Limb apraxia: a paradigmatic cognitive – (psycho?) motor disorder

Stephan Bohlhalter
Abteilung für Kognitive und Restorative Neurologie, Universitätsklinik für Neurologie, Inselspital Bern

There is no actual or potential conflict of interest in relation to this article.

Summary

This article focuses on limb apraxia as a paradigmatic cognitive-motor disorder affecting gestural communication and tool use. It is frequently seen in left-hemispheric stroke and neurodegenerative diseases. Furthermore, the possible relationship between cognitive-motor and psychic dysfunction is discussed, based on apraxic-like symptoms in schizophrenia. A model of limb praxis is introduced, which involves the recruitment of semantic and mechanical knowledge (conceptual system) and time-space engrams (production system) guiding skilled actions. Based on the dichotomy of this model, apraxia has been traditionally classified in two major subtypes. In the more severe form, called ideational apraxia, concepts of skilled actions are lost, that is, patients no longer know for *what* purpose gestures and tools are utilized, whereas in ideomotor apraxia stored information on *how* they are properly executed is primarily impaired. Recent anatomical and functional neuroimaging studies suggest that gesture pantomiming critically engages the left inferior frontal lobe, irrespective of the hand involved. Furthermore, tool use of both hands appears to be controlled predominantly by the left inferior parietal lobe, particularly if based on mechanical knowledge, and by the temporal lobe bilaterally if supported by semantic knowledge. Gesture performance and fine motor control are impaired in schizophrenia, but seem not to correlate with psychopathology. However, whether psychic dysfunction is related to clinically relevant apraxia is largely unexplored and therefore remains an open question.

Key words: gestures; tool use; pantomime; imitation

Limb praxis: cognitive basis of skilled and/or learned movements

Limb praxis is defined as the ability to correctly perform skilled and/or learned movements, most commonly manual, which can be classified in two main categories: gestures and real object (tool) use. Gestures mainly play a communicative role, either supporting or substituting language. Gestures represent a body language that enhances verbal communication, for instance, beckoning someone when asked to come over or making a threatening sign to enforce a demand. In a noisy environment or over long distance gestures may replace verbal communication, for example asking for a tool near loud machines by pantomiming its use or waving goodbye at the railway station.

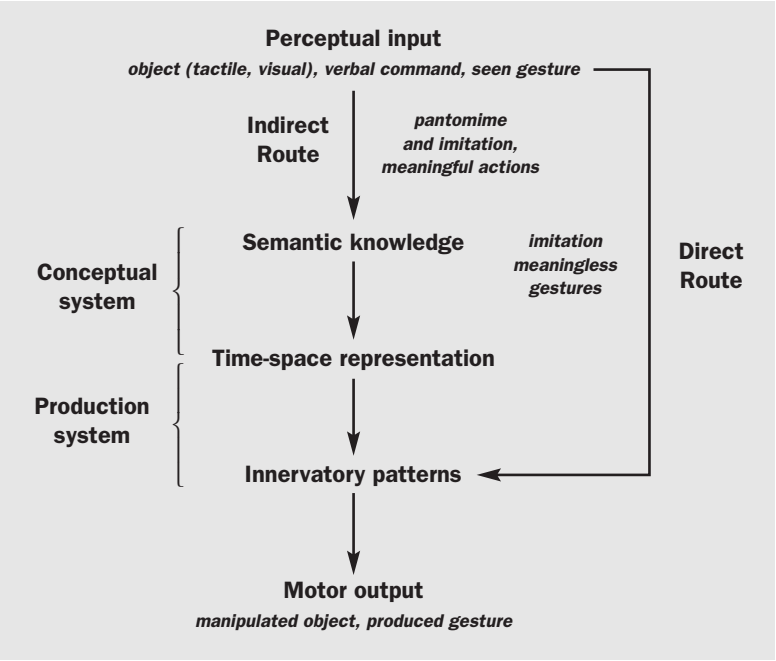
There are two cognitive-motor domains of gestures: *imitation* and *pantomime*. In a natural context, imitation plays an important role in motor learning and may support the comprehension of demonstrated actions, while the spontaneous performance of pantomimes, as pointed out above, serves mainly non-verbal communication. In the clinical setting, gestures of different semantic content (non-symbolic versus symbolic) are routinely tested in both domains, that is, imitation of gestures demonstrated by the examiner and pantomime on command (elicited verbally or by pictures). Gestures are non-symbolic if they are *meaningless* and novel for the examinee (e.g. index finger on top of nose) and symbolic if they are *meaningful*. Symbolic gestures are further classified as being intransitive, communicative in nature (e.g. military salute) or being transitive, related to specific object/tool use (e.g. hammer use).

