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INTENSIVE LANGUAGE ACTION THERAPY AND RECOVERY IN CHRONIC APHASIA

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ABSTRACT

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Intensive Language Action Therapy (ILAT) is a short-term aphasia therapy that emphasises massed-practise of language, where communication is framed through language action games that approximate everyday interactions. Despite increasing interest in ILAT, a comprehensive description of its methods has thus far been missing. Furthermore due to inconsistent results, further exploration of cortical reorganisation of language functions following ILAT is warranted.

The underlying principles and practical features of ILAT methods and of language-action games are fully described, including the structure and materials for two specific games. 14 English speaking patients with chronic aphasia underwent two weeks of ILAT utilising the methods outlined. Pre and post measures of language performance were collected through standardised clinical assessments, along with functional Magnetic Resonance Imaging scans from a subset of 8 patients. Accuracy and response times for speech output and comprehension during language-action games were also recorded to measure success during the therapy interval.

Data analysis showed significant improvements in clinical assessments of naming and comprehension, but not in auditory or syntactic processing tasks. Significant increases were also seen in patients' self-ratings of quality of communication following therapy. Video and voice recordings during therapy sessions demonstrated significantly faster response times in production and comprehension of language, alongside an increase in the complexity of patients' spoken output. Cortical activation was recorded whilst patients heard low-level noise, sentences containing ambiguous words and low-ambiguity sentences. Although the results showed no changes in cortical activation in the group of patients whilst processing low-level noise or low ambiguity sentences, increases in language-induced activation were seen in single-subject analyses in both the left and right hemispheres. Furthermore the group of patients recruited the right hemisphere significantly more than the left hemisphere following ILAT when processing complex sentences containing ambiguous words.

Clinical assessments and measures of everyday communication showed undergoing two weeks of ILAT significantly improved speech output and comprehension in patients with chronic aphasia. Gains made in communicative performance during therapy highlight the importance of recording therapy sessions for additional assessment of therapy efficacy. Although conclusions regarding cortical reorganisation are not entirely clear, they indicate the important role of the right hemisphere in reorganisation of language after stroke.

Key words: aphasia, neurorehabilitation, cortical reorganisation, intensive language therapy, constraint-induced aphasia therapy, communicative aphasia therapy

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LIST OF ACRONYMS

ALI	Automatic lesion identification
ANOVA	Analysis of variance
BDAE	Boston Diagnostic Aphasia Battery
BNT	Boston Naming Test
CAL	Communicative Activity Log
CI	Complexity Index
CIAT	Constraint-Induced Aphasia Therapy
CIAT-G	Constraint-Induced Aphasia Therapy with grammatical constraints
CILT	Constraint-Induced Language Therapy
CIMT	Constraint-Induced Motor Therapy
CONV	Conventional therapy
CVA	Cerebrovascular accident
EEG	Electroencephalography
fMRI	functional Magnetic Resonance Imaging
FWE	Family wise error
IFG	Inferior frontal gyrus
ILAT	Intensive Language Action Therapy
IPC	Inferior parietal cortex
ITG	Inferior temporal gyrus
LAG	Language action game
LH	Left hemisphere
LIFG	Left inferior frontal gyrus
MCA	Middle cerebral artery
MEG	Magnetoencephalography

MRI	Magnetic Resonance Imaging
MTG	Middle temporal gyrus
PACE	Promoting Aphasic's Communicative Effectiveness
PSA	Post-stroke aphasia
RCT	Randomised controlled trial
RH	Right hemisphere
RIFG	Right inferior frontal gyrus
ROI	Region of interest
RT	Response time
SCN	Signal correlated noise
SFG	Superior frontal gyrus
SLT	Speech and language therapy
SPM	Statistical Parametric Mapping
STG	Superior temporal gyrus
SWA	Slow wave activity
TMS	Transcranial magnetic stimulation
TP	Temporal pole
TT	Token Test

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INTENSIVE LANGUAGE ACTION THERAPY AND RECOVERY IN CHRONIC APHASIA

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CHAPTER 1: INTRODUCTION

1.1 BACKGROUND

Stroke represents one of the major health problems worldwide and is a frequent cause of severe long term disability, often leading to post-stroke aphasia (PSA). In PSA, damage to cortical language areas, i.e. around the left perisylvian region, and to underlying functional connections in the brain leads to a chronic condition where patients are left with mild to severe speech and language deficits. It is reported that around 40 per 100,000 individuals in Europe suffer from PSA each year following a first ischemic stroke, and that this incidence rate increases with age (Engelter et al., 2006). Furthermore at onset of stroke, a diagnosis of severe aphasia is given in a quarter to a half of all PSA patients (Engelter et al., 2005; Pederson, Vinter & Olsen, 2004).

Spontaneous recovery is often seen within the first few weeks to months following a stroke (Berthier, 2005; Berthier & Pulvermüller, 2011) and frequently the severity of aphasia improves over the first year post-stroke, with more severe cases developing into less severe forms (Klebic, Salihovic, Softic & Salihovic, 2011). However since stroke patients can often face long-term problems in communication, PSA can often lead to dependence on others and further potentially detrimental social and emotional consequences, including isolation and depression (Berthier & Pulvermüller, 2011; Feigin, Lawes, Bennett & Anderson, 2003).

Theory and research regarding therapeutic interventions which may improve language capacities therefore, is of utmost importance. There is evidence of improvement in language abilities following speech and language therapies (SLTs; Cicerone et al, 2005). A number of authors corroborate the merits of SLT, particularly when it is executed in a rigorous fashion and initiated early after brain injury (Robey, 1998; Sarno & Levita, 1979). Furthermore there is evidence to suggest more intense therapies may be beneficial (Bhogal, Teasell & Speechley, 2003; Cherney, Patterson, Raymer, Frymark & Schooling, 2008).

There are several neural mechanisms reported to be involved in functional language recovery. Patients with limited damage to the left hemisphere (LH) may engage the spared language regions or recruit compensatory perilesional areas – i.e. areas surrounding the damaged LH parts. Patients with more extensive LH damage may also engage, at least partly, the homologous right hemisphere (RH) regions – i.e. the corresponding undamaged RH areas (Berthier et al., 2011; Saur et al, 2006; Turkeltaub, Messing, Norise & Hamilton, 2011). However the literature is characterised by a widespread dearth of scientific evidence and to date, the changes which occur in the brain due to recovery from aphasia remain to a large degree, unknown.

1.2 INTENSIVE LANGUAGE ACTION THERAPY

Intensive Language Action Therapy (ILAT) refers to a set of techniques for SLT that emphasise: massed practise; action-embedded use of language that is relevant for daily life; and the focusing and tailoring of treatment to the individual patients' communicative abilities and needs. It has been shown that one form of ILAT, called Constraint-Induced Aphasia Therapy (CIAT), is successful in improving language in chronic PSA within a short period of time (Pulvermüller et al, 2001). The success of CIAT (also known as Constraint Induced Language Therapy, CILT) in the treatment of chronic aphasia has been replicated by several studies (Berthier et al., 2009; Faroqi-Shah & Virion, 2009; Goral & Kempler, 2009; Kirmess & Maher, 2010; Kurland, Pulvermüller, Silva, Burke & Andrianopoulos, 2012; Maher et al., 2006; Meinzer, Djundja, Barthel, Elbert & Rockstroh, 2005; Szaflarski et al., 2008).

