**Treatment of Limb Apraxia: Moving Forward to Improved Action**

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**Abstract**

Limb apraxia is a common disorder of skilled purposive movement that is frequently associated with stroke and degenerative diseases such as Alzheimer Disease. Despite evidence that several types of limb apraxia significantly impact functional abilities, surprisingly few studies have focused on development of treatment paradigms. Additionally, although the most disabling types of apraxia reflect damage to gesture and/or object memory systems, existing treatments have not fully taken advantage of principles of experience known to affect learning and neural plasticity. We review the current state of the art in the rehabilitation of limb apraxia, indicate possible points of contact with the learning literature, and generate suggestions for how translational principles might be applied to the development of future research on treatment of this disabling disorder.

Key Words: Apraxia,Ideomotor Apraxia, Treatment, Rehabilitation

## Introduction

Apraxia is a common disorder of skilled, purposive movements. Praxis is mediated by a complex system that stores components of skilled movements, thus providing them a processing advantage (i.e., in terms of accuracy and response time) as compared with less-practiced movements. Although several types of apraxia have clear impact upon functional abilities, and are common consequences of stroke, Alzheimer Disease, and corticobasal degeneration, fundamental knowledge in a number of areas necessary to guide informed treatment is surprisingly lacking. There remains confusion about the definitions, distinctiveness, and mechanisms of various types of apraxia, and indeed, whether any have critical functional significance. In addition, although the most disabling types of apraxia reflect damage to systems involved in movement and gesture representation (i.e., *memory*), the nascent apraxia treatment literature has not taken advantage of principles of experience known to affect *skill learning*. The aim of this article is to review the current state of the rehabilitation of limb apraxia, and based on the learning and plasticity literature, generate suggestions for how translational principles might be applied to guide future treatment research.

## Definitions of apraxia

The term 'apraxia' was introduced by Steinthal [1]. While this word is derived from Greek and literally means *without action,* the term apraxia is used to describe a *decrease or disorder* in the ability to perform purposeful skilled movements. The greatest advance in the description and understanding of these disorders is contained in a series of papers written between 1900 and 1920 by Hugo Liepmann [2-4]. Liepmann described three forms of apraxia which, by virtue of his careful evaluations and

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discussions, brought about a 'paradigmatic shift' in our understanding of motor control. These three types were limb kinetic apraxia (also called melokinetic apraxia or innervatory apraxia), ideomotor apraxia, and ideational apraxia. To this triad Rothi, Heilman, Ochipa and colleagues [5-7] added another type, termed conceptual apraxia, and DeRenzi as well as Heilman [8, 9] described a fifth type now called dissociation apraxia.

In this manuscript we will focus on ideomotor apraxia (hereafter, IMA), for two reasons. First, as will be discussed, it is extremely common in stroke and degenerative disease (Alzheimer's disease and corticobasal degeneration). Second, it is increasingly recognized that IMA has important functional consequences, and the disorder is thus in need of continued critical investigation, particularly in the area of treatment.

IMA is usually diagnosed on the basis of spatiotemporal errors in the production of transitive (object-related) gesture pantomime to sight of objects, to command, and upon imitation of others [10-14]. Kinematic analyses have revealed that IMA patients pantomime skilled tool-use movements with abnormal joint angles and limb trajectories, and with uncoupling of the spatial and temporal aspects of movement [13]. Spatiotemporal errors persist to a lesser degree with actual tool use [15, 16]. The deficit is not restricted to meaningful movements, and has also been observed in meaningless postures [17-19] and sequences [20, 21]. IMA is also associated with cognitive deficits in declarative knowledge of the action appropriate to objects [22], impairments in mechanical problem-solving [23], deficits in motor planning [21, 24-26], and difficulty learning new gestures [27, 28]. Testing for IMA frequently includes pantomiming to command of transitive (familiar actions with objects, e.g., brush teeth) and intransitive (symbolic movements without objects, e.g., sign for crazy) movements, imitation of the examiner performing transitive, intransitive,

and novel meaningless movements, and gesture in response to seeing and holding actual tools, as well as the objects upon which tools act.

Several investigators have distinguished between IMA with impaired gesture recognition ("representational" IMA) and IMA with intact recognition ("dynamic" IMA; [11, 29, 30]. In representational IMA, inability to discriminate correctly from incorrectly performed meaningful object related hand movements correlates strongly with ability to produce the same movements, suggesting that the same representations are likely to underlie both [31]. Additionally, representational (but not dynamic) IMA patients are significantly more impaired when producing object-related than symbolic, non-object related movements [32]. This in turn suggests that the damaged system underlying representational IMA is specialized for movements related to skilled object use.

**The Functional Implications of Limb Apraxia: Does Limb Apraxia Matter in the Real World?**

Historically, most clinicians and researchers believed that limb apraxia had little or no real world implications [4, 10, 33-35]. This is emphasized by DeRenzi, who wrote, "…apraxia rarely appears in everyday situations and spontaneous motor behaviour, predominantly emerging when gestures are produced out of context as a purposeful response to an artificial request." Although not specified, it appears that this view was particular to IMA and stemmed from the notion that apraxia was present when pantomimes to command and imitation were tested but improved when the use of actual objects were examined.

It is now widely believed that IMA impairs real world functioning, but there are still remarkably few studies demonstrating such a relationship. In addition, most studies to date are fraught with problems. First, these studies usually do not rule out the

influence of all other factors, such as hemiparesis. They commonly compare the performance of apraxic and nonapraxic patients with left hemisphere damage [36-41], but relative to nonapraxics, apraxics are often more impaired in other domains, such as language and sensory and motor skills. Therefore, it is difficult to know if limb apraxia is the *best* predictor of functional skills. Second, apraxics typically have larger lesions than patients without apraxia, and those lesions more frequently damage the left parietal and frontal regions [42] that are also important for many other cognitive functions that could again confound the findings. Regression approaches have been used in order to evaluate the unique impact of various factors including limb apraxia on activities of daily living [41, 43-45], in some cases after controlling statistically for factors such as lesion size, primary motor deficits, and/or other cognitive deficits. However, these studies usually suffer from statistical problems related to a small number of subjects relative to the number of predictors examined.

Another problem in efforts to understand the influence of apraxia on disability is the use of a wide variety of functional measures, including object use [46, 47], performance-based measures of activities of daily living [36, 37, 39, 41, 43, 48, 49], and caregiver or patient report of daily functioning [39, 44, 45, 50]. These outcome measures vary in complexity from isolated object use, such as brushing teeth [51], to simulated activities of daily living, such as picking up a bean with a spoon [38, 39, 41], to instrumental activities of daily living, such as eating a meal [36], dressing [49, 52], preparing food [43, 48, 53-55] or changing batteries in a recorder [37]. It is common in performance-based studies to use instruments that do not have demonstrated reliability; thus, validity is frequently demonstrated only in the context of the specific study. In addition, there are significant problems with obtaining

reliable measures of these skills because the tasks are usually quite complex and the number of possible errors is large. Furthermore, because performance-based tasks are dependent upon a great number of cognitive abilities, patients may be impaired for different reasons [56, 57].

