INVITED REVIEW

Limb apraxias
Higher-order disorders of sensorimotor integration

Ramón C. Leiguarda and C. David Marsden

1Raúl Carrea Institute of Neurological Research, FLENI, Buenos Aires, Argentina, 2University Department of Clinical Neurology, Institute of Neurology and National Hospital for Neurology and Neurosurgery, London, UK

Correspondence to: Ramón C. Leiguarda, Raúl Carrea Institute of Neurological Research, FLENI, Montañeses 2325, Buenos Aires (1428), Argentina E-mail: rleiguar@fleni.org.ar

†Deceased

Summary
Limb apraxia comprises a wide spectrum of higher-order motor disorders that result from acquired brain disease affecting the performance of skilled, learned movements. At present, limb apraxia is primarily classified by the nature of the errors made by the patient and the pathways through which these errors are elicited, based on a two-system model for the organization of action: a conceptual system and a production system. Dysfunction of the former would cause ideational (or conceptual) apraxia, whereas impairment of the latter would induce ideomotor and limb-kinetic apraxia. Currently, it is possible to approach several types of limb apraxia within the framework of our knowledge of the modular organization of the brain. Multiple parallel parietofrontal circuits, devoted to specific sensorimotor transformations, have been described in monkeys: visual and somatosensory transformations for reaching; transformation of information about the location of body parts necessary for the control of movements; somatosensory transformation for posture; visual transformation for grasping; and internal representation of actions. Evidence from anatomical and functional brain imaging studies suggests that the organization of the cortical motor system in humans is based on the same principles. Imitation of postures and movements also seems to be subserved by dedicated neural systems, according to the content of the gesture (meaningful versus meaningless) to be imitated. Damage to these systems would produce different types of ideomotor and limb-kinetic praxic deficits depending on the context in which the movement is performed and the cognitive demands of the action. On the other hand, ideational (or conceptual) apraxia would reflect an inability to select and use objects due to the disruption of normal integration between systems subserving the functional knowledge of actions and those involved in object knowledge.

Keywords: limb apraxia; object-oriented behaviour; parietofrontal circuits; sensorimotor integration

Abbreviations: AIP = anterior intraparietal area; IPL = inferior parietal lobule; MIP = medial intraparietal area; PM = premotor cortex; SMA = supplementary motor area; SPL = superior parietal lobule; STS = superior temporal sulcus

Introduction
Limb apraxia comprises a wide spectrum of higher-order motor disorders that result from acquired brain disease affecting the performance of skilled and/or learned movements with the forelimbs, with or without preservation of the ability to perform the same movement outside the clinical setting in the appropriate situation or environment. An impairment in gesturing cannot be termed apraxia, however, if it results from a language comprehension disorder or from dementia, or if the patient suffers from any elementary motor–sensory deficit that could fully explain the abnormal motor behaviour. This is not a negative approach, for praxic errors are well defined clinically and kinematically and can be superimposed on elementary motor disorders such as weakness, rigidity, tremor, dystonia and ataxia (Heilman and Rothi, 1985; Roy and Square, 1985; De Renzi, 1989; Poizner et al., 1999, 1995).

De Renzi and co-workers (De Renzi et al., 1982) and Geschwind and Damasio (Geschwind and Damasio, 1985)
emphasized the significance of the stimulus by means of which the learned movement is normally elicited: ‘for the overwhelming majority of clinical situations, one can use the following operational definition of apraxia: (i) failure to produce the correct movement in response to a verbal command, or (ii) failure to imitate correctly a movement performed by the examiner, or (iii) failure to perform a movement correctly in response to a seen object, or (iv) failure to handle an object correctly’ (Geschwind and Damasio, 1985). Thus, at present, limb apraxia is basically classified by both the nature of the errors made by the patient and the means by which these errors are elicited.

Skilful differs from unskilful motor behaviour because (i) its performance is characterized by preprogrammed processes; (ii) it is context-dependent; and (iii) individual differences increase with the degree of skill (Halsband and Freund, 1993; Schlaug et al., 1994; Brooks et al., 1995).

The learning of a skilful motor behaviour is initially subject to conscious, cognitive, even verbal control, and such control diminishes progressively as a function of practice to give way to automatic processes (Halsband and Freund, 1993). The cerebral representation of learned motor skills would change with extended practice and automatization and would become independent from areas involved in the initial acquisition and performance of novel motor tasks (Roland, 1984; Brooks et al., 1995), as well as from the cerebral commissures, allowing them to be controlled by either hemisphere (Zaidel and Sperry, 1977). PET studies in humans have provided evidence for the non-unitary mechanism of motor learning. During the early phases of learning, changes occur mainly in the parietal association cortex, premotor cortex (PM) and primary motor and sensory cortices. However, when an everyday skill has been well established and overlearned, its execution becomes largely relegated to the supplementary motor area (SMA), primary sensory motor cortex, basal ganglia and cerebellum (Roland, 1984; Seitz et al., 1990; Grafton et al., 1992; Passingham, 1997) without the participation of higher-order parietal and frontal association cortices. Thus, it is apparent that at least two cerebral systems can become operative to represent a motor plan depending on the level of practice and according to the complexity of the cognitive demands placed on the brain (Grafton et al., 1995).

In this review we will first briefly describe the development of concepts of limb apraxia, the evaluation of limb praxis and the interhemispheric differences in the control of praxic skills, and will then present the relevant clinical aspects of apraxic syndromes as well as their possible anatomofunctional substrates. We then depart from the currently more widely accepted neuropsychological models to work out the different types of limb praxic deficits within the framework of our present knowledge concerning the distributed modular organization of the brain (Houk and Wise, 1995; Gallese et al., 1997; Rizzolatti et al., 1998).

Since its original definition by Steinthal (Steinthal, 1871), the classification of limb praxic disorders has been subject to multiple modifications and is still under debate. Advances in behavioural motor neurophysiology over recent decades have provided mounting evidence that focal inactivation of functional nodes within distributed modular networks causes, in monkeys, highly selective motor and sensorimotor abnormalities, such as grasping deficits after injections of muscimol in the anterior intraparietal area (AIP) (Gallese et al., 1997). Lesion studies have demonstrated that a similar selective dysfunction may appear in humans (Binkofski et al., 1998). Furthermore, functional neuroimaging studies have shown activation in normal subjects of nodes similar to those making up the networks defined neurophysiologically in monkeys, and interference over such functional areas with transcranial magnetic stimulation produces effects similar to those observed in inactivation and lesion studies (Fadiga et al., 1995; Rizzolatti et al., 1996; Gerloff et al., 1997). Therefore, we will discuss limb apraxia in this context in a modest attempt to open new avenues for the future understanding of these complex higher-order motor disorders.

**Development of concepts of limb apraxia**

Contemporary ideas concerning apraxia stem from the classical work of Liepmann (Liepmann, 1900, 1905, 1908, 1920). He posited that the idea of the action, or movement formulae, containing the space–time form picture of the movement were stored in the left parietal lobe. In order to carry out a skilled movement, the space–time plan has to be retrieved and associated via cortical connections with the innervatory pattern stored in the left sensorimotorium (the precentral and postcentral gyri and the pes of the superior, middle and inferior frontal convolutions), which conveys the information about the formulae to the left primary motor areas. When the left limb performs the movement, the information has to be transmitted from the left to the right sensorimotorium through the corpus callosum to activate the right motor cortex (Liepmann, 1905, 1908, 1920). Liepmann conceived ideational apraxia as a disruption of the space–time plan or its proper activation, so that it was impossible to construct the idea of the movement. In contrast, in ideomotor apraxia the space–time plans are intact but can no longer guide the innervatory engrams which implement the movements because they are disconnected from them; the patient knows what to do but not how to do it. Limb-kinetic apraxia appears when the disruption of the innervatory engrams interferes with the selection of the required muscle synergies to perform the skilled movement (Liepmann, 1920). Ideomotor and limb-kinetic apraxia frequently coexist, and were both considered by Liepmann to be motor apraxias (Liepmann, 1920).

