespective of the type of the gesture and the modality for evoking them'. They stated that these difficulties were more than one could expect based on the severity of rigidity and/or bradykinesia and they were more obvious in the most affected hand. This description is very suggestive of LKA. The authors also assessed patients for features of orofacial and respiratory apraxia. Of the PSP patients, 10 demonstrated OFA and 8 had respiratory apraxia. The most striking feature noted was that of an overall final correct performance preceded by long pauses during which unsuccessful attempts were made. The authors commented, however, that it was sometimes difficult to interpret the nature of errors in the presence of the typical dystonic facial appearance of PSP.

In a case report of a patient who fitted the clinical description of PSP except that he had 'moderate to severe apraxia', a postmortem demonstrated pathology consistent with PSP but also senile plaques and tangles in the frontoparietal areas suggestive of early Alzheimer's disease (Pharr *et al.*, 1999). The authors suggested that when a patient with presumed PSP demonstrates moderate to severe apraxia, the diagnosis of PSP must be questioned. However, although brainstem and basal ganglia pathology was initially emphasized in PSP, it has become increasingly clear that cortical involvement is a feature of the disorder. In a series of 10 cases of definite PSP, cortical lesions were a constant feature and the density of neurofibrillary tangles was highest in the precentral and angular gyri (Verny *et al.*, 1996). These cortical lesions may play a significant role in the clinical phenomenology. In a clinical-pathological study comparing PSP patients with classic presentation to those with unusual signs (i.e. limb apraxia, focal

dystonia and arm levitation) and to those with CBD, PSP patients with atypical signs had more severe cortical degeneration than classic PSP patients but less cortical pathology than patients with CBD. The cortical changes for all three patient groups were most severe in the frontal lobe (Bergeron *et al.*, 1997). This again supports the argument made earlier that it is the location of the pathology and the degree of changes present, and not the nature of the pathological changes, that lead to the clinical features of the CBS.

Idiopathic Parkinson's disease

Apraxia has also been described in idiopathic Parkinson's disease. In the report by Leiguarda *et al.*, 1997 discussed above, bilateral IMA for transitive movements was found in 27% (12) of the patients with Parkinson's disease versus 75% of patients with PSP. The scores in the levodopa responsive patients did not differ between the ON and OFF states. The most common error type was spatial organization. None of the Parkinson's disease patients exhibited IMA for intransitive tasks, had errors of recognition of pantomimes or had orofacial or respiratory apraxia. As in the PSP group, apraxia scores in patients with Parkinson's disease correlated with cognitive disturbances, namely frontal lobe dysfunction, again emphasizing the importance of corticostriatal connections in the generation of IMA. Importantly, there was no correlation between apraxia scores and motor disability, as measured by the Unified Parkinson's Disease Rating Scale, reemphasizing the point that limb apraxia can be examined in the presence of, and is not explained by, classical parkinsonian motor disability.

A few other studies have also examined praxis in idiopathic Parkinson's disease. One study compared the performance of 15 Parkinson's disease patients with controls on two tasks: (i) a symbolic representation of implement usage on verbal command and on imitation and (ii) an imitation of non-symbolic hand positions (Sharpe *et al.*, 1983). The patients with Parkinson's disease performed at a lower gestural level on the representational task and made more spatial errors on the non-representational task. Another study evaluated imitation of movement sequences in 42 patients with moderate to severe Parkinson's disease compared with controls (Goldenberg *et al.*, 1986). Again, the patients with Parkinson's disease had worse total apraxia scores, and these scores correlated with visuospatial disability but not with motor severity. Not surprisingly, Villardita *et al.* (1982) found that visuo-perceptive disabilities were responsible for 'constructional apraxia' in a group of 20 patients with Parkinson's disease. This disorder is distinct from the forms of motor apraxia that are the main subject of this review. Finally, a series evaluating motor praxis (gestural functioning) in 22 non-demented patients with relatively mild Parkinson's disease (27% Hoehn & Yahr stage 1; 69% Hoehn & Yahr stage 2) found that 63% of these patients differed from controls in praxis performance (Grossman *et al.*, 1991). The majority of errors involved substitution of body part for object. Although responses were

slow, as might be expected as a result of bradykinesia, the degree of gestural impairment did not correlate with degree of motor disability. Finally, neuropsychological screening was performed in this study but did not include specific tests of perseveration and frontal lobe functions.