Taken together, these problems in the literature suggest that future studies must 1) examine the relationship of different types of limb apraxia to real world functioning (activities of daily living and instrumental activities) of various kinds; and 2) utilize sufficiently large groups of patients to provide sufficient power for analysis. It is also reasonable to consider at least two different approaches for subject recruitment. The first approach examines well- characterized patients with unilateral focal lesions, and the second approach examines a broader range of patients with and without limb apraxia without regard to lesion location. The latter approach may yield patients more broadly representative of the patients typically seen in the clinic.

Finally, some of the most innovative work in this area attempts to identify cognitive mechanisms that are associated with ideomotor limb apraxia and potentially with the resulting deficits in real world functioning (see [58] for a review). These cognitive processes include mechanical problem solving [46], sequence planning and organization [21], the ability to develop and/or retrieve optimal motor programs [13], knowledge of *how* to manipulate an object [22, 25, 59], and knowledge of optimal hand position when real world objects provide minimal cues [25, 39].

**Treatment of Limb Apraxia**

A recent review of the literature on treatment of limb apraxia yielded reports of ten treatment approaches, many of which were single case studies. Methods reported were varied and can be summarized as follows:

Multiple Cues. The multiple cues treatment method was developed in 1991 by Maher, Rothi & Greenwald [60] for a 55 year old male with chronic ideomotor apraxia and intact gesture recognition. It focused on treatment of gestures using presentation of multiple cues, including tools, objects, visual models, and feedback. Errors were corrected using imitation and physical manipulation. As performance improved, cues were systematically withdrawn. The individual participated in one hour sessions daily for two weeks. The multiple cues method resulted in positive effects, with treated gestures showing some lasting improvement. Generalization to untreated gestures was not assessed.

Error Reduction. In an attempt to define the active components of the multiple cues method, Ochipa and colleagues [61, 62] conducted a treatment study aimed at treating specific error types. Two males, 44 and 66 years old, with chronic Broca's aphasia and ideomotor apraxia but preserved gestural recognition participated in the treatment. Treatment duration and intensity varied, with the 44 year old receiving treatment four times per week (n=44 sessions) and the 66 year old receiving treatment two times a day twice a week (n=24 sessions). The goals of treatment consisted of reduction of external configuration, movement, and internal configuration errors, depending upon the error types exhibited by the individual. Reduction of external configuration errors involved training the individual to correctly orient his hand to objects, while reduction of internal

configuration errors involved positioning of hand and fingers to accommodate a tool. Movement errors were reduced through verbal descriptions to guide joint movement while gesturing.  Only one error type was addressed at a time and feedback was only provided about the error type being trained.  Error reduction treatment resulted in a significant and lasting improvement on treated gestures for both individuals.  However, no generalization to untreated error types or gestures was noted.  Improvements were noted to continue at 2 week post treatment follow-up, but later follow-ups were not performed.

Six Stage Task Hierarchy.  The task hierarchy method was developed by Code & Gaunt [63] who studied in an individual with severe chronic aphasia, ideomotor apraxia and ideational apraxia. This six stage task hierarchical treatment for limb apraxia was a modification of an Eight-Step Continuum used for treatment of apraxia of speech [64].  The Code and Gaunt method involves requiring the patient to produce target words and signs in various combinations and in concert with the therapist in response to a therapist model or in response to a picture elicitation. The patient participated in 45 minute sessions once weekly for 8 months.  The six stage task hierarchy method resulted in acquisition of trained signs and a non-significant trend toward improvement in untrained signs during treatment.   Maintenance of effects was not formally tested, but the authors provide anecdotal reports of the patient's continued use of signs in group treatment sessions. Treatment did not impact limb apraxia.

Conductive Education.   The conductive education method was developed by Pilgrim & Humphreys [65] for a patient with head injury and chronic unimanual apraxia of the non-dominant limb. Treatment focused on a task-analysis of the movements and articulation

of goal-directed tasks.  The treatment began with physical manipulation plus verbalization of task elements (e.g., "reach the beaker, clasp the beaker, carry to my lips, drink, stop") and those cues were systematically withdrawn as performance improved. There were daily 15 minute sessions for 3 weeks. The conductive education method improved this patient's performance on treated items as compared to untreated items. There was no generalization to untreated objects.  Maintenance of effects were not assessed.

Strategy Training.  The strategy training method was developed as a compensatory technique for individuals with ADL (Activities of Daily Living) impairment secondary to apraxia.  This method was first described in the literature in a study of 33 individuals with apraxia secondary to left hemisphere stroke [66]. The patients were trained on three ADLs, and the specific method of treatment was chosen based on each individual's performance in baseline testing of those tasks.  A similar strategy training method utilizing 5ADLs was studied in another group of 56 individuals with left hemisphere stroke and subsequent apraxia. Both strategy training approaches focused on the use of internal compensatory strategies (ie, self-verbalization) and external compensatory strategies (ie, use of pictures) to maximize independence.  The duration and intensity of treatments varied among individuals in both studies. Strategy training resulted in positive outcomes across all domains measured (effect sizes .37 for the ADL tasks and .47 for the Barthel ADL index;  both significantly greater than for patients receiving usual occupational therapy treatment), but the improvements were not lasting [67, 68].  In the final study in this series, there was an additional finding of interest; namely, maintenance of gains in trained tasks at 5-month followup. . Transitive/Intransitive Gesture Training.

The transitive/intransitive gesture training method was investigated by Smania and colleagues [69] in 22 individuals at least two months post onset of a left hemisphere stroke with subsequent ideomotor limb apraxia. Treatment focused on the training of transitive and intransitive gestures. Transitive gesture training consisted of three phases in which the individual was (1) shown use of common tools, (2) shown a static picture of a portion of the transitive gesture and asked to produce the pantomime, and (3) shown a picture of common tool and asked to produce the associated gesture. The intransitive gesture training also consisted of three phases in which the individual was (1) shown two pictures, one illustrating a context and the other showing related symbolic gesture, and asked to reproduce the gesture (2) shown the context picture alone, and asked to reproduce the gesture (3) shown a picture of a different but related contextual situation and asked to reproduce the gesture. Fifty-minute treatment sessions were administered three times per week for approximately 10 weeks, with the number of total treatment sessions ranging from 30-35. A control group was administered aphasia treatment only for a similar intensity and duration. Results indicated there was a difference between the two groups post-treatment, with the gesture training method resulting in improved performance on an IMA test ($U=69.00$, $p= .016$), a gesture comprehension test ($U=64.00$, $p= .018$) and an ADL questionnaire ($U=53.50$, $p<.01$). Importantly, patients and caregivers reported more independence in ADLs following treatment. Nine patients showed maintenance of gains at two months post treatment.

"Rehabilitative Treatment". Smania and colleagues [70] reported a positive outcome with a so-called rehabilitative treatment. It was noted that the treatment was "devised to treat a wide range of gestures and to reduce several types of praxic errors…" and that it "used

different contextual cues in order to teach patients how to produce the same gesture under different contextual situations" (p. 2052). Thus, although details were not provided, the treatment appears substantially similar to the one previously reported by this group [69]. Forty-one post-acute left hemisphere stroke patients with limb apraxia (either ideational or IMA – not defined) were assigned randomly to treatment or no-treatment groups. The no-treatment group received aphasia therapy. Patients attended 30 fifty-minute sessions over the course of 10 weeks. Although the groups were equivalent in ADL performance, apraxia scores, and ADL questionnaire scores prior to treatment, they differed significantly on these measures after treatment, both immediately and after a 2 week delay.

