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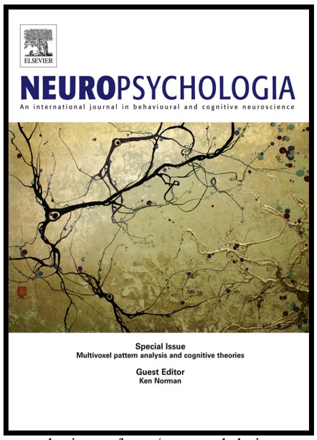

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Perceptual decisions regarding object manipulation are selectively impaired in apraxia or when tDCS is applied over the left IPL

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Abstract

This study evaluated whether apraxia can be understood as due to impaired motor representations or motor imagery necessary for appropriate object-use, imitation, and pantomime. The causal role of the left inferior parietal lobe (IPL), which is heavily implicated in apraxia, is also evaluated. These processes are appraised in light of the proposed ventro-dorsal sub-stream of the classic two visual pathway model, where perceptual information from the ventral stream and the dorsal action stream are integrated and essential for object manipulation. Using a task assessing object-use perception, stroke patients with apraxia demonstrated a selective deficit during perceptual decisions reliant on the integration of visible and known object properties to select the appropriate grasp for object-use. This deficit increased with apraxia severity. A dissociation was evident in these patients showing intact non-motoric perceptual decisions regarding the functional semantic relationship between two objects in the absence of the actor (e.g. how a hammer hits a nail). Converging evidence was found using a modified version of the same task in a neuromodulation study that directly targeted the left IPL in healthy participants using transcranial direct current stimulation (tDCS). Application of inhibitory stimulation over the left IPL reduced performance during perceptual decisions regarding object manipulation whilst performance was unaffected during functional semantic decisions. Excitatory stimulation of the left IPL did not affect performance in either task. Combined, these results suggest that the left inferior parietal lobe is critical for motor imagery, and that apraxia may be caused by an inability to use internal motor representations of object manipulation. These results are discussed in terms of motoric and non-motoric perceptual processes and the proposal of an additional ventro-dorsal sub-stream within the dorsal and ventral visual pathways model.

Keywords

Perception and action, Apraxia, left inferior parietal lobe, dorsal and ventral streams, motor imagery, object manipulation.

INTRODUCTION

The selection of an appropriate object-use grasp is based on the recruitment of stored knowledge of the object, including knowledge of the object's identity and typical function, as well as circumstantial information about the structure and location of the object in the given situation. Recent evidence suggests that integration of known and visible properties of an object is carried out by a purported 'ventro-dorsal' sub-stream within the visual pathways model, with the left inferior parietal lobe (IPL) being the critical juncture where these object properties are combined (Rizzolatti & Matteli, 2003; Binkofski & Buxbaum, 2013; Vingerhoets, 2014).

Further to the classic dorsal 'action' and ventral 'perception' streams of the visual pathways model (Milner & Goodale, 2006) there is evidence for an additional sub-stream that incorporates ventral information into the dorsal action circuit through a reciprocal connection between the temporal lobe and the IPL. The integration of long-term action representations of objects into movement plans allows objects to be grasped for use. Predominantly left lateralised, the ventro-dorsal stream extends from occipital cortex to the left IPL, to the ventral premotor cortex and frontal eye fields (Frey 2007; Rizzolatti, Fogassi, & Luppino, 2011). The ventro-dorsal stream is purportedly critical in skilled action execution, movement perception, and mental representations of movement (or motor imagery) that may be necessary when retrieving postural requirements related to skilled object-use and object manipulation (Jeannerod, 1994; Buccino et al., 2001; Kosslyn, Ganis, & Thompson, 2001; Solodkin, Hlustik, Chen, & Small, 2004; Johnson-Frey, Newman-Norland, & Grafton, 2005; Buxbaum, Kyle, Tang, & Detre, 2006; Lotze & Cohen, 2006; Creem-Regehr, 2009; Rizzolatti & Craighero, 2004; Buxbaum & Kalénine, 2010; Gao, Duan, & Chen, 2011). It is therefore possible that skilled action execution, motor imagery and movement perception may involve a common process that critically relies on the ventro-dorsal stream.

In particular, the left IPL has been heavily implicated in the ventro-dorsal stream (Hétu et al., 2013), though it is not currently understood what specific role it has in motor imagery. Neuroimaging studies exploring the neural correlates of object knowledge indicates that the left IPL is consistently and selectively activated during motoric elements of object-use including object manipulation perception, and when participants observe, imagine or pantomime object-use (Chao & Martin, 2000; Mozaz, Rothi, Anderson, Crucian, & Heilman, 2002; Rumiati et al., 2004; Boronat et al., 2005; Frey, 2007; Vingerhoets, 2008; Króliczak & Frey, 2009; Vingerhoets, Acke, Vandemaele, & Achten, 2009; Caspers et al., 2010). Non-motoric decisions about object function on the other hand show more temporal activation (Kellenbach et al., 2003; Rumiati et al., 2004; Buxbaum et al., 2006; Lewis, 2006; Frey, 2007; Canessa et al., 2008; Vingerhoets et al., 2008; Chen, Garcea, & Mahon, 2015).

A direct relationship between left IPL integrity and perceptual decisions regarding skilled object manipulation can be observed in apraxia, a high level motor disorder that impairs imitation of hand or finger gestures, or demonstration of appropriate actions associated with using an object through pantomime or actual use. Depending on the type and severity of apraxia, errors are observed in one or all behaviours (Goldenberg, 1996; Buxbaum, 2001; Daprati & Sirigu, 2006). Apraxia can emerge from lesions across the motor network and is heavily associated with damage to the left IPL, most markedly when examining transitive movements (Goldenberg & Hagmann, 1998; Johnson-Frey, 2004; Buxbaum, Johnson-Frey, & Bartlett-Williams, 2005; Buxbaum, Kyle, Grossman, & Coslett, 2007; Sunderland, Wilkins, & Dineen, 2011).

The relationship between apraxia and left IPL damage implies that apraxic symptoms may reflect a disruption to the ventro-dorsal stream resulting in impaired access to internal motor representations necessary for accurate perception of object-use manipulation (Haaland, Harrington, & Knight, 2000; Buxbaum & Saffran, 2002; Randerath, Li, Goldenberg, & Hermsdörfer, 2009; Buxbaum & Kalénine, 2010). Akin to the dissociations found in neuroimaging data, apraxic patients make errors matching objects manipulated similarly (e.g. a computer keyboard and piano), but appropriately match items with a similar function (e.g. a lighter and a matchstick both make a flame) (Buxbaum & Saffran, 2002; Myung et al., 2010; Lee, Mirman, & Buxbaum, 2014). Notably, an eye-tracking task found that apraxic patients took longer to fixate on manipulation-related stimuli compared to non-apraxics, indicating that processing of manipulation features of object-use is maintained but less accessible (Myung et al., 2010). Apraxic patients' maintained ability to identify objects and accurately grasp visually presented objects for transfer demonstrate that the ventral and dorsal pathways are intact, which confirms that errors appear restricted to movements reliant on integration of these visible and known properties (Haaland et al., 2000; Daprati & Sirigu, 2006; Ietswaart, Della Sala, & Carey, 2006; Frey, 2007).

By using non-invasive brain stimulation, the critical role of the left IPL in perceptual decisions regarding object-use can be evaluated directly. Using repetitive transcranial magnetic stimulation (rTMS), stimulation of the left IPL slows object manipulation judgements whereas anterior temporal lobe stimulation slows function judgements (Ishibashi, Lambon Ralph, Saito, & Pobric, 2011). The perception of object function appears to be attributed to more ventral and semantic systems (Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000). These findings suggest that the left IPL enables the perception of motoric elements of object-use, but is not necessary when making non-motoric functional judgements. Such a premise might indicate a critical role of the left IPL in motor imagery. In apraxia, damage to the left IPL either directly or indirectly through disruption along the ventro-dorsal pathway may lead to impaired integration of known and visible properties of objects necessary to generate internal motor representations for skilled object-use.

However, as these studies use of pictures or words of objects in isolation during function decisions, it remains possible that apraxic patients may understand the functional *goal* of object-use (e.g. a match is used to make a flame) but not the actions required by both the object and the actor to achieve that goal. In other words, if apraxic patients are unimpaired in their perception of how the functional parts of each object *interact* (e.g. how the flame of a match is used to light a candle) and these patients understand the functional goal of the object by appropriately matching objects of a similar function (e.g. a match and a lighter both make a flame), it can be asserted that apraxic impairments lie in the integration of known and visible object properties (ventro-dorsal cross talk) through motor imagery. By exploring performance when making non-motoric functional semantic decisions of object-object interactions, the current study confirms more definitively than previous research that apraxic impairments cannot be attributed to a more general deficit in the understanding of skilled object-use based on stored semantic (ventral) perceptual processes. As this distinction has not previously been assessed, it cannot be established whether the role of the left IPL is specific to decisions about the motoric elements of object-use relying on motor imagery.

Using a series of perceptual matching tasks, the integrity of internal motor representations for skilled object-use was evaluated in a study with apraxic patients and a neuromodulation study with healthy volunteers. A critical distinction was made between 'motoric perceptual decisions' of object manipulation requiring motor imagery to simulate how the object is handled for use, versus 'non-motoric functional semantic perceptual decisions' that do not require motor imagery. Rather these latter decisions are based on the action representations of objects, principally the representation of how an object typically interacts with another object in the absence of the actor (e.g. how a hammer hits a nail). A perceptual matching task allowed clear-cut distinctions to be made between each aspect of object-use, and enabled the control object affordance cues to prevent patients from relying on the objects' physical properties to indicate the appropriate object-use grasps (Randerath, Goldenberg, Spijkers, Li, & Hermsdorfer 2011; Vingerhoets, 2014). In addition to assessing dissociations in apraxic behaviour, using transcranial direct current stimulation (tDCS) with healthy participants enabled the neural correlates of perceptual decisions regarding object-use to be explored directly. It was hypothesised that if perceptual judgements of motoric features of object-use rely on the integration of known and visible properties via the purported ventro-dorsal sub-stream, then disruption to this pathway would disturb motoric manipulation perception. Therefore, for the two studies, a selective impairment of motoric perceptual decisions was expected in apraxic patients or when the left IPL was stimulated in non-brain damaged participants using tDCS.

Study 1: Object manipulation perception of apraxic patients

The patient study aimed to tease apart the different representations of skilled object-use maintained in left hemisphere stroke patients with apraxia compared to healthy age-matched controls. By dissecting each aspect of object-use to account for the distinctions outlined above, these findings will confirm more confidently whether apraxia is attributed to impaired integration of known and visible properties necessary for skilled object-use. If apraxia reflects deficient access and implementation of motor representations associated with skilled object-use due to disrupted integration of these properties impairing motor imagery, these patients should perform well when making non-motoric semantic or functional semantic decisions about how objects are used, but show a selective difficulty making perceptual decisions about how objects are manipulated for use.

METHOD

Participants

A total of 39 participants were recruited; 14 acute stroke patients with apraxia that have lesions directly or indirectly implicating the left IPL (M_{age} = 68 ± 11, 7 male) and 25 age-matched healthy control participants (M_{age} = 70 ± 8, 12 male). All participants were right-handed and gave informed consent to participate in the study. The study received ethical approval from the local NHS ethics committee and the ethics committee within Northumbria University's Department of Psychology.

Apraxia patients were recruited from National Health Hospitals and rehabilitation centres in the North East of England. Based on CT, MRI scans and clinical notes, patients were selected having suffered a brain haemorrhage or an infarct in the left hemisphere within the last six months. Patients presented with degrees of right-sided weakness, aphasia, or sensory loss. Symptoms of apraxia were determined based on gesture imitation and object-use (pantomime and actual use) tests; patients were recruited if they performed abnormally in one or more of the apraxia screening tools. The full screening battery was given within a few days of experimental testing. The presence of a pathological score on one or more of these standard apraxia assessment tests was confirmed through reassessment at the time of testing. These patients presented with ideomotor (imitation and pantomime) and/or ideational (actual object-use) errors. See Table 1.1 for patient details and Appendix A Table A1 for details on apraxia screening performance.