1.3 NEUROSCIENTIFIC PRINCIPLES AND THEIR PRACTICAL IMPLICATIONS

ILAT developed from two major roots: communicative and pragmatic SLT (Aten, Caligiuri & Holland, 1982; Davis & Wilcox, 1985; Pulvermüller & Roth, 1991) and constraint-induced therapy of motor deficits caused by stroke and other brain diseases (Constraint-Induced Motor Therapy, CIMT; see Taub, Crago & Uswatte, 1998; Taub, Uswatte & Pidikiti, 1999). Similar to CIMT, ILAT employs the three neuroscientific principles of *massed practise*, *behavioural relevance*, and *focussing* of patients by guidance provided by the training context, shaping, and other behavioural techniques. Similar to pragmatic and communicative aphasia therapy, speech acts and their sequences from everyday dialogues constitute the frames for therapeutic interaction, thus rendering these interactions behaviourally relevant. Focussing is provided by the structure of the training interactions, which are inspired by Wittgenstein's (1953) concept of language games. Speech act sequences are embedded into game-like activities, which allow for repeated practice of words, utterances and sentence structures. Materials which connect speaking and writing with non-linguistic actions, allow the tailoring of SLT to the patients' communicative needs. Further guidance comes from communication partners (particularly therapists) acting as role models and from communicative success in the games.

The new term 'intensive language-action' therapy is now used instead of the old term 'constraint-induced' aphasia therapy as the term constraint has given rise to misunderstandings in the past. One type of concern had arisen based on the forceful suppression association of the word 'constraint'. As the method itself gives no reason for any concern of this sort, the friendlier terminology, speaking for example about 'guiding' patients instead of 'constraining' them is used, thus hoping to avoid the misunderstanding in future (Difrancesco, Pulvermüller & Mohr, 2012). A further misunderstanding had arisen based on the relationship between ILAT and CIMT of stroke-related lateralised motor deficits. The latter includes putting the unaffected arm in a sling to thereby constrain its use and force use of the affected extremity. In analogy CIAT had been understood to prohibit any kind of non-verbal communication and gesturing, although as is discussed below, its aim is to encourage verbal communication, also if it is accompanied and supported by nonverbal action. Nonverbal communication replacing verbal activity should be avoided, but the concordant verbal communication and other body actions are in fact desirable (see Section 1.3.2).

The new term ILAT, may not only help to overcome the above misunderstandings, but is also informative as it highlights two important features of the approach: first that it is an *intensive* method, typically applied several hours per day, and second, that language is being practised in *action-contexts*. An additional advantage of the new term is the fact that its use can be slightly wider. Whereas CIAT primarily covered one specific type of communication, that is request interactions, a broader and gradually increasing spectrum of communication types and speech acts is targeted in the ILAT context. The neuroscience foundation of the three main principles constituting ILAT: intensive practice, communicative and behavioural relevance, and focussing, will now be explained.

1.3.1 Intensive Practise

Neuroscience research demonstrates that when networks of neurons in the brain are frequently simultaneously active, they become strongly connected with each other. In contrast, asynchronous firing weakens established synaptic links (Hebb, 1949; Tsumoto, 1992). The correlation learning implied by the ‘fire together – wire together’ rule has implications for the representation and processing of language in the human brain (Pulvermüller, 1999). In early language learning, babbling in human infants becomes fine-tuned to specific speech sounds or phonemes they frequently hear. Connections between inferior frontal regions which control articulations and the auditory areas in the superior temporal regions become strengthened leading to action-perception circuits for phonemes and words (Pulvermüller & Fadiga, 2010). Correlation learning may therefore be relevant for the basic mapping between articulations and speech signals. Such learning may however, also play a role for acquiring semantic and linguistic-pragmatic knowledge. As words are frequently used in the context of their referent objects or actions, simultaneous activation of neuronal circuits, for example in the visual or motor systems and in the language cortex, results. Hebbian learning principles therefore imply the formation of a connection and semantic linkage between word form representations in the cortical language system (left-perisylvian cortex) and their related concept representations in other parts of the cortex, including sensorimotor and multimodal areas (Pulvermüller, Kiff & Shtyrov, 2012). Similar correlation learning may also occur for syntax (Pulvermüller, 2001; Pulvermüller & Fadiga, 2010).

Conversely, if connected neurons are frequently active independently from each other, their connections undergo synaptic weakening. Such ‘anti-Hebb’ learning (Tsumoto, 1992) may become relevant to language in cases of brain injury, for example when partial damage to the circuit connecting word form and concept does not allow the conceptual circuit to spark the linguistic one, and vice versa. Use of an inappropriate word may lead to further anti-Hebb learning, which could therefore imply further weakening of the already damaged word-concept links (Berthier & Pulvermüller, 2011; Pulvermüller & Berthier, 2008).

These considerations have clear implications for neurorehabilitation. As much as co-activation of crucial neuronal circuits should be encouraged, the independent activation of circuit parts should be avoided. ILAT aims to re-strengthen links between phonological, lexical, semantic, and conceptual circuits, which include action- and perception-related circuits, by co-activating these neuronal ensembles (Berthier & Pulvermüller, 2011). Regular, intensive practise may facilitate coincidence learning to obtain rewiring of synaptic connections and behavioural (language) changes in patients. Critically, increasing the frequency of daily practice and therefore reducing the time delay between therapy sessions should minimise the possibility that circuit parts are activated in isolation and crucial connections degrade, for example when words are used in an inappropriate context so that synaptic weakening of word-concept links may result.

It therefore appears useful to aim at practicing language in an intensive training regime, with many therapy hours applied in as short a time as possible. One potential problem frequently suggested regarding ILAT, relates to this high-intensity aspect and a related practicability issue. As the therapy is so intense, it has been claimed that the clinical day-to-day practice cannot deal with such high demand. This is a false argument. Randomised controlled trials (RCT) have shown *the same amount of* SLT delivered in a short time period, in an intensive language-action setting, is more efficient than stretched out over several weeks in a classical training regime (Pulvermüller et al., 2001). Therefore it is not required to provide overall more treatment hours to make therapy more efficient, but it is important to *re-structure the delivery of therapy* so that the same patient can receive treatment within a shorter time interval, ideally on a day-to-day basis in order to enhance the learning effects.

1.3.2 Behavioural and Communicative Relevance

The second theoretical principle addresses the communicative and behavioural relevance of language use in the therapeutic settings. This principle builds on work in communicative and pragmatic SLT which aims to improve patients' abilities to communicate in everyday-life conversations (Aten et al, 1982; Davis & Wilcox, 1985; Pulvermüller & Roth, 1991). In one form of communicative therapy called PACE (Promoting Aphasic's Communicative Effectiveness; Davis and Wilcox, 1985), drawings, pictures, and other visually-stimulating items are used to promote information dialogues and spontaneous communication including turn taking. Building on PACE, communicative-aphasia therapy was further developed to widen the spectrum of speech acts and communication forms targeted in aphasia therapy (Pulvermüller & Roth, 1991). To this end, Wittgenstein's (1953) concept of *language games* was systematically exploited and a range of therapeutic language action games (LAGs) were created to approximate and allow the practise of different communication forms, including requesting, joint planning, storytelling, giving directions etc. (Pulvermüller & Roth, 1991). These LAGs form the therapy frames of ILAT (Pulvermüller & Berthier, 2008).