Proper object/tool use is supported by various cognitive functions. Firstly, for familiar objects the *semantic knowledge* of its prototypical use is required (e.g. a hammer is used to pound a nail, a nail clipper to cut fingernails etc.). Semantic knowledge is considered a part of semantic memory, which stores information about the typical purpose of objects [1, 2]. Secondly, prototypical use of objects is supported by *manipulation knowledge* mediating proper handling of tools [3]. For instance, for an effective stroke a hammer has first to be moved away from its target (nail) or the appropriate use of a knife requires sliding movements back and forth. Thirdly, skilled use of objects may need *mechanical knowledge* if the prototypical tool for the action is not available or is damaged [4]. Consequently, based on their mechanical properties, alternative tools may have to be selected to complete the intended action. For instance, the impact surface of a pliers head is usually hard and big enough to pound a nail, to replace a hammer. Mechanical knowledge also allows judgment of whether an altered instrument is still useful (e.g. a twisted spoon could still be used to eat soup, if not damaged by a hole). Finally, to reach an action goal, sequential knowledge of how to correctly use multiple objects (e.g. closing an envelope after having put in the letter) is required.

Most theoretical models on cognitive-motor control of limb praxis share two principal components: a conceptual and a production system [5]. The basic notion is that the conceptual system represents the semantic knowledge for *what* typical purpose the objects and gestures are utilized, while the production system stores temporal-spatial engrams about *how* object use and gestures are properly executed. Herein, a modified dual route model [6–8] is presented

Correspondence:
Stephan Bohlhalter
Abteilung für Kognitive und Restorative Neurologie
Neurologische Universitätsklinik
Inselspital
CH-3010 Bern
stephan.bohlhalter@insel.ch

Figure 1
Cognitive-motor model of limb praxis.



(fig. 1). According to this model, meaningful actions are processed mainly in an indirect route and meaningless gestures through a direct route.

After perceptual analysis, use of objects and meaningful gestures are intuitively evaluated for action meaning based on semantic (including mechanical) knowledge. Further processing involves the recruitment of time-space representations (including manipulation knowledge) of actions, which are responsible for their skilled execution. Finally, it is believed that translation of temporal-spatial plans into detailed motor output is mediated by so-called innervatory patterns, which channel information to appropriate motor areas. Pantomime of meaningful gestures is processed mainly through the indirect route, while their imitation may engage both pathways. Meaningless novel gestures are exclusively controlled by the direct route as their imitation cannot rely on stored semantic knowledge or temporal-spatial engrams. It corresponds to a visuo-motor transformation linking perceptual analysis directly to innervatory patterns.

This cognitive-motor model of limb praxis takes into account some behavioural dissociations that are frequently observed in patients with brain lesions. For instance, in apraxic stroke patients, pantomiming is typically more vulnerable than imitating gestures, particularly if gestures are transitive in nature. This is thought to be mainly related to their degradated temporo-spatial representation or impaired access to it [9]. Furthermore, in some patients with corticobasal syndrome, at least in early stages, imitation of meaningless gestures may be worse than meaningful gestures pointing to a predominant impairment of the direct route with relatively intact semantic and time-space representation of actions [10]. Real tool use is generally more severely affected when multiple subsystems are affected (e.g. in patients with large stroke lesions or with dementia), particularly when semantic knowledge is lost or when innervatory patterns are disrupted.

Limb apraxia: assessment and traditional classification

Apraxia is a cognitive-motor disorder of skilled and/or learned movements, which is not explained by elementary sensorimotor or language comprehension deficits. It impairs pantomime and imitation of gestures, as well as real object/tool use, although these domains may be differentially affected in distinct subtypes of apraxia. Elementary neurological deficits have to be taken into account when assessing apraxia. For instance, left hemispheric stroke patients should be examined primarily on the ipsilateral side, as apraxia on the contralateral side is frequently superimposed on, or masked by, weakness. Furthermore, if apraxia is associated with severe aphasia the clinical assessment may rely more on the performance in the imitation than in the pantomime domain, as the former requires no language comprehension. Recently, a new scale has been developed with separate cut off scores for all relevant domains and semantic features of gestures, allowing a differential evaluation of patients [11].