Based on clinical notes and additional standard test batteries, patients were excluded if they showed i) any global cognitive deficit or known dementia, ii) severe receptive aphasia or were unable to follow one-stage commands (based on the token test for language comprehension, De Renzi & Faglioni, 1978), iii) a history of alcohol dependence or evidence of substance abuse, iv) significant signs of visuospatial neglect (based on the Apples Test by Bickerton, Samson, & Humphreys, 2011).

Table 1.1 *Description of each apraxic patient; includes MS and GW who were excluded due to poor performance on the screening conditions of the experimental task.*

Patient	Sex	Age at test (years)	Days post stroke at test	Right sided motor weakness on admission	Aphasia noted on admission	Neglect/ hemianopia	Language comprehension (stage reached of Token Test)	Apraxia Screen performance (%)[a]
FR	M	81	40	Y	N	N	6	96
JAH	M	72	41	Y	N	N	6	93
JH	F	66	35	Y	N	N	6	95
HG	M	81	64	Y	Y	N	6	88
DF	M	68	63	Y	Y	N	6	90
MAS	F	75	20	Y	Y	N	5	85
AA	F	81	19	Y	Y	n.t.	n.t.	58
JA	F	46	61	Y	Y	N	2	83
PB	F	63	51	Y	Y	N	5	67
AH	F	72	61	Y	Y	R neglect	6	88
WM	M	78	62	Y	N	N	6	85
TM	M	61	160	Y	Y	N	6	95
MS	F	60	58	Y	Y	L neglect	4	24
GW	M	49	101	Y	Y	n.t.	3	52

Note. F: Female; M: Male; Y: Yes; N: No; L: Left; R: Right; n.t.: not tested
[a]Apraxia screen performance (%) is the overall accuracy across all the apraxia screening tests: imitation (hand and finger gestures) and object-use tasks (pantomime and actual use).

Details of each patient's lesion as described in the CT and/or MRI reports can be found in Table 1.2. This table specifies the Brodmann areas implicated including areas 39 (angular gyrus) and 40 (supramarginal gyrus), which are equivalent to the IPL. To determine which Brodmann areas were damaged, each patient's lesions were mapped onto the digital brain image on the basis of the radiologist's report using MRIcron software package (Rorden, Karnath, & Bonilha, 2007; http://www.mccauslandcenter.sc.edu/mricro/ mricron/). Scans were normalised (using Clinical Tool box software through SPM; Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012;

http://www.mricro.com/clinical-toolbox/) and applied to the Brodmann Atlas included in MRIcron to determine which Brodmann areas were damaged. Figure 1.1 includes an overlay of apraxic patients' lesions on a template scan. Both Table 1.2 and Figure 1.1 were used to describe each patient's lesion and not used to statistically confirm the brain regions implicated.

Healthy control participants were recruited from the Psychology Department's participant database. These participants were age-matched to the apraxic patients and did not have a history of brain damage or stroke. As compensation for their time, participants received an honorarium.

Table 1.2. *Description of each patient's lesion as described in the radiologist's CT and/or MRI reports and when mapped onto the Brodmann atlas.*

Patient	Lesion includes IPL	Lesion – left hemisphere lesion information on basis of acute CT/MRI report	Brodmann Areas damaged on basis of clinical scan (% = amount lesioned)		
			>75%	25-75%	<25%
FR	Y	New infarct L posterior horn of internal capsule; old L parieto-occipital lesion	2	**40,** 41	4, 21, **39,** 42, 48
JAH	N	L cerebellar infarct			
JH	N	L thalamic bleed			
HG	Y	L parietal infarct			2, 3, 6, 19, **39**, **40**, 48
DF	-	Evolving L fronto-temporo-parietal infarct & L insula			
MAS	N	Small vessel disease affecting periventricular white matter, L temporal lobe, & L internal capsule			
AA	Y	L MCA infarct involving parietal white matter and cortex	42	17, **40**, 41	21, 37, **39**
JA	N	L MCA infarct	34, 38	47	6, 11, 20, 21, 22, 41, 44
PB	Y	Large L frontal bleed	3, 4, 6	8	9, 32, **40**, 43, 44, 46
AH	N	L MCA infarct involving L putamen, internal capsule, & caudate head. Extending into L frontal white matter	34		10, 11, 25, 32, 47, 45, 46
WM	-	L total anterior circulation infarct			
TM	N	Ischaemic change in the L MCA occlusion			42

Note. Y: Yes; N: No; L: Left; R: Right; ACA: Anterior Cerebral Artery; MCA: Middle Cerebral Artery.
Brodmann areas attributed to the inferior parietal lobe (areas 39 & 40) are indicated in bold.

Scan reports details only are included for JH and WM because their scans could not be obtained for digitation, for DF because the scan was performed too early for the lesion to be accurately localised, and for JAH because his lesion was confined to the cerebellum. MS and GW do not feature because they were excluded on failing the perceptual screening (for lesion details see the data analysis section of the method).

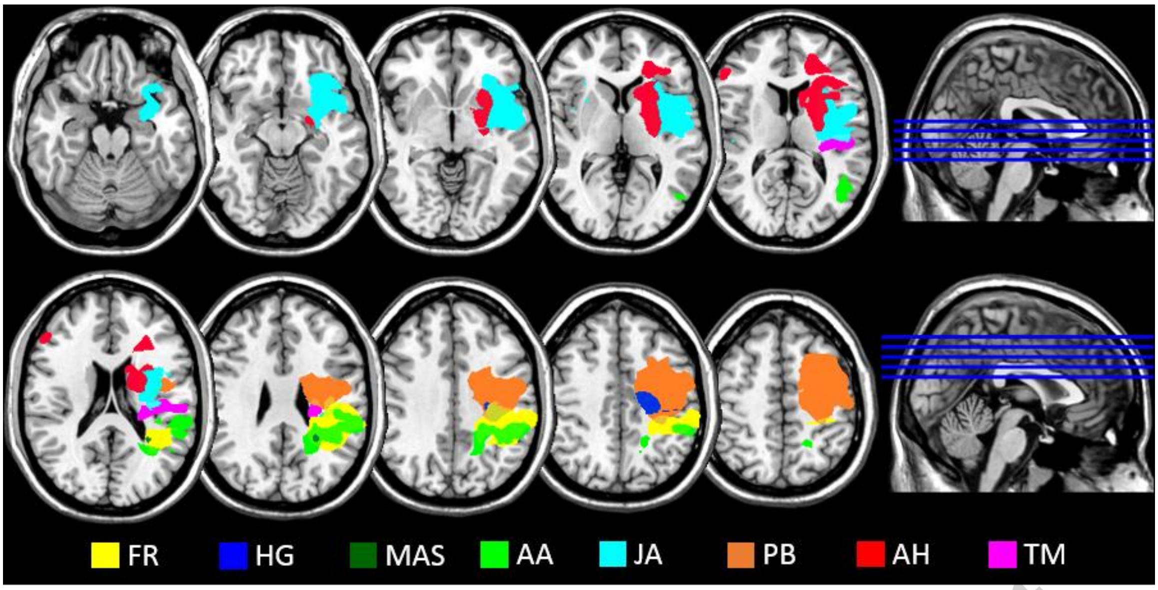


Figure 1.1. Scan slices of lesions of each patient were overlaid and applied to a template scan allowing clear visualisation of the anatomical landmarks using MRIcron software package (Rorden et al., 2007; http://www.mccauslandcenter.sc.edu/mricro/ mricron/). Clinical scans could not be obtained for patients JH and WM; the scan for DF was performed too early for the lesion to be accurately localised. JAH is not featured as his lesion was confined to the cerebellum. Scans for patients MS and GW are not shown here because they were excluded on failing the perceptual screening (for lesion details see the data analysis section of the method).

Procedure

Healthy control participants were tested within the Psychology Department and patients were tested at home or at the bedside over two to three sessions, each session lasting approximately 30 minutes. Initially, patients were screened for cognitive, motor, or sensory deficits before being assessed for symptoms of apraxia. After screening, patients were given the experimental task. All tasks were presented on paper.

Materials

1. Apraxia Screening

Imitation of hand and finger postures (Goldenberg, 1996). Patients were required to imitate hand and finger postures demonstrated by the experimenter. Hand postures consisted of different hand positions relative to the head and finger postures defined by configurations of the fingers irrespective of the hands position relative to the body. The experimenter sat opposite the patient and demonstrated each gesture 'like a mirror', performing each posture with their right hand to be imitated with the patients' left hand. Imitation was permitted after the demonstration had ended. Two points were given for successful imitation on the first trial; one point if the patient was successful after a second demonstration; zero points if the patient failed to imitate the posture correctly. Ten gestures of each kind were presented and a total score of 20 could be achieved.

Pantomime of object use (based on Goldenberg, Hermsdörfer, Glindemann, Rorden, & Karnath, 2007). Drawn images of 19 objects taken from Cycowicz, Friedman, Rothstein, and Snodgrass (1997) were presented and patients were asked to demonstrate their use. The examiner named the action and patients were marked on the presence or absence of predefined movement features; a maximum of 53 points could be obtained, with less than 43 points considered pathological. For example, when demonstrating how to "write with a pencil", patients received three points if they used a "precision" grip, made "movements of small amplitude in the horizontal plane", and the "grip is close to but does not touch the table". Body-part-as-object errors were marked as incorrect except when demonstrating the use of scissors.

Actual object use (based on De Renzi & Lucchelli, 1988). 18 of the objects presented in the pantomime test were given to the participant to demonstrate their use. One point was given for every object used correctly, and zero for incorrect movements. It was considered pathological if errors were made when demonstrating the use of two or more objects.

2. Experimental Task

Across four conditions, participants' made perceptual decisions regarding object-use. The first two conditions screened semantic object understanding; the third required a functional semantic decision; and fourth an object manipulation decision. The stimuli included drawn pictures of objects taken from Cycowicz et al. (1997) and pictures taken from an Internet search engine and then modified. Hand postures featured were created using a 12.1 mega pixel camera. Each posture was created by holding the target object, removing it, and maintaining the posture whilst the photograph was taken. The photos were edited and grey scaled using an image manipulation program. Two independent assessors evaluated whether the photos clearly depicted correct or incorrect gestures for object-use. Any postures that were considered ambiguous were replaced until both assessors unanimously agreed on the final selection.

In each condition, participants were given simple verbal instructions and asked to point to the correct image amongst distractors. The same target objects were used across all conditions to directly assess the point at which individuals' object-use perception deteriorated. The distractor images consisted of an 'afforded' distractor, defined as physically plausible but highly unlikely for effective object-use, and 'unafforded' distractor, defined as physically implausible/impossible for object-use. There were 20 trials in each of the four conditions, totalling 80 overall. Accuracy and response times were recorded; after the stimuli were presented, a stopwatch was used to record the response times to select an image out of the array. Participants were given one point for correct trials and zero for incorrect.

Non-motoric semantic object understanding (screening): The initial *Object Identification* condition required participants to point to the target object amongst three distractors in a 2x2 array. Distractors consisted of random objects; some of which also appeared in the other conditions to minimise the number of new stimuli seen by the participant. In the second condition, *Object Pairing* required participants to point to the object typically used with the target. The paired object was presented with two distractors, one affordance-related and one affordance-unrelated. For example, the target 'hammer' could be paired with a 'nail' (correct), 'drum' (affordance-related/incorrect), and 'doorknob' (affordance-unrelated/incorrect).