As discussed in the previous section, semantic links established during language learning can connect neuronal ensembles in left-perisylvian language regions with sensorimotor areas. Inferior frontal and parietal sensorimotor areas are strongly active during language perception and comprehension in general (Berthier & Pulvermüller, 2011; Fadiga, Craighero, Buccino & Rizzolatti, 2002; Pulvermüller, 2005; Pulvermüller & Fadiga, 2010; Pulvermüller, Kiff & Shtyrov, 2012; Pulvermüller, Shtyrov, & Ilmoniemi, 2003; Watkins, Strafella & Paus, 2003). Interestingly, specific semantic relationships of words are also manifest in sensory and motor systems of the brain. Reading or hearing the word 'grasp' co-activates the specific motor areas that would be active if the person actually performed the word-related action (i.e. grasping; Hauk, Johnsrude & Pulvermüller, 2004). Semantic action links between motor and linguistic regions appear to be bi-directional whereby stimulation (using transcranial magnetic stimulation, TMS) of topographical areas of the motor cortex such as the leg or arm area has been shown to improve reaction time to the recognition of leg-related and arm-related words, respectively (Pulvermüller, Hauk, Nikulin & Ilmoniemi, 2005). Similarly, specific brain activation to semantic features occurs in visual, auditory, gustatory and olfactory brain areas when processing linguistic expressions relating to visual information (about colour or form), tastes, odours or sounds (Barrós-Loscertales et al., 2012; González et al., 2006; Kiefer, Sim, Herrnberger, Grothe & Hoenig, 2008; Pulvermüller & Hauk, 2006).

These findings have strong implications for aphasia therapy. If language and action systems of the brain are strongly interwoven, one of the two can help the other to activate in case of focal lesion. Therefore practising language in interactions where words appear in their natural context of nonlinguistic actions and object perceptions should be of utmost relevance to re-activate language circuits. One example for this would be to pick up (a card depicting) an apple and handing over the (card depicting an) apple when asked by someone else. Alternatively, verbally agree to join in playing tennis whilst simultaneously performing/mimicking the action of using a tennis racket. In this case, neural activity may spread from sensorimotor areas to facilitate processing in those parts of the language networks that are affected by brain damage (Berthier & Pulvermüller, 2011; Pulvermüller & Berthier, 2008). The focus on linking language with sensorimotor networks in ILAT differentiates this therapeutic approach from SLT aimed purely at producing linguistic utterances or structures, with little attention to action embedding and speech act features of the verbal output.

In essence, the close functional links between language and action systems of the brain, along with the well-known a priori knowledge about the pragmatic role of language as a communicative tool in interaction between people, lead to the aim of practising language structures in communication and action context.

1.3.3 Focussing

There is strong evidence that adaptation to stroke-related deficits is a major issue in functional recovery and that it may hinder poststroke rehabilitation (Taub, 2004; Taub et al., 1998; Taub, Uswatte & Elbert, 2002; Tau et al., 1999). For example, a patient who following a stroke is unable to move one arm might learn to avoid using the affected limb. Similarly, patients with aphasia may quickly realize that owing to their disorder, they cannot speak properly. As a result, these patients may resort to strategies such as using simplified sentences (‘telegraphic style’, agrammatism) to communicate with others or, in extreme cases might avoid verbal communication altogether and limit themselves to gesturing (Kolk & Heeschen, 1990). Thus an important feature of neurorehabilitation is to avoid such strategic or learned nonuse of potentially available capacities. To make patients with stroke-related motor deficits use their affected limbs, Taub and colleagues developed CIMT (Taub et al., 1998). In CIMT, constraints are employed that force the patient to use their affected limb. Compensatory activity using the intact arm and other adaptation to stroke-related deficits is prohibited by constraints in order to facilitate rewiring and re-strengthening of neuronal connections supporting the functionality of the affected limb.

In a similar manner, aphasia patients can be guided (or ‘constrained’) to use verbal utterances that they normally would avoid due to lack of success in the past and resultant avoidance behaviour or learned nonuse. Due to practising of verbal communication skills which are still available to stroke patients, they may regain some of their lost language skills that would otherwise have remained unused. Thus ensuring that patients with aphasia make use of the full range of their available verbal abilities is a valuable aim of neurobehavioural rehabilitation (Taub et al., 1999; Taub, 2004).

Linguistic ‘constraints’ cannot be applied in a similar fashion to the slings and restraints applied to the unaffected arm, which are used in CIMT to guide the use of the affected extremity. In ILAT, it is the use of language games and related materials that provides the guidance for patients to systematically explore, apply and elaborate on a repertoire of verbal utterances and actions they might still be able to use, but wouldn’t typically in their day-to-day behaviour because of lack of success in the past. Note that the focussing on patients’ full range of verbal communication skills does not imply that nonlinguistic actions be prevented. As discussed in section 1.3.2, it is of importance to allow relevant nonlinguistic actions in context of verbal activities, including the use of gestures complementing verbal utterances. What should be avoided is the isolated use of gestures in replacement of verbal communication, which is a typical strategy of learned nonuse.

In ILAT, the most important therapeutic tools to provide guidance and focusing for patients are:

(1) the action structure of the language game

(2) the materials (typically specific sets of picture cards) used in the game and the framing of the game (e.g., barriers between players, double card sets, impossibility to see each other’s cards),

(3) behavioural techniques such as modeling, shaping and positive reinforcement,

(4) explicit rule descriptions.

These focusing tools are addressed fully in Chapter 3.

1.4 THE PRESENT STUDY

Despite the demonstrated success of ILAT's most researched form, CIAT, in aphasia treatment and despite the increasing interest in this method from a neuroscientific point of view, there is still a lack of detailed guidance on how to run the procedures practically in clinical settings and how to adjust the method to the spectrum of deficits of individual patients. Furthermore, the precise implementation of speech acts, their embedding in other actions, and the choice of language materials has previously not been described in much detail.

1.4.1 Aims

This thesis aims to close this gap by outlining the exemplary procedures involved in ILAT. As well as further exploring the efficacy of ILAT, through intervention with a group of patients with chronic aphasia, this thesis presents an alternative method for assessing success during the intervention. The final aim of this thesis is to explore the neural reorganisation that occurs alongside improvements in language function due to ILAT. Analyses in this thesis will be mainly exploratory. However they may help in being able to identify relationships between different measures of therapy outcome, including clinical and behavioural data, and neural activation, which could serve as starting points for future studies. Chapter 2 will provide an overview of previous studies employing ILAT, outlining the behavioural gains shown by chronic aphasia patients who have undergone this intervention and summarising the investigation and understanding thus far of brain plasticity triggered by ILAT.

In Chapter 3, special attention will be given to the rules and settings of ILAT; practical samples of therapy elements will capitalise on two types of language games. In Chapter 4, a study utilising an extended version of ILAT is reported which investigates the efficacy of ILAT in English speaking aphasia patients. Fourteen patients with chronic aphasia participated in two weeks of ILAT for three hours per day each weekday. Immediately before and after therapy, patients underwent standardised clinical assessments of language and reported on subjective measures of their communication.

A novel measurement of *communicative* performance gains induced by ILAT is exemplified in Chapter 5. 'Communicative' performance refers to the question of how patients succeed in performing speech acts such as informing, requesting, making suggestions etc. and how they succeed in understanding such linguistic actions.

Finally Chapter 6 will serve to augment the current understanding of brain plasticity due to language therapy by exploring the specific functional changes in the brain triggered by ILAT and their connection to improvement in patients' language abilities after therapy. A subset of 8 patients from Chapter 4 also underwent a functional Magnetic Resonance Imaging (fMRI) scan before and after therapy. During the scan patients engaged in a language comprehension task. By looking at brain reorganisation processes in space using high resolution fMRI, this thesis will potentially help to further elucidate the specific factors related to recovery from stroke and will have important implications for neurorehabilitation and specifically the neuronal principles underlying ILAT induced plasticity.

If ILAT leads to significant language improvements in chronic aphasic patients, accompanied by neurophysiological changes in the brain, it would not only help to understand mechanisms of brain recovery after stroke, but could potentially have a huge impact on the provision of health care for chronic stroke patients. As ILAT is a short term (two weeks) therapy, it could easily be implemented in an outpatient setting, providing easy and cost effective access to language therapy for chronic aphasia patients.