Geschwind followed Liepmann’s interpretations and advanced a neuronal system for limb praxis similar to that proposed by Wernicke for language processing (Wernicke, 1874; Geschwind, 1965). The verbal command is first registered in Wernicke’s area. Information flows subsequently to the ipsilateral motor association cortex, probably via the
Evaluation of limb praxis

A systematic evaluation of limb praxis is critical in order (i) to identify the presence of apraxia; (ii) to classify correctly the nature of the limb praxis deficit according to the errors committed by the patient; and (iii) to gain insight into the underlying mechanism of the patient’s abnormal motor behaviour, which may be further defined by kinematic analysis (Table 1).

Several types of transitive movements are used in the evaluation of praxis, and it is not an uncommon finding that apraxic patients perform some but not all movements in a particularly abnormal fashion and/or that individual differences appear in some but not all components of a given movement. Therefore, the dissimilar complexity and features of transitive movements should be considered if praxic errors are to be analysed and interpreted accurately. For instance, (i) movements may or may not be repetitive in nature (e.g. hammering versus using a bottle-opener to remove the cap of a bottle); (ii) an action may be composed of sequential movements (e.g. reaching for a glass and taking it to the lips when drinking); (iii) a movement may primarily reflect proximal limb control (transport) (as in transporting the wrist when carving a turkey), proximal and distal limb control (as in reaching and grasping a glass of water) or primarily distal control (as when the patient is asked to manipulate a pair of scissors); and (iv) movements may be performed away from the body in the peripersonal space (e.g. carving a turkey) or in body-centred space (e.g. brushing the teeth), or they may require the integration of actions in both spaces (e.g. the actions involved in drinking).

Analysis of the performance of patients is based on both accuracy and error patterns (Table 2). Patients with ideational apraxia have difficulty mainly in sequencing actions, whereas patients with conceptual apraxia commit content errors: the movement itself is performed well but the target of the action is wrong or the patient performs the movement without the benefit of a tool. Ideomotor apraxia patients show primarily temporal and spatial errors, which are more evident when they are performing transitive gestures. Errors in limb-kinetic apraxia represent slowness, coarseness and fragmentation, particularly of manipulative movements; the deficit affects simple and complex finger and hand movements, regardless of whether they involve the use of an object.

Three-dimensional motion analysis of the spatiotemporal characteristics of gestural movements has provided an accurate method to capture objectively the nature of the praxis errors observed in clinical examination (Poizner et al., 1990, 1995; Clark et al., 1994). Patients with ideomotor apraxia, resulting from focal left hemisphere lesions (Poizner et al., 1990, 1995; Clark et al., 1994), or different asymmetrical cortical degenerative syndromes (Rapcsak et al., 1995; Leiguarda and Starkstein, 1998), have shown slow and hesitant build-up of hand velocity, irregular and non-sinusoidal velocity profiles, abnormal amplitudes, alterations of the plane of motion and of the direction and shapes of wrist trajectories, decoupling of hand speed and trajectory curvature, and loss of interjoint co-ordination. All these studies have evaluated gestures, such as carving a turkey or slicing a loaf of bread, which mainly involve the transport or reaching phase of the movement. However, the majority of transitive gestures included in most apraxia batteries are prehension (reaching and grasping) movements, which reflect proximal (transport) and distal limb control (grasping) as well as the coupling of transport and grasping components.

The analysis of prehension movements provides further insight into the specific neural mechanisms underlying distinct types of limb praxic disorders. Although few, the studies that have been designed to explore these components of the action system in patients with apraxia have provided consistent results. Charlton and colleagues evaluated an apraxic patient and demonstrated that the co-ordination of the transport and grasp component and the grasp component itself were markedly abnormal (Charlton et al., 1988). Caselli and colleagues and Leiguarda and colleagues studied patients with progressive apraxia resulting from corticobasal degeneration and Alzheimer’s disease (Caselli et al., 1999; Leiguarda et al., 2000). Compared with controls, apraxic patients show disruption of both the transport and grasp phases of the movements as well as the uncoupling of transport from grasping. Furthermore, manipulating finger movements during exploration of an object has revealed...
Table 1 Assessment of limb praxis

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<th>1. Evaluation of the praxis production system</th>
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<tr>
<td>Intransitive movements</td>
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<td>Non-representational (e.g. touch your nose, wriggle your fingers).</td>
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<td>Representational (e.g. wave goodbye, hitch-hike).</td>
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<td>Transitive movements</td>
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<td>(E.g. use a hammer, use a screwdriver) under verbal, visual and tactile modalities.</td>
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<td>Imitation of meaningful and meaningless movements, postures and sequences.</td>
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<th>2. Evaluation of the praxis conceptual system</th>
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<td>Multiple step tasks</td>
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<td>To select the appropriate tool to complete a task, such as a hammer for a partially driven nail.</td>
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<td>Tool* selection tasks</td>
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<td>To select an alternative tool such as pliers to complete a task such as pounding a nail, when the appropriate tool (e.g. hammer) is not available.</td>
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<tr>
<td>Alternative tool selection tasks</td>
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<td>Gesture recognition tasks</td>
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<td>To assess the capacity to comprehend gestures either verbally (to name gestures performed by the examiner) as well as non-verbally (to match a gesture performed by the examiner with cards depicting the tool or object† corresponding to the pantomime).</td>
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Source: De Renzi, 1989; Rothi and Heilman, 1997. *Tool: implement with which an action is performed (e.g. hammer, screwdriver); †object: the recipient of the action (e.g. nail, screw).

abnormal workspace and breakdown of the temporal profiles of the scanning movements in patients with limb-kinetic apraxia (Leiguarda et al., 2000). Thus, exploration of the kinematics of reaching, grasping and manipulating not only provides information regarding the specific neural subsystems involved in patients with different types of praxic disorders of the limbs, but may also help in the further understanding of how these systems are integrated with those involved in the representations of objects.

Patients with apraxia exhibit several types of sequential errors, such as deletions, transpositions, additions, perseverations and unrelated types of substitutions (Roy and Square, 1985; Rothi and Heilman, 1997). Abnormalities in sequencing movements have been reported more commonly in patients with parietal, frontal and basal ganglion involvement (Kimura and Archibald, 1974; Luria, 1980; Kolb and Milner, 1981; De Renzi et al., 1983; Benecke et al., 1987; Harrington and Haaland, 1992; Halsband et al., 1993). Luria emphasized the role of the frontal lobes in controlling actions requiring the sequencing of different movements over time (Luria, 1980). Kolb and Milner studied meaningless movement sequences in a group of epileptic patients with cortical ablations, and found that those with left parietal lesions were more impaired than those with right or left frontal lesions (Kolb and Milner, 1981). Similar results were found by Kimura and by De Renzi and colleagues using a multiple hand movement task and the imitation of three unrelated movements carried out in a sequence (Kimura, 1982; De Renzi et al., 1983). Patients with frontal or parietal lesions had deficits in sequencing movements, but the impairment in those with frontal damage became evident only with more complex sequences (Kimura, 1982).

**Interhemispheric differences in the control of praxic skills**

Since Liepmann postulated that the left hemisphere of right-handed subjects contains the ‘movement formulae’ that control purposeful skilled movements of the limbs on both sides of the body (Liepmann, 1905), every subsequent study on limb apraxia has confirmed the dominance of the left hemisphere in praxis (Basso et al., 1980; De Renzi et al., 1980, 1982; Kertesz and Ferro, 1984). However, apraxia, as tested by the imitation of gestures and object use pantomime, has been found in ~50% of patients with left hemisphere damage and in <10% of those with right hemisphere damage, which means that in many subjects praxic functions have bilateral representations (De Renzi, 1989).

Liepmann himself was cautious enough to point out that the right hemisphere may also possess some praxic skills, especially for the left half of the body (Liepmann, 1920). Since then, the possibility that in right-handers the right hemisphere may have some capacity to control complex skilled movements has also been posited by several authors as a likely explanation for the sparing of certain left-hand praxic functions after callosal or left hemisphere lesions (Geschwind and Kaplan, 1962; Zaidel and Sperry, 1977; Kertesz and Ferro, 1984; Graff-Radford et al., 1987). Most of the errors exhibited by ideomotor apraxia patients are seen equally in left and right hemisphere-damaged patients when they pantomime non-representative and representative/intransitive gestures, but are observed predominantly for left hemisphere-damaged patients when they pantomime transitive movements, because it is this action which is carried on outside the natural context (Haaland and Flaherty, 1984). Schnider and colleagues also emphasized that the motor dominance of the left hemisphere reflected by ideomotor apraxia refers to spatially and temporally complex movements performed in an artificial context (Schnider et al., 1997). Moreover, Rapcsak and colleagues have suggested that the left hemisphere is dominant not only for the ‘abstract’ performance (pantomiming to verbal command) of transitive movements but also for the imitation of meaningless movements (Rapcsak et al., 1993).