Errorless Completion + Exploration Training. The errorless completion/exploration training method was developed by Goldenberg & Hagmann [51] for 15 individuals with IMA (impairment on gesture imitation and gesture to sight of objects) who were on average 6.1 weeks post onset of a left hemisphere stroke with subsequent aphasia and severe limb apraxia. The errorless completion method utilized physical manipulation during ADLs, simultaneous demonstration of ADL by the examiner and imitation by the patient, and copy by the patient after demonstration during performance of three ADLs. The exploration training method directed attention to functional significance of details and critical features of action but did not incorporate direct practice of actions with actual objects. These two methods were combined and treatment was applied to one ADL at a time daily for 20-40 minutes for 2-5 weeks. Combined errorless completion/exploration training resulted in positive effects that were lasting for individuals who remained active in ADLs at home. A subsequent study was conducted by Goldenberg, Daumuller, &

Hagmann [37] comparing these two methods in 6 individuals with left hemisphere stroke and subsequent chronic aphasia and limb apraxia. Each treatment type was applied on a different pair of ADLs. The exploration training method had no effect. The errorless completion method yielded a positive and lasting effect. When different objects were used to test ADL, however, the rate of errors increased, and were comparable to untrained gestures. Therefore, there was no evidence of generalization.

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Table 1 provides a summary of the 10 apraxia treatment approaches discussed in the literature to date. Several trends are worth noting. First, apraxia type is frequently poorly characterized. For example, although gesture recognition is clearly an important index of the integrity of gesture representations (which in turn, may have important implications for rehabilitation strategies), recognition testing is usually not performed. Second, while some studies provide data on treatment effects and generalization to untreated items, they are more sparse with regards to treatment effect upon degree or nature of limb apraxia, maintenance of treatment effect, and impact of treatment upon ADLs. Third, the duration and intensity of treatment differs within and across studies making it difficult to determine the active components of the treatment. Fourth, the length of time between termination of treatment and follow-up differs across studies, which renders it difficult to compare the lasting effects of treatment upon limb apraxia or ADLs. Finally, methods such as the nature of the feedback or correction are commonly underspecified in these reports if described at all, making replication in additional subjects nearly impossible.

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Despite these issues, the data consistently suggest that intervention yields a treatment effect. Furthermore, in the cases where it is reported, there is indication of maintenance of treatment effects, and impact upon nature/degree of limb apraxia as well as upon ADL facility. Thus, it appears that the evidence based on these 10 Phase I studies suggests that limb apraxia is amenable to treatment. However, according to Robey [71], the purpose of Phase I research is to develop hypotheses, protocols, and methods, establish safety and activity, determine the best outcome measures, identify responders vs. nonresponders, determine optimal intensity and duration, and determine why the treatment is producing an effect [71]. Little of this information is found in these 10 reports and thus, we must continue to promote systematic inquiry until the objectives of Phase I research are satisfied for limb apraxia.

Evidence suggests that 9 of the 10 treatments reported in the literature yielded a treatment effect. However, only 4 of these 9 treatments resulted in generalization. Since the ultimate goal of rehabilitation is the use of acquired skill in the individual's natural environment, it is important to consider why certain treatments resulted in generalization while others did not.

Nadeau et al [72] recently identified seven treatment attributes that may contribute to generalization in language rehabilitation: 1) Intrinsic: application of knowledge acquired in therapy; 2) Cross function: development of knowledge that can be applied to multiple tasks; 3) Extrinsic: acquisition of a technique that can be applied outside of treatment to rebuild function (requires motivation); 4) Mechanistic: training of key brain resources (i.e., working memory capacity, distributed concept representations, intentional bias); 5) Substrate mediated: development of a critical mass of skill needed to further the

therapeutic process; necessary for intrinsic/extrinsic mechanisms to operate; 6)

Contextual: learning environment resembles retrieval environment; 7) Socially mediated:

restoration of social context and change in perception regarding roles to promote activity

in the environment.

Unfortunately, in the realm of apraxia rehabilitation, there is no clear relationship

between these putatively critical mechanisms and treatment generalization.  All 4

treatments that generalized included cross function and extrinsic mechanisms, but some

treatments that did not generalize included these mechanisms as well.  Similarly, some

treatments that were mechanistic generalized while others did not.  Of the 3 treatments

that incorporated home practice (contextual mechanism), none resulted in generalization.

In addition, based on the available information, there appears to be no consistent

relationship between duration/intensity/type of items trained and generalization of results.

These equivocal results suggest that while limb apraxia may be amenable to treatment,

systematic investigation of factors promoting generalization is still essential.

## Motor Learning and Motor Plasticity: An Overview

The learning of skilled movements is called procedural learning, and its

underlying mechanisms and neuroanatomical correlates differ from declarative

learning[73]).  In the following sections, we will provide a brief introduction to the

literature on motor learning and plasticity, with an eye toward applying this literature to

the study of IMA.

Some of the actions typically assessed in motor learning studies differ in complexity

and/or meaningfulness from the skilled actions that comprise praxis. A number of motor

learning studies, however, have used complex, learned actions that are arguably akin to

what we commonly term "praxis movements". Other motor learning studies have examined complex spatiomotor transformations that may have relevance to spatial coding of complex action. Thus, it is important to carefully examine the motor learning literature for points of possible convergence with the study of learning in apraxia.

<u>Neuroanatomical Considerations</u>.

The primary motor cortex, in particular,exhibits a great deal of plasticity as a function of motor learning . Using transcranial magnetic stimulation, a number of investigations have mapped the degree and extent of excitability of individual muscles on the scalp surface. Body parts that are used more have a larger representation, and this representation shrinks if the body part is not used (e.g., [74] ). Based on neuroimaging paradigms, a variety of brain regions have been demonstrated to be active depending on the task and the stage of motor learning; in nearly all cases, however, there is activation of primary motor cortex [75].

In most neuroimaging studies, cerebellar activation is evident in the learning phase and declines when the movement is learned. This certainly indicates a role in learning, and in particular suggests that the cerebellum may critical for developing the movement representation but not storing it. The frontal and parietal lobes are also clearly involved in motor learning, but the precise structures involved in early versus later stages of learning are unclear. For example, a frontal to parietal shift in activation has been observed as a sequence task is learned [76], a prefrontal to premotor, posterior parietal, and cerebellar shift in activation has been observed in force adaptation learning [77]. On the other hand, several studies using motor sequence tasks and at least one using a rotational learning task have demonstrated that parietal activation is associated with *early* stages of

learning, with greater cerebellar and/or premotor involvement in later stages [78-81]. At this juncture, we may conclude that the parietal regions so frequently lesioned in apraxic patients are clearly important in aspects of skill learning.

There is evidence that perilesional plasticity may play a role in recovery of function after stroke. It has been shown, for example, that after finger tracking movements, paretic stroke patients improved in finger pointing accuracy and grasp and release capabilities [82]. These functional gains were accompanied by increased fMRI activations in sensorimotor areas of the lesioned hemisphere, and diminished activations in the intact hemisphere (and see [83]).