Motoric manipulation decision (hand-object): Participants pointed to the correct hand posture for using the target object. Two postures were presented, one correct and one affordance-related incorrect. Participants were requested not to pantomime the movement. Left-handed postures were presented so that participants were able to imagine the movement with their unaffected hand in the event of right-sided weakness. The experimental Manipulation task was designed to capture covert motor imagery. There is little consensus in the literature about the validity of more established motor imagery tasks (Ietswaart, Butler, Jackson & Edwards, 2015). The motor imagery task in this study was carefully constructed on the basis of existing theory. The task was designed such that it cannot be performed on the basis of manipulation knowledge alone and instead requires online imagery of movement to complete perceptual matching. This task assessed the integration of ventral stored representations with dorsal motor processes, whereas other tasks assess knowledge of object manipulation (for example, Buxbaum & Saffran, 2002).

Non-motoric functional semantic decision (object-object)*:* In this condition, participants were required to identify the scenario in which the target object was being used correctly with the paired object shown in the previous condition. Three 'object-object interaction' images were presented, one correct and two incorrect (affordance-related and affordance-unrelated). The paired object (e.g. the nail when used with the target hammer) maintained the same orientation in all images. Selection of the appropriate object-object interaction is not reliant on intact movement representations. Figure 1.2 shows an example of each experimental condition.

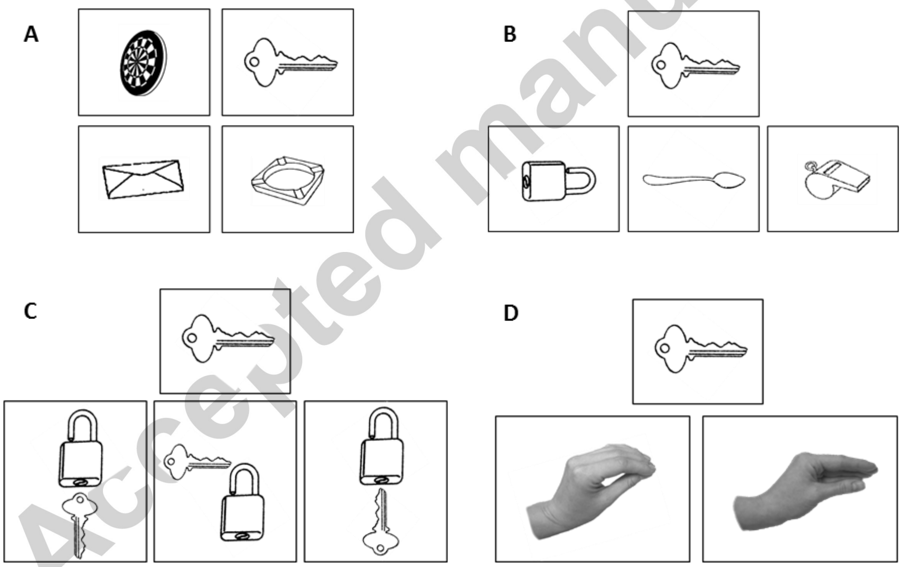


Figure 1.2. Stimuli presentation in each condition of the experimental task using a 'key' as the example target object. A) & B) screened non-motoric object understanding with Object Identification and Object Pairing conditions. Respectively, participants pointed to the target object and the object typically used with it. C) Non-motoric Functional Semantic decision assessed perception of object-object interaction; participants indicated how the paired objects are typically used together by selecting the target image (right) from affordance-related (left) and affordance-unrelated (middle) distractors. D) Motoric Manipulation decision assessed hand-object perception; how an object is typically held for use between the correct posture (left) and affordance-related incorrect (right).

Data Analysis

Participants were excluded from the study if accuracy was less than 90 percent (less than 18 correct of the 20 trials) in either condition of the non-motoric *Semantic Object Understanding* screening, as this suggested a level of semantic deficit. Based on this criterion, patient MS and GW were excluded due to 70 and 85 percent accuracy respectively in the *Object Pairing* condition. CT and MRI scan reports confirmed MS suffered a left temporal lobe sub-acute infarct (implicating Brodmann areas 2, 3, 4, 8 and 40) whilst GW had infarcts in the left temporo-parietal, basal ganglia, and parieto-occipital regions (Brodmann areas 6, 19, 20, 22, 31, 34, 36-39) consistent with more semantic impairments. The remaining 12 apraxic participants' performance was equal to or greater than 95 percent in both conditions of the semantic screening. A one-sample t-test confirmed that performance was comparable to 100 percent accuracy; *Object Identification* (M=99.615 ± 1.387), $t(12)$=-1.0, p=.337, *Object Pairing* (M=98.846 ± 2.193), $t(12)$=-1.897, p=.082. Alpha level for significant scores was less than .05.

The aim of the study was to confirm whether patients with apraxia differed from control participants, and if so, whether these differences were specific to perceptual decisions regarding skilled object-use (thought to rely on ventro-dorsal processing). A mixed model analysis of variance (ANOVA) was conducted to compare performance of apraxic and control participants during the non-motoric *Functional Semantic* and motoric *Manipulation* conditions. A score of accuracy (%) divided by reaction time (RT) in seconds was measured to account for any speed-accuracy trade-off of each participant. A more positive score characterises high accuracy and fast RT. Additional ANOVAs explored differences in Reaction Time (s) and Accuracy (%) separately and can be found in Appendix B. Post-hoc analyses were conducted using independent samples t-tests with a Bonferonni correction for multiple comparisons.

Finally, using the data from the apraxic participants alone, the relationship between apraxia severity and task performance was explored using a non-parametric one-tailed Spearman's rho correlation. Apraxia Screen performance was calculated as the overall accuracy (%) across all the apraxia screening tests: imitation (hand and finger gestures) and object-use tasks (pantomime and actual use). A Difference score of task performance was calculated: non-motoric *Functional Semantic* condition (Accuracy/RT) minus motoric *Manipulation* condition (Accuracy/RT). This calculation assessed the extent to which performance when making manipulation decisions differed from performance during functional semantic decisions, and whether this difference could be associated with apraxia severity. In other words, as apraxia severity increases, does performance in the manipulation condition decrease compared to the functional semantic condition. Use of a difference score also reduces the introduction of variance in performance based on individual differences. If the difference score deviated from zero this indicated a greater difference in performance between conditions; a positive difference score illustrated a poorer performance in the motoric *Manipulation* condition compared to the non-motoric *Functional Semantic* condition and a negative score illustrated a comparably poorer performance in the *Functional Semantic* condition.

RESULTS

Functional Semantic and Manipulation Task performance – Apraxic patients versus Healthy controls.

Mixed model ANOVAs explored the effect of Task (Functional Semantic vs. Manipulation) x Apraxia (Apraxia Patients vs. Healthy Controls) on performance. This was carried out for Accuracy/RT to account for any speed-accuracy trade-off in performance of each individual. Separate analyses of Reaction Time (s) and Accuracy (%) are reported in Appendix B.

Accuracy/RT. An initial main effect of Task ($F_{(1,35)}$ = 55.440, p <.001) indicated that performance in the motoric Manipulation condition was poorer overall (M = 1.271 ± .242) compared to the non-motoric Functional Semantic condition (M = 1.533 ± .164) across participants. Further, a significant main effect of Apraxia ($F_{(1,35)}$ = 10.369, p =.003) confirmed that apraxic patients performed worse (M = 1.309 ± .272) than controls (M = 1.495 ± .133) in both task conditions.

Of interest, the significant interaction Task x Apraxia ($F_{(1,35)}$ = 7.367, p =.010) revealed that performance differed between each participant group and task condition (see Figure 1.3). Post-hoc independent samples t-tests confirmed that apraxic patients performed significantly worse (M = 1.131 ± .320) than controls (M = 1.412 ± .164) during the motoric Manipulation condition ($t_{(13.841)}$ = -2.863, p = .013). Alternatively, performance was comparable between apraxic and control participants during the non-motoric Functional Semantic condition ($t_{(13.255)}$ = -1.321, p = .209). A Spearman's rho correlation of apraxic patients also confirmed a non-significant relationship between patient's performance in the Manipulation and Functional Semantic tasks ($r_{s(12)}$ = .511, p = .089).

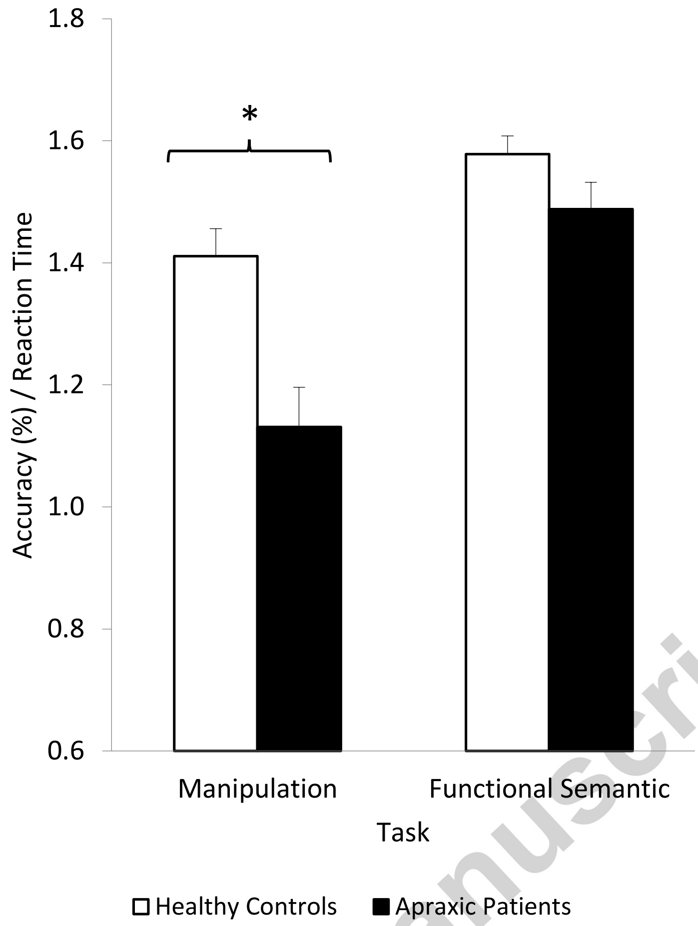


Figure 1.3. Performance of apraxic and healthy control participants in the motoric Manipulation and non-motoric Functional Semantic conditions of the experimental task. A high score represents high accuracy and fast reaction time (RT). Standard Error (SE) bars are plotted for each condition and participant group. An asterisk marks the significant difference between apraxic and control participants in the Manipulation condition.

Apraxia Severity

The relationship between apraxia severity and task performance was explored using a non-parametric one-tailed Spearman's rho correlation. It was anticipated that increase in apraxia severity would correlate with a decrease in performance in the motoric Manipulation condition. A significant negative correlation between apraxia screen performance and difference score ($r_{s(12)}$ = -.522, p = .041) was confirmed. Figure 1.4 indicates a linear trend in difference performance score and apraxia severity, with performance in the motoric Manipulation task decreasing as apraxia severity increases.