Dementia with Lewy bodies, Parkinson's disease dementia or Alzheimer's disease

Dementia with Lewy bodies is another parkinsonian disorder that may manifest apraxia. Distinguishing between diseases that manifest the combination of parkinsonism and cognitive decline (such as DLB and Alzheimer's disease) can sometimes be difficult, especially because it is widely recognized that Alzheimer's disease pathology (senile plaques and neurofibrillary tangles) often coexists with Lewy bodies (Crystal *et al.*, 1993; Lippa *et al.*, 1994; McKeith *et al.*, 1996). Some suggest that the timing of apraxia in relation to the disease onset and coexistence with other features (e.g. hallucinations, fluctuations in level of awareness) may actually be of diagnostic value. In a series evaluating the effect of coexisting Alzheimer-type lesion load, clinical and pathological features were assessed in two groups of patients with DLB (del Ser *et al.*, 2001). The authors studied 35 Alzheimer's disease, 11 pure DLB and 18 Alzheimer's disease plus DLB pathologically confirmed cases. Not surprisingly, the most useful criteria in distinguishing DLB from Alzheimer's disease were similar to the DLB consensus criteria, including hallucinations and cognitive fluctuations, especially when present early in the disease course (McKeith *et al.*, 1996). The Alzheimer's disease and Alzheimer's disease plus DLB patients in this series had lower (worse) scores on the Extended Scale for Dementia. Ideational apraxia was less frequent in the pure DLB group (18%) compared with the groups with Alzheimer's disease (54%) and Alzheimer's disease plus DLB (27%).

In contrast to the higher prevalence of ideational apraxia in Alzheimer's disease, constructional apraxia, as tested by drawing pentagons, has been found to be significantly worse in patients with DLB (Cormack *et al.*, 2004). Constructional apraxia indicates a drawing disturbance without general impairment of intelligence, visual or motor capabilities and is usually caused by parietal lesions involving either hemisphere. This study found that non-demented Parkinson's disease patients showed no abnormality of pentagon drawing but those with Parkinson's disease dementia made errors comparable to the DLB group. This is not unexpected given the current accepted continuum between Parkinson's disease and DLB and the clinical and pathological similarities between Parkinson's disease dementia and DLB (Burton *et al.*, 2004; McKeith and Mosimann, 2004). Although performance on this task correlated with global cognitive dysfunction in those with Alzheimer's disease and Parkinson's disease dementia, this was not the case in those with DLB, in whom drawing was linked only to perception and praxis. Therefore, one might expect to find constructional apraxia earlier in the disease course in DLB, whereas the occurrence of ideational apraxia

later in the course of the illness may be helpful in distinguishing Alzheimer's disease from DLB. Ideomotor apraxia, on the other hand, has been found in up to one-third of patients with mild dementia of the Alzheimer's type (Della *et al.*, 1987; Taylor, 1994; Derouesne *et al.*, 2000). Although, to our knowledge, this feature, has not been assessed in DLB, the 27% incidence in Parkinson's disease found by Leiguarda *et al.* (1997), especially in those with cognitive dysfunction, might predict a similar or greater incidence in DLB. This suggests that the presence of this type of apraxia early in the course of a dementing illness may not be a very useful distinguishing feature.

Multiple system atrophy

Relatively little has been published on the presence of apraxia in MSA. No studies have examined apraxia in MSA separately, but rather this group of patients is usually studied in comparison with other parkinsonian syndromes. In the study by Leiguarda *et al.* (1997), none of the patients with MSA ($n = 10$) or neuroleptic-induced parkinsonian demonstrated any praxic errors. In another study by the same group, three-dimensional computer graphic analysis was used to study the repetitive gesture of slicing bread. None of the four patients with MSA had apraxia clinically, but on three-dimensional analysis they did show deficits in control of the direction of the movement axis and in spatial patterns, albeit that these were much milder than in the patients with Parkinson's disease and PSP (Leiguarda *et al.*, 2000b). Finally, in one series IMA was described in 2 of 19 patients with MSA, although the majority of this group also showed evidence of executive dysfunction (Monza *et al.*, 1998). It is presumably the relative lack of frontal/cognitive impairment in MSA patients that spares the praxis system.