At least one previous account has attributed preserved function in apraxia to preservation of non-dominant (right) hemisphere fronto-parietal regions involved in praxis function [84]. On the other hand, non-dominant hemisphere plasticity changes have been demonstrated to be maladaptive in recovery from aphasia [85], and may plausibly be similarly counterproductive in apraxia recovery. Additional investigations are required to shed light on this question.

Implicit and Explicit Skill Learning. A considerable literature attests to important differences between skill learning that is unavailable to conscious experience (implicit learning) and that which is cognitively accessible. Ideally, the study of learning in apraxia could tap into this large body of evidence to support the framing of hypotheses and predictions. However, one critical concern is that it is not clear whether to align praxis learning with explicit or implicit knowledge, or both. The types of complex skills that fall under the rubric of "praxis" are not typically verbalized, yet they can be made explicit under certain circumstances. It is perhaps most reasonable to begin with the

hyptothesis that praxis learning is more similar to implicit procedural learning than to learning of declarative information. Specific investigations that test predicted patterns of results based on this hypothesis need to be performed.

A typical exploration of skill learning entails the use of serial reaction time tasks (SSRT). Participants are usually faster to perform sequences of key presses that are repeated throughout and experiment, even though they are unaware of the repetition. This is an example of implicit learning. With additional practice, the sequence can frequently be specified; in this case, the learned information has become declarative as well as procedural. Performance gets even better at this stage, but the subject's strategy can change since the stimuli can be consciously anticipated.

Honda et al. [86] examined the dynamic involvement of different brain regions in implicit and explicit motor sequence learning using a SRTT and Positron Emission Tomography. During the implicit learning phase, when the subjects were not aware of the sequence, improvement of the reaction time was associated with increased activity in the contralateral primary sensorimotor cortex. Explicit learning, reflected by a positive correlation with correct recall of the sequence, was associated with increased activity in the posterior parietal, precuneus and premotor cortices bilaterally, supplementary motor area predominantly in the left anterior part, left thalamus, and right dorsolateral prefrontal cortex. In a study by Grafton et al. [87], there was activation of the contralateral primary motor cortex, supplementary motor area and putamen in an implicit learning task, and activation of ipsilateral dorsolateral prefrontal cortex and premotor cortex as well as bilateral parietal cortex during explicit learning.

In summary of the studies of motor learning in healthy subjects, it appears that multiple structures in the brain are involved, and that differential involvement arises at different stages.  The primary motor cortex and cerebellum (and sometimes parietal cortex) are active early and at least the former appears to play a role in implicit learning. Premotor and parietal cortical areas are active later and appear to play a role in explicit learning, perhaps in part by storage of the sequence.  This concept is supported by the observation that the premotor and parietal areas increase their activation in proportion to the length of a sequence performed from memory [88].  The relation to regions that when damaged cause apraxia is obvious.

**Principles of motor learning as they may be relevant to apraxia rehabilitation**

Several basic principles of motor learning have been explored in other aspects of motor control rehabilitation, but have received relatively little attention in the study of IMA.

Internal Models of Movement.  The motor system in healthy participants is adept at developing internal models that represent the kinematics (geometry and speed) and dynamics (forces) of a motor task.  Forward models calculate the movements resulting from a given pattern of force (dynamics) or the limb positions resulting from a given pattern of joint rotation (kinematics). Inverse models compute the muscle forces or movements needed to reach a visual goal or goal posture [89].  The learning (that is, practice-dependent reduction of error) of kinematic and dynamic internal models appears to be separable, and may be disrupted by different brain lesions [90].

Several models of motor performance distinguish a mode of action concerned with planning, learning, and motor prediction, and another specialized for motor

execution and control (see [91]). One influential account, for example, distinguishes semantic representations necessary for motor learning and planning from pragmatic representations subserving the control and execution of action [92]. The planning mode has been proposed to generate movement parameters by way of internal models. The execution mode, in contrast, emphasizes on-line control that is sensitive to current environmental conditions.

Recent investigations provide indirect evidence that patients with IMA may be impaired in learning and/or accessing internal models of movement. Motor imagery has been proposed by several investigators to serve as a proxy for motor planning in the absence of execution [93-97]. Sirigu et al. [98] and Buxbaum, Johnson-Frey, & Bartlett-Williams [25] demonstrated that participants with left parietal lesions and IMA were impaired in motor imagery. In contrast, these patients perform well on tasks more reliant upon on-line control, such as reaching and grasping with visual feedback [13, 26]. The nature and extent of putative deficiencies in generating and accessing internal models are being explored in several of the authors' laboratories using visuomotor and force-field adaptation paradigms borrowed from the motor control literature. Such studies are an important step in developing rehabilitation paradigms targeted at relearning of appropriate internal models.

Practice Schedules. It is clear that practice benefits motor learning, but optimal types and schedules of training remain unclear, and may vary across tasks. In most motor tasks, practice that is distributed over (rather than massed in) time appears to result in optimized learning and retention [99]. In learning new sensorimotor transformations, rest breaks between sessions is of benefit, and may allow for the consolidation of newly

acquired internal models [100]. It is also frequently beneficial to train a variety of similar movements to encourage so-called contextual interference. Shea & Kohl [101], for example, found in a force-learning task that filling the inter-test-trial interval with related motor tasks significantly improved retention. Ollis et al. [102] demonstrated that learning a variety of knot-tying movements enhances learning, even for novices practicing complex knots. There is some suggestion, however, that the benefit of contextual interference may be task specific [103]. Additionally, a contextual interference manipulation in patients with Parkinson's disease did not enhance learning, suggesting that successful learning strategies in healthy controls may not generalize to brain-damaged patients [104]. It is also of interest to note that training of items that share many features with other items is disruptive and not beneficial in the lexical-semantic domain [105, 106]. As object-related praxis movements are complex skills with close ties to semantic knowledge [22], it remains unclear whether training on shared or distinctive motor features, semantic features, or both will be optimal in praxis rehabilitation.

The Role of Feedback and Error Correction. Feedback and knowledge of results frequently facilitate motor skill acquisition. Recent investigations have probed the types of feedback that may be most optimal, and here, as in other areas of motor learning, the answer is unclear. For example, varying the movement component about which feedback is provided may benefit simple skill learning, but disrupt more complex motor skill learning [107].

In the domain of cognitive implicit learning, error may be disruptive. As a result, rehabilitation paradigms have evolved that emphasize "errorless learning". Performance may be "shaped" by minimizing opportunities to make errors and by

rewarding successful performance. In contrast, in the domain of simple movements, such as reaching under visual guidance, performance appears to be "tuned" by the opportunity to correct error (e.g., [108]). The role of error in these different types of learning remains poorly understood; moreover, it is not clear whether and where praxis movements may fall on this continuum.

Hemiparetic stroke patients without IMA are able to adapt to forces applied perpendicular to the moving hemiparetic arm [109] as well as to spring-like forces that act against movement [110] when they receive feedback about error. This suggests that hemiparetic patients can use error to adjust internal models of movement to achieve an intended goal [109, 111]. It has also been suggested that perception of gross errors may enhance the recovery process in stroke [112].

Unfortunately, patients with apraxia frequently exhibit some degree of anosognosia, or unawareness of deficit. They may recognize that they are unable to move correctly, but fail to recognize the extent of deficit, or may attribute it to clumsiness, memory loss, or intellectual decline [113]. It may be necessary to provide augmented feedback about error. Fortunately, a number of virtual reality paradigms under recent development present promising opportunities to do just this (see [114]).