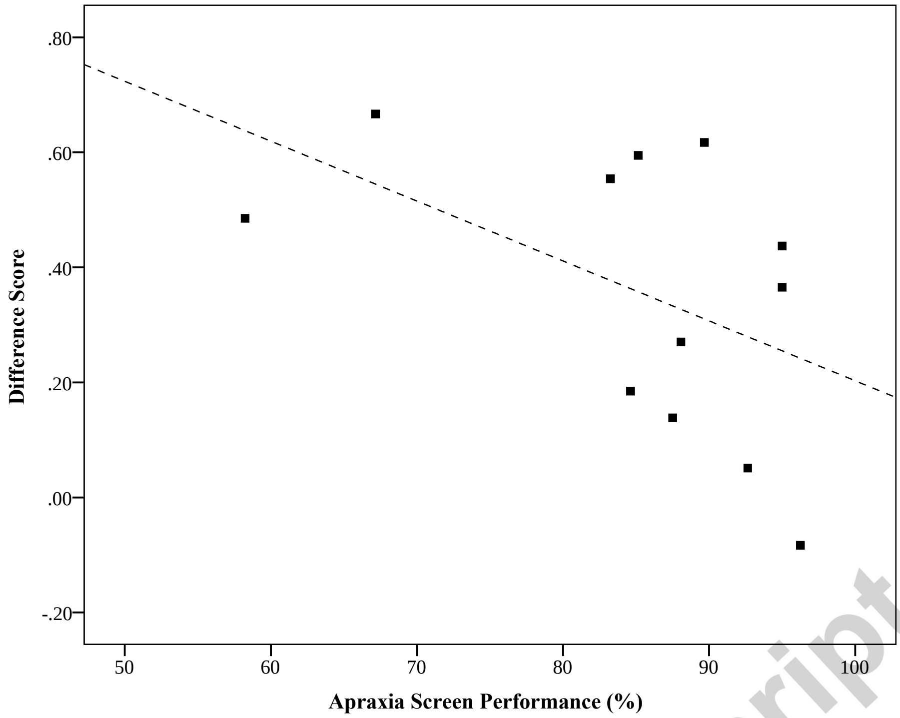


Figure 1.4. Scatterplot of the correlation between difference score of Accuracy/RT for Functional Semantic minus Manipulation conditions and apraxia screen performance(%). A dashed line of fit is plotted, R^2 = .242. The greater the difference score deviated from zero the greater the difference in performance between the Functional Semantic and Manipulation conditions; a positive difference score indicated a comparably poorer performance in the latter condition and a negative difference score indicated a comparably poorer performance in the former. A high percentage indicated accurate performance in apraxia screening.

Study 2: the effect of left IPL tDCS on object manipulation perception

The results from Study 1 suggest that apraxia selectively disturbs perceptual decisions concerning motoric object manipulation whilst non-motoric functional semantic perceptual decisions are unaffected. Using the same perceptual matching task, the role of the left IPL in motor imagery of manipulation features of object-use was explored directly using the neuromodulation technique transcranial direct current stimulation (tDCS). TDCS involves the application of a weak electrical current onto the scalp through a pair of electrodes (the positive anode and the negative cathode electrode) to modulate cortical function by inducing prolonged, reversible, shifts in cortical excitability. Classic assumptions regarding the polarity effects of tDCS indicates that cathodal stimulation inhibits neuronal excitability whereas anodal stimulation enhances neuronal excitability (Nitsche et al., 2008). For clarity, these classic modulatory effects will be defined when referring to each electrode: ‘cathodal-inhibitory’ and ‘anodal-excitatory’.

Over two experiments with different participants, either cathodal-inhibitory tDCS was applied over the left parietal cortex (approximately over the IPL) with anodal-excitatory stimulation over the contralateral supraorbital ridge (Experiment 2.1), or anodal-excitatory left parietal and cathodal-inhibitory contralateral supraorbital ridge stimulation (Experiment 2.2) was applied. It was hypothesised that if the left IPL of the ventro-dorsal stream were critical in the integration of known and visible object properties important for the retrieval of postural requirements for object-use, cathodal-inhibitory stimulation of the left parietal cortex would reduce task performance, akin to the pattern of results in lesion patients, whereas anodal-excitatory stimulation would enhance task performance when making manipulation judgements. Stimulation of the left parietal cortex however would not affect task performance when making functional semantic decisions.

METHOD

Participants

An opportunity sample of healthy participants was recruited; all participants were right handed (in accordance with the revised Edinburgh Handedness Inventory, Oldfield 1971; Cohen, 2008), received a health screening questionnaire based on Rossi, Hallett, Rossini, & Pascual-Leone (2011) to confirm their eligibility for tDCS stimulation, and gave informed consent. Monetary compensation or course points were offered for their time. For the cathodal-inhibitory study protocol (Experiment 2.1) 24 participants (M_{age} 22 ± 7, 19 female, laterality quotient 82.50) were recruited. For the anodal-excitatory study protocol (Experiment 2.2) a further 23 participants (M_{age} 23 ± 10, 12 female, laterality quotient 78.12) were recruited. The participant groups used in Experiment 2.1 and 2.2 were comparable in terms of age and laterality.

Transcranial direct current stimulation

A constant direct current was applied during both tasks using a battery driven stimulator (neuroConn, Germany). Two rubber electrodes were inserted into separate sponge pouches that were soaked in saline solution. A lycra cap was placed on the participants head to keep the electrodes in place and a 1.5mA current was applied through a 25cm^2 (5x5cm) electrode over the target site and a 100cm^2 (10x10cm) electrode over the reference site. A large reference electrode was selected in order to spread stimulation over a larger area and minimise the potential for the electrode impacting cognition. Stimulation was ramped up for 10 seconds and remained online throughout the experimental tasks in accordance with current safety limits for healthy volunteers (Nitsche et al., 2003): experiment one, average stimulation duration 11 minutes ± 2 and experiment two an average of 11 minutes ± 1, at a maximum current density of 0.06mA (1.5 mA/25 cm^2). During the sham condition, stimulation was applied for 30 seconds before being switched off.

Based on the international 10/20 system for electrode placement, the target electrode was placed over the left parietal cortex, approximately over the left IPL; the centre of the electrode was positioned between P3 and CP3 (Harris and Minuissi, 2003) and the reference electrode was placed over the contralateral supraorbital ridge. In Experiment 2.1, cathodal-inhibitory stimulation was applied to the left parietal cortex (target) with anodal-excitatory stimulation using the large ‘diffuse’ electrode applied to the reference site. In Experiment 2.2, anodal-excitatory stimulation was applied to the left parietal cortex and cathodal-inhibitory stimulation to the reference site. Both experiments consisted of two testing sessions where either real or sham stimulation was applied.

Stimuli

Participants completed the experimental motoric object manipulation task and non-motoric functional semantic task used in Study 1, however these were altered to suit computer presentation and included additional stimuli to extend the number of trials (see Figure 2.1). These additional trials were added in order to capture the more subtle effect of tDCS on performance compared to those observed in patients. The experiment was run on a 19-inch computer monitor (1280 x 1024 pixels) and programmed using E-Prime. The centre of the screen was at eye level at a viewing distance of 63cm, which was maintained using a chin rest. The reliability of the additional stimuli being identifiable as the correct or incorrect interactions for object-use was evaluated by two independent assessors and based on pilot data from six participants (average accuracy of 94% ± 10). Stimuli were changed if the average accuracy fell below 75%.

Motoric Manipulation task. Stimuli consisted of target objects taken from the Bank of Standardized Stimuli (BOSS) (Brodeur, Dionne-Dostie, Montreuil, & Lepage, 2010) or modified images from an Internet search engine. After the central fixation cross, the target object was displayed for 500ms before being replaced by a correct or incorrect hand posture. Participants identified whether the hand posture displayed was appropriate to use the object presented previously. The target object was presented in a non-functional orientation whereas the hand posture was oriented appropriately for object-use. This prevented participants simply matching the images. Participants saw both left and right hand postures for each target object.

Non-motoric Functional Semantic task. Additional drawn pictures of objects to those used in Study 1 were taken from a stimulus set (Cycowicz et al., 1997) and modified from an Internet search engine. Following a central fixation cross, participants saw one drawn image of an 'object-object interaction' and were required to identify whether the target object was being used correctly with the paired object. Interactions were presented equally in orientations for left- or right-handed use.

Procedure

An initial practice block was completed prior to stimulation enabling participants to have sufficient practice with the task. For respective non-motoric Functional Semantic and motoric Manipulation tasks, this consisted of 33 and 38 trials. After practice, five minutes of stimulation was applied prior to task onset to ensure stimulation effects were being experienced. Participants then repeated each task whilst stimulation was on going. During stimulation, 66 trials of the Functional Semantic task and 89 trials of the Manipulation task were presented. Each task was split into two main test blocks consisting of 33 trials per block for the Functional Semantic task and 45 and 44 trials in Block 1 and 2 for the Manipulation task. Over two testing sessions, 132 and 178 trials were completed for each task respectively.

Across each task, participants were required to respond as quickly and accurately as possible when deciding whether the functional relationship between the objects or hand postures presented were correct or incorrect for use. Responses were given on a keypad: participants responded 'correct' by pressing number '1' with their left index finger and 'incorrect' by pressing number '3' with their right index finger. Stimulation was switched off after the final task was completed. To avoid response priming for subsequent images, participants did not see both the correct and incorrect image for each target object in one session. In addition to counterbalancing the presentation of correct or incorrect images, task order and stimulation protocol were counterbalanced across participants.

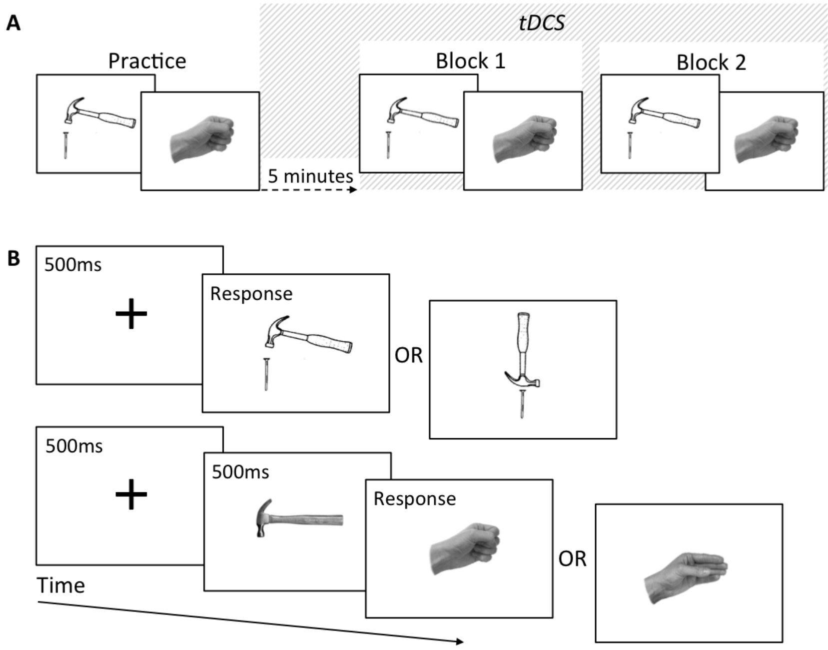


Figure 2.1. (A) Schematic of the experimental procedure. Note the diagonal striped box depicts the period of tDCS stimulation. (B) Schematic of the stimulus presentation for the Functional Semantic task (top) and the Manipulation task (bottom). The correct stimulus is presented on the left and the incorrect affordance stimulus on the right.

Design

Two experiments were completed with different stimulation protocols. For each experiment, a within-subject repeated-measures design was used with three independent variables: Task (non-motoric functional semantic vs. motoric manipulation) and Stimulation (left parietal tDCS vs. sham) and Stimulation Block (1 vs. 2). The dependent variables were response reaction times (RT) in milliseconds and response accuracy (%).

Data Analysis

Participants' reaction times (RT) and response accuracy (%) were recorded using E-prime and analysed separately in three-way repeated-measures analyses of variance (ANOVA) for each experiment. These measures were analysed separately in Study 2; where composite measures were used in Study 1, separate analyses are provided in the Appendix. The reason for this difference is that Study 1 required a higher level of data reduction: to make the link to apraxia severity, difference scores between the two conditions were needed including both speed and accuracy. As this level of data reduction was not required for Study 2, separate analyses for speed and accuracy are reported to allow detection of potentially subtle effects of tDCS.

Specifically, performance was compared between each Task (Functional Semantic and Manipulation), and Stimulation condition (real stimulation and sham). Unlike more conventional paradigms, where the effects of tDCS are explored after stimulation, the current study explored performance changes during stimulation. This was done to ensure the effects of stimulation were evident, as little is known about the duration of after-effects of tDCS over these densely connected parietal lobes. The effect of tDCS over time was analysed by measuring performance differences across stimulation Blocks (1 and 2), as it was uncertain whether stimulation effects were stable due to so few parietal tDCS perception studies being conducted with continuous stimulation. Further, tDCS effects are state dependent and can change when the brain regions being stimulated are active (Silvanto, Muggleton, & Walsh, 2008; Walsh, 2013). Significant scores were those below the alpha level .05. All participants were included in the final analyses, with average performance 85% ± 7 in Experiment 1, and 85% ± 6 in Experiment 2. RTs greater than three standard deviations from the mean were excluded.