Huntington's disease

Ideomotor limb apraxia also occurs in Huntington's disease. In a small series of nine patients, 33% met criteria for IMA (Shelton and Knopman, 1991). The degree of apraxia correlated with the duration of Huntington's disease and with overall motor disability but not with cognitive dysfunction, chorea, dystonia, rigidity or bradykinesia. The authors postulated that this was primarily due to basal ganglia dysfunction because some of the patients who made errors had only mild cognitive dysfunction [based on mini-mental state examination scores and a 12-point auditory comprehension test similar to the Token Test used for testing receptive aphasia (De Renzi *et al.*, 1982)], suggesting that cortical structures were not yet involved; however, two of these patients had mini-mental state examination scores of 21 and 22, respectively. Because of the small sample size and the fact that the most severely affected patients made the greatest apraxic errors, a second group went on to study a larger set of patients with a wider range of disease severity (Hamilton *et al.*, 2003). In 20 patients with Huntington's disease, they also found a

Table 3 Studies of apraxia in movement disorders

Reference	No. of patients	Type of apraxia	Types of errors	Major differences between groups	Observations
PSP only					
Nath <i>et al.</i> , 2003	187 PSP	'Eyelid apraxia', present 32, absent 52, not recorded 103	No mention of other types of apraxia		
PSP and CBD					
Pharr <i>et al.</i> , 2001	13 CBD, 14 PSP	PSP and CBD both had IMA. They both had more difficulty with transitive than intransitive tasks	CBD patients made more internal configuration errors and more unclassifiable errors than PSP, but otherwise performance was similar across various error types	CBD scores were worse overall and showed preferential worsening on tasks requiring distal upper extremity manoeuvring	
Monza <i>et al.</i> , 2003	24 CBD, 25 PSP	CBD patients had worse total apraxia scores than PSP	CBD patients had worse apraxia for whole upper limb and hand/finger movements		
Soliveri <i>et al.</i> , 2005	24 CBD, 25 PSP, 19 controls	72% CBD and 32% PSP had total scores in the apraxia range	Simple gesture performance was worse in CBD group. Sequencing errors did not differ between the PSP and CBD group. CBD patients made more awkwardness and spatial errors than PSP group	CBD scores were worse overall. Errors in CBD were thought to be consistent with LKA	
PD					
Sharpe <i>et al.</i> , 1983	15 PD	PD patients performed at lower gestural level on representational tasks	Patients made more spatial errors on non-representational tasks		Degree of impairment correlated with visuospatial and visuoperceptive abilities
Goldenberg <i>et al.</i> , 1986	42 PD	IMA	Errors were mainly in sequencing		Patients were not demented and scores did not correlate with motor deficit
Grossman <i>et al.</i> , 1991	22 PD patients	64% of PD patients had compromised gestural performance	Most common errors were body substitution, and errors were made on representational more than non-representational gestures		
Other parkinsonian disorders including PD and PSP					
Leiguarda <i>et al.</i> , 1997	45 PD, 12 PSP, 10 MSA, 12 NIP	IMA for transitive in 85% PSP (8/12) and 27% PD (12/45). Orobulcal apraxia was found in 10 PSP patients. LKA was found in 5 PSP patients	Mainly spatial errors. No problems with gesture recognition in any group	IMA for intransitive gestures was found in 4 PSP, no PD	Correlation between IMA in PD and deficits in frontal lobe. In PSP IMA correlated with MMSE

Table 3 Continued

Reference	No. of patients	Type of apraxia	Types of errors	Major differences between groups	Observations
Monza <i>et al.</i> , 1998	19 MSA, 19 PSP, 14 PD	All groups made some errors suggestive of IMA with PSP being the most affected. 2/19 MSA, 3/15 PSP had De Renzi scores of praxis significance	After errors owing to clumsiness, sequencing errors were the most common	PSP had more variable errors, i.e. sequencing (50%), clumsiness (30%), location (10%) and orientation (10%), whereas MSA were due to clumsiness (85%) and sequencing (15%)	All subjects recognized gestures
HD Hamilton <i>et al.</i> , 2003	20 HD	7/20 (35%) with IMA	Gestural impairment more evident for transitive than intransitive		Apraxia correlated with duration illness and QNE (motor impairment), especially eye movement deficits but not with MMSE Apraxia correlated with duration of disease
Shelton and Knopman, 1991	9 HD patients	33% (3) patients exhibited IMA, 22% (2/9) made no apraxic errors and 26% had some impairment of gestures	Apraxia was present for transitive and intransitive tasks but no errors were made in recognition of gestures		