Paradigms using robot-assisted devices (e.g., [115, 116]) can launch correct actions based on electromyographic activity that is associated with the intention to act. Thus, preparatory activity is linked to a correct response, and errors are prevented. This would seem to be an extremely useful feature. However, given that IMA patients may fail at the level of planning and intention, it is not obvious that robot-assisted therapies will be

helpful in the rehabilitation of IMA, unless the correct performance of an act can feed back to augment the putatively deficient internal model.

## V. Summary and Recommendations

There are several different subtypes of apraxia, resulting in some cases from damage to differing underlying neural systems. Ideomotor, ideational, and conceptual apraxia all appear to impact real world-functioning. Development of appropriate treatment paradigms is clearly needed. A review of the apraxia treatment literature to date reveals that the field is in the early stages of efforts to develop effective treatments, and that most studies have relied upon individual case experimental designs. Additional problems include poor specification of patient characteristics, including incidence and of aphasia, variable criteria for diagnosing apraxia, vague description of treatments applied, unequal application of treatment even within a given study, and absence of information about treatment generalization. Most central to the aims of this review, principles from the existing motor learning literature have not yet informed the development of treatment studies.

The motor learning literature identifies several principles that may benefit the rehabilitation of apraxia, if appropriately applied. For example, distributed practice of the target task appears to improve learning and retention. Creating contextual interference by interleaving the target task with other similar tasks may aid [117] or disrupt (c.f. [106]) generalization. Feedback of results should be provided. Intensity of practice is also clearly important.

One potential strategy in development of apraxia treatment studies is to systematically vary one treatment feature at a time (e.g., massed versus distributed

practice schedule, similarity or distinctiveness of items, presence or absence of feedback, shaping of easier to harder items to maximize success, as opposed to allowing errors) while systematically holding the others constant.  This is clearly preferable from the perspective of clarifying the features of the training that are critical.  On the other hand, there is unfortunately very little to suggest how these motor learning principles are best parameterized (e.g., in terms of strength, duration, or intensity) or applied to the treatment of IMA.  Another strategy, then, is to attempt to obtain a beneficial effect by "loading" the treatment on all of the motor learning features that may plausibly be beneficial, and if an effect is obtained, follow up with studies designed to disentangle the critical versus non-critical factors.  Of course, if no training benefit is observed, then it would be unclear which features were applied incorrectly, and this in turn would necessitate a return to the "one feature at a time" strategy.

As an exercise, at least, we can imagine a treatment study based on the strategy of "loading" the treatment with principles derived from the motor learning literature.  One might predict, for example, that deficits in naturalistic action may be most successfully treated by providing an intense but distributed schedule of practice on a variety of targeted naturalistic tasks, interleaved with other similar tasks.  Principles of shaping might be predicted to be beneficial, such that easy tasks are used early in training and harder tasks later in training such that performance is successful.  On the other hand, opportunities to correct errors should be provided should they arise.

The apraxia literature also provides some hints about other factors that may impact rehabilitation.  A recent learning study from the lab of one of the authors [118] assessed the role of the "affordances" of unfamiliar objects – in this case, the degree to

which the unfamiliar objects signal the actions associated with them by virtue of their shape – in learning new object-related gestures. Patients with IMA, but not age- and education-matched non-apraxic left hemisphere stroke patients, were significantly better at learning new gestures when the gestures were highly afforded by their associated objects. This "affordance benefit" could clearly be exploited in the design of future treatment studies by focusing early treatment on high affordance objects.

Tasks trained early in a shaping procedure may be designed to be "easy" in a number of other critical ways. Clearly, these early tasks should have few steps. Arrays should be simple, with few visual elements, and no distractor (task-irrelevant) objects. Spatial consistency of object placement from trial to trial is also critical [119]. These task and object features may all be titrated gradually such that tasks higher up in the shaping hierarchy are increasingly complex with respect to these features.

Treatments must be applied identically across all treated subjects. Treated and untreated patients must either be matched across a large number of putatively important variables, including lesion size, severity of cognitive and language deficits, apraxia type (and subtype) and severity, and motor impairment, or sample sizes must be large and patients randomly assigned to treated and untreated groups. Efficacy of treatment should be assessed by applying pre- and post-treatment measures of caregiver burden, performance of ADLs, and/or functional independence that are different from the trained tasks.

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REFERENCES

1.    Steinthal P: Abriss der sprachwissenschaft. Berlin, 1871.

2.    Liepmann H: Das krankheitsbild der apraxie. Monatsschr Psychiatr Neurol
      1900;8:102-132,182-197.

3.    Liepmann H: Die linke hemisphare und das handeln. Munchener Medizinische
      Wochenschrift 1905;40; 49(2322-2326; 2375-2378).

4.    Liepmann H: Apraxie. Ergebnisse der Gesamten Medizin 1920;1:516-543.

5.    Hanna-Pladdy B, Rothi LJG: Ideational apraxia: Confusion that began with
      Liepmann. Neuropsychol Rehabil 2001;11(5):539-547.

6.    Ochipa C, Rothi LJG, Heilman KM: Ideational apraxia:  A deficit in tool selection
      and use. Annals of Neurology 1989;25:190-193.

7.    Ochipa C, Rothi LJG, Heilman KM: Conceptual apraxia in Alzheimer's disease.
      Brain 1992;115:1061-1072.

8.    DeRenzi E, Faglioni P, Sorgato P: Modality-specific and supramodel mechanisms
      of apraxia. Brain 1982;105:301-312.

9.    Heilman KM, Gonzalez Rothi LJ: Apraxia, In: Heilman KM, valenstein E, (eds).
      Clinical Neuropsychology. 3rd ed. New York, Oxford University Press;
      1993:141-150.

10.   DeRenzi E, Motti F, Nichelli P: Imitating gestures:  A quantitative approach to
      ideomotor apraxia. Achives of Neurology 1980;37:6-10.

11.   Heilman KM, Rothi LJ, Valenstein E: Two forms of ideomotor apraxia.
      Neurology 1982;32:342-346.

12.  Goldenberg G: Imitating getures and manipulating a mannikin-the representation of the human body in ideomotor apraxia. Neuropsychologia 1995;33(1):63-72.

13.  Haaland KY, Harrington DL, Knight RT: Spatial deficits in ideomotor limb apraxia: A kinematic analysis of aiming movements. Brain 1999;122:1169-1182.

14.  Foundas A, Maccauley B, Raymer A, Maher L, Rothi L, Heilman K: Ideomotor apraxia in Alzheimer's disease and left hemisphere stroke:  Limb transitive and intransitive movements. Neuropsychiatry, Neuropsychology, and Behavioral Neurology 1999;12(161-166).

15.  Poizner H, Clark M, Merians A, Macauley B, Gonzalez Rothi L, Heilman K: Joint coordination deficits in limb apraxia. Brain 1995;118:227-242.

16.  Poizner H, Mack L, Verfaellie M, Rothi LJG, Heilman KM: Three-dimensional computergraphic analysis of apraxia:  Neural representations of learned movement. Brain 1990;113:85-101.