The left hemisphere also seems to be dominant for...
Table 2 Types of praxis error

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<th>Type</th>
<th>Description</th>
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<tr>
<td>I. Temporal</td>
<td>Sequence: some pantomimes require multiple positionings that are performed in a characteristic sequence. Sequencing errors involve any perturbation of this sequence including addition, deletion, or transposition of movement elements as long as the overall movement structure remains recognizable.</td>
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<td>Timing: this error reflects any alterations from the typical timing or speed of a pantomime and may include abnormally increased, decreased, or irregular rate of production or searching or groping behavior.</td>
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<td>Occurrence: pantomimes may involve either single (i.e., unlocking a door with a key) or repetitive (i.e., screwing in a screw with a screwdriver) movement cycles. This error type reflects any multiplication of single cycles or reduction of a repetitive cycle to a single event.</td>
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<td>II. Spatial</td>
<td>Amplitude: any amplification, reduction, or irregularity of the characteristic amplitude of a target pantomime.</td>
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<td>Internal configuration: when pantomiming, the fingers and hand must be in specific spatial relation to one another to reflect recognition and respect for the imagined tool. This error type reflects any abnormality of the required finger/hand posture and its relationship to the target tool. For example, when asked to pretend to brush the teeth, the subject's hand may close tightly into a fist with no space allowed for the imagined toothbrush handle.</td>
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<td>Body-part-as-object: the subject uses his/her finger, hand or arm as the imagined tool of the pantomime. For example, when asked to smoke a cigarette, the subject might puff on his or her index finger.</td>
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<td>External configuration orientation: when pantomiming, the fingers/hand/arm and the imagined tool must be in a specific relationship to the object receiving the action. Errors of this type involve difficulty orienting to the object or in placing the 'object' in space. For example, the subject might pantomime brushing the teeth by holding their hand next to their mouth without reflecting the distance necessary to accommodate an imagined toothbrush. Another example would be when asked to hammer a nail—the subject might hammer in differing locations in space, reflecting difficulty in placing the imagined nail in a stable orientation or in a proper plane of motion (abnormal planar orientation of the movement).</td>
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<td>Movement: when acting on an object with a tool, a movement characteristic of the action and necessary to accomplish the goal is required. Any disturbance of the characteristic movement reflects a movement error. For example, when asked to pantomime using a screwdriver, a subject may orient the imagined screwdriver correctly with respect to the imagined screw, but instead of stabilizing the shoulder and wrist and twisting at the elbow the subject stabilizes the elbow and twists at the wrist or shoulder.</td>
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<td>III. Content</td>
<td>Perseverative: the subject produces a response that includes all or part of a previously produced pantomime.</td>
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<td>Related: the pantomime is an accurately produced pantomime associated in content with the target. For example, the subject might pantomime playing a trombone for a target of a bugle.</td>
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<td>Non-related: the pantomime is an accurately produced pantomime not associated in content with the target. For example, the subject might pantomime playing a trombone for a target of shaving.</td>
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<td></td>
<td>The patient performs the action without a real or imagined tool. For example, when asked to cut a piece of paper with scissors, he or she pretends to rip the paper.</td>
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<td>IV. Other</td>
<td>Concretization: the patient performs a transitive pantomime not on an imagined object but instead on a real object not normally used in the task. For example, when asked to pantomime sawing wood, the patient pantomimes sawing on his or her leg.</td>
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<tr>
<td></td>
<td>No response.</td>
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<td></td>
<td>Unrecognizable response: the response shares no temporal or spatial features of the target.</td>
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of the lateral premotor and parietal cortex, basal ganglia, thalamus and white matter fascicles would participate in the selection of limb movement responses, whereas an adjacent system integrated by lateral area 8 and possibly interconnected parietal regions, thalamus, striatum and white matter fascicles would be concerned with the selection of object-oriented responses (Rushworth et al., 1998). The process of motor attention has also been lateralized to the left hemisphere, so left hemisphere-damaged patients would exhibit abnormalities in the sequencing of movements due to inability to shift the focus of motor attention from one movement in the sequence to the next (Rushworth et al., 1997b).

In conclusion, it seems quite likely that the interhemispheric differences in the control of praxic skills depend largely on the context in which the movement is performed and on the cognitive requirements of the task: that is, when a single movement and/or a sequence of object-oriented movements are performed outside the usual context and depend on higher-level cognitive abilities for planning and self-monitoring the action, the left hemisphere emerges as the dominant one (Kimura and Archibald, 1974; Kimura, 1982; Haaland and Harrington, 1996; Rushworth et al., 1997b, 1998).

**Types of limb apraxia**

**Ideational or conceptual apraxia**

Patients with impairment of the conceptual system exhibit primarily content errors in the performance of transitive movements (e.g. the patient pantomimes shaving for a target of toothbrushing or uses the toothbrush as if it were a shaver), because they are unable to associate tools and objects with the corresponding action. They may also lose the ability to associate tools with the objects that receive their action; thus, when a partially driven nail is shown, the patient may select a pair of scissors rather than a hammer from an array of tools to perform the action. Not only are patients unable to select the appropriate tool to complete an action, but they may also fail to describe the function of a tool or point to a tool when the function is described by the examiner, even when the patient names the tool properly when it is shown to him/her. Patients with conceptual apraxia lose the mechanical advantage afforded by tools (mechanical knowledge). For example, when asked to complete an action and the appropriate tool is not available (e.g. a hammer to drive a nail), they may not select the most suitable tool for that action (e.g. a spanner) but rather one which is inadequate (e.g. a screwdriver) (Ochipa et al., 1992; Heilman et al., 1997). These patients may also be impaired in the sequencing of tool/object use (Pick, 1905; Liepmann, 1920; Pocek, 1983). Patients with ideational or conceptual apraxia are disabled in everyday life, because they use tools/objects improperly, they misselect tools/objects for an intended activity, perform a complex sequential activity (e.g. make espresso coffee) in a mistaken order or do not complete the task at all (Foundas et al., 1995).

The terminology applied to behavioural disturbances arising from the disruption of the conceptual system for praxis has been confusing. Pick coined the term ‘ideational apraxia’ to denote the inability to carry out a series of acts involving the utilization of several objects (e.g. preparing a letter for mailing), although his first case also showed impairment in the use of single objects (Pick, 1905). As we have already seen, Liepmann, as well as De Ajuriaguerra and colleagues, Hecaen and Pocek, advanced a similar concept and attributed it to damage to the left parieto-occipital or temporoparietal regions (Liepmann, 1920; De Ajuriaguerra et al., 1960; Hecaen, 1972; Pocek, 1983). However, other authors use the term to denote failure to use single tools appropriately. Denny-Brown considered ideational apraxia as an agnosia for object use (Denny-Brown, 1958), and De Renzi and co-workers interpreted it as an inability to remember the general configuration of the action when attempting to use a tool (De Renzi, 1989). To overcome this confusion, Ochipa and colleagues have suggested restricting the term ‘ideational apraxia’ to the failure to sequence correctly a series of acts leading to an action goal, and introducing the term ‘conceptual apraxia’ to denote precisely the loss of different types of tool–action knowledge (Ochipa et al., 1992).

Ideational apraxia in its pure form is an unusual disorder, although the presence of associated aphasia in many patients probably masks this type of praxic deficit. Ideational apraxia is characterized by impairment in carrying out sequences of actions requiring the use of various objects in the correct order so as to achieve an intended purpose. They recognize single objects well and name them correctly, but they may be unable to recognize correct and incorrect sequences of actions represented in photographs (Pocek, 1983).