Herein a traditional classification of apraxia subtypes is presented, which dates back to Hugo Liepmann [12], a German neurologist and psychiatrist, who pioneered it in the field at the beginning of 20th century. The following table summarizes a refined taxonomy suggested by Dr. K. Heilman in an International Workshop for Ideomotor apraxia in Washington, 2005.

Table 1
Classification of Apraxias (according to Dr. K. Heilman, International Workshop on Ideomotor Apraxia, 2005, Rockville, USA, (see also [8]).

Multimodal apraxias	Ideational apraxia • Conceptual apraxia (CA) • Sequential apraxia (SA)
	Ideomotor apraxia (IMA)
	Limb kinetic apraxia (LKA)
Modality-specific Apraxia	Dissociation apraxias (visuo-imitative, speech command, tactile)

Most apraxia subtypes are multimodal, that is the disorder is present irrespective of the modality of perceptual input. They comprise of *ideational apraxia* (IA), further subdivided into *conceptual* (CA) and *sequential* apraxia (SA), which basically results when the conceptual system of limb praxis is defective, and *ideomotor* (IMA) as well as *limb kinetic* apraxia (LKA), both reflecting an impairment in the production system. Rarely, apraxic deficits may occur only if stimuli are presented in a specific modality, qualifying for so-called dissociation apraxias. Accordingly, skilled actions may be impaired exclusively if elicited by seen gestures (visual imitative) [13], speech commands [14] or tactile stimuli [15]. This article will focus on multimodal apraxias, which are clinically the most relevant.

Patients with CA do no longer know what to do when asked to demonstrate the use of a tool. In everyday life they

may be observed using a tooth brush instead of a comb. During clinical examination, the patients show content errors when pantomiming tool use (e.g. screwdriver for hammer) or they may be unable to select appropriate tools when presented with other objects, for example tooth paste and a tooth brush out of three related foil objects (comb, shampoo, and hair brush). They also typically have difficulties to select alternative tools to complete a task when the tool for prototypical use is not available (e.g. pliers for hammer). In patients with SA, if asked to prepare a letter for mail, they may close the envelope before inserting the paper sheet or may put the stamp on the letter instead of the envelope. However single object use remains intact.

IMA is thought to result when time-space representations of skilled movements are defective, being most obvious when pantomiming and imitating gestures. For instance, when cutting bread the patients may show chopping movements in vertical direction instead of sliding movements back and forth, or when demonstrating the use of a screwdriver they may rotate in the shoulder instead of the elbow (impaired interjoint coordination). The patients also typically produce "body-part-as-object- (BPO-)" errors by using a body part as a tool (e.g. finger as tooth brush, fist as hammer etc.), which persist despite the instruction of the examiner to imagine holding the object in hand and not to use body parts. The skilled movements are frequently delayed and clumsy, characterized by multiple interruptions and seeking activity ("conduite d'approche"), but usually recognizable as the conceptual knowledge of gestures and prototypical object use is typically preserved. Therefore, patients with IMA know what to do but not how to do it. They usually improve when actually using tools, but their manipulation often remains defective as demonstrated clinically [16] and by kinematical analysis [17].

LKA is characterized by a loss of precise and independent finger movements not explained by elementary sensorymotor deficits. In particular, inappropriate selection for simultaneous and/or sequential movements of individual fingers is a hallmark. LKA has been considered a higher-order motor disorder since it is thought to be based on the dysfunction of brain areas, which are located upstream to primary motor cortex [18]. Furthermore, if based on a left hemispheric lesion, LKA is a bilateral disorder, although affecting the contralateral side more than the ipsilateral side [19]. However, in contrast to other types of apraxia it does not represent a true cognitive-motor disorder with conceptual and temporal-spatial deficits. LKA rather results when access of motor cortex to time-space representations of skilled movements is interrupted by degradated innervatory patterns, thereby adopting an intermediate position between higher-level apraxia and elemental motor disorder. Limb kinetic deficits can be assessed by imitation of finger postures [20] or the so-called coin rotation (CR) task [19, 21], in which the subjects are instructed to rotate a coin as rapidly as possible (Swiss 50-Rappen, corresponding exactly in size to a US-Nickel) between their thumb, index and middle finger. The limb kinetic deficit is indicated by the increased time needed to complete 20 half turns (e.g. >20 seconds) and by the number of coin drops.