17.  Goldenberg G, Hagmann S: The meaning of meaningless getures: a study of visuo-imitative apraxia. Neuropsychologia 1997;35:333-341.

18.  Weiss PH, Dohle C, Binkofski F, Schnitzler A, Freund HJ, Hefter H: Motor impairment in patients with parietal lesions: Disturbances of meaningless arm movement sequences. Neuropsychologia 2001;39:397-405.

19.  Rumiati R, Weiss P, Tessari A, et al.: Common and differential neural mechanisms supporting imitation of meaningful and meaningless actions. Journal of Cognitive Neuroscience 2005;17(9):1420-1431.

20. DeRenzi E, Faglioni P, Lodesani M, Vecchi A: Performance of left brain-damaged patients on imitation of single movements and motor sequences. Frontal and parietal-injured patients compared. Cortex 1983;19:333-343.

21. Harrington DL, Haaland KY: Motor sequencing with left hemisphere damage: Are some cognitive deficits specific to limb apraxia? Brain 1992;115:857-874.

22. Buxbaum LJ, Saffran EM: Knowledge of object manipulation and object function: Dissociations in apraxic and non-apraxic subjects. Brain and Language Under Review 2002;82:179-199.

23. Spatt J, Bak T, Bozeat S, Patterson K, Hodges J: Apraxia, mechanical problem solving and semantic knowledge: Contibutions to object usage in corticobasal degeneration. Journal of Neurology 2002;249:601-608.

24. Clark M, Merians AS, Kothari A, et al.: Spatial planning deficits in limb apraxia. Brain 1994;117:1093-1106.

25. Buxbaum LJ, Johnson-Frey SH, Bartlett-Williams M: Deficient internal models for planning hand-object interactions in apraxia. Neuropsychologia 2005;43(6):917-929.

26. Jax SA, Buxbaum LJ, Moll AD: Deficits in movement planning and intrinsic coordinate control in ideomotor apraxia. J Cogn Neurosci Dec 2006;18(12):2063-2076.

27. Gonzalez Rothi LJ, Heilman KM: Ideomotor apraxia: Gestural learning and memory, In: Roy EA, (ed). Neuropsychological studies in apraxia and related disorders. New York, Oxford University Press; 1985:65-74.

28. Faglioni P, Basso A, Botti C, Aglioti S, Saetti C: Gestural learning in apraxia, In: Jeannerod M, (ed). Attention and performanc XIII. Hillsdale (NJ), Lawrence Erlbaum; 1990:837-856.

29. Buxbaum LJ: Ideomotor apraxia: A call to action. Neurocase 2001;7:445-458.

30. Buxbaum LJ, Giovannetti T, Libon D: The role of the dynamic body schema in praxis: evidence from primary progressive apraxia. Brain and Cognition 2000;44:166-191.

31. Buxbaum LJ, Kyle KM, Menon R: On beyond mirror neurons: internal representations subserving imitation and recognition of skilled object-related actions in humans. Brain Res Cogn Brain Res Sep 2005;25(1):226-239.

32. Buxbaum LJ, Kyle K, Grossman M, Coslett HB: Left inferior parietal representations for skilled hand-object interactions: Evidence from stroke and corticobasal degeneration. Cortex In Press.

33. Geschwind N: Disconnection syndromes in animals and man. Brain 1965;8:237-294, 585-644.

34. Kimura D: Translations from Liepmann's Essays on Apraxia. 506 ed. London, University of Western Ontario, 1980.

35. Poeck K: The clinical examination for motor apraxia. Neuropsychologia 1986;24(1):129-134.

36. Foundas AL, Macauley BL, Raymer AM, Maher LM, Heilman KM, Roth LJG: Ecological implications of limb apraxia: Evidence from mealtime behavior. Journal of the International Neuropsychological Society 1995;1:62-66.

37.     Goldenberg G, Daumuller M, Hagmann S: Assessment and therapy of complex activities of daily living in apraxia. Neuropsychological Rehabilitation 2001;11(2):147-169.

38.     Sunderland A, Bowers MP, Sluman SM, Wilcock DJ, Ardron ME: Impaired dexterity of the ipsilateral hand after stroke and the relationship to cognitive deficit. Stroke May 1999;30(5):949-955.

39.     Sunderland A, Sluman SM: Ideomotor apraxia, visuomotor control and the explicit representation of posture. Neuropsychologia 2000;38:923-934.

40.     van Heugten CM, Dekker J, Deelman BG, Stehmann-Saris JC, Kinebanian A: Rehabilitation of stroke patients with apraxia: the role of additional cognitive and motor impairments. Disability and Rehabilitation 2000;22(12):547-554.

41.     Wetter S, Poole JL, Haaland KY: Functional implications of ipsilesional motor deficits after unilateral stroke. Arch Phys Med Rehabil Apr 2005;86(4):776-781.

42.     Haaland KY, Harrington DL, Knight RT: Neural representations of skilled movement. Brain 2000;123:2306-2313.

43.     Donkervoort M, Dekker J, Deelman B: Sensitivity of different ADL measures to apraxia and motor impairments. Clinical Rehabilitation 2002;16(3):299-305.

44.     Hanna-Pladdy B, Heilman KM, Foundas AL: Ecological implications of ideomotor apraxia: evidence from physical activities of daily living. Neurology Feb 11 2003;60(3):487-490.

45.     Sundet K, Finset A, Reinvang I: Neuropsychological predictors in stroke rehabilitation. Journal of Clinical & Experimental Neuropsychology 1988;10(4):363-379.

46. Goldenberg G, Hagmann S: Tool Use and Mechanical problem solving in apraxia. Neuropsychologia 1998;36(7):581-589.

47. Laimgruber K, Goldenberg G, Hermsdorfer J: Manual and hemispheric asymmetries in the execution of actual and pantomimed prehension. Neuropsychologia 2005;43:682-692.

48. van Heugten CM, Dekker J, Deelman BG, van Dijk AJ, Stehmann-Saris FC, Kinebanian A: Measuring disabilities in stroke patients with apraxia: A validation study of an observational method. Neuropsychological Rehabilitation 2000;10(4):401-414.

49. Walker CM, Sunderland A, Sharma J, Walker MF: The impact of cognitive impairment on upper body dressing difficulties after stroke: a video analysis of patterns of recovery. J Neurol Neurosurg Psychiatry Jan 2004;75(1):43-48.

50. Sunderland A: Recovery of ipsilateral dexterity after stroke. Stroke Feb 2000;31(2):430-433.

51. Goldenberg G, Hagmann S: Therapy of activities of daily living in patients with apraxia. Neuropsychological Rehabilitation 1998;8(2):123-141.

52. Walker MF, Lincoln NB: Factors influencing dressing performance after stroke. J Neurol Neurosurg Psychiatry Aug 1991;54(8):699-701.

53. Buxbaum LJ, Schwartz MF, Montgomery M: Ideational apraxia and naturalistic action. Cognitive Neuropsychology 1998;15:617-643.

54. Schwartz MF, Montgomery, M.W., Buxbaum, L.J., Lee, S.S., Carew, T.G., Coslett, H.B., Ferraro, M., Fitzpatrick-DeSalme, E., Hart, T., & Mayer, N.:

Naturalistic action impairment in closed head injury. Neuropsychology 1998;in press.