Although Pocek and Lehmkuhl maintained that patients with ideational apraxia ‘quite often are able to correctly manipulate single objects’ (Pocek and Lehmkuhl, 1980), when these patients were systematically investigated they were also found to be impaired in demonstrating the use of single objects (De Renzi, 1989). De Renzi and Lucchelli tested 20 left brain-damaged patients with a single object and with a multiple-object test, and found that performance in the two tests was strongly correlated. Omission (the patient neglects to spread the paste on a toothbrush), misuse (the patient uses a key as a hammer) and mislocation (the patient holds a pen upside down) were the most frequent errors (De Renzi and Lucchelli, 1988). These errors were observed whether the test involved a single object or multiple objects. Thus, it appears that strict differentiation between ideational and conceptual apraxia, as Ochipa and colleagues have proposed (Ochipa et al., 1992), may not be possible in every patient, because in many cases object use is impaired even outside the context of sequence.

Heilman and colleagues evaluated patients with focal hemisphere lesions for deficits in the conceptual praxis system (Heilman et al., 1997). The main conclusions of their study were as follows: (i) in some patients, dissociation was
observed between tests assessing different types of tool–action knowledge, which suggests the possible existence of subtypes of conceptual apraxia; (ii) dissociation between conceptual apraxia and ideomotor apraxia was found, suggesting independent systems for praxis knowledge and praxis production, although the two systems appeared to be closely related because both types of apraxia frequently coexisted; (iii) most patients with conceptual apraxia had damage in the left hemisphere; and (iv) among patients with left hemisphere damage, only about half exhibited ideomotor apraxia and conceptual apraxia. Although there were no specific anatomical areas in the left hemisphere that were damaged in the group with apraxia and spared in the non-apraxic group, the parietal and frontal association areas, together or separately and with or without subcortical involvement, were affected in most patients (Heilman et al., 1997). Similar findings were described by De Renzi and Luchelli: parietal, temporal and parietotemporal lesions were found in 10 of their patients, frontal lesions in six and frontotemporal, parietofrontal, basal ganglion and occipital lesions in one patient each (De Renzi and Luchelli, 1988).

It is still unclear what kind of knowledge about an object is necessary for its use (Roy and Square, 1985; Ochipa et al., 1992; Buxbaum et al., 1997; Goldenberg and Hagmann, 1998; Moreaud et al., 1998). Object recognition seems to be subserved mainly by a viewpoint-independent mechanism which relies on the occipitotemporal system (or ventral stream) but is complemented by a viewpoint-dependent mechanism which relies on the occipitoparietal system (or dorsal stream). A third system, centred on the IPL, would be additionally involved in the ‘binding’ of information from the two visual systems (for review, see Turnbull et al., 1997). The study by Faillenot and colleagues, which showed that the dorsal stream participates in object perception whenever it is required for object-oriented action (Faillenot et al., 1997), supports this notion. Moreover, it has also been proposed that the left dorsolateral frontal cortex subserves the interaction between object/tool manipulation and functional knowledge, since this region becomes activated in a task involving the recognition of man-made tools (Perani et al., 1995).

Thus, it might be posited that the use and selection of objects/tools depends on the integration of systems involved in the functional knowledge of actions (i.e. reaching, grasping, manipulating, sequencing) with those devoted to the knowledge of objects and tools. Disruption of these complex integration processes may lead to different types of ideational or conceptual praxic deficits.

**Ideomotor apraxia**

Ideomotor apraxia has been thought to reflect ‘a disturbance in programming the timing, sequencing and spatial organization of gestural movements’ (Rothi et al., 1991). As described above, patients with ideomotor apraxia exhibit mainly temporal (i.e. irregular speed, sequencing abnormalities) and spatial errors (i.e. abnormal amplitude, improper spatial orientation of objects and movements, abnormal hand and limb configuration, use of body parts as objects) (Table 2). The movements are incorrectly produced but the goal of the action can usually be recognized. Occasionally, however, the performance is so severely deranged that the examiner cannot recognize the movement. Transitive movements are more affected than intransitive ones on pantomiming to commands. Acting with tools/objects is carried out better than pantomiming their use, but in most instances movements are not normal. Patients with ideomotor apraxia usually improve on imitation when performance is compared with responses to verbal commands, although some patients may find similar difficulties in the two types of task (Heilman and Rothi, 1985; De Renzi, 1989). The improvement in performance observed when the patient actually uses the tool/object might result from the advantage provided by visual and tactile–kinaesthetic cues emanating from the tool/object and/or by the fact that in this condition the patient is performing the movement in a more natural context and is therefore less dependent on the left hemisphere. The tactile kinaesthetic information provided by holding the tool/object may not only help to establish the postural context but also facilitate a correct hand position for the gesture (Frank and Earl, 1990).

Since the first formal report of apraxia by Liepmann (Liepmann, 1900), it has been widely accepted that apraxic patients show a voluntary–automatic dissociation, which means that the patient does not complain about the deficit and that the execution of the movement in the natural context is relatively well preserved; the deficit appears mainly in the clinical setting when the patient has to represent explicitly the content of the action outside the situational props. However, recent studies have demonstrated that even patients with ideomotor apraxia may manifest deficits when interacting with their everyday environment (for review, see Cubelli and Della Sala, 1996).

Unilateral lesions of the left hemisphere in right-handed patients produce bilateral deficits, usually less severe in the left than in the right limb (Liepmann, 1920; Heilman and Rothi, 1985; De Renzi, 1989). Ideomotor apraxia is commonly associated with damage to the parietal association areas, less frequently with lesions of the PM and SMA, and usually with disruption of the intrahemispheric white matter bundles which interconnect them, as well as with basal ganglion and thalamic damage.

Liepmann’s original postulate about the crucial role played by the dominant parietal lobe in the genesis of apraxia (Liepmann, 1900) has been largely confirmed by subsequent studies (Morlaas, 1928; De Ajuriaguerra et al., 1960; Kolb and Milner, 1981; De Renzi et al., 1983; Fogliani and Basso, 1985). Lesions centred in the supramarginal gyrus, the superior parietal lobe and the underlying white matter would cause ideomotor apraxia through damage of the parietal associative areas or by interrupting pathways connecting
these areas with the premotor cortex (Liebermann, 1908; Geschwind, 1965; Heilman and Rothi, 1985).

After the parietal lobes, the PM and the SMA are the regions that play the most important role in praxis (Liebermann, 1905; Morlaas, 1928; Kleist, 1931; De Ajuriaguerre et al., 1960; Geschwind, 1965; Hecaen, 1972). Surprisingly, however, only a few well-documented cases of ideomotor apraxia with PM (Faglioni and Basso, 1985; Raymer et al., 1999) and SMA lesions (Watson et al., 1986; Marchetti and Della Sala, 1997) have been described. Two possible reasons for the paucity of reports are as follows: (i) most premotor lesions have also involved the primary motor cortex, causing a contralateral paresis or paralysis; therefore, if a detailed and properly oriented clinical evaluation were not carried out, the mild or subtle spatial and temporal errors that the patient may have committed when performing with the non-dominant limb would not have been captured; and (ii) a defect caused by a unilateral dominant premotor lesion may be compensated for largely by the contralateral hemisphere, because of the close interaction between the two frontal lobes during the performance of a unilateral movement, as demonstrated by functional studies (Roland and Zilles, 1996).

Heilman and colleagues and Rothi and colleagues studied patients with ideomotor apraxia resulting from anterior and posterior lesions on the left hemisphere, and found that only those patients with a damaged parietal lobe displayed impairment in the recognition of gestures (Heilman et al., 1982; Rothi et al., 1985). Therefore, the authors suggested the existence of posterior and anterior forms of ideomotor apraxia, with and without gesture-recognition disturbances, respectively. However, most of the studies designed to correlate action-recognition deficits with lesion location have revealed the involvement of many structures other than the parietal lobe, including the frontal and temporal lobes, and even the basal ganglia (Ferro et al., 1983; Rothi et al., 1985, 1986; Varney and Damasio, 1987; Wang and Goodglass, 1992).