Controversies of the traditional classification

The term IA has produced significant confusion [22]. Some authors have considered IA a disorder of actual tool use (single or multiple) and IMA a pure gestural deficit [23]. For others, IA denoted a disturbance mainly of action sequence involving multiple objects and IMA defective single object use [24]. Therefore, to overcome some of the controversy, the term CA has been introduced indicating the loss of semantic knowledge of single object use and gestures [25] and SA (Dr. K. Heilman, International Workshop, 2005) for a disorder of action sequence. Further distinction of CA and IMA is based mainly on the type of apraxic errors, the former characterized by predominantly semantic and the latter by temporal-spatial errors occurring during both gesturing and real tool use [26]. Finally, the relevance of the somewhat arbitrary cognitive-motor dichotomy between IA and IMA has been questioned overall [27], based on the observation that apraxic patients show similar impairment when imitating gestures with their own body or on life-sized manikins [28], indicating that production errors in apraxia may simply reflect a reaction to the core conceptual impairment. Herein, the traditional classification has been introduced as it is still widely used. However, it has to be emphasized that the appearance of apraxia subtypes is frequently not exclusive, but may significantly overlap in individual patients.

Clinical relevance of limb apraxia

Clinico-anatomical studies demonstrated that apraxia is a cognitive-motor syndrome affecting both sides of the body, which is largely based on left parieto-frontal damage [12, 29]. It is therefore frequently seen in left-hemispheric stroke as well as various neurodegenerative disorders involving parietal lobes (e.g. Alzheimer's disease and corticobasal degeneration). It is a major source of disability in stroke patients and significantly affects everyday life [30]. After stroke, it may be more predictive for caregiver dependency than other deficits such as aphasia [30–32]. Therefore, the clinical importance of apraxia is increasingly recognized in restorative neurology [33].

In stroke patients, conceptual impairment frequently improves in subacute stages, while temporal-spatial errors, indicating IMA, tend to persist. Tool-related apraxic deficits are usually most prominent during clinical testing of transitive pantomimes, while actual tool use may be seemingly normal, a phenomenon that has been referred to as voluntary-automatic dissociation. The clinical significance of IMA has therefore been questioned by some authors [34, 35]. However, although the disability in everyday life is less obvious in IMA than other apraxia subtypes, detailed kinematic analysis suggest that feedback-driven improvement by holding the tool in hand may not be sufficient to compensate for its defective use [17]. Furthermore, difficulties may be underestimated as stroke patients rarely complain about ideomotor apraxic deficits. Patients are often anosognostic and ascribe, if right-handed and right-hemiparetic, their difficulties with the left hand to handedness. Moreover, the fact that patients are usually able to complete everyday tasks

may mask the underlying difficulty. The patients compensate for the deficit by repeating single components of everyday actions or need simply more time to think about their realization. Therefore, the disability is reflected by the increased time needed to accomplish everyday tasks, which is a frequent complaint. Finally, in the rehabilitation of aphasic patients, teaching gestural communication as a compensation for language deficits is often more difficult.

LKA is frequently seen in stroke [19] and neurodegenerative disorders [36], particularly corticobasal degeneration (CBD). Recent studies suggest that patients with Parkinson's disease (PD) may also suffer from limb kinetic deficits [21, 37, 38] as manual dexterity measured with CR is much less responsive to levodopa than bradykinesia. However, whether impaired digital dexterity in PD should be really called limb kinetic apraxia or just considered a different face of bradykinesia/akinesia is subject of a current debate [37, 39].