55.  Schwartz MF, Buxbaum L, Montgomery MW, et al.: Naturalistic action production following right hemisphere stroke. Neuropsychologia 1999;37:51-66.

56.  Hartmann K, Goldenberg G, Daumuller M, Hermsdorfer J: It takes the whole brain to make a cup of coffee: the neuropsychology of naturalistic actions involving technical devices. Neuropsychologia 2005;43(4):625-637.

57.  Mayer NH, Reed ES, Schwartz MF, Montgomery MW, Palmer C: Buttering a hot cup of hot coffee:  An approach to the study of errors of action after brain damage, In: Cicerone K, Tupper D, (eds). The neuropsychology of everyday life: Assessment and basic competencies. Boston, Kluwer Academic Publishers; 1990:259-283.

58.  Sunderland A, Shinner C: Ideomotor apraxia and functional ability. Cortex in press.

59.  Buxbaum LJ, Veramonti T, Schwartz MF: Function and manipulation tool knowledge in apraxia: Knowing 'What for' but not 'how'. Neurocase 2000;6:83-97.

60.  Maher L, Rothi L, Greenwald M: Treatment of gesture impairment: a single case. American Speech and Hearing Association 1991;33:195.

61.  Maher LM, Ochipa C: Management and treatment of limb apraxia, In: Gonzalez-Rothi LJ, Heilman KM, (eds). Apraxia: The Neuropsychology of Action. United Kingdom, Psychology Press; 1997:75-91.

62. Ochipa C, Maher L, Rothi L: Treatment of ideomotor apraxia. Journal of the International Neuropsychological Society 1995;2:149.

63. Code C, Gaunt C: Treating severe speech and limb apraxia in a case of aphasia. Br J Disord Commun Apr 1986;21(1):11-20.

64. Deal JL, Florance CL: Modification of the eight-step continuum for treatment of apraxia of speech in adults. J Speech Hear Disord Feb 1978;43(1):89-95.

65. Pilgrim E, Humphreys GW: Rehabilitation of a case of ideomotor apraxia, In: Riddoch MJ, Humphrey GW, (eds). Cognitive Neuropsychology and Cognitive Rehabilitation. Hillsdale, Lawrence erlbaum associates; 1994:271-285.

66. van Heugten CM, Dekker J, Deelman BG, van Dijk AJ, Stehmann-Saris JC, Kinebanian A: Outcome of strategy training in stroke patients with apraxia: a phase II study. Clin Rehabil Aug 1998;12(4):294-303.

67. Donkervoort M, Dekker J, Stehmann-Saris FC, Deelman BG: Efficacy of strategy training in left hemisphere stroke patients with apraxia: a randomized clinical trial. Neuropsychological Rehabilitation 2001;11(5):549-566.

68. Geusgens C, van Heugten C, Donkervoort M, van den Ende E, Jolles J, van den Heuvel W: Transfer of training effects in stroke patients with apraxia: an exploratory study. Neuropsychol Rehabil Apr 2006;16(2):213-229.

69. Smania N, Girardi F, Domenicali C, Lora E, Aglioti S: The rehabilitation of limb apraxia: a study in left-brain-damaged patients. Arch Phys Med Rehabil 2000;81:379-388.

70.    Smania N, Aglioti SM, Girardi F, et al.: Rehabilitation of limb apraxia improves daily life activities in patients with stroke. Neurology Dec 12 2006;67(11):2050-2052.

71.    Robey RR, Schultz MC: A model for conducting clinical-outcome research: An adaptation of the standard protocol for use in aphasiology. Aphasiology 1998;12:787-810.

72.    Nadeau SE, Rothi LJG, Rosenbek JC: Language rehabilitation from a neural perspective, In: Chapey R, (ed). Language intervention strategies in adult aphasia. Baltimore, Williams and Wilkins; In Press.

73.    Hallett M: Motor Learning, In: Freund HJ, Jeannerod M, Hallett M, Leiguarda R, (eds). Higher-order Motor Disorders: From Neuroanatomy and Neurobiology to Clinical Neurology. Oxford, Oxford University Press; 2005:123-140.

74.    Pascual-Leone A, Dang N, Cohen LG, Brasil-Neto JP, Cammarota A, Hallett M: Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. J Neurophysiol 1995;74:1037-1045.

75.    Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerleider LG: Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature Sep 14 1995;377(6545):155-158.

76.    Hikosaka O, Nakamura K, Sakai K, Nakahara H: Central mechanisms of motor skill learning. Curr Opin Neurobiol Apr 2002;12(2):217-222.

77.    Shadmehr R, Holcomb H: Neural correlates of motor memory consolodation. Science 1997;277:821-825.

78. Bapi RS, Miyapuram KP, Graydon FX, Doya K: fMRI investigation of cortical and subcortical networks in the learning of abstract and effector-specific representations of motor sequences. Neuroimage Aug 15 2006;32(2):714-727.

79. Graydon FX, Friston KJ, Thomas CG, Brooks VB, Menon RS: Learning-related fMRI activation associated with a rotational visuo-motor transformation. Brain Res Cogn Brain Res Mar 2005;22(3):373-383.

80. Muller RA, Kleinhans N, Pierce K, Kemmotsu N, Courchesne E: Functional MRI of motor sequence acquisition: effects of learning stage and performance. Brain Res Cogn Brain Res Aug 2002;14(2):277-293.

81. Toni I, Krams M, Turner R, Passingham RE: The time course of changes during motor sequence learning: a whole-brain fMRI study. Neuroimage Jul 1998;8(1):50-61.

82. Carey DP: Multisensory integration: attending to seen and felt hands. Curr Biol Nov 30 2000;10(23):R863-865.

83. Fridman EA, Hanakawa T, Chung M, Hummel F, Leiguarda RC, Cohen LG: Reorganization of the human ipsilesional premotor cortex after stroke. Brain Apr 2004;127(Pt 4):747-758.

84. Rapcsak SZ, Ochipa C, Beeson PM, Rubens AB: Praxis and the right hemisphere. Brain and Cognition 1993;23:181-202.

85. Winhuisen L, Thiel A, Schumacher B, et al.: Role of the contralateral inferior frontal gyrus in recovery of language function in poststroke aphasia: a combined repetitive transcranial magnetic stimulation and positron emission tomography study. Stroke Aug 2005;36(8):1759-1763.

86.     Honda M, Deiber MP, Ibanez V, Pascual-Leone A, Zhuang P, Hallett M: Dynamic cortical involvement in implicit and explicit motor sequence learning. A PET study. Brain Nov 1998;121 ( Pt 11):2159-2173.

87.     Grafton ST, Hazeltine E, Irvy R: Functional mapping of sequence learning in normal humans. Journal of Cognitive Neuroscience 1995;7:497-510.

88.     Catalan MJ, Honda M, Weeks RA, Cohen LG, Hallett M: The functional neuroanatomy of simple and complex sequential finger movements: a PET study. Brain Feb 1998;121 ( Pt 2):253-264.

89.     Wise SP, Shadmehr R: Motor control, In: Ramachandran VS, (ed). Encyclopedia of the Human Brain, Vol 3. San Diego, Academic Press; 2002:137-157.

90.     Krakauer JW, Ghilardi MF, Ghez C: Independent learning of internal models for kinematic and dynamic control of reaching. Nat Neurosci Nov 1999;2(11):1026-1031.