Recently, the basal ganglia and thalamus have also been included in the modular neural network which mediates praxis (Sharpe et al., 1983; Goldenberg et al., 1986; Della Sala et al., 1992; Pramstaller and Marsden, 1996; Leiguarda et al., 1997). Pramstaller and Marsden reviewed 82 cases of ‘deep’ or ‘subcortical’ apraxia and found that (i) most of the patients had lesions on the left hemisphere; (ii) small isolated lesions of the putamen and thalamus or lesions restricted to the lenticular nucleus, with or without caudate or thalamic involvement, were uncommon; (iii) the majority of patients sustained larger lesions with damage to the basal ganglia and/or thalamus together with the internal capsule and periventricular and peristriatal white matter, interrupting association fibres, in particular those of the superior longitudinal fasciculus and frontostriatal connections; and (iv) ideomotor apraxia was present in most patients, orofacial apraxia was less common and ideational apraxia was rare.

Most studies exploring a possible clinical–anatomical correlation for ideomotor apraxia have found a strong association of apraxia with large corticospinalcortical lesions in the suprasylvian, perirolandic region of the left dominant hemisphere (Kertesz and Ferro, 1984; Alexander et al., 1992; Schneider et al., 1997), but no specific lesion site which correlated with apraxia. Smaller apraxia-producing lesions have been reported to be located in the parietal lobe (Faglioni and Basso, 1985), the deep central paraventricular region (Kertesz and Ferro, 1984), the deep anterior two-thirds of the paraventricular white matter (Alexander et al., 1992), and even the basal ganglia and thalamus (Pramstaller and Marsden, 1996).

Papagno and colleagues found 10 apraxic non-aphasic and 129 aphasic, but not apraxic, patients among a cohort of 699 patients with vascular lesions in the left hemisphere (Papagno et al., 1993). Seven of the apraxic non-aphasic patients had subcortical lesions (in the frontal and parietal white matter in six patients and the caudate nucleus in one), whereas in the other three the lesion also encroached upon the cortex; these latter cases had more severe ideomotor apraxia. On the other hand, most of the aphasic non-apraxic patients had predominantly pure cortical lesions. These findings further support the role of white matter damage and the interruption of corticocortical and corticospinalcortical connections in the causation of apraxia.

**Callosal apraxia**

Patients with naturally occurring or surgically caused callosal lesions involving the genu and body (Liepmann and Maas, 1907; Sweet, 1941; Watson and Heilman, 1983; Graff-Radford et al., 1987; Leiguarda et al., 1989) or only the body of the corpus callosum (Kazui and Sawada, 1993) may develop unilateral apraxia of the non-dominant limb whose characteristics vary according to the type of test given and the lateralization pattern of praxic skills in each patient. Some patients could not correctly pantomime to verbal commands with their left hand but performed normally on imitation and object use (Geschwind and Kaplan, 1962; Gazzaniga et al., 1967; Zaidel and Sperry, 1977), whereas others could not use their left hand on command, by imitation or while holding the object (Liepmann and Maas, 1907; Watson and Heilman, 1983; Leiguarda et al., 1989; Kazui and Sawada, 1993). Moreover, a few patients could not pantomime to verbal commands and while holding the object but performed fairly well on imitation (Graff-Radford et al., 1987) or improved over time on imitation and object use (Watson and Heilman, 1983). Thus, the most enduring callosal type of praxic defect is demonstrated when verbal–motor tasks, such as pantomiming to command, are used (Graff-Radford et al., 1987).

**Modality-specific or disassociation apraxias**

The modality-specific (De Renzi et al., 1982) or disassociation (Rothi and Heilman, 1997) apraxias are those types of praxic deficits exhibited by patients who commit errors only, or
predominantly, when the movement is evoked by one but not all modalities. Thus, the impairment of patients who performed abnormally only under verbal commands was attributed to a left hemisphere lesion most likely affecting the audio-verbal inputs to the parietal lobe (Heilman, 1973; De Renzi et al., 1982) or to a callosal lesion (Geschwind and Kaplan, 1962; Gazzaniga et al., 1967). Patients who performed poorly to seen objects but were able to pantomime gestures normally to verbal command have been reported as having lesions interrupting the flow of visual information towards the parietal lobe (Assal and Regli, 1980; De Renzi et al., 1982; Peña-Casanova et al., 1985; Pilgrim and Humphreys, 1991). On occasion, praxic deficits may be confined to the tactile modality (Renzi et al., 1982). Finally, patients have been reported who, unlike those with ideomotor apraxia improving on imitation, were more impaired when imitating than when pantomiming to command (Ochipa et al., 1994), or could not imitate but performed flawlessly under other modalities (Mehler, 1987; Goldenberg and Hagmann, 1997; Merians et al., 1997). The deficits may be restricted solely to the imitation of meaningless gestures with preserved imitation of meaningful gestures. Furthermore, patients may show abnormal imitation of hand postures but with normal imitation of finger configuration (Goldenberg and Hagmann, 1997). The anatomical correlates of imitation deficits have not been studied specifically, although abnormal performance on imitation was found in patients with parietal, frontal, temporal, subcortical or basal ganglion lesions (Hermsdorfer et al., 1996).

**Limb-kinetic apraxia**

Limb-kinetic apraxia is a controversial type of praxis disorder which has been largely neglected. Recently, however, renewed interest has arisen mainly from the study of patients with corticobasal degeneration and the syndrome of primary progressive apraxia (Okuda et al., 1992; Fukui et al., 1996; Tsuchiya et al., 1997; Denes et al., 1998).

This type of apraxia was originally described by Kleist, who called it ‘innervatory apraxia’ to stress the loss of hand and finger dexterity resulting from inability to connect and to isolate individual innervation: ‘the patient is unable to manipulate scissors and shows a complete failure when trying to knot a thread’, ‘... the deficit being proportional to the innervatory complexity, the greater the innervatory complexity of hand functions, the greater the disorder’ (Kleist, 1907).

The deficit is confined mainly to finger and hand movements contralateral to the lesion, regardless of its hemispheric side, with preservation of power and sensation. Manipulatory finger movements are affected predominantly, but in most cases all movements, either complex or routine, independently of the modality that evokes them, are coarse and mutilated. The virtuosity given to movements by practice is lost and they become clumsy, awkward and rough: ‘for many motions, the starting point cannot even be found, or the motion becomes amorphous’ (Liepmann, 1908). Fruitless attempts usually precede wrong movements, which in turn are frequently contaminated by extraneous movements. Imitation of finger postures is also abnormal and some patients use the less affected or normal hand to reproduce the posture requested. The severity of the deficit is consistent, exhibiting the same degree in everyday activities as in the clinical setting; thus, there is no voluntary-automatic dissociation (Kleist, 1907, 1931; Liepmann, 1908; Faglioni and Basso, 1985; Denes et al., 1998).

Most authors have dismissed limb-kinetic apraxia as merely the expression of basic motor (pyramidal) deficits (Geschwind, 1965; Heilman and Rothi, 1985; De Renzi, 1989). However, Luria (Luria, 1980) and Freund (Freund, 1992) both recognized the category and, following Kleist (Kleist, 1931), attributed it to damage to the PM cortex. We also agree that limb-kinetic apraxia is a higher-order motor disorder over and above a corticospinal or basal ganglion deficit, which would mainly result from frontal lobe damage centred on the PM cortex, most likely associated with parietal and/or basal ganglion involvement.

Limb-kinetic apraxia is an uncommon type of praxic deficit which has been scantily reported with focal lesions (Faglioni and Basso, 1985). We believe there are basically two possible explanations. First, most PM lesions also involve the precentral cortex, and, therefore, the contralateral paresis or paralysis precludes the expression of the praxic deficit. Secondly, bilateral activation of the PM cortex and SMA is often observed with unilateral movements (Roland and Zilles, 1996); thus, a unilateral lesion would not be enough for the deficit to become clearly manifested, since bilateral involvement would most likely be necessary. As a matter of fact, all recently pathologically confirmed cases of limb-kinetic apraxia have shown a degenerative process such as corticobasal degeneration and Pick’s disease, involving the frontal and parietal cortices (Fukui et al., 1996) or, predominantly, the PM cortex (Tsuchiya et al., 1997).

**The anatomofunctional substrates of limb praxis**

The fact that most studies exploring possible clinical–anatomical correlations for different types of limb apraxia have failed to unveil a consistent and specific lesion site for the disorder strongly suggests that praxic functions are distributed across several distinct anatomofunctional neural systems working in concert, but each one controlling specific processes (i.e. parietofrontal systems and reaching/grasping, frontostratial system and sequential motor events). Damage to these systems would produce selective praxic-related deficits depending on the context of the movement and the cognitive demand of the action.