Neural basis of cognitive-motor dysfunction in limb apraxia

The traditional classification of apraxia, despite the controversies, has still proved to be of some usefulness in characterizing major apraxic deficits in patients. However, the nosological labels reflecting differential combinations of cognitive-motor dysfunctions are likely to be not appropriate to elucidate their neural basis [27, 40]. Therefore, to understand the pathophysiological mechanism leading up to apraxic syndromes, the cognitive-motor functions have to be studied separately.

Accordingly, a recent lesion-symptom mapping study demonstrated that pantomiming of transitive gestures may be mediated mainly by the left inferior frontal cortex [40]. By contrast, analysis in the same cohort of stroke patients revealed that impaired imitation of meaningless gestures was associated with inferior parietal lesions [41]. This dichotomy is corroborated by functional neuroimaging studies showing that during pantomime, parietal-premotor networks are particularly engaged inferior frontal [42, 43] and during imitation inferior parietal [44, 45]. The neuroimaging findings for pantomime, along with the premotor activation during gesture recognition [46, 47], both relying particularly on stored cognitive-motor information, challenge an influential model that localized temporal spatial representation of praxis movements to inferior parietal lobe [48, 49].

Advances in elucidating the neural basis of gesturing were also made for real tool use. A very recent study demonstrated that real tool use critically requires an intact left parietal lobe, particularly if supported by mechanical knowledge [2]. Interestingly, the temporal lobe, considered the neuro-anatomical site for conceptual knowledge of familiar object use [50, 51], seems to persistently affect real tool use only if damaged bilaterally [1, 2]. Little is known about the neural basis of fine motor control mediated by innervatory patterns. Based on clinico-anatomical case reports, the premotor areas, including supplementary motor area, are major candidate regions [26]. Functional neuroimaging studies concur with this view by showing that a higher complexity of movements is associated with increasing premotor activation [52, 53] compensating for impaired motor skill [54–56].

Limb apraxia: related to psychic dysfunction?

The topic of this issue, namely, the interrelationship not only of cognitive and motor, but also of psychic dysfunction raises the question of how limb apraxia may be related to mental disorders. In this context, it is interesting that Hugo Liepmann originally attributed IA to the realm of intrapsychic dysfunction [27]. At the end of 19th century, some authors (including Nothnagel) even used the term "Seelenlähmung" to signify a higher-order motor disorder of skilled actions not explained by weakness [12]. Historically, intrapsychic processes were considered non-localizable brain functions, which are maintained by the whole brain. Accordingly, in the early writings Liepmann viewed the movement plan of a skilled action as a non-localizable idea produced by the whole cortex, although finally considering lesions involving left parieto-occipital lobe most vulnerable for IA [12].

Motor impairment described as clumsiness has been reported early in schizophrenia [63] and seems, in contrast to affective disorders, to be almost invariably present in this patient group [58]. Motor awkwardness is not explained by neuroleptic treatment [57, 58] and only two studies have assessed praxis-related movements in schizophrenic patients in more detail [60, 61]. Although in schizophrenic patients with predominant negative symptoms "clear-cut" apraxia was not found, as the authors stated, apraxic features such as BPO errors were much more prevalent than in healthy controls [61]. The abnormalities in praxis assessment did not correlate with psychopathology. BPO errors also seemed not to be explained by concretistic thinking, often seen in schizophrenia. The authors described the praxis performance of patients as "... generally more clumsy, coarse and less extensive in space and time ..." [61]. It is therefore conceivable that the dextrous difficulties in schizophrenic patients may best fit with the concept of LKA. This would also correspond with the predominant frontal-lobe dysfunction underlying negative symptoms of schizophrenia [62] as innervatory patterns are thought to be stored in premotor region (see above). Interestingly, parieto-motor disconnection, which is likely to be based on premotor interruption (direct parieto-motor connections are rudimentary in humans), has been recently demonstrated using paired-pulse TMS in schizophrenia, though studied on the right hemisphere only [63]. Could impairment of dexterity in schizophrenia simply reflect psychomotor retardation, that is, a hypokinetic disorder based on lack of motivation and drive? In contrast to goal-directed praxis movements psycho-motor activity, per se, generally refers to aimless motor behaviour, which may be increased (e.g. agitation, stereotypies, wringing of hands) or diminished (slow, hesitant, perseverative), and therefore should not account for apraxic deficits. However, the boundary between cognitive and psychic dysfunction may be similarly arbitrary, as for cognitive and motor dysfunction discussed in previous sections. The attempt to distinguish cognitive, psychic and motor function finally touches on the fundamental mind-brain problem, which still exists in

contemporary times, as in Hugo Liepmann's times. In any event, further research to disentangle dextrous difficulties and psychopathological disturbance is needed.