91.     Keele SW: Motor control., In: Brooks WB, (ed). Handbook in Physiology, Section 1:  The Nervous System, Vol Vol.2. Baltimore, Williams & Williams; 1981:1391-1414.

92.     Jeannerod M: Object oriented action. Amsterdam, Elsevier, 1994.

93.     Blakemore SJ, Sirigu A: Action prediction in the cerebellum and in the parietal lobe. Exp Brain Res Nov 2003;153(2):239-245.

94.     Glover S: Separate visual representations in the planning and control of action. Behav Brain Sci Feb 2004;27(1):3-24; discussion 24-78.

95.     Jeannerod M: Neural simulation of action: A unifying mechanism for motor cognition. Neuroimage 2001;14(S103-S109).

96.    Johnson SHR, M., Grafton, S.T., Hinrichs, H., Gazzaniga, M.S. & Heinze, H-J.: Selective activation of a parieto-frontal circuit during implicity imagined prehension. Neuroimage 2002;17:1693-1704.

97.    Prinz W: Motor images are action plans (commentary). Behavioral and Brain Sciences 1994;17(2):218.

98.    Sirigu A, Duhamel J-R, Cohen L, Pillon B, Dubois B, Agid Y: The mental representation of hand movements after parietal cortex damage. Science 1996;273(1564-1568).

99.    Krakauer JW, Ghez C, Ghilardi MF: Adaptation to visuomotor transformations: consolidation, interference, and forgetting. J Neurosci Jan 12 2005;25(2):473-478.

100.    Bock O, Thomas M, Grigorova V: The effect of rest breaks on human sensorimotor adaptation. Exp Brain Res May 2005;163(2):258-260.

101.    Shea CH, Kohl RM: Composition of practice: influence on the retention of motor skills. Res Q Exerc Sport Jun 1991;62(2):187-195.

102.    Ollis S, Button C, Fairweather M: The influence of professional expertise and task complexity upon the potency of the contextual interference effect. Acta Psychol (Amst) Mar 2005;118(3):229-244.

103.    Tong C, Flanagan JR: Task-specific internal models for kinematic transformations. J Neurophysiol Aug 2003;90(2):578-585.

104.    Haaland KY, Harrington DL, O'Brien S, Hermanowicz N: Cognitive-motor learning in Parkinson's disease. Neuropsychology Apr 1997;11(2):180-186.

105.    Park H, Arndt J, Reder LM: A contextual interference account of distinctiveness effects in recognition. Mem Cognit Jun 2006;34(4):743-751.

106.    Plaut DC, McClelland JL, Seidenberg MS, Patterson K: Understanding normal and impaired word reading:  computational principles in quasi-regular domains. Psychological Review 1996;103(1):56-115.

107.    Wulf G, Horger M, Shea CH: Benefits of Blocked Over Serial Feedback on Complex Motor Skill Learning. J Mot Behav Mar 1999;31(1):95-103.

108.    Rossetti Y, Rode G, Pisella L, et al.: Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. Nature 1998(166-169).

109.    Patton JL, Stoykov ME, Kovic M, Mussa-Ivaldi FA: Evaluation of robotic training forces that either enhance or reduce error in chronic hemiparetic stroke survivors. Exp Brain Res Jan 2006;168(3):368-383.

110.    Dancause N, Ptito A, Levin MF: Error correction strategies for motor behavior after unilateral brain damage: short-term motor learning processes. Neuropsychologia 2002;40(8):1313-1323.

111.    Gandolfo F, Mussa-Ivaldi FA, Bizzi E: Motor learning by field approximation. Proc Natl Acad Sci U S A Apr 30 1996;93(9):3843-3846.

112.    Rossetti Y: Implicit short-lived motor representations of space in brain damaged and healthy subjects. Consciousness and Cognition 1998;7:520-558.

113.    Heilman KM, Gonzalez-Rothi LJ: Apraxia, In: Heilman KM, Valenstein E, (eds). Clinical Neurophysiology. New York, Oxford University Press; 2003:215-235.

114.    Holden MK: Virtual environments for motor rehabilitation: review. Cyberpsychol Behav Jun 2005;8(3):187-211; discussion 212-189.

115.    Kahn L, Rymer W, Reinkensmeyer D: Adaptive assistance for guided force training in chronic stroke. Conf Proc IEEE Eng Med Biol Soc 2004;4:2722-2725.

116. Masiero S, Celia A, Rosati G, Armani M: Robotic-assisted rehabilitation of the upper limb after acute stroke. Arch Phys Med Rehabil Feb 2007;88(2):142-149.

117. Hanlon RE: Motor learning following unilateral stroke. Arch Phys Med Rehabil 1996;77:811-815.

118. Barde L, Buxbaum L, Moll A: Abnormal reliance on object structure in apraxics' learning of novel actions. Journal of the International Neuropsychological Society In Press.

119. Giovannetti T, Schwartz MF, Buxbaum LJ: The effect of divided attention on action slips:  A new error elicitation paradigm. Journal of Clinical and Experimental Neuropsychology In Press.

**Table 1: Summary of Apraxia Treatment Studies**

| | Apraxia Type(s) | Trained Items | Duration | Intensity | Treatment Effect | Generalization | Maintenance | Apraxia Impact | ADL Impact |
|---|---|---|---|---|---|---|---|---|---|
| *Multiple Cues* (n=1) | IMA | gestures | 2 weeks | One hour daily | Y | Y | Y-treated items only (2 weeks) | NA | NA |
| *Error Type Reduction* (n=2) | IMA | gestures | Varied; 6-11 weeks | Varied; once daily 4 days/week- twice daily 2 days/week | Y | N | Y- treated error types only (2 weeks) | N | NA |
| *Six Stage Task Hierarchy* (n=1) | IMA + IA | gestures | 8 months | 45 minutes; once weekly | Y | N | NA | N | NA |
| *Conductive Education* (n=1) | IMA | gestures | 3 weeks | Daily | Y | N | NA | NA | NA |
| *Strategy Training* (n=89) | IA? * | ADL | Varied; 8-12 weeks | Varied; 25 sessions, 15 hours total | Y | Y | N (5 months) | Y | Y |
| *Transitive/Intransitive Gesture Training* (n = 13) | IMA | gestures | 10-11 weeks | 35 sessions, 50 minutes each | Y | Y | NA | Y | NA |
| *"Rehabilitative Treatment"* (n=20) | IA or IMA | gestures | 10 weeks | 30 sessions, 50 minutes each | Y | Y | Y (2 weeks) | Y | Y |
| *Errorless Completion+Exploration Training* (n=15) | NA | ADL | 2-5 weeks | 5 days/week plus 20-40 minutes practice daily | Y | N | Y (6-30 months) | NA | NA |
| *Errorless Completion* (n=6) | IMA | ADL | 2 weeks | 6 sessions, one hour each | Y | N | Y (3 months) | NA | NA |
| *Exploration Training* (n=6) | IMA | ADL | 2 weeks | 6 sessions, one hour each | N | N | N (3 months) | NA | NA |

Legend: IMA = ideomotor apraxia, IA = ideational apraxia, Y = yes, N = no, NA = not assessed/no information provided

* "Inability to carry out purposeful activities"