RESULTS

Study 2 aimed to find convergence for the findings from Study 1 by confirming whether neuromodulation of the left inferior parietal lobe would selectively affect motoric object manipulation perception decisions, as observed in patients with apraxia. This would not only confirm this regions importance during perceptual decisions of motor elements of object-use, but that the left IPL may be critical when making manipulation judgements that may be reliant on motor imagery.

Cathodal-inhibitory stimulation of the left IPL.

Reaction Time (ms). The three-way ANOVA confirmed a significant main effect of Task ($F_{(1,23)}$ = 10.868, p =.003, η_p^2 = .321): RTs were faster in the Functional Semantic task (M= 1033.060 ± 245.130) compared to the Manipulation task (M= 1157.915 ± 358.982). Whereas, the main effects of Stimulation ($F_{(1,23)}$ = .531, p =.473, η_p^2 = .023) and Block ($F_{(1,23)}$ = 2.600, p =.121, η_p^2 = .102) were non-significant. Two-factor comparisons indicated a significant Task x Block interaction ($F_{(1,23)}$ = 5.598, p =.027, η_p^2 = .196), and non-significant interactions between Task x Stimulation ($F_{(1,23)}$ = 1.139, p =.297, η_p^2 = .047) and Stimulation x Block ($F_{(1,23)}$ = .941, p =.342, η_p^2 = .039). Crucially, a significant three-factor interaction for Task x Stimulation x Block ($F_{(1,23)}$ = 4.906, p =.037, η_p^2 = .176) was identified.

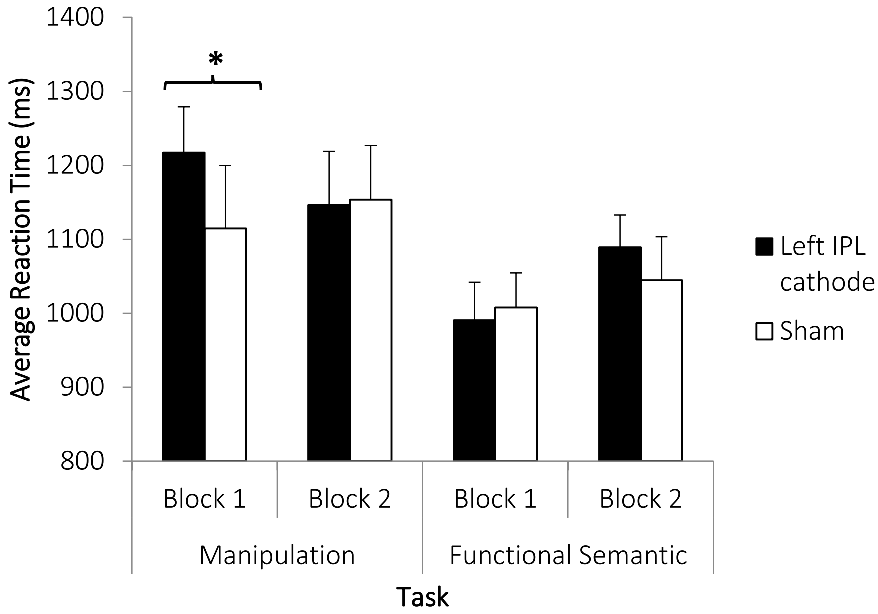
To analyse the three-factor interaction, two-way ANOVAs for Block x Stimulation were carried out for each Task separately. This revealed a significant interaction of Stimulation x Block for the motoric Manipulation task ($F_{(1,23)}$ = 5.481, p =.028, η_p^2 = .192), but not for the non-motoric Functional Semantic task ($F_{(1,23)}$ = 1.835, p =.189, η_p^2 = .074). The graph on the left of Figure 2.2 demonstrates the task specific effects of inhibitory stimulation on Manipulation task performance in Block 1. Post-hoc paired-samples t-tests were used to explore the differences between cathodal-inhibitory stimulation (black bars in Figure 2.2) and sham (white bars in Figure 2.2) for each of the blocks and task conditions. The difference between stimulation and sham in Block 1 of the Manipulation condition was expressed in a trend in the post-hoc analysis ($t_{(23)}$ = 1.869, p =.074), while all other all other post-hoc comparisons were firmly non-significant (Functional Semantic stimulation versus sham: $p \geq .721$). It appears that stimulation may be slowing performance during the first test block of the Manipulation task only.

Accuracy (%). Stimulation was not found to have an effect on task accuracy: Stimulation, $F_{(1,23)} = .071$, $p = .792$, $\eta_p^2 = .003$; Task x Stimulation, $F_{(1,23)} = .447$, $p = .510$, $\eta_p^2 = .019$; Stimulation x Block, $F_{(1,23)} = .035$, $p = .853$, $\eta_p^2 = .002$; Task x Stimulation x Block, $F_{(1,23)} = 035$, $p = .853$, $\eta_p^2 = .002$. A main effect of Task ($F_{(1,23)} = 76.489$, $p < .001$, $\eta_p^2 = .769$) confirmed that participants were more accurate when making Functional Semantic decisions (M=90% ± 5) compared to Manipulation decisions (M=81% ± 7). Accuracy was higher in Block 1 (M= 87% ± 6) compared to Block 2 (M= 84% ± 7) ($F_{(1,23)} = 22.900$, $p < .001$, $\eta_p^2 = .499$). A significant interaction Task x Block ($F_{(1,23)} = 12.441$, $p = .002$, $\eta_p^2 = .351$) was found but not explored.

Anodal-excitatory stimulation of the left IPL

Reaction Time (ms). Opposed to Experiment 1, the three-way ANOVA exploring the effect of anodal-excitatory left IPL stimulation compared to sham on task performance did not find a significant interaction Task x Stimulation x Block ($F_{(1,22)} = 2.347$, $p = .140$, $\eta_p^2 = .096$). Non-significant results were also found for Stimulation ($F_{(1,22)} = .812$, $p = .377$, $\eta_p^2 = .036$), Task x Stimulation ($F_{(1,22)} = .029$, $p = .867$, $\eta_p^2 = .001$), and Stimulation x Block ($F_{(1,22)} = .003$, $p = .958$, $\eta_p^2 < .001$). The main effects of Task ($F_{(1,22)} = 1.809$, $p = .192$, $\eta_p^2 = .076$) and Block ($F_{(1,22)} = 2.155$, $p = .156$, $\eta_p^2 = .089$) were also non-significant. The interaction Task x Block however was significant ($F_{(1,22)} = 10.675$, $p = .004$, $\eta_p^2 = .327$), but was not pursued as it was not directly relevant to the hypotheses. These data suggest that RTs were not in any way affected by anodal-excitatory stimulation.

Accuracy (%). Results reveal non-significant effects of stimulation on task accuracy: Stimulation, $F_{(1,22)} = .052$, $p = .821$, $\eta_p^2 = .002$; Task x Stimulation, $F_{(1,22)} = .021$, $p = .886$, $\eta_p^2 = .001$; Stimulation x Block, $F_{(1,22)} = .253$, $p = .620$, $\eta_p^2 = .011$; Task x Stimulation x Block, $F_{(1,22)} = .485$, $p = .494$, $\eta_p^2 = .022$. A significant main effect of Task ($F_{(1,22)} = 57.400$, $p < .001$, $\eta_p^2 = .723$) confirmed that accuracy was greater in the Functional Semantic task (M= 90% ± 5) compared to the Manipulation task (M= 80% ± 9). Main effect of Block ($F_{(1,22)} = 57.629$, $p < .001$, $\eta_p^2 = .724$) indicated that accuracy was greater in Block 1 (M= 89% ± 7) compared to Block 2 (M= 83% ± 8). Finally a significant Task x Block interaction ($F_{(1,22)} = 6.680$, $p = .017$, $\eta_p^2 = .233$) was found but not explored.



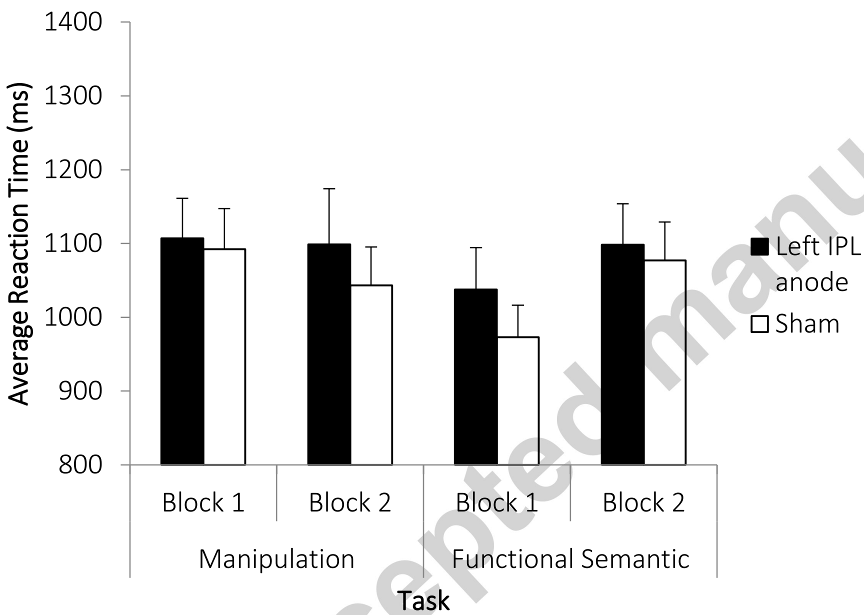


Figure 2.2. Average reaction times (ms) of participants in Experiment 2.1 (left) and Experiment 2.2 (right) during stimulation or sham for both testing blocks of the Functional Semantic and Manipulation tasks. Standard error bars included. The asterisk marks the post-hoc analysis trend *p*=.07 further to the significant interactions.

DISCUSSION

To confirm the critical role of left IPL in apraxia, and in turn the possible role of motor imagery in explaining apraxia as an impairment of internal movement representations due to ventro-dorsal damage, it was important to assess whether apraxic patients were selectively impaired on perceptual decisions of motoric elements of object-use (object manipulation) while unimpaired on perceptual decisions of non-motoric 'action representations' of how an object typically interacts with another object in the absence of the actor (functional semantic perception). Previous studies have overlooked this distinction. By documenting each apraxic patient's lesion and dissociable impairments in these tasks, Study 1 aimed to confirm whether apraxia was attributed to impaired integration of known and visible object properties due to disruption of the purported ventro-dorsal stream of the visual pathways model. Study 2 assessed directly the neural correlates of object manipulation perception with the expectation of modulatory effects of tDCS over the left IPL selectively affecting perceptual object manipulation decisions reliant on motor representations while leaving functional semantic perceptual decisions unaffected. TDCS, like patient studies, is uniquely placed to beyond the science of correlations where dependent relationships are inferred, and confirm the critical role of brain regions, in this case in the interaction between perception and action.

In Study 1, when comparing apraxic performance to healthy controls, apraxic patients made considerably more errors relating to motoric hand-object interactions in the Manipulation condition compared to control participants. This is consistent with the errors apraxic patients make when imagining or pantomiming object-use, and with previous apraxia research showing impairments when matching objects based on similar manipulation (such as a computer keyboard and piano) (Goldenberg, 1995; Buxbaum & Saffran, 2002; Daprati & Sirigu, 2006; Myung et al., 2010). When analysing accuracy and response times separately (as detailed in the Appendices), results indicated that there was no significant difference in accuracy between apraxic and healthy participants in either the Functional Semantic of Manipulation conditions. Yet the variable performance of apraxic patients in the Manipulation condition, which could partly be attributed to the variance in apraxia severity across participants, may be concealing any interaction effects. Apraxic patients were however significantly slower when making manipulation decisions compared to control participants, whilst response times were comparable when making functional semantic conditions, corroborating the modulatory effects of tDCS in Study 2, as discussed later. Critically, by combining the accuracy and reaction time performance of each patient to account for speed/accuracy trade-off, apraxic patients performed significantly worse than healthy controls in the Manipulation condition while performance in the Functional Semantic condition was maintained. This finding indicates that apraxic patients that performed accurately took longer to respond, which confirms that these patients were performing abnormally. As such, these results suggest that apraxic patients do indeed show a selective deficit when making manipulation decisions dependent on internal movement representations.