References

1 Hodges JR, Bozeat S, Lambon Ralph MA, Patterson K, Spatt J. The role of conceptual knowledge in object use evidence from semantic dementia. Brain. 2000;123(Pt 9):1913–25.
2 Goldenberg G, Spatt J. The neural basis of tool use. Brain. 2009;132:1645–55.
3 Buxbaum LJ, Saffran EM. Knowledge of object manipulation and object function: dissociations in apraxic and nonapraxic subjects. Brain Lang. 2002;82:179–99.
4 Goldenberg G. Apraxia and the parietal lobes. Neuropsychologia. 2009;47:1449–59.
5 Roy EA, Square PA. Common considerations in the study of limb, verbal, and oral apraxia. In: Roy E.A., editor. Neuropsychological studies of apraxia and related disorders. Amsterdam: North-Holland, 1985;111–61.
6 Rothi LJG, Ochipa C, Heilman KM. A Cognitive Neuropsychological Model of Limb Praxis and Apraxia. In: Rothi LJG and Heilman KM. Apraxia, eds. The neuropsychology of action. Hove (UK): Psychology Press 1997; 29–49.
7 Tessari A, Canessa N, Ukmar M, Rumiati RI. Neuropsychological evidence for a strategic control of multiple routes in imitation. Brain. 2007;130:1111–26.
8 Wheaton LA, Hallett M. Ideomotor apraxia: a review. J Neurol Sci. 2007;260:1–10.
9 Heilman KM, Watson RT. The disconnection apraxias. Cortex. 2008;44:975–82.
10 Buxbaum LJ. Ideomotor apraxia: A call to action. Neurocase. 2001; pp. 445–58.
11 Vanbellingen T, Kersten B, Van Hemelrijk B, Van de Winckel A, Bertschi M, Muri R, et al. Comprehensive assessment of gesture production: a new test of upper limb apraxia (TULIA). Eur J Neurol 2009. [Epub ahead of print].
12 Liepmann H. Apraxie. Ergebnisse der Gesamten Medizin 1920;1:516–43.
13 Goldenberg G, Hagmann S. The meaning of meaningless gestures: a study of visuo-imitative apraxia. Neuropsychologia. 1997;35:333–41.
14 Heilman KM. Ideational apraxia – a re-definition. Brain. 1973;96:861–4.
15 Binkofski F, Kunesch E, Classen J, Seitz RJ, Freund HJ. Tactile apraxia: unimodal apractic disorder of tactile object exploration associated with parietal lobe lesions. Brain. 2001;124:132–44.
16 Goldenberg G, Hagmann S. Tool use and mechanical problem solving in apraxia. Neuropsychologia. 1998;36:581–9.
17 Poizner H, Clark MA, Merians AS, Macauley B, Gonzalez Rothi LJ, Heilman KM. Joint coordination deficits in limb apraxia. Brain. 1995;118:227–42.
18 Heilman KM, Meador KJ, Loring DW. Hemispheric asymmetries of limb-kinetic apraxia: A loss of deftness. Neurology. 2000;55:523–6.
19 Hanna-Pladdy B, Mendoza JE, Apostolos GT, Heilman KM. Lateralised motor control: hemispheric damage and the loss of deftness. J Neurol Neurosurg Psychiatry. 2002;73:574–7.
20 Leiguarda RC, Merello M, Nouzeilles MI, Balej J, Rivero A, Nogues M. Limb-kinetic apraxia in corticobasal degeneration: clinical and kinematic features. Mov Disord. 2003;18:49–59.
21 Gebhardt A, Vanbellingen T, Baronti F, Kersten B, Bohlhalter S. Poor dopaminergic response of impaired dexterity in Parkinson's disease: Bradykinesia or limb kinetic apraxia? Mov Disord. 2008;23:1701–6.
22 Hanna-Pladdy B, Gonzalez Rothi LJ. Ideational apraxia: Confusion that began with Liepmann. Neuropsychological Rehabilitation. 2001;11:539–47.
23 De Renzi E, Lucchelli F. Ideational apraxia. Brain. 1988;111: 1173–85.
24 Poeck K. The two types of motor apraxia. Arch Ital Biol. 1982; 120:361–9.