CHAPTER 2: ILAT - EFFICACY AND BRAIN REORGANISATION

2.1 BACKGROUND

Evidence indicates that speech and language therapy (SLT) in general is effective for both acute and chronic post-stroke aphasia (PSA) patients (Robey, 1998) and is particularly beneficial when executed in an intense manner (Bhogal et al., 2003; Cherney et al., 2008; Kelly, Brady, & Enderby, 2010). Previous research applying the Intensive Language-Action Therapy (ILAT) method in a randomised controlled trial (RCT) has demonstrated improvements of language and communication performance in patients with chronic PSA (Pulvermüller et al., 2001). Notably all PSA patients included in this trial had shown no change in language performance for years prior to the commencement of ILAT. Other studies have replicated the beneficial effects of ILAT (or one of its variants – CIAT/CILT, Constraint-Induced Aphasia/Language Therapy) for acute as well as chronic aphasia patients, which in several studies, remained stable over weeks and up to six months (Faroqi-Shah & Virion, 2009; Goral & Kempler, 2009; Kirmess & Maher, 2010; Maher et al., 2006; Meinzer et al., 2005; Szaflarski et al., 2008). Additional drug therapy has led to a further increase of therapy success (Berthier et al., 2009). This chapter will review the trials of ILAT thus far, outlining behavioural and neural changes reported following this intervention.

2.2 BEHAVIOURAL RECOVERY IN INTENSIVE LANGUAGE ACTION THERAPY

In 2001, Pulvermüller et al. reported for the first time that the methods of ILAT could improve language abilities in patients with chronic PSA. In a RCT, 17 native German speakers were assigned to either a group receiving CIAT or Conventional Therapy (CONV). The CONV group were treated for the same amount of time as the CIAT group (approximately 30 hours), but over a less intensive period (30 hours over 3-5 weeks, compared to 30 hours over 10 days in CIAT). Patients in the CONV group were treated for their particular linguistic deficits with tasks such as naming, repetition, sentence completion and following instructions. All patients were assessed immediately before and after the therapy period using a standardised clinical aphasia battery (subtests of the Aachen Aphasia Battery; Huber, Poeck, Weniger & Willmes, 1983) and a measure of communicative performance in everyday life (Communicative Activity Log, CAL; Pulvermüller et al., 2001). The results indicated significant improvements following therapy in six out of eight language assessments in the group of patients treated with CIAT. Comparatively, the CONV group improved in only one out of the eight tests.

Gains in language performance following ILAT have also been illustrated in subsequent studies, including positive responses after just a single week of therapy (Szaflarski et al., 2008) and in patients in early recovery from stroke (Kirmess & Maher, 2010). Improvements have also been demonstrated when employing modified versions of ILAT including: an increase in the number of verbs generated following therapy which specifically aimed to practise the use of verbs (Goral & Kempler, 2009; Kempler & Goral, 2011); improvements in narrative discourse after individualised ILAT (Szaflarski et al., 2008); and CIAT-G, which included grammatical constraints on language for patients suffering with agrammatism (Faroqi-Shah & Virion, 2009). Gains reported were not always significant at the group level, but in single patients across test-retest sessions (Faroqi-Shah & Virion, 2009). Interestingly it has been noted that patients who scored lower at pre-therapy testing sessions showed more dramatic improvements of language following ILAT or one of its variants (Faroqi-Shah & Virion, 2009; Szaflarski et al., 2008).

2.2.1 Efficacy of Different Approaches in Communicative Aphasia Therapy

Although the 2001 RCT (Pulvermüller et al., 2001) showed gains in language performance following ILAT, it is unclear how each of the three principles: massed practise, language-action structure and focusing, contributed to the gains made. When comparing CIAT to CONV, the CONV group were treated for the same overall amount of time but spread less intensively over 3 – 5 weeks. Therefore both *therapy-type* and *intensity* were varied. In an attempt to separate these two factors, one research group has compared CIAT with patients receiving an intervention focussed on individual functional deficits (Barthel, Meinzer, Djundja & Rockstroh, 2008; Meinzer et al., 2004). Critically the two groups engaged in intensive therapy, practising language use for approximately three hours per day for ten days. Results from these studies demonstrated no differences in improvements between the two groups, suggesting intensity of therapy is a critical contribution in improving chronic aphasia.

Further attempts to separate the factors of ILAT has indicated similar improvements following therapy for groups of patients receiving either CILT or a modified version of PACE (Promoting Aphasic's Communicative Effectiveness, Davis and Wilcox, 1985) therapy (Maher et al., 2006). Critically CILT and PACE therapy were delivered using the same language-action structures and at the same intensity and therefore the groups differed only in terms of whether communication modality was constrained to speech (CILT group) or was unconstrained (total-communication approach in PACE). Interestingly, gains made following CILT were more consistent and longer lasting than after PACE. CILT improvements were sustained and even improved further at a one month follow up period. Furthermore out of the two patients from the PACE group who showed significant improvements in single-subject analysis, Maher et al. (2006) reported that one "refused to use any other modality than speech" (p.847). Therefore the improvements shown in the comparison group in this study included significant gains by a patient who actually underwent CILT-like therapy.

Finally, in the version of CILT utilised in their study, Maher et al. (2006) reported, “No…gestured or any other non-verbal self-cuing strategies were allowed” and that patients “were reminded to use only speech and to ‘sit on their hands’ if necessary” (p. 846). As was highlighted in Difrancesco et al. (2012), although gestures are ignored in ILAT, they are not actively discouraged. On the contrary, in line with the principle of behavioural relevance on which ILAT is based, language and action are tightly linked in the brain and therefore gestures may actually help to activate a word-concept link (see Chapter 1; Difrancesco et al., 2012). Barriers are used in order to ensure no gestures are seen by other players, but gestures are not in any way discouraged. Discouraging gestures therefore could have played an inhibitory role in allowing further improvement in patients in the CILT group.

A recent single-subject multiple baseline study compared the effects of PACE therapy with CIAT, where two patients underwent two weeks of intensive PACE followed by two weeks of intensive CIAT (Kurland et al., 2012). Both interventions employed the same language-action structure and similar materials and therefore varied only on whether communication was constrained to speech or not. Each patient was tested at three time points (pre-therapy, post PACE and post CIAT), as well as assessed every other day with ‘test’ cards for naming. Again, although significant gains were seen in each therapy condition, patients made faster and stronger improvements during CIAT.

Together these findings suggest that an intense and repetitive therapy structure, where language is practised in communicatively-relevant action-based contexts is important in aiding improvement in language performance in patients with chronic

PSA. Combined with guiding patients to communicate through speech alone, as in ILAT, gains are made quicker and appear to be longer lasting. Indeed given the neuroscientific background of the principles of massed practise, behavioural relevance and focusing of language, it is reasonable that an intervention employing all three is likely to ensure the best outcome.

2.2.2 Long-term Improvements after ILAT

In addition to gains made immediately following ILAT, it is important to determine whether improvements are sustained after a period where no additional therapy is given. Maher et al. (2006) reported that gains made following CILT were stable after a one month post-therapy period and that some patients actually made further behavioural improvements to those seen immediately post-therapy. Moreover sustained improvement in language performance has also been documented after a 6 month post-ILAT period (Meinzer et al, 2005). This was demonstrated on both standardised assessments and subjective self- and relative-reports. Interestingly improvements were found irrespective of age and severity and duration of aphasia, suggesting there is potential for long-term improvement across a range of PSA patients.