The association between apraxia severity and the selective deficit on perceptual decisions of motoric object manipulation is evidence for the relationship between apraxia and motor representations of object-use; as severity of apraxic symptoms increased, performance in the Manipulation condition decreased while performance in the the Functional Semantic control condition was unaffected. Although a causal link cannot be verified through correlation, coupled with the dissociable performance between apraxics and healthy controls and non-significant correlation between apraxic patient's performance between both conditions, the current data strongly suggests that deficits seen in apraxia are associated with impaired perception of motoric features of object-use. This supports the suggestion that apraxia is associated with impaired internal movement representations.

The selectivity of this impairment in internal movement representations was demonstrated by normal performance in the Functional Semantic condition where apraxic patients were comparable to controls. Coupled with accurate performance in the semantic screening tasks, these results support the proposal that non-motoric features of object-use, including 'action representations' of how objects interact with each other, are not associated with apraxia. By maintaining the same target objects throughout each experimental condition, accurate performance in the semantic screening tasks confirmed that any errors in later conditions could not be attributed to impaired semantic representations. Likewise the use of visually afforded distractor stimuli confirms that accurate performance in the non-motoric Functional Semantic condition was attributed to maintained understanding of object-use in apraxic patients and not by 'process of elimination' by selecting the image that looked most plausible based on its physical properties. These findings support previous research indicating that apraxic patients have maintained ventral processing and can appropriately match objects of a similar function (Buxbaum & Saffran, 2002; Myung et al., 2010).

Moreover, the dissociation in this study between impaired perceptual decisions regarding object manipulation and intact perceptual decisions regarding non-motoric features of object-use, offers support for a supposed ventro-dorsal sub-stream necessary for tasks relying on the integration of visible and known object properties. Yet apraxic patients have shown appropriate memory-driven reach and grasp movements believed to be reliant on the integration of ventral and dorsal processes (Ietswaart, Carey, Della Sala, & Dijkhuizen, 2001). However, the reliance of memory-driven reach and grasp movements on cross-talk between the two visual pathways has since been questioned; the dorsal stream is believed to play a dominant role in both immediate and delayed action, whilst the role of the ventral stream increases with extended delay of movement onset (Schenk & McIntosh, 2010). Appropriate memory-driven grasping in these patients could therefore be attributable to sufficient information remaining present in the dorsal stream. Instead the experimental, perceptual based task in this study may better reflect the current understanding of the two visual pathway model. The current results are also in line with findings from a recent action execution task conducted by our lab that demonstrated impaired grasping behaviour of apraxic patients when ventro-dorsal processing was required to account for the weight distribution of each object (Evans, Edwards, Taylor, & Ietswaart, 2016).

Another goal of the current study was to confirm whether the left IPL is the critical juncture where known and visual properties are integrated via the purported ventro-dorsal sub-stream, allowing accurate decisions regarding manipulation perception. If this is the case, patients with lesions implicating the left IPL were expected to perform poorly in the object manipulation condition. Based on the descriptive data from the radiologist reports and scan images, the lesioned areas in the patients in this study appear to follow the traditional pattern associated with apraxia involving the left IPL either directly or indirectly. Approximately half of the apraxic patients had lesions encompassing the left IPL. In the remaining apraxic patients, lesions did not involve the left IPL itself, but were in other regions of the frontoparietal network including the cerebellum, thalamus, broca's area, and underlying white matter, that are heavily associated with disruption of left IPL function, apraxia and object-use deficits (Goldenberg & Hagmann, 1998; Johnson-Frey, 2004; Buxbaum et al., 2005; Buxbaum et al., 2007; Sunderland et al., 2011). A review of apraxia from subcortical damage found that of 82 cases, a majority of patients had lesions implicating the putamen, thalamus, basal ganglia, internal capsule, and periventricular and peristriatal white matter (Pramstaller & Marsden, 1996). In cases where white matter damage disrupts corticocortical and corticosubcortical connections, apraxia can be persistent and severe (Leiguarda, 2001). A review by Lewis (2006) also confirmed that a majority of these regions are part of the cortical network activated during imagined object-use. Therefore, errors in the perception of object manipulation can occur after damage external to left IPL, suggesting that the ventro-dorsal stream can be indirectly disturbed by disrupting communication at different parts of the pathway. These findings support previous research confirming that lesions implicating the left IPL can give rise to apraxia and result in impaired perception of object-use manipulation (Buxbaum et al., 2005; Daprati & Sirigu, 2006; Buxbaum et al., 2007; Goldenberg 2009; Ishibashi et al., 2011). They also suggest that apraxia may be associated with deficits in motor imagery, which in turn compromise the integration of known and visual object properties.

However, due to the small number of apraxic patients in this study, it was not possible to conduct detailed voxel-based lesion-symptom mapping (VLSM) that would confirm whether, and to what degree, the left IPL has a critical role in performance errors during motoric judgements regarding object manipulation. Therefore the relationship between left IPL integrity and object-related movement representations can only be inferred in these patients. Nevetheless it is always difficult to make direct inferences from patient lesions because the pattern of results tends to be somewhat mixed. We therefore pursued to provide more direct evidence on whether the left IPL is the critical juncture where stored and visible properties are integrated using the same experimental paradigm in an analogous brain stimulation study.

By using the neuromodulation technique tDCS, Study 2 explored this question by directly targeting the left IPL. As indicated in the three-way interaction, perceptual decisions regarding object-use manipulation does seem to be modulated by left parietal cathodal-inhibitory stimulation (Experiment 2.1). Specifically, response times of perceptual decisions on the motoric manipulation task were slower during the first test block compared to sham. Critically, parietal inhibitory stimulation did not impact on reaction times when making non-motoric functional semantic decisions. These results therefore provide evidence that critically converges with the current findings in left hemisphere patients. Although the effects of inhibitory stimulation were found, akin to the impairment seen in lesioned patients, it was not the case that anodal-excitatory parietal stimulation (Experiment 2.2) generated performance enhancement.

Notably, tDCS had a somewhat marginal impact on manipulation decisions, where its effects were only seen during earlier trials (Block 1), but not during the later half of the task (Block 2). However, the effect of tDCS is not necessarily continuous. TDCS modulates cortical excitability rather than directly disrupting the neurons by causing an action potential (as with TMS), the effects of stimulation may change (Silvanto, Muggleton, & Walsh, 2008; Walsh, 2013) or be compensated for over time. Likewise, different cognitive processes may start to be recruited to compensate for the disruption of motor representations, for example by relying on visual opposed to motor strategies. The current findings would support the idea that less efficient alternative strategies kick in with time as the accuracy scores in the second block were found to be consistently reduced in all tasks and in both stimulation protocols (in fact this is the only effect found on accuracy in this study). This would account for a mild, and over time weakening, effect of tDCS on cognitive function. Furthermore, tDCS inhibiting the parietal cortex reduced performance but no effects of excitatory stimulation enhanced performance, despite recent reviews suggesting that achieving excitatory effects of stimulation during cognitive tasks are more likely (Nitsche & Paulus, 2011; Jacobson, Koslowsky, & Lavidor, 2012).

Nonetheless the effect of left parietal cathodal-inhibitory stimulation found on motoric manipulation decisions is consistent with selective deficit identified in apraxic patients during manipulation perception in this work, in particular when observing the substantially slowed reaction times of apraxic patients during this task (Appendix B). Further, it provides converging evidence for a wealth of neuroimaging data demonstrating increased left IPL activity when generating internal representations of movement, in particular when perceiving object related action (Kellenbach et al., 2003; Boronat et al., 2005; Buxbaum et al., 2006; Canessa et al., 2008), and observation or pantomime of object-use (Chao & Martin, 2000; Mozaz et al., 2002; Rumiati et al., 2004; Frey, 2007; Vingerhoets, 2008; Króliczak & Frey, 2009; Vingerhoets et al., 2009; Caspers et al., 2010). Unlike the correlational link between left IPL and manipulation perception provided by neuroimaging, the effects of tDCS support a causal relationship between left IPL integrity and object manipulation perception.

Conversely, performance during the non-motoric functional semantic task was unaffected when comparing sham to either left parietal cathodal-inhibitory or anodal-excitatory stimulation. In accordance with the patient study (Study 1), these results not only suggest that non-motoric functional semantic action representations do not rely on the integrity of the left parietal cortex, but also that it is independent from motoric manipulation perception. The selective effect of tDCS on manipulation perception decisions with maintained functional semantic judgements regarding object-use adds weight to the proposal that motoric action representations are generated in the ventro-dorsal sub-stream.

The experimental Manipulation task and the control Functional Semantic task were designed to make the tasks features as comparable as possible although matched task difficulty may have been compromised in this design process. Indeed, in both studies the Functional Semantic task was statistically easier than the Manipulation task. There are no indications however that poorer performance in the latter task could be applicable to task difficulty as opposed to impaired manipulation perception. In apraxic patients, the correlation between increased apraxia severity and reduced performance in the Manipulation condition relative to the Functional Semantic condition suggest that dissociations in task performance cannot be explained by task difficulty. This calculation also disentangled apraxia severity from stroke severity; correlation between performance in each task separately and apraxia severity may otherwise be attributed to stroke severity as opposed to apraxia. As most patients had comparable left hemisphere symptoms of receptive aphasia, it can be inferred that this correlation is not attributed to stroke severity as opposed to symptoms of apraxia. Further, if dissociations in task performance were applicable to task difficulty rather than impaired manipulation perception, the isolated effects of cathodal-inhibitory stimulation of the left IPL on manipulation decisions would not be present. This modulation suggests that performance in the Manipulation condition is dependent on the integrity of the ventro-dorsal sub-stream. Finally, inherent to the task design reaction times would not be comparable as response on the control task would always be faster because knowledge-based while the experimental task was designed to rely on motor imagery allowing time for this action simulation to take place.

Secondly, the stimuli in the Functional Semantic and Manipulation conditions differed; both conditions used line drawings of objects whereas photographs of hand postures were used in the latter condition. It is possible that by using different types of illustration unwanted variance was introduced between each task that may affect performance. However, in designing the tasks to maximise recognition gold-standard line drawings of objects were used to depict the object-object interactions in the Functional Semantic condition. In the Manipulation condition, photographs were chosen as they better illustrated the subtle differences in hand posture for each object, such as grip size and wrist orientation. As such, the risk of introducing variance between tasks had less consequence than having illustrations that did not clearly depict the object-object and object-hand relationships targeted in each task.

CONCLUSION

Left hemisphere patients with apraxia or healthy populations receiving cathodal-inhibitory stimulation over the left IPL demonstrated a selective impairment in perceptual decisions of motoric object manipulation that required motor imagery, whilst non-motoric functional semantic decisions that did not rely on motor imagery were maintained. Combined, these selective behavioural impairments support the suggestion that apraxia is associated with impaired internal movement representations due to damage to the purported ventro-dorsal stream of the visual pathways model. This stream can be compromised directly through disruption of the left IPL, confirming that the left IPL is likely to have an integral role in motoric action representations necessary for appropriate object-use including motor imagery, adding important causal evidence to neuroimaging findings.

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References

Benninger, D. H., Lomarev, M., Lopez, G., Wassermann, E. M., Li, X., Considine, E., & Hallett, M. (2010). Transcranial direct current stimulation for the treatment of Parkinson's disease. *Journal of Neurology, Neurosurgery, & Psychiatry, 81,* 1105-1111.

Bickerton, W-L., Samson, D., & Humphreys, G. W. (2011). Separating forms of neglect using the Apples Test: Validation and functional prediction in chronic and acute stroke. *Neuropsychology, 25*(5), 567-580.