25 Ochipa C, Rothi LJ, Heilman KM. Conceptual apraxia in Alzheimer's disease. Brain 1992;115(Pt 4):1061–71.
26 Heilman KM, Watson RT, Rothi LJG. Disorders of skilled movements: limb apraxia. in: Feinberg TE, Farah MJ, eds. Behavioral Neurology & Neuropsychology, second edition. New York: McGraw-Hill: 2003; 217–24.
27 Goldenberg G. Chapter 16 Apraxia. Handb Clin Neurol. 2008; 88:323–38.
28 Goldenberg G. Imitating gestures and manipulating a mannikin – the representation of the human body in ideomotor apraxia. Neuropsychologia. 1995;33:63–72.
29 Haaland KY, Harrington DL, Knight RT. Neural representations of skilled movement. Brain 2000;123:2306–13.
30 Hanna-Pladdy B, Heilman KM, Foundas AL. Ecological implications of ideomotor apraxia: Evidence from physical activities of daily living. Neurology. 2003;60:487–90.
31 Sundet K, Finset A, Reinvang I. Neuropsychological predictors in stroke rehabilitation. J Clin Exp Neuropsychol. 1988; 10:363–79.
32 Wetter S, Poole JL, Haaland KY. Functional implications of ipsilesional motor deficits after unilateral stroke. Arch Phys Med Rehabil. 2005;86:776–81.
33 Buxbaum LJ, Haaland KY, Hallett M, Wheaton L, Heilman KM, Rodriguez A, Gonzalez Rothi LJ. Treatment of limb apraxia: moving forward to improved action. Am J Phys Med Rehabil. 2008;87:149–61.
34 De Renzi E, Motti F, Nichelli P. Imitating gestures. A quantitative approach to ideomotor apraxia. Arch Neurol. 1980;37:6–10.
35 Poeck K. The clinical examination for motor apraxia. Neuropsychologia. 1986;24:129–34.
36 Zadikoff C, Lang AE. Apraxia in movement disorders. Brain. 2005;128:1480–97.38
37 Quencer K, Okun MS, Crucian G, Fernandez HH, Skidmore F, Heilman KM. Limb-kinetic apraxia in Parkinson disease. Neurology. 2007;68:150–1.
38 Stewart KC, Fernandez HH, Okun MS, Alberts JL, Malaty IA, Rodriguez RL, Hass CJ. Effects of dopaminergic medication on objective tasks of deftness, bradykinesia and force control. J Neurol 2009 [Epub ahead of print].
39 Landau WM, Mink JW. Is decreased dexterity in Parkinson disease due to apraxia? Neurology. 2007;68:90–1.
40 Goldenberg G, Hermsdorfer J, Glindemann R, Rorden C, Karnath HO. Pantomime of tool use depends on integrity of left inferior frontal cortex. Cereb Cortex 2007;17:2769–76.
41 Goldenberg G, Karnath HO. The neural basis of imitation is body part specific. J Neurosci. 2006;26:6282–7.
42 Fridman EA, Immisch I, Hanakawa T, Bohlhalter S, Waldvogel D, Kansaku K, Wheaton L, Wu T, Hallett M. The role of the dorsal stream for gesture production. Neuroimage. 2006;29:417–28.
43 Bohlhalter S, Hattori N, Wheaton L, Fridman E, Shamim EA, Garraux G, Hallett M. Gesture subtype-dependent left lateralization of praxis planning: an event-related fMRI study. Cereb Cortex. 2009;19:1256–62.
44 Hermsdorfer J, Goldenberg G, Wachsmuth C, Conrad B, Ceballos-Baumann AO, Bartenstein P, Schwaiger M, Boecker H. Cortical correlates of gesture processing: clues to the cerebral mechanisms underlying apraxia during the imitation of meaningless gestures. Neuroimage. 2001;14:149–61.
45 Muhlau M, Hermsdorfer J, Goldenberg G, Wohlschlager AM, Castrop F, Stahl R, et al. Left inferior parietal dominance in gesture imitation: an fMRI study. Neuropsychologia. 2005; 43:1086–98.
46 Pazzaglia M, Smania N, Corato E, Aglioti SM. Neural underpinnings of gesture discrimination in patients with limb apraxia. J Neurosci. 2008;28:3030–41.