**Parallel parietofrontal circuits for sensorimotor integration**

Recent anatomical and functional studies have identified in primates a series of segregated parietofrontal circuits, working
in parallel and each one involved in a specific sensorimotor transformation process: that is, their function is to transform the sensory information encoded in the coordinates of the sensory epithelia (e.g. retina, skin) into information for movements (Rizzolatti et al., 1998). The transformation process involves parallel mechanisms that simultaneously engage functionally related parietal and frontal areas linked by reciprocal corticocortical connections, supplemented by additional local computations (Wise et al., 1997; Rizzolatti et al., 1998). The posterior parietal cortex comprises a multiplicity of areas, each involved in the analysis of particular aspects of sensory information (i.e. somatosensory, visual, auditory, vestibular). The coordinate system may vary in different parts of the parietal cortex according to the nature of the actions evoked by sensory input (Kalaska et al., 1997). The motor cortex, in turn, is also made up of many areas, each containing an independent representation of body movement and playing a specific role in motor control according to its afferent and efferent connections. The proposed functions of the main circuits originating from the superior parietal lobule (SPL) include visual and somatosensory transformation for reaching (medial intraparietal area, MIP-F5), somatosensory transformation for reaching (PEn/PEn-F5), somatosensory transformation for posture (PEc-F5) and transformation of body part location data into information necessary for the control of body part movements (PE-F5). The circuits originating in the IPL are devoted to visuomotor transformation for grasping (AIP-F5), the internal representation of actions (PF-F5), coding peripersonal space for limb and neck movements (VIP-F5) and visual transformation for eye movements (LIP-PEF) (Fig. 1) (Rizzolatti et al., 1998).

The parietofrontal circuits subserving the transport (reaching) phase of movements towards an object originate in the SPL. Several areas in the monkey’s SPL use visual as well as somatosensory information for movement organization, whereas others are mainly involved in the analysis of somatosensory stimuli for planning and controlling arm movements. Lacquaniti and colleagues showed that area 5 (dorsal SPL) cell activity signalled arm postures and movements in a body-centred frame of reference (Lacquaniti et al., 1995). About 70% of the neurons have tuning functions that cluster around distance, azimuth (horizontal position) or elevation (vertical position); the global reconstruction of a limb position can be accomplished by the summation of individual contributions in a population of neurons (Lacquaniti et al., 1995). The SPL is the major source of projections to the dorsal premotor cortex (PMd). The PMd is somatotopically organized and seems to play a key role in trajectory planning. As cells in the primary motor cortex, PMd cells are tuned to movement direction, with a tendency to follow the position of the arm in space (Johnson et al., 1996; Kalaska et al., 1997). On the other hand, numerous studies have described signal- and set-related activity in the rostral PMd (F7), indicating a role in movement preparation and in the conditional selection of action (Passingham, 1993).

Moreover, it has been proposed that neurons in F7 also contribute to the spatial localization of external stimuli for reaching movements (Rizzolatti et al., 1998).

The SMA proper (F3), as part of one of the SP–frontal circuits, appears to play an important role in the control of posture, in particular in the postural adjustments that precede voluntary movements. The pre-SMA (F4) receives substantial projections from the prefrontal lobe, suggesting that it is involved in the control of potential actions encoded in the parietofrontal circuits. Its degree of activity would depend on external contingencies and motivational factors (Rizzolatti et al., 1998).

The skilful handling of objects requires the use of visual information to encode the intrinsic properties of the object (size and shape) and to produce appropriate patterns of hand and finger movements. This visuomotor transformation process takes place in a circuit made up by the IPL and the PM ventral cortex (PMv), as well as by their interconnection with the basal ganglia and cerebellum. This circuit may be considered as a lateral subsystem devoted to grasping and hand manipulation, parallel to the medial subsystem involved in the transport phase of reaching (Jeannerod et al., 1995).

Recent neurophysiological studies in monkeys have disclosed several classes of neurons involved in hand actions located in the IPL. Some neurons were activated by the sight of objects during fixation, representing perception of egocentric distance to the visual target, while others showed precise correspondence between the pattern of hand movements and the spatial characteristics of the object to be manipulated. Still other manipulation-related neurons discharged only when the monkey used the real object or tool (Taira et al., 1990; Sakata et al., 1995).

Area F5 lies in the rostral part of the ventral premotor cortex (PMv) and it is reciprocally connected with the AIP. It is also connected with the hand area of M1, and is therefore specifically related to distal movements (Matelli et al., 1985). Hand neurons discharge during specific goal-related movements such as grasping, tearing, manipulation and holding, whereas others are specific for a particular movement in relation to certain types of hand grip (e.g. precision grip or finger prehension) (Rizzolatti et al., 1988). Thus, different populations of neurons might encode different motor acts (schemas). Some schemas represent general categories of actions, such as grasping, holding and tearing; others indicate how the objects are to be grasped (e.g. held and torn) and the effectors (fingers) appropriate for the action; whereas still other schemas are concerned with the temporal co-ordination of the action. The motor schemas form a basic ‘vocabulary’ from which many dexterous movements can be constructed as co-ordinated control programmes (Jeannerod et al., 1995).

The final updating of the motor (or sensory–motor) schemas related to the physical properties of an object seems to be based on afferent information about specific mechanical events in the skin–object contact areas during manipulation (Johansson and Cole, 1992).

Graziano and Gross have suggested that a general principle
of sensory–motor integration is that the space surrounding the body be represented by body part-centred coordinates (Graziano and Gross, 1998). Cells within PMv, areas 7b and VIP and the putamen respond both to tactile stimulation of the face, arm or trunk, and to the presentation of visual stimuli. These areas are monosynaptically connected and
appear to form a system for the representation of the peripersonal space somatotopically. This system would be particularly suitable for guiding and adapting movements towards (or away from) everyday objects that surround us (Graziano and Gross, 1998).

Functional brain imaging studies support the proposed neurophysiological mechanisms for reaching and grasping. Matsumura and colleagues studied reaching and grasping neutral objects. Compared with reaching, grasping was associated with increased activation bilaterally in the PM, the prefrontal and posterior parietal areas, and in the contralateral cerebellum, thalamus and basal ganglia (globus pallidus and caudate) (Matsumura et al., 1996). Rizzolatti and colleagues found that the regions significantly activated during the execution of grasping movements were the precentral and mesial motor areas, SPL and cuneus, putamen and cerebellum (Rizzolatti et al., 1996), whereas Faillenot clearly demonstrated activation of the premotor as well as mesial frontal cortices in addition to the parietal and primary motor and somatosensory cortices during grasping (Faillenot, 1997).

A recent functional MRI study in control subjects during reaching and grasping a familiar object showed activation of the contralateral sensorimotor cortex, bilateral premotor cortex, SMA and bilateral posterior parietal cortices. Significant bilateral activation, more marked on the contralateral side of the lateral bank of the anterior intraparietal sulcus, was observed during grasping (Binkofski et al., 1998).

Selective apraxia-related deficits resulting from damage to the parietofrontal circuits

Lesions in the SPL involving circuits which subserve somatosensory transformation for reaching, somatosensory transformation for posture and transformation of body part location data into information for the control of body part movements would explain the external configuration and movement types of praxic errors such as faulty orientation and abnormal limb configuration. Monkeys with bilateral lesions of area 5/7b/MIP showed misreaching in the dark but not in the light, further confirming the essential role of area 5/7b/MIP for the spatial co-ordination of arm movements in relation to propropioceptive and efference copy information (Rushworth et al., 1997a). Heilman and colleagues described a right-handed patient with an apraxia resulting from a right superior parietal lesion. Her performance with her left hand was characterized by minor temporal but gross spatial errors, particularly with her eyes closed; she moved her arm erroneously in space and oriented the limb abnormally in relation to the object. She did not have visuomotor ataxia, and grasping appeared to be preserved (Heilman et al., 1986).