CBD = corticobasal degeneration; HD = Huntington's disease; IMA = ideomotor apraxia; LKA = limb-kinetic apraxia; MMSE = mini-mental state examination; MSA = multiple system atrophy; NIP = neuroleptic-induced parkinsonism; PD = Parkinson's disease; PSP = progressive supranuclear palsy; QNE = quantified neurological examination.

Table 4 Comparison of limb apraxia in selected movement disorders

	CBD	PSP	Parkinson's disease	DLB	MSA	Huntington's disease
LKA, distal hand, unilateral	Common	Uncommon	Not present	Not present	Not present	Not present
IMA, proximal bilateral, but asymmetric	Common; transitive and intransitive movements affected	Common; transitive affected more than intransitive movements	Uncommon; intransitive movements not affected; not formally studied in PDD	Not routinely studied. Presence probably correlates with degree of dementia	Rare	Present
Ideational apraxia	Present	Uncommon	Not present in uncomplicated Parkinson's disease; not formally studied in PDD	Present later in disease course	Not present	Rare

CBD = corticobasal degeneration; DLB = dementia with Lewy bodies; IMA = ideomotor apraxia; MSA = multiple system atrophy; PDD = Parkinson's disease dementia; PSP = progressive supranuclear palsy.

35% frequency of apraxia. Again the apraxia scores did not correlate with chorea or cognitive status, but apraxic patients did have more severe motor disability (namely, oculomotor deficits) and longer disease duration. Although basal ganglia neuronal loss might play a role in producing apraxia in Huntington's disease, it is important to acknowledge that the more severely affected patients who demonstrate apraxia also have greater evidence of cortical involvement. As pointed out in the section discussing the role of the basal ganglia in apraxia, it is more likely that interruption of corticostriatal connections rather than pure basal ganglia dysfunction underlies limb apraxia in Huntington's disease.

Finally, although little has been written about OFA in Huntington's disease, this is probably a relatively common feature. Bruyn and Went referred to it as 'mimical apraxia' in which impairment in facio-labio-glosso-pharyngeal movements is not explained by chorea or other elementary motor disturbances. He described errors in performance of simple tasks such as protrusion of the tongue and putting the tongue into the cheek, as well as in more complex tasks such as coughing, winking and whistling. These errors were often accompanied by limb apraxia as well (Bruyn and Went, 1986) (Tables 3 and 4).

Conclusion

Various types of apraxia have been described in patients with movement disorders particularly those combining parkinsonism and cognitive dysfunction. It is important to recognize that the presence of one type of apraxia does not exclude the presence of other types and, in fact, multiple types can coexist in the same patient. At times, apraxia is a dominant feature that contributes substantially to the patient's disability, especially in the cases of ideational apraxia, in which everyday object use is affected, and LKA, in which control over fine finger movements is lost. On the other hand, motor disturbances sufficient to constitute IMA may result in little or no interference with function, particularly in the case of voluntary automatic dissociation, where task performance may normalize when the patient is given the actual object to use. It is unclear whether the presence of these motor disturbances supports a role of the basal ganglia in praxis. The term 'apraxia' is also misapplied to some motor disturbances that may be seen in movement disorder patients. Finally, it is unclear whether the motor dysfunction encompassed by the term 'limb-kinetic apraxia' is best considered a form of apraxia or a more 'primary' or 'essential' motor disturbance. Further studies, including careful clinical assessment and analysis, functional imaging, kinematic evaluations and prospective clinical-pathological studies, are needed to clarify these issues and answer the many questions that arise in the evaluation of apraxia in movement disorder patients. Standardized methods of evaluating such patients are required, with an effort to reach wider consensus on the quantification, characterization and applied terminology. Only then will it be

possible to begin to understand the role of the different neural networks involved in producing these complex disorders of movement.

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