Other research however shows less clear results in terms of long-term stability. Breier et al. (2009) reported stable increases after three months in half of the patients who showed a good-initial response to ILAT; and in single-subject analysis, only some subtests showed evidence of maintained gains three months post-therapy (Faroqi-Shah & Virion, 2009). In a multiple-baseline trial, Kurland et al. (2012) reported a large drop in therapy-induced gains in one patient, 7 months after CIAT. Therefore additional research following up the effects ILAT is warranted in order to further evaluate the long-term benefits of the intervention.

2.2.3 The Effects of ILAT Training by Laypersons

One issue regarding the on-going provision of SLT is the cost associated with long-term therapy which may be needed for further improvements. One way which may prove to be beneficial to the cost-effectiveness of therapy is to include patient's relatives in training. Meinzer et al. (2005) investigated an extended version of CIAT where patients' relatives were asked to try to engage the patients in as much communication at home as possible. Patients were also given activities in the afternoons following therapy where they had to perform simple, but behaviourally relevant language tasks, such as going to the bakery and asking for a loaf of bread. Although there was no difference between the typical- and extended-CIAT groups in standardised testing, reports from relatives showed they perceived greater improvements in the CIATplus group at the 6 month follow up stage.

Extending upon this, Meinzer, Streiftau & Rockstroh (2007) compared a group of patients who received CIAT from trained therapists with a group who received the same amount and intensity schedule, but who instead were trained by laypersons. Laypersons in this group consisted of relatives of the patients who were trained to run CIAT sessions. No difference was found between the two groups, suggesting intensive therapy could be effectively delivered by laypersons.

However as will be discussed in Chapter 3 and is highlighted in Difrancesco et al. (2012), the role of the lead therapist is a complex one. As ILAT is delivered in a group setting, it is not always possible to have a homogenous group as was set up in Meinzer et al. (2007). In these circumstances it is vital to be able to successfully adjust rules and materials in order that the more able patients are challenged, yet the patients who struggle do not become frustrated at lack of success. Those with substantial training and experience may therefore be more suited to this role. Friends and relatives however, may prove vital in sustaining initial therapy gains through post-therapy activities such as those employed in Meinzer et al. (2005).

2.3 REORGANISATION IN THE BRAIN AFTER ILAT

Understanding how the brain adapts following a stroke, through exploring changes in the brain triggered by language therapy and the relationship with behavioural outcomes, is vital in being able to best aid those with language disorders. Restitution of language subsequent to stroke is linked to a complex pattern of reorganisation in the brain. Some restoration of language functions following stroke typically occurs in the acute (first months) phase of recovery but may also occur in patients with chronic PSA who have suffered from speech and language disorders for a number of years. Three principal mechanisms for recovery from stroke have been suggested. First, in cases of limited damage to the left hemisphere (LH) regions, patients may regain abilities due to spared, almost ‘normal’ functioning. Second, spared or sub-networks of peri-lesional areas in the LH may play a cardinal role in the restoration of language. Finally, in cases of more severe or extended damage (particularly to the left inferior frontal gyrus, LIFG), there is evidence to suggest that restitution processes of language functions may involve compensation of corresponding regions in the right hemisphere (RH) of the brain (Kurland et al., 2012; Saur et al., 2006; Turkeltaub et al., 2011).

However a complex interaction between lesion extent and location, pre-stroke factors such as language representation in the brain, sex and handedness, and aphasia type and severity, largely influence individual variability in recovery from PSA (Berthier & Pulvermüller, 2011; Kurland et al., 2012). To date therefore, the association between brain plasticity - the ability for the brain to reorganise and change through learning, recovery of language function and language therapy remains to a large degree, unknown.

2.3.1 Neural Reorganisation following ILAT

Electroencephalography/Magnetoencephalography (EEG/MEG) and functional Magnetic Resonance Imaging (fMRI) are brain imaging techniques which allow for high temporal and spatial resolution, important for precise mapping of brain activation and regions involved in cognitive processes such as language. As ILAT is a short-term therapy and has proven effective in improving language functions in aphasia patients, it is a useful tool in which to study therapy-induced reorganisation in patients where spontaneous neural changes are unlikely to occur (after one year post-stroke). First steps have been undertaken in elucidating the plastic functional changes directly related to ILAT (Breier et al., 2009; Breier, Maher, Novak & Papanicolaou, 2006; Breier, Maher, Schmadeke, Hasan & Papanicolaou, 2007; Kurland et al., 2012; Meinzer et al., 2004; Meinzer et al., 2008; Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005; Richter, Miltner & Straube, 2008).

2.3.1.1 Evidence of Neural Reorganisation after ILAT: EEG Studies

Support for cortical reorganisation following ILAT has been shown in EEG recordings, where stronger activation to words but not pseudowords occurred following CIAT (Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005b). Pulvermüller et al. (2005) suggest this word-evoked response may reflect an indicator of recovery or what the authors refer to as an 'Aphasia Recovery Potential'. This increase in activation correlated with improvements in behavioural performance on standardised tests and importantly was seen in the left and right hemispheres, therefore supporting the notion that both hemispheres play a role in reorganisation of language after stroke.

2.3.1.2 Evidence of Neural Reorganisation after ILAT: MEG Studies

Evidence of bilateral contribution to recovery from stroke has also been shown using MEG. In a single-patient case study, Breier et al. (2007) showed RH-only activation in homotopic language areas prior to CILT, with an increase in this activation following therapy, followed by a shift to bilateral activation at a 3 month follow up session. These changes were accompanied by improvements in language functions, indicating an important role for both hemispheres in recovery. The results also highlight the fact that changes in the brain may not be linear, but dynamic over a period of time.

In contrast to reports for beneficial effects of increased activation in the RH, Brier et al. (2006) showed that initial pre-therapy activation in the RH, but no increase in this activation may indicate improvements following therapy. Although prior to therapy, both the left and right hemisphere were significantly more active in patients who responded well to therapy compared to non-responders, only RH pre-CILT activation was correlated with behavioural improvements following therapy. However it is possible that the apparent contrast in results may be due to underlying differences in severity of damage in respective patients. As Breier et al. (2007) discuss, their patient showed no LH activation before therapy, whereas the patients reported in Breier et al. (2006) showed both left and right pre-therapy activation. Therefore due to differences in initial language-induced activation, these patients may have had to adopt different strategies for recovery from language.

Indeed Meinzer et al. (2004) have indicated that reorganisation strategies may be related to time and severity of stroke. Using MEG, the authors showed that changes in abnormal slow wave activity (SWA) in LH perilesional areas of the brain, correlated with improvement in performance on standardised language assessments (Meinzer et al., 2004). The increase of SWA, which may correspond to active but non-functional areas of the brain, tended to occur in patients with a longer duration since time of stroke and therefore may reflect permanent damage to peri-lesional areas. Conversely a decrease in SWA may reflect re-integration of spared language areas.

Although Meinzer et al. (2004) reported that both the increase and decrease of SWA was positively correlated with behavioural improvement, other research suggests the most efficient recovery occurs when reintegration of spared LH regions is possible (Heiss & Thiel, 2006). Brier et al. (2009) found three distinct patterns of reorganisation across a large group of 23 patients. Patients who showed and maintained gains from ILAT after a three month period demonstrated an increase in LH temporal activation following therapy. Conversely, patients who showed initial improvement after ILAT but lost this at the follow up session had greater RH activation than both responders and non-responders across all time periods. These results would suggest RH activation may support initial recovery of language functions, but that this recovery may not be stable. For the most efficient recovery following ILAT, it appears an increase in LH language-area activation is vital.

2.3.1.3 Evidence of Neural Reorganisation after ILAT: fMRI Studies

Results from fMRI studies also show the importance of the LH in therapy-induced recovery from aphasia, although contributions from the RH remain unclear. Meinzer et al. (2008) reported that significant increases in LH perilesional activity following therapy were correlated with behavioural improvement. However when two patients with the lowest pre-therapy scores were included in analysis, increased activation was also seen in RH homologues of perilesional regions, accompanied by an increase in behavioural functions.