Selective deficits limited to the grasping phase of the movement, which can mirror some of the internal configuration types of praxic errors, have also been described in animals and humans with damage to parietofrontal circuits in the IPL. Gallese and colleagues found deficits mainly restricted to the grasping phase in monkeys with inactivation of the AIP (Gallese et al., 1997). Jeannerod and colleagues reported a patient who, after a bilateral parieto-occipital infarction, showed a severe and bilateral grasping impairment; the hand was widely open, without correlation between grip and object size, and the grasp was awkward and inaccurate (Jeannerod et al., 1994). Binkofski and colleagues studied three patients with left hemisphere lesions (two of the patients having ideomotor apraxia) and two patients with right hemisphere lesions involving the anterior lateral bank of the intraparietal sulcus, possibly the human homologue of the AIP, who had selective temporal and spatial kinematic deficits in the co-ordination of the finger movements required for grasping a switch, with minor disturbances of the reaching phase of the movement. An extended time to achieve maximal hand aperture and a prominent disturbance of hand-shaping was observed in all five patients (Binkofski et al., 1998).

In clinical terms, as the authors suggested, this visuomotor deficit would represent a focal deficit of the unimodal apraxic type, as described by Freund (Freund, 1992). The report of Sirigu and colleagues clearly demonstrated the relationship between grasping and praxis (Sirigu et al., 1995). Their patient, with bilateral hypometabolism in the posterior parietal regions, showed a selective praxic deficit for hand postures during the grasping of objects in the context of utilization gestures, with apparently normal movement trajectories and accurate scaling of manual grasp during simple reaching movements. Thus, object attributes are likely to be processed differently according to the task in which the subject is involved. When a subject is requested to grasp an object but not to use it, the brain extracts the structural attributes of the object (i.e. form, size, orientation) relevant to action to generate the appropriate movement. However, during utilization gestures, in addition to data about object characteristics, prior knowledge about the functional properties of objects needs to be integrated into the grasping subsystem to produce an accurate manual grasp (Jeannerod et al., 1995; Sirigu et al., 1995).

Lesions in animals and humans involving those areas of the motor cortex making up the parietofrontal circuits also cause distinct types of praxic-like deficits, though less selectively than those observed when there is damage to the parietal component of the circuits.

Earlier studies in monkeys with extensive ablations of the PMd cortex, some of them also involving the SMA and/or prefrontal cortex, have shown groping reaching movements and impairment of skilled arm movements (Fulton et al., 1932). On examining a problem box-trained chimpanzee after the paralysis of a premotor cortex ablation had remitted, Jacobsen noticed that the animal appeared unable to ‘organize’ the necessary manipulations and had to relearn them, because it was incapable of setting about the proper movements (Jacobsen, 1934). Similar results were reported in monkeys with periarcuate lesions (Deuel, 1977).

Kurata and Hoffman found that muscimol injections in the
PMd caused directional errors in a visually cued delayed response task, whereas when muscimol was injected in the PMv the movements were in the correct direction, although they were slower and of small amplitude (Kurata and Hoffman, 1994). Gallese and colleagues observed that inactivation of F7 caused a deficit similar to that caused by inactivation of the AIP: a severe disruption of hand preshaping and object grip without reaching deficits (Gallese et al., 1997). However, the ability to grasp was not totally disrupted, since the animal was still able to grasp the objects after a series of corrections that relied on tactile explorations.

Kennard and colleagues described a patient with persistent impairment of skilled movement after removal of a glioma from the right premotor area (Kennard et al., 1934). Luria stressed the ‘loss of the kinetic melody’, resulting in disintegration of the dynamics of the motor act and of complex skilled movements in patients with premotor lesions, which is mainly apparent when the task requires the learning of a new skilled movement (Luria, 1980). Patients with frontal lobe lesions may exhibit deficits in visually steering the arm accurately, particularly during rapid movements (catching a thrown ball) because of abnormal temporal sequencing of muscular activation (Freund and Hummelstein, 1985). As mentioned above, patients with premotor lesions exhibit a deficit in conditional motor learning (Halsband and Freund, 1990; Passingham, 1993; Rushworth et al., 1997b).

Therefore, it might be posited that the disintegration of skilled hand movements may be attributed mainly to damage to the PMv (F4 and F5) and dysfunction of those populations of neurons encoding the ‘motor vocabulary’ in the frontal component of the circuit involved in grasping and manipulating. On the other hand, lesions in the PMd (F2 and F7) may cause (i) coordination breakdown of proximal arm muscles when these muscles are used for the generation of reaching movements, (ii) abnormal orientation and trajectory defects, and (iii) deficit in conditional motor learning, which may underlie the inappropriate selection of actions in relation to the context exhibited by apraxic patients (Passingham, 1993).

Patients with ideomotor apraxia may show abnormal performance of transitive movements directed away from the body (e.g. hammering), whereas self-directed movements (e.g. combing) are relatively well executed. This dissociation might be due to the fact that the target of self-directed actions, an important part of the context, is invariably present, or that associated damage to the circuit subserving the somatotopic representation of peripersonal space causes a deficit in transforming object locations into appropriate movements towards them (Graziano and Gross, 1998). In contrast, poorer performance of self-directed compared with externally directed movements may reflect the fact that the former require the participation of another circuit, or that gestures directed towards the body demand greater movement precision than those performed away from the body (Roy and Square, 1994).

Frontostriatal and frontoparietal systems: sequencing of movements

Functional brain imaging studies have shown that different neural systems are actively engaged in the preparation and generation of a sequential action depending on whether a sequence has been prelearned or is a new one, and contingent on the complexity of the attentional demands of the task (Jenkins et al., 1994; Grafton et al., 1995; Catalan et al., 1998).

The SMA, primary sensorimotor cortex, basal ganglia (mid-posterior putamen) and cerebellum may be mainly involved in the execution of automatic, overlearned, sequential movements, whereas the prefrontal, premotor and posterior parietal cortices and the anterior part of the caudate/putamen would be particularly recruited—in addition to such areas engaged in the execution of simple movement sequences—when a complex or newly learned sequence, which requires attention, integration of multimodal information and working memory processes for its appropriate selection and monitoring, has to be performed (Grafton et al., 1995; Miyachi et al., 1997; Catalan et al., 1998; Harrington et al., 1998).

Scheduling or timing a series of actions has been suggested to be an emergent property of interactions of the left cerebral cortex with the basal ganglia (Harrington and Haaland, 1992). Cortical systems with reciprocal pathways to the basal ganglia (e.g. SMA, PM cortex), which receive projections from the cerebellum (e.g. PM cortex) or send bilateral projections to the putamen and caudate, such as the inferior parietal cortex, are important candidates that may support timing processes (Harrington et al., 1998). Rubia and colleagues have recently suggested a neural network for temporal bridging and timing movements made up by the left prefrontal cortex, the SMA and the supramarginal gyrus (Rubia et al., 1998). The frontal lobes have been considered to be a crucial structure for bridging temporal gaps in the action perception cycle and for the temporal organization of the motor output (Fuster, 1990). The findings of Halsband and colleagues in patients with unilateral lesions of the frontal lobe have further emphasized the critical roles of both the SMA and the PM cortex in the generation of motor sequences from memory that fit into a precise timing plan (Halsband et al., 1993).

Thus, different neural systems would be engaged depending on the type of movement sequence requested to be executed during the evaluation of praxis. When the sequence is well known or automated, or else performed from memory, the SMA–basal ganglia system would be recruited preferentially. However, most of the sequences used to test praxis are new (e.g. sequencing of movement in the movement imitation test for ideomotor apraxia), or the content of an otherwise well learned goal-directed action (e.g. the multiple sequential use of objects test for ideational apraxia) has to be represented explicitly. In any case, the system composed of the prefrontal, premotor and parietal cortices, the striatum and white matter fascicles would be engaged specifically. In addition, it might
be possible that, within this system, there are many different subsystems subserving functionally separate cognitive computations that are involved in motor sequencing (i.e. timing, motor attention, selection of limb movements and object-oriented responses), which may be selectively damaged by the pathological process and so produce different types of sequencing impairment in apraxic patients (Harrington and Haaland, 1992; Roy and Square, 1994; Rushworth et al., 1997b, 1998).