Binkofski, F., & Buxbaum, L. J. (2013). Two action systems in the human brain. *Brain and Language*, *127*(2), 222–229.

Boronat, C. B., Buxbaum, L. J., Coslett, H. B., Tang, K., Saffran, E. M., Kimberg, D. Y., & Detre, J. A. (2005). Distinctions between manipulation and function knowledge of objects: evidence from functional magnetic resonance imaging. *Cognitive Brain Research*, *23*, 361–373.

Bracci, S., Cavina-Pratesi, C., Ietswaart, M., Caramazza, A., & Peelen, M. V. (2012). Closely overlapping responses to tools and hands in left lateral occipitotemporal cortex. Journal of neurophysiology, 107(5), 1443-1456.

Brodeur, M. B., Dionne-Dostie, E., Montreuil, T., & Lepage, M. (2010). The bank of standardized stimuli (BOSS), a new set of 480 normative photos of objects to be used as visual stimuli in cognitive research. *PloS ONE, 5*(5), e10773.

Buccino, G., Binkofski, F., Fink, G. R., Fadiga, L., Fogassi, L., Gallese, V., … Freund, H. J. (2001). Action observation activates premotor and parietal areas in a somatotopic manner: an fMRI study. *The European Journal of Neuroscience*, *13*(2), 400–404.

Buxbaum, L. J. (2001). Ideomotor apraxia: a call to action. *Neurocase*, *7*(6), 445–458.

Buxbaum, L. J., & Kalénine, S. (2010). Action knowledge, visuomotor activation, and embodiment in the two action systems. *Annals of the New York Academy of Sciences*, *1191*, 201–218.

Buxbaum, L. J., & Saffran, E. M. (2002). Knowledge of object manipulation and object function: dissociations in apraxic and nonapraxic subjects. *Brain and Language*, *82*(2), 179–199.

Buxbaum, L. J., Johnson-Frey, S. H., & Bartlett-Williams, M. (2005). Deficient internal models for planning hand-object interactions in apraxia. *Neuropsychologia*, *43*(6), 917–929.

Buxbaum, L. J., Kyle, K. M., Tang, K., & Detre, J. a. (2006). Neural substrates of knowledge of hand postures for object grasping and functional object use: evidence from fMRI. *Brain Research*, *1117*(1), 175–185.

Buxbaum, L. J., Kyle, K., Grossman, M., & Coslett, H. B. (2007). Left inferior parietal representations for skilled hand-object interactions: evidence from stroke and corticobasal degeneration. *Cortex*, *43*, 411–423.

Canessa, N., Borgo, F., Cappa, S. F., Perani, D., Falini, A., Buccino, G., … Shallice, T. (2008). The Different Neural Correlates of Action and Functional Knowledge in Semantic Memory: An fMRI Study. *Cerebral Cortex*, *18*, 740–751.

Caspers, S., Zilles, K., Laird, A. R., & Eickhoff, S. B. (2010). ALE meta-analysis of action observation and imitation in the human brain. *NeuroImage*, *50*(3), 1148–1167.

Chao, L. L., & Martin, A. (2000). Representation of manipulable man-made objects in the dorsal stream. *Neuroimage, 12,* 478-484.

Chen, Q., Garcea, F. E., & Mahon, B. Z. (2015). The Representation of Object-Directed Action and Function Knowledge in the Human Brain. *Cerebral Cortex*, bhu328.

Cohen, M. S. (2008, August 19). Handedness Questionnaire. Retrieved February, 2011, from http://www.brainmapping.org/shared/Edinburgh.php#.

Creem-Regehr, S. H. (2009). Sensory-motor and cognitive functions of the human posterior parietal cortex involved in manual actions. *Neurobiology of Learning and Memory*, *91*(2), 166–171.

Cycowicz, Y. M., Friedman, D., Rothstein, M., & Snodgrass, J. G. (1997). Picture Naming by Young Children: Norms for Name Agreement, Familiarity, and Visual Complexity. *Journal of Experimental Child Psychology, 65,* 171-237.

Daprati, E., & Sirigu, A. (2006). How we interact with objects: learning from brain lesions. *TRENDS in Cognitive Sciences*, *10*(6), 265–270.

De Renzi, E., & Faglioni, P. (1978). Normative data and screening power of a shortened version of the Token Test. *Cortex, 14*(1), 41-49.

De Renzi, E., & Lucchelli, F. (1988). Ideational apraxia. *Brain*, *111*, 1173–1185.

Evans, C., Edwards, M. G., Taylor, L. J., & Ietswaart, M. (2016). Impaired communication between the dorsal and ventral stream: indications from Apraxia. *Frontiers in Human Neuroscience, 10*(8).

Frey, S. H. (2007). What puts the how in where? Object use and the divided visual streams hypothesis. *Cortex*, *43*, 368–375.

Gao, Q., Duan, X., & Chen, H. (2011). Evaluation of effective connectivity of motor areas during motor imagery and execution using conditional Granger causality. *NeuroImage*, *54*(2), 1280–1288.

Goldenberg, G. (1995). Imitating gestures and manipulating a manikin – the representation of the human body in ideomotor apraxia. *Neuropsychologia, 33*(1), 63-72.

Goldenberg, G. (1996). Defective imitation of gestures in patients with damage in the left or right hemispheres. *Journal of Neurology, Neurosurgery, and Psychiatry, 61,* 176-180.

Goldenberg, G., & Hagmann, S. (1998). Tool use and mechanical problem solving in apraxia. *Neuropsychologia*, *36*(7), 581–589.

Goldenberg, G., Hermsdörfer, J., Glindemann, R., Rorden, C., & Karnath, H-O. (2007). Pantomime of tool use depends on integrity of left inferior frontal cortex. Cerebral Cortex (New York, N.Y. : 1991), 17(12), 2769–76.

Haaland, K. Y., Harrington, D. L., & Knight, R. T. (2000). Neural representations of skilled movement. *Brain*, *123*, 2306–2313.

Harris, I. M., & Miniussi, C. (2003). Parietal Lobe Contribution to Mental Rotation Demonstrated with rTMS. *Journal of Cognitive Neuroscience*, *15*(3), 315–323.

Hétu, S., Grégoire, M., Saimpont, A., Coll, M. P., Eugène, F., Michon, P. E., & Jackson, P. L. (2013). The neural network of motor imagery: An ALE meta-analysis. Neuroscience and Biobehavioral Reviews, 37(5), 930–949.

Hodges, J. R., Bozeat, S., Lambon Ralph, M. a, Patterson, K., & Spatt, J. (2000). The role of conceptual knowledge in object use evidence from semantic dementia. *Brain : A Journal of Neurology*, *123*, 1913–25.

Ietswaart, M., Butler, A., Jackson, P., & Edwards, M.G. (2015). Mental Practice: clinical and experimental research in imagery and action observation. *Frontiers in Human Neuroscience*, 9, 573.

Ietswaart, M., Carey, D. P., & Della Sala, S. (2006). Tapping, grasping and aiming in ideomotor apraxia. *Neuropsychologia*, *44*(7), 1175–84.

Ietswaart, M., Carey, D. P., Della Sala, S., & Dijkhuizen, R.S. (2001) Memory-driven movements in limb apraxia: Is there evidence for impaired communication between the dorsal and ventral streams? *Neuropsychologia,* 39, 950-961.

Ishibashi, R., Lambon Ralph, M. a, Saito, S., & Pobric, G. (2011). Different roles of lateral anterior temporal lobe and inferior parietal lobule in coding function and manipulation tool knowledge: evidence from an rTMS study. *Neuropsychologia*, *49*(5), 1128–1135.

Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: a meta-analytical review. *Experimental Brain Research*, *216*(1), 1–10.

Jeannerod, M. (1994). The representing brain: Neural correlates of motor intention and imagery. *Behavioral and Brain Sciences*, *17*(02), 187–245.

Johnson-Frey, S. H. (2004). Stimulation through simulation? Motor imagery and functional reorganization in hemiplegic stroke patients. *Brain and Cognition*, *55*(2), 328–31.

Johnson-Frey, S. H., Newman-Norlund, R., & Grafton, S. T. (2005). A distributed left hemisphere network active during planning of everyday tool use skills. *Cerebral Cortex (New York, N.Y. : 1991)*, *15*(6), 681–95.

Kellenbach, M. L., Brett, M., & Patterson, K. (2003). Actions Speak Louder Than Functions: The Importance of Manipulability and Action in Tool Representation. *Journal of Cognitive Neuroscience*, *15*(1), 30–46

Kosslyn, S. M., Ganis, G., & Thompson, W. L. (2001). Neural foundations of imagery. *Nature Reviews Neuroscience, 2,* 635-642.

Króliczak, G., & Frey, S. H. (2009). A common network in the left cerebral hemisphere represents planning of tool use pantomimes and familiar intransitive gestures at the hand-independent level. *Cerebral Cortex (New York, N.Y. : 1991)*, *19*(10), 2396–410. doi:10.1093/cercor/bhn261

Lee, C.-I., Mirman, D., & Buxbaum, L. J. (2014). Abnormal dynamics of activation of object use information in apraxia: Evidence from eyetracking. *Neuropsychologia*, *59C*, 13–26.

Leiguarda, R. (2001). Limb apraxia: cortical or subcortical. *NeuroImage*, *14*, 137–41.

Lewis, J. W. (2006). Cortical networks related to human use of tools. *The Neuroscientist*, *12*(3), 211–231.

Lotze, M., & Cohen, L. G. (2006). Volition and Imagery in Neurorehabilitation. *Cognitive & Behavioural Neurology, 19*(3),135-140.

Milner A. D., & Goodale M. A. (2006). *The Visual Brain in Action* (2nd ed.). Oxford: Oxford University Press.

Mozaz, M., Rothi, L. J. G., Anderson, J. M., Crucian, G. P., & Heilman, K. M. (2002). Postural knowledge of transitive pantomimes and intransitive gestures. *Journal of the International Neuropsychological Society*, *8*(7), 958–962.

Myung, J., Blumstein, S. E., Yee, E., Sedivy, J. C., Thompson-Schill, S. L., & Buxbaum, L. J. (2010). Impaired access to manipulation features in Apraxia: evidence from eyetracking and semantic judgment tasks. *Brain and Language*, *112*(2), 101–12.

Nitsche, M. a, Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., … Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. Brain Stimulation, 1(3), 206–23.

Nitsche, M. a, Liebetanz, D., Lang, N., Antal, A., Tergau, F., & Paulus, W. (2003). Safety criteria for transcranial direct current stimulation (tDCS) in humans. *Clinical Neurophysiology*, *114*, 2220–2222.

Nitsche, M. A, & Paulus, W. (2011). Transcranial direct current stimulation--update 2011. *Restorative Neurology and Neuroscience*, *29*(6), 463–92.

Oldfield, R.C. "The assessment and analysis of handedness: the Edinburgh inventory." Neuropsychologia. 9(1):97-113. 1971.

Pramstaller, P. P., & Marsden, C. D. (1996). The basal ganglia and apraxia. *Brain*, *119*(1), 319-340.

Randerath, J., Li, Y., Goldenberg, G., & Hermsdörfer, J. (2009). Grasping tools: effects of task and apraxia. *Neuropsychologia*, *47*(2), 497–505.

Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., & Hermsdörfer, J. (2011). From pantomime to actual use: how affordances can facilitate actual tool-use. *Neuropsychologia*, *49*(9), 2410–6. s

Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience*, *27*, 169–92.

Rizzolatti, G., & Matelli, M. (2003). Two different streams form the dorsal visual system: anatomy and functions. *Experimental Brain Research*, *153*(2), 146–157.

Rizzolatti, G., Fogassi, L., & Luppino, G. (2011). The Two Dorsal Visual Streams and Their Role in Perception. In L. M. Chalupa, N. Berardi, M. Caleo, L. Galli-Resta, & T. Pizzorusso (Eds.), *Cerebral Plasticity: New Perspectives* (pp. 259–273). Cambridge, Massachusetts: MIT Press.