Furthermore in a recent single-subject crossover design, Kurland et al. (2012) demonstrated more RH activation following an intensive form of PACE therapy compared to baseline. However a subsequent block of CIAT therapy, where faster and more improvements were made, was paralleled by mainly LH activation, and one significant cluster in the RH homologue of Broca's area. Both of these studies support the idea that a more effective recovery process involves the LH language areas.

Few studies have included a post-therapy follow up period to assess stability of neural changes following ILAT and this may help to explain the lack of consistency in imaging results. In the largest fMRI study investigating the effects of CIAT, Richter et al. (2008) compared 16 patients pre- and post-therapy and found that right frontal brain activation measured with fMRI was a strong predictor of language improvements after therapy. These results appear to fit with the findings from Breier et al. (2006), but contrast with the view that RH activation alone may indicate a less-efficient reorganisation strategy (Breier et al., 2009). However as studies have shown the reintegration of language functions is dynamic across time (Breier et al., 2007; Breier et al., 2009), it is unclear whether the improvements made in patients demonstrating significant RH pre-therapy activation were sustained after a period with no intervention.

The thus far inconsistent results could additionally be due to a number of factors including use of different tasks during scanning and the dynamic factors in PSA patients, including severity of lesion. Indeed Richter et al. (2008) discuss the fact a group analysis may disguise the partially opposite changes that occurred in patients for whom there was an increase in RH activation and those for whom there was a decrease in activation.

2.4 SUMMARY

Together these findings suggest that intensive daily practise using ILAT methods leads to clinical improvements of language functions, possibly because it entails re-learning of word-concept links and re-wiring of neuronal connections in language networks. Imaging studies have provided strong evidence that the change in behavioural improvements is accompanied by neural reorganisation. However the plastic changes that occur in the brain are highly dynamic and thus far it is still unclear to what extent each hemisphere plays in the improvement of language functions. Evidence suggests the reintegration of partially damaged or spared LH regions may result in the most efficient improvements in language functions following therapy (Brier et al., 2009). However it is also clear contributions from the RH are significant (Breier et al., 2006; Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005; Richter et al., 2008). Despite the variability in results from imaging studies, there is strong evidence for the beneficial effects of ILAT in behavioural language functions, accompanied by changes in the brain.

CHAPTER 3: ILAT - THE METHODS

3.1 INTRODUCTION

Intensive Language Action Therapy (ILAT) aims to implement the three main guidelines for the neurorehabilitation of language derived from neuroscience and linguistic sciences: massed practice, language-action embedding in a behaviourally relevant context, and focusing on the individuals' communicative abilities and needs through shaping their use of language. Despite the demonstrated success of ILAT's variants, CIAT and CILT, in aphasia treatment (see Chapter 2) and despite the increasing interest in this method from a neuroscientific point of view, there has thus far been a lack of detailed guidance on how to run the procedures practically in clinical settings and how to adjust the method to the spectrum of deficits of individual patients. Furthermore the precise implementation of speech acts, their embedding in other actions, and the choice of language materials has previously not been described in much detail. In this chapter, which forms Part II of a recent article (Difrancesco et al., 2012), the methods of ILAT are described in detail, closing this gap by highlighting the principles of this type of SLT and by outlining the procedures involved in the intervention. Special attention is given to the rules and settings and practical samples of therapy elements will capitalise on two types of language games.

3.2 ILAT PROCEDURES

3.2.1 Basic Setting

Although there is in principle no upper limit for the amount and frequency of therapy, real world limitations constrain the implementation of the high-therapy-frequency principle. A therapy frequency of three hours per day for ten consecutive working days represents a high therapeutic intensity which can be tolerated by many patients and may even be applicable in clinical contexts.

In the ILAT context, language-action embedding is realized through verbal communication in the context of other communicative and nonlinguistic overt actions. Language use is a crucial component of card games with picture cards showing objects or actions. These games include both non-communicative actions, such as showing, handing over, or taking and putting aside a card, as well as verbal communicative actions, such as asking for one of the cards, or objects depicted. These communicative interactions are called *language action games*, or LAGs.

When specifying LAGs, the following terminology will be used: a *game*, or LAG, consists of several *rounds* characterised by a communicative goal (requesting and passing an object/card), which in turn consist of a sequence of *moves* or *turns*, that is *speech acts*, *nonverbal communicative actions* and other, *not communicative action turns* (e.g., the request, the handing-over of the requested, or a clarifying question).

For performing LAGs, participants typically sit around a table with barriers between them (see Figure 3.1). Barriers ensure that participants cannot see each other's cards. In addition, the barriers also make it more difficult for participants to efficiently use and perceive any non-verbal communication, such as gestures or pointing. Especially, this set-up ensures that gestures cannot easily be used to replace verbal output (see Section 3.2.2 on gesturing), while still allowing participants to use them in addition to their spoken output, if they wish.

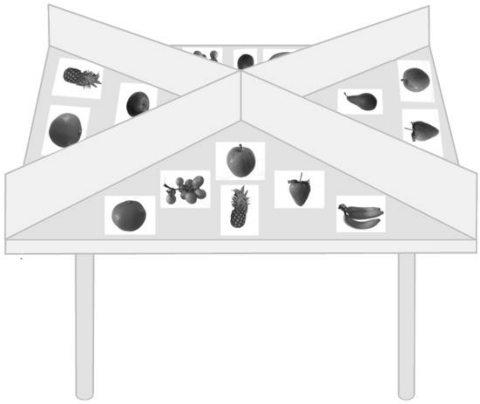


Figure 3.1. Therapeutic setting for ILAT: Four players, usually 3 aphasic patients and one therapist sit around a table, with a set of 12 matching pairs of cards distributed between them.

At the start of the LAG, each of the participants or ‘players’ is given a set of picture cards. Patients and the therapist act as players following the same rules for communicating in the LAG. Two copies of each picture card are used in the game, although each with a different player. At the beginning of each ‘round’ of the LAG, one player selects one picture card from their set. The aim is to obtain the matching card from a different participant. Note again that each player can only see his or her own cards or objects, as the barriers prevent seeing any co-players’ cards. In one type of LAG, the REQUEST game, the only tool for obtaining the matching card is *making verbal requests*. In a different type of game, the PLANNING game, participants have to propose activities to their co-players. The players can propose an activity or agree in participating in the activity, only if they have a corresponding action picture in their set of cards. In these contexts patients have to perform a series of different speech acts in interaction with other players to achieve success in the game.

All speech acts are embedded into sequences although these sequences, similar to natural conversations, are not necessarily linear. They are normally best represented as action trees rather than action chains, because one speech act can be followed by *a range of* other different but well-defined acts. For example, a REQUEST to hand over an object (or a card depicting it) can be responded to by FOLLOWING this request, that is handing over of the object (card), but in case the player does not have the object/card in his or her set, a REJECTION of the request must follow. If there are problems in understanding – either because the speaker has articulated not clearly enough, used an (in the context) ambiguous expression or because the addressee did not understand precisely enough – there is motivation to initiate a repair sequence to CLARIFY what has been meant. Also each of these ‘second moves’ has a range of possible continuations. Similar sequences characterise other language games, too. The specific action-sequence structure of different LAGs will be addressed in Section 3.8.

Importantly, the action sequences allow patients to practice both speech production and comprehension and (with minor modifications of the game) can also be used to practise reading and writing. Note in this context that a standard procedure applies to comparing the cards after they have been verbally identified. The speaker would first select the card and make his or her request or proposal, the addressee would then, ideally respond by agreeing, selecting the corresponding card and handing over the card. In turn the speaker would then also show his/her card and only if a match between cards has been achieved, thus proving successful communicative interaction, the sequence finishes as successful. Feedback about successful speech acts and successful comprehension therefore, is given by way of the card matching procedure.

Making requests or planning an activity with someone else are communicative speech acts which often occur in everyday life situations. Such relevance to everyday communication has long been emphasised to be highly relevant in aphasia therapy (Davis & Wilcox, 1985; Elman & Bernstein-Ellis, 1999). Taking into account different speech acts in everyday life, and varying levels of patients' language abilities, materials for use in ILAT have been created which ensure that patients engage in different forms of communication in a behaviourally relevant language-action context. One set of materials will be described in more detail in section 3.3.

3.2.2 Gesturing in ILAT

Before addressing more specific features of ILAT, it is important to comment on the role of non-verbal communication and gesturing in ILAT. As emphasised in Chapter 1, a common misunderstanding of the CIAT (and therefore also ILAT) method had been that non-verbal communication of any sort always needs to be 'suppressed'. Note however that from the point of view of brain science where language and action systems have been demonstrated to be functionally connected and to interact synergistically, it would not be advisable to forbid gesture in the context of verbal communication attempts. Facilitation of linguistic brain systems by excitation from still intact action/gesture systems may be one of the keys for the success of language-action embedding. On the other hand, the focussing principle suggests not allowing patients to replace demanding actions which they have reason to practice, with easy ones. The solution is obviously to allow, even encourage gesturing and non-verbal activity, *not in replacement* but *rather as a complement* of, verbal communication. Therefore to make it possible to efficiently practice verbal language use, *substitution* of spoken language by gesture is typically discouraged. Note again that it is a side effect of the barriers on the table between players that it is difficult to see each other's hands and gestures. This is desirable in the context of the nonuse avoidance strategy: the aim is to practice verbal abilities, speaking and writing, possibly accompanied and facilitated by gestures (e.g., saying "letter" plus gesture writing), but not to replace words by isolated gestures.

3.2.3 Speech Acts and their Sequential Structure

Language games can be more or less complex. In everyday communication it is sometimes advantageous to get as much done with one single utterance as possible. In other circumstances, it is more advisable to move carefully and slowly, ascertaining at each step that addressees fully understand and that one doesn't request too much from communicative partners. Correspondingly the pragmatic structure of speech act sequences can be more or less elaborate in LAGs, too. In ILAT, a typical form of LAGs is used in which one player addresses one other player with a REQUEST or a PROPOSAL. This one-to-one mode requires selecting a partner, focusing attention on that partner and taking turns with that partner only. A more challenging version would be if one player addresses all other players. In this one-to-all mode there is an increased demand on divided attention and turn-taking abilities, as several participants may start to speak at a time and therefore compete for attention. A further modification divides the action structure into four sub-moves. Here a QUESTION-ANSWER sequence first aims at clarifying whether a given co-player is in possession of the required object (or is able/willing to take part in the suggested activity) and the third move then is the key speech act, REQUEST or ACTION PROPOSAL followed by its specific response options for the fourth move. This four-move version can be realized in the one-to-one or one-to-all modes. In order to illustrate the different speech acts during a LAG, we use so-called 'action trees' which demonstrate the sequential structure of speech acts. Several examples of action trees are outlined below.

Typical action sequences would thus be the following in three variants of the REQUEST game:

- 2 move – specific
  - Player A requests object from player B
  - Player B follows the request or rejects

- 2 move – general - Player A REQUESTS object from any co- player
  - Player B (who has the matching card) follows the request while others reject
- 4 move – specific - Player A asks B whether s/he has a given object
  - Player B agrees or denies
  - Player A request the object from B
  - B follows the request

More details as well as specific examples will be given below with regard to the sequence structure of the REQUEST and PLANNING LAGs (see section 3.8 on *Specific features of LAGs).*

3.3 ILAT MATERIALS

The materials described here are picture cards developed recently specifically for English speaking patients with aphasia (Difrancesco et al., 2012). All items are photographs of either objects or people taking part in a range of activities/actions (n=624) and presented in colour on laminated cards sized 6 by 4 inches on a blank white background (see examples of pictures cards in Appendix 1). Each object/activity depicted on the cards had a best-matching single noun or verb, or more complex noun phrase or sentence. Cards with best-matching single noun/verb were subdivided into frequency classes according to the standardized lexical frequency of these items. To this end, Kučera-Francis word frequencies were taken from the Medical Research Council's Psycholinguistic database (Coltheart, 1981). For therapeutic use, all picture cards were duplicated to obtain matching pairs of cards.

Choice of materials can be adjusted to patients' needs, abilities and interests. The materials chosen may challenge patients and encourage them to use language they may normally avoid. However care must be taken that materials are not too difficult, so that patients might become frustrated. With patients improving their performance, appropriate increase in difficulty of LAGs can be controlled by material choice. At the same time it is useful to use some items as 'repeat cards' so as to monitor trivial therapy effects on the items practiced, as well as 'test cards', which have not been used before but are of comparable difficulty. These latter items are matched for psycholinguistic features and are essential for assessing non-trivial generalisation effects brought about by therapy.

Below, seven categories of picture cards are presented for the REQUEST LAG. These are not meant to represent a linearly increasing difficulty ladder, but rather different points in a multidimensional difficulty space, with some items (pictures of objects with names of high lexical frequency) relatively easy to process by patients, and others (minimal pairs, multi-feature objects and object sets) being experienced as more challenging. Only one full set of cards in the PLANNING LAG was used as not so many patients with specific difficulty in action description were available.

Category 1-3: Word Frequency: 1) The simplest set of cards (n = 60 items) are those depicting objects whose most characteristic verbal label has high lexical frequency; these items, typically nouns, were used more than 100 times per million words. These included words such as 'table' and 'door'. Higher frequency words are often easier for aphasic patients than words used less often in everyday language (Pulvermüller & Berthier, 2008). Therefore difficulty of the LAG can be increased by reducing the lexical frequency of typical names of the objects depicted. 2) Middle frequency items (n=60) showed objects with a word frequency of their typical names between 20 and 100 per million. Examples are 'plate' and 'key'. Once patients are relatively confident making requests with middle frequency items, it makes sense to introduce 3) low frequency items (n=60). These are object cards with nouns of corresponding word frequency of 20 per million or below, such as ‘candle’ and ‘vase’. Along the frequency axis, the level of difficulty can therefore be adjusted to patients’ ability and progress throughout the therapy.

4. Minimal pairs: Minimal pairs are words that only differ in one speech sound or letter. The 30 picture cards of this set show pictures typically named by English nouns that are only minimally different phonologically and/or orthographically. Examples are ‘ball’ and ‘wall’; or ‘glass’ and ‘grass’. Identifying these items in the context of their minimal pair-objects requires rather precise pronunciation (or letter writing) and is thus especially appropriate for patients suffering from apraxia of speech and pronounced speech production deficits (or writing deficits). Corresponding difficulty in phonological discrimination in speech perception (and letter discrimination in reading) can also be addressed using this set.

5. Semantic Categories: Difficulty in distinguishing between items can be introduced by making them more and more similar. Distinguishing an animal from a tool is relatively easy and can be done using many different words. However if similar animals need to be distinguished, such as different mammals, or even smaller sub-categories such as cats, the demand on linguistic processing gets greater. A set of cards include 84 items from different hierarchically organized semantic categories. Semantic groups include pictures of animals, clothing, fruit and vegetables, furniture, tools and vehicles. Using this card set, and especially a specific sub-category set of cards, fine-grained distinction and verbal description between items are needed. It would not be enough to simply ask for an ‘animal’ or ‘animal with four legs’, for example, but the species ‘cat’ would need to be distinguished and even a specific subtype such as the ‘black cat’ from the ‘white kitten’. Note furthermore that certain kinds of language deficits come with category-specific impairments so that tool or animal names may be selectively impaired in individual patients (Gainotti, 2000).

6. Multi feature objects and object arrangements: To further increase difficulty, card sets were created which required a more complex description for unique identification of a given card. 180 cards include subsets differing by colour, shape, size, or a mix of all of these. Note that the attributes of the objects and their size necessitate more elaborate descriptions and therefore introduce a constraint to use more complex linguistic forms in the game. For success in LAGs using this category of picture cards, it is necessary to uniquely specify the set of objects on a given card against the alternatives in the set. This may require verbal explication of all information available, using forms such as ‘four round biscuits’ or ‘one green and one red pepper’. Thus this card set can be used to focus communication on two and three word utterances along with more complex constructions.

7. Spatial relationships: A final set of object-related cards includes objects in different spatial relationships thus requiring the use of prepositions (n= 60) in order to uniquely identify the depicted scenarios. As the different cards can show the same two or more objects but arranged in different ways, the players are required to use spatially-specific linguistic structures, such as ‘the cup *on* the saucer’; ‘the cup *under* the saucer’; ‘the cup *next* to the saucer’, to perform a successful request. Note furthermore that prepositions and spatial language are difficult to process in specific kinds of aphasia (Tranel & Kemmerer, 2004) and in dementia with predominant posterior-parietal involvement.

8. Action cards: In the PLANNING LAG, the aim of the interaction is to propose and agree on an activity several players could perform together. Therefore picture cards need to show actions, and typical actions are best “named” using verbs or longer expressions including verbs. The 60 cards in this extended set depict a range of everyday activities, either ones which can be performed alone such as ‘brushing teeth’ or ‘licking an envelope’, or group activities such as ‘hiking’ or ‘playing a board game’. This card set and game is especially appropriate for patients with deficits in speaking about actions and using verbs. There is ample evidence for deficits in verb and action processing in certain types of aphasia and specific dementias (Miceli, Silveri, Villa, & Caramazza, 1984; Kemmerer, Rudrauf, Manzel & Tranel, 2012).

3.4 INTRODUCING THE GAMES AND RULES TO PATIENTS: MODELLING, SHAPING AND REINFORCEMENT.

The rules of the therapeutic language action games are typically introduced by playing them. As many patients suffer from severe comprehension deficits, a verbal explanation may not always be effective. So starting with the barriers, cards in front of each of the participants and the therapist making a request, is typically the best possible strategy. In this introductory phase of the therapy, it may help to have available a co-therapist to demonstrate the interactive nature of the games. Aphasic patients may just join in, as pictures and verbal actions provide relevant cues. Modelling and shaping can also be used to encourage desirable activities by patients. Within the first rounds of the game, the therapist may also illustrate the different possibilities to respond to the key speech acts of the game (REQUESTING in the REQUEST game and PROPOSING an action in the PLANNING game). It also makes good sense that the therapists demonstrate not only using the 'best possible' match (the word 'house' for a card depicting a house), but alternative expressions that may function equally well in solving the communication problem. Note that depending on the cards from which the target object needs to be distinguished within the given context, the expressions 'home', 'to live in', 'thing with a roof', may be sufficient and equally functional, whereas more specificity may be needed in other contexts ('red house with a long chimney' in case of a card set including several houses). The *materials* section above shows how the game can be tuned to control utterance complexity by choosing the appropriate materials requiring more or less complex and challenging utterances.

Patients will typically stick to sets of utterances which they know they can easily produce (e.g. single words, simple sentences). However through modelling, new utterance types and speech acts can be introduced easily and by systematic positive reinforcement, their application can be established. For example, it is has been observed that if the therapist uses full sentences, politeness formulae, or even specific grammatical constructions repeatedly, patients will start making attempts towards mirroring such linguistic activity (Difrancesco et al., 2012). Note that there are neuroscience reasons for assuming that 'syntactic priming' (Branigan, Pickering & Cleland, 1999; Pulvermüller, 2010) and 'mirroring' (Rizzolatti & Sinigaglia, 2010; Pulvermüller & Fadiga, 2010) are automatic mechanisms built into the human brain.

3.4.1 Explicit Rule Descriptions

As mentioned before, much of the burden of introducing the therapeutic language games is through learning-by-doing. However if patients have sufficient comprehension abilities explicit rule descriptions may be important to adjust and fine-tune the game to patients' communicative abilities and needs. A problem that frequently arises is that some participating patients do not have difficulty with a given type of game, whereas others still struggle. In this case, it is advisable to introduce additional constraints by explicit rules that make the game more difficult for best-performers. Note that explicitly introduced rules can easily be adjusted to each patient depending on ability levels. Different explicit rules can apply for each player, whereas the material constraints, which serve similar purposes of adjusting difficulty level, always apply to all players. To explicitly introduce a rule for one or more participants, the therapist would request that they use utterances of specific types, for example:

- regarding the length of utterances:
  - any utterance, including single words ('clock?')
  - single words ('clock?')
  - only two word expressions or longer utterances, including adjective-noun or noun-verb minimum ('pass clock?')
  - only full grammatical sentences ('Could you pass me the clock?')
  - only grammatically complex forms (embedded sentences; 'Could you pass the apple that is red?')
- regarding the way to address other players:
  - no restriction ('Could you pass me the fork?)
  - always use of co-player's name ('Joe, could you pass me the fork?')
- regarding politeness:
  - no restrictions ('Pass the bread?')
  - use of politeness formula obligatory ('Please could you pass the bread?')

Please note again that all of these rules can also be introduced by modeling, although this is more difficult if rules are adjusted to individual patients. Note furthermore that some of these focusing tools only make sense for specific deficit patterns, for example a constraint on complex linguistic forms primarily for patients with specific grammatical impairments, especially agrammatism. It may be best not to overemphasize explicit rules and draw more heavily on material constraints, as described above. If rules are established explicitly, success of the speech act should depend on adhering to the rules. For example, a patient asked to follow the politeness and name-usage rules should only receive a requested object card or be allowed to participate in any proposed activity if indeed, a politeness formula and the name of the addressee had been used. This can be motivated by everyday-communication, as in some contexts, making a request or proposition in a polite way and speaking to the addressee by using their name is of great importance for success.

Although it has been argued that the therapist function in CIAT can be taken on by non-specialists (Meinzer et al., 2007), the complex role of the therapist in CIAT or ILAT can be difficult to master for interested lay persons who have little background in language sciences and pathology (Difrancesco et al., 2012). In addition to serving as a communication partner with the same function as any of the LAG-participating patients, the role of the therapist includes modeling and shaping, adjustment, introduction and keeping track of patient-specific rules, keeping track of communicative success and failure, possibly in the form of a protocol, and most importantly, adjusting their own language activities to most efficiently help patients who participate in the LAGs. Such a demanding and complex task may be difficult for a layperson to take on without substantial training and experience. Using language-action games at home, between patients and their partners or friends and in aphasia self-help/community groups amongst patients, can however be beneficial and motivating for patients suffering from language difficulties (Pulvermüller & Roth, 1991).

3.5 ROLE OF A CO-THERAPIST

The typical composition of participants in ILAT is one therapist and two or three aphasic patients. In addition, a co-therapist can be present during all sessions. Whereas the main therapist engages in LAGs and models possible speech acts for patients, the optional co-therapist - whose role can also be taken on by experienced therapists, on top of their LAG-playing function - is responsible for:

- taking notes of communicative moves of each individual patient
- keeping track of difficulties and improvements during each therapeutic session, and