The temporoparietal–frontal system: recognition and imitation of action
Di Pellegrino and colleagues discovered a particular subset of neurons in F5 which discharge while a monkey observes meaningful hand movements made by the experimenter, in particular when interacting with objects; they called them ‘mirror neurons’ and speculated that they belong to an observation/execution matching system involved in understanding the meaning of motor events (Di Pellegrino et al., 1992). Neurons with properties similar to those of mirror neurons in F5 are also found in the posterior superior temporal sulcus (STS) in monkeys (the superior temporal polysensory region, which might be the monkey’s homologue of part of the human IPL) (Morel and Bullier, 1990; Perret et al., 1990a; Milner, 1995; Oram and Perret, 1996). These neurons respond not only to the sight of the monkey’s own hand performing the action, but also to the sight of the experimenter’s hand performing the same action, an equivalence that may be crucial for recognizing, imitating or shaping one’s own actions to match those witnessed (Carey et al., 1997).

Two other types of neurons which may contribute to the recognition and imitation of postures and actions have also been found in the STS by Perrett and co-workers. One type encodes the visual appearance of particular parts of the body (i.e. fingers, hands, arms) while static or in motion, and these neurons combine in such a way that the collection of components can specify a particular meaningful posture or action (Perret et al., 1995), whether novel actions or stereotyped social signals. The second type encodes specific body movements, such as walking and turning (Perret et al., 1990b).

Cells responding to hand–object interaction might also be present in area 7b (Fogassi et al., 1998). Area 7b in the rostral part of the convexity of the IPL sends its cortical output to the convexity F5; area 7b receives projection from the STS region, and the latter is interconnected with the frontal lobe (Matelli et al., 1985; Seltzer and Pandya, 1989), thus closing a cortical circuit involved in the perception of hand–object interaction. The crucial cognitive role of the STS–7b–F5 network would be the internal representation of actions which, when evoked by an action made by others, would be involved in two related functions: action recognition and action imitation (Rizzolatti et al., 1998).

PET studies in humans support neurophysiological findings in monkeys. Observation of grasping markedly increased cerebral blood flow in the cortex of the STS, the rostral part of Broca’s area and in the rostral part of the left intraparietal sulcus on the left hemisphere of right-handed subjects (Bonda et al., 1996; Grafton et al., 1996; Rizzolatti et al., 1996). Furthermore, when a gesture was observed with the intention that it should be imitated rather than recognized, the activation was observed predominantly in structures usually involved in the planning of action, such as the dorsolateral prefrontal cortex and the SMA. If the action had a semantic content referring to objects, it would be processed mainly by the ‘ventral’ visual pathway (occipitotemporal cortex, hippocampus and PMv cortex) of the left hemisphere, whereas an unfamiliar action would activate the ‘dorsal’ visual pathway (occipitoparietal and PMd cortices) of the right hemisphere with the contribution of regions within the ventral pathway (Decety et al., 1997).

Thus, the imitation of meaningful actions seems to be mediated by implicit knowledge about the form as well as the meaning of the gesture, which is processed by regions involved in the planning and generation of actions plus the temporal cortex (Decety et al., 1997). On the other hand, imitation of meaningless actions would depend on the decoding of their spatiotemporal layout in the occipitoparietal–PM cortex pathway (Decety et al., 1997), or on the analysis of arbitrary body movements or components (i.e. hand open, finger extended) by cells in the temporal cortex and their corresponding parietal and/or premotor connections (Carey et al., 1997). That imitative movements may be generated by direct connections between the occipitotemporal and frontal cortices, without the participation of the occipitoparietal pathway, is suggested by the lack of correlation between the transport phase of a movement and end-point errors in apraxic patients when they imitate meaningful hand positions (Hermsdorfer et al., 1996).

In left brain-damaged patients with left limb apraxia, the improvement on imitation may be explained by the participation of the right hemisphere, or by the use of the undamaged temporofrontal component of the putative system in the left hemisphere if the lesion is more posterior and dorsally located (Carey et al., 1997). On the other hand, several mechanisms may explain why patients are impaired when imitating meaningless gestures but perform flawlessly when imitating a meaningful one. A perceptive deficit due to a parietal lesion may cause an abnormal mental transformation of another person’s body part (Bonda et al., 1995), or the defective imitation can be produced by inability to store temporarily and/or manipulate spatial relationships in visuospatial working memory. Both of these mechanisms may be bypassed when the meaningful gesture has access to meaning. Alternatively, the deficit may be due to damage to those populations of temporal cells encoding arbitrary hand postures and movements with preservation of those engaged in encoding expressive body movements (or postures) and object-oriented actions (Carey et al., 1997), or to a lesion
which disrupts the decoding of the spatiotemporal layout in the occipitoparietal–PM cortex pathway (Decety et al., 1997). Imitation deficit restricted to hand positions but with normal finger configuration (Goldenberg and Hagmann, 1997) may be explained by selective involvement of cell populations in the temporal cortex which encode static hand but not finger postures (Carey et al., 1997), although alternative interpretations have been advanced (Goldenberg, 1999).

Limb apraxias due to dysfunction of the parietofrontal circuits: higher-order defects of sensorimotor integration

Disruption of parietofrontal circuits and their subcortical connections, subserving the transformation of sensory information into action, would give rise to most of the praxic errors observed in ideomotor apraxia. Damage to circuits devoted to sensorimotor transformation for grasping, reaching and posture, as well as for the transformation of body part location into the information necessary for the control of body part movements, would produce incorrect finger and hand posture and abnormal orientation of the tool/object, inappropriate configuration of the arm and faulty orientation of the movement (with respect to both the body and the target of the movement in extrapersonal space), as well as movement trajectory abnormalities. These errors may be observed in the limb contralateral to a left or right parietal lesion, if an associated elemental motor or sensory deficit does not preclude their proper interpretation. However, they would be particularly reflective of ideomotor apraxia, and would then also be observed in the limb ipsilateral to a left hemisphere lesion, when the patient pantomimes a transitive movement under verbal command. Thus, the praxic quality of the errors in ideomotor apraxia would be determined by the context in which the movement is performed and the cognitive requirements of the task.

Selective praxic deficits may be observed when specific circuits are involved in the parietal or frontal lobes. Damage to the SPL in circuits subserving somatosensory transformation for reaching, posture and movements would produce praxic errors, such as abnormal limb orientation and configuration, resembling those observed in patients with apraxia secondary to superior parietal lesions (Heilman et al., 1986). When the circuits subserving grasping mechanisms are damaged in the IPL, a praxic deficit characterized by a mismatch between finger and hand postures and the object to be grasped will be observed (Sirigu et al., 1995). An additional deficit in the transformation of object location into accurate movements towards such objects would appear if the circuit encoding peripersonal space were also involved.

Lesions in the PMd cortex and SMA involving the corresponding parietofrontal circuits will most likely cause milder errors in limb position, configuration, orientation and trajectory than those observed with parietal lesions. These deficits will be more evident in the contralateral limb because of close interrelation between both premotor cortices during movements, although subtle abnormalities may be observed in the limb ipsilateral to a damaged left hemisphere, particularly when the subject pantomimes transitive movements to verbal command.

Involvement of the circuits subserving sensorimotor transformation for grasping in the PMv cortex may produce some of the ideomotor type of praxis errors confined to hand movements. However, we believe that damage to this region of the premotor cortex would primarily disrupt particular segments of the action and the specificity for different hand and finger movements and configurations. The motor vocabulary necessary for the proper selection of finger and hand movements would be impaired and a limb-kinetic type of praxis deficit would appear in the hand contralateral to the more affected hemisphere regardless of the pattern of cerebral dominance. An associated sensory deficit—as occurs in most patients with corticobasal degeneration—that would in addition interfere with the information necessary for the final updating of the finger and hand schemas to the object’s physical characteristics, further undermining the process of manipulation, might be required for the adexterous hand typical of limb-kinetic apraxia to finally develop.

The complexity of limb praxis disorders requires a multidisciplinary approach which should encompass expertise ranging from clinical and cognitive neurology and neuropsychology to the basic neurosciences. Future studies exploring normal praxis functions with functional neuroimaging, as well as kinematic analysis of reaching, grasping and manipulating components of object-oriented actions (particularly when combined with activation studies), in patients with different types of limb praxis deficits due to restricted focal cortical and subcortical lesions, will most likely allow the specific underlying neural mechanisms to be identified and limb praxis disorders to be classified within the framework of the modular organization of the brain.

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