Rorden, C., Karnath, H-O., & Bonilha, L. (2007). Improving lesion-mapping. *Journal of Cognitive Neuroscience, 19*(7), 1081-1088.

Rorden, C., Bonilha, L., Fridriksson, J., Bender, B., & Karnath, H-O. (2012). Age-specific CT and MRI templates for spatial normalization. NeuroImage, 61(4), 957-965.

Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. (2011). Screening questionnaire before TMS: an update. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *122*(8), 1686.

Rumiati, R. I., Weiss, P. H., Shallice, T., Ottoboni, G., Noth, J., Zilles, K., & Fink, G. R. (2004). Neural basis of pantomiming the use of visually presented objects. *NeuroImage*, *21*(4), 1224–1231.

Schenk, T., & McIntosh, R. D. (2010). Do we have independent visual streams for perception and action? *Cognitive Neuroscience, 1*(1), 52-78.

Silvanto, J., Muggleton, N., & Walsh, V. (2008). State-dependency in brain stimulation studies of perception and cognition. *Trends in Cognitive Sciences*, *12*(12), 447–454.

Sirigu, A., Cohen, L., Duhamel, J.-R., Pillon, B., Dubois, B., & Agid, Y. (1995). A Selective Impairment of Hand Posture for Object Utilization in Apraxia. *Cortex*, *31*(1), 41–55.

Solodkin, A., Hlustik, P., Chen, E. E., & Small, S. L. (2004). Fine Modulation in Network Activation during Motor Execution and Motor Imagery. *Cerebral Cortex*, *14*(11), 1246–1255.

Sunderland, A., Wilkins, L., & Dineen, R. (2011). Tool use and action planning in apraxia. *Neuropsychologia*, *49*(5), 1275–86.

Vingerhoets, G. (2008). Knowing about tools: neural correlates of tool familiarity and experience. *NeuroImage*, *40*(3), 1380–91.

Vingerhoets, G. (2014). Contribution of the posterior parietal cortex in reaching, grasping, and using objects and tools. *Frontiers in Psychology*, *5*, 151.

Vingerhoets, G., Acke, F., Vandemaele, P., & Achten, E. (2009). Tool responsive regions in the posterior parietal cortex: effect of differences in motor goal and target object during imagined transitive movements. *NeuroImage*, *47*(4), 1832–1843.

Walsh, V. Q. (2013). Ethics and social risks in brain stimulation. *Brain Stimulation*, *6*(5), 715–717.

APPENDICES

Appendix A

Table A1. *Apraxia screening performance and error types including excluded participants MS and GW.*

Patient	Apraxia Screening Gesture Imitation (total score)				Object use (total score)			
	Hand (20)	*Errors*	Fingers (20)	*Errors*	Pantomime (53)	*Errors*	Actual (18)	*Errors*
FR	20		17	*fe*	53		18	
JAH	16	*hm; sm*	20		48	*bpo*	18	
JH	19		17	*fe*	53		18	
HG	10	*hm; sm*	18/18		53		18	
DF	15	*Hm*	19		47	*bpo; sm*	18	
MAS	17	*Hm*	19		31	*bpo; sm*	18	
AA	10	*hm; sm*	12	*p of hands; fe.*	21	*so; ss*	15	*so; ss*
JA	19		20		26	*ao; aa; gm; sm*	16	*ao; aa; gm; sm*
PB	17	*hm; sm*	17	*fe*	14	*so; aa; bpo; ss*	13	*ao; aa*
AH	19		19		33	*ao; bpo; sm; ss;*	18	
WM	18	*Sm*	12	*sm*	48		18	
TM	17	*fe; sm*	19		53		18	
MS	5	*p; hm; fe*	0	*fe; sm*	3	*ao; bpo; ss*	12	*ao; so; aa; ss*
GW	16	*Hm; sm*	4	*p of hands; sm*	10	*ao; aa*	16	*aa*

Note. Types of performance error have been given the following acronyms: GESTURE IMITATION: perseveration (p); hand misorientation (hm): misorientation of the hand relative to the face; finger extension (fe): incorrect fingers extended from hand; spatial misorientation (sm): hand misorientation relative to the experimenter, e.g. back of hand instead of palm facing. OBJECT USE: action addition (aa): miscellaneous actions not interpretable as a step in the task, e.g. waving; action omission (ao): failed to perform any recognisable action; step omission (so): failed to complete some parts of the movement, e.g. rotating hand when squeezing a lemon; body-part-as-object (bpo): e.g. brush teeth with finger; semantic substitution (ss): e.g. stir with fork; grasp misestimation (gm): incorrect grasp size/type for object, e.g. pincer grip for cup; spatial misestimation (sm): incorrect relationship between object relative to body or another (reference) object.

Appendix B

Mixed Model ANOVA results for Accuracy (%) of participants in Study 1.

Accuracy (%). A main effect of Task ($F_{(1,35)}$ = 36.252, p <.001) revealed that both apraxic and control participants performed worse in the motoric Manipulation condition (M = 83% ± 13) compared to the non-motoric Functional Semantic condition (M = 96% ± 6). A non-significant main effect of Apraxia ($F_{(1,35)}$ = 2.670, p =.111) and Task x Apraxia ($F_{(1,35)}$ = 2.758, p =.106) was also confirmed. Although these results suggest there was no great difference in accuracy performance between apraxic and control participants, descriptive data indicates that both control groups performed similarly in the Functional Semantic condition (apraxic patients M = 95% ± 6, healthy controls M = 96% ± 5) yet apraxic patients' accuracy was markedly poorer and more varied than controls in the Manipulation condition (apraxic patients M = 80% ± 16, healthy controls M = 87% ± 9). The variance in apraxic performance may be accounted for by the variance in apraxia severity of these patients, which may also be masking any interaction effects (see Figure A1).

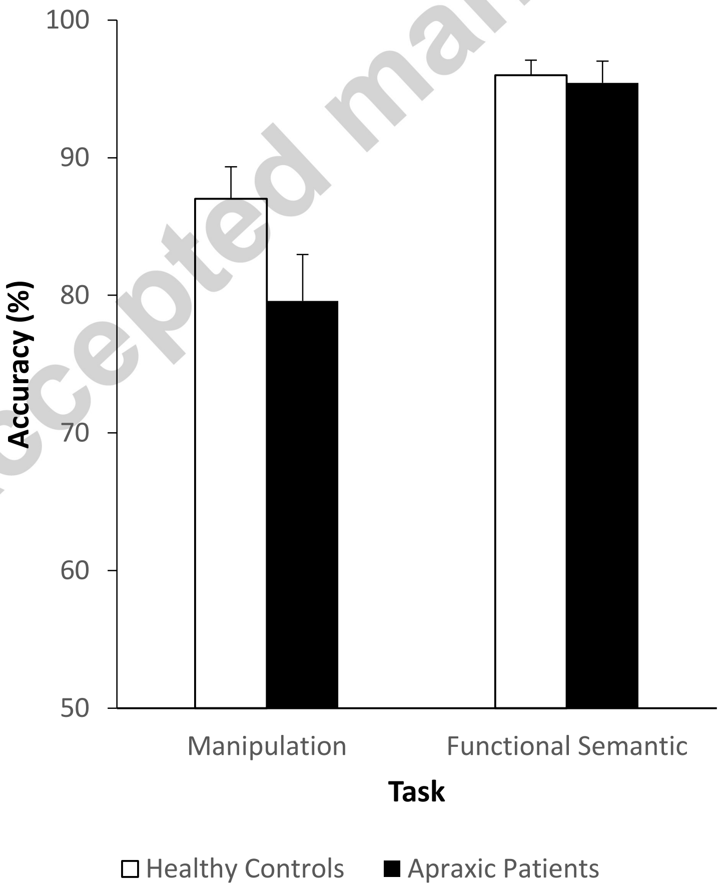

Figure A1. Accuracy (%) results for apraxic and healthy control participants in the motoric Manipulation and non-motoric Functional Semantic conditions of the experimental task. Standard Error (SE) bars are plotted for each condition and participant group.

Mixed Model ANOVA results for Reaction Time (s) of participants in Study 1.

Reaction Time (s). The mixed model ANOVA revealed a significant main effect of Task ($F_{(1,35)}$ = 14.595, p =.001) indicating that both apraxic patients and controls were slower when making motoric Manipulation decisions (M = 63.168 ± 5.977) compared to non-motoric Functional Semantic decisions (M = 67.295 ± 8.290). A main effect of Apraxia ($F_{(1,35)}$ = 12.699, p =.001) also confirmed that apraxic patients were slower overall (M = 69.083 ± 11.297) compared to controls (M = 61.380 ± 2.970). Notably, a significant Task x Apraxia interaction ($F_{(1,35)}$ = 8.813, p =.005) was observed. Post-hoc independent samples t-tests showed that apraxic patients were significantly slower (M = 72.750 ± 12.700) when making Manipulation decisions ($t_{(11.997)}$ = 2.911, p =.013) compared to controls (M = 61.840 ± 3.880), whereas RTs were comparable between apraxic patients and controls when making Functional Semantic decisions ($t_{(11.460)}$ = 1.558, p =.146).

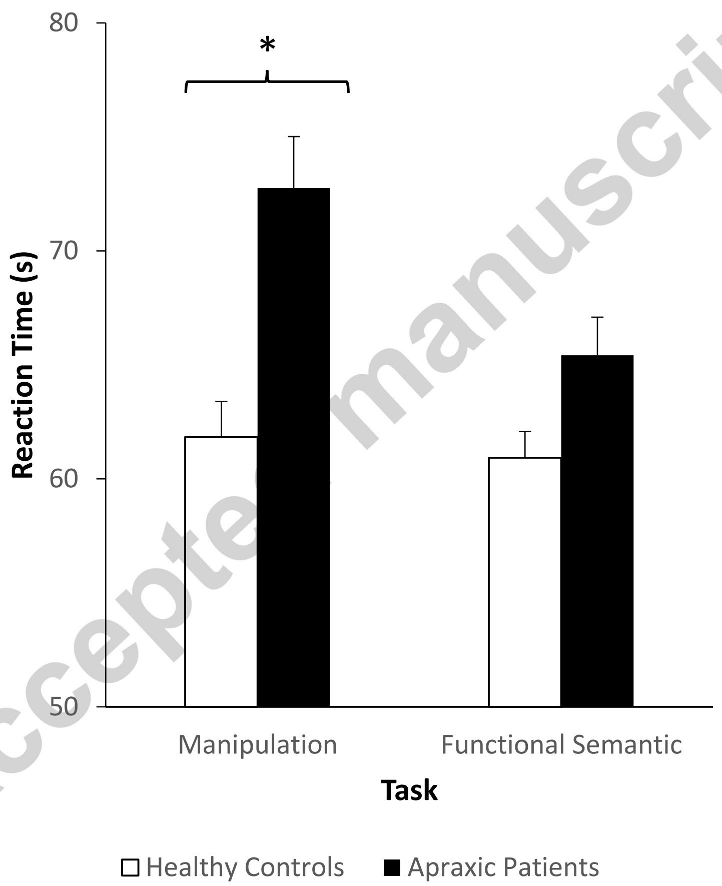

Figure A2. Reaction Time (s) results for apraxic and healthy control participants in the motoric Manipulation and non-motoric Functional Semantic conditions of the experimental task. Standard Error (SE) bars are plotted for each condition and participant group. An asterisk marks the significant difference between apraxic and control participants in the Manipulation condition.

Highlights

- Apraxia is associated with deficits in motor imagery due to compromised integration of known and visible object properties or ventro-dorsal cross talk.

- Motoric perceptual decisions of object-use are compromised through left inferior parietal brain stimulation, indicating a critical role of this region in apraxia and motor imagery.
- Representations of motoric object manipulation are independent from representations of non-motoric semantic object interaction.
- Motor representations are implicated in the ventro-dorsal sub-stream of the two visual pathway model.