47 Villarreal M, Fridman EA, Amengual A, Falasco G, Gerscovich ER, Ulloa ER, Leiguarda RC. The neural substrate of gesture recognition. Neuropsychologia. 2008;46:2371–82.
48 Heilman KM, Rothi LJ, Valenstein E. Two forms of ideomotor apraxia. Neurology. 1982;32:342–6.
49 Buxbaum LJ, Johnson-Frey SH, Bartlett-Williams M. Deficient internal models for planning hand-object interactions in apraxia. Neuropsychologia. 2005;43:917–29.
50 Damasio H, Grabowski TJ, Tranel D, Ponto LL, Hichwa RD, Damasio AR. Neural correlates of naming actions and of naming spatial relations. Neuroimage. 2001;13:1053–64.
51 Ebisch SJ, Babiloni C, Del Gratta C, Ferretti A, Perrucci MG, Caulo M, Sitskoorn MM, Romani GL. Human neural systems for conceptual knowledge of proper object use: a functional magnetic resonance imaging study. Cereb Cortex. 2007;17: 2744–51.
52 Catalan MJ, Ishii K, Honda M, Samii A, Hallett M. A PET study of sequential finger movements of varying length in patients with Parkinson's disease. Brain. 1999;122:483–95.
53 Lehericy S, Bardinet E, Tremblay L, Van de Moortele PF, Pochon JB, Dormont D, et al. Motor control in basal ganglia circuits using fMRI and brain atlas approaches. Cereb Cortex. 2006;16:149–61.
54 Wu T, Hallett M. A functional MRI study of automatic movements in patients with Parkinson's disease. Brain. 2005;128:2250–9.
55 Lotze M, Markert J, Sauseng P, Hoppe J, Plewnia C, Gerloff C. The Role of Multiple Contralesional Motor Areas for Complex Hand Movements after Internal Capsular Lesion. J Neurosci. 2006;26:6096–102.
56 Schaechter JD, Perdue KL. Enhanced cortical activation in the contralesional hemisphere of chronic stroke patients in response to motor skill challenge. Cereb Cortex. 2008;18: 638–47.
57 Kleist K. Untersuchungen zur Kenntnis psychomotorischer Bewegungsstörungen bei Geisteskranken. Klinkhardt, Leipzig, 1908.
58 Manschreck TC, Maher BA, Rucklos ME, Vereen DR. Disturbed voluntary motor activity in schizophrenic disorder. Psychol Med. 1982;12:73–84.
59 Gunther W, Gunther R, Eich FX, Eben E. Psychomotor disturbances in psychiatric patients as a possible basis for new attempts at differential diagnosis and therapy. II. Cross validation study on schizophrenic patients: persistence of a "psychotic motor syndrome" as possible evidence of an independent biological marker syndrome for schizophrenia. Eur Arch Psychiatry Neurol Sci. 1986;235:301–8.
60 Merriam AE, Kay SR, Opler LA, Kushner SF, van Praag HM. Neurological signs and the positive-negative dimension in schizophrenia. Biol Psychiatry. 1990;28:181–92.
61 Martin P, Tewesmeier M, Albers M, Schmid G, Scharfetter C. Investigation of gestural and pantomime performance in chronic schizophrenic inpatients. Eur Arch Psychiatry Clin Neurosci. 1994;244:59–64.
62 Ho BC, Andreasen NC, Nopoulos P, Arndt S, Magnotta V, Flaum M. Progressive structural brain abnormalities and their relationship to clinical outcome: a longitudinal magnetic resonance imaging study early in schizophrenia. Arch Gen Psychiatry. 2003;60:585–94.
63 Koch G, Ribolsi M, Mori F, Sacchetti L, Codeca C, Rubino IA, Siracusano A, Bernardi G, Centonze D. Connectivity between posterior parietal cortex and ipsilateral motor cortex is altered in schizophrenia. Biol Psychiatry. 2008;64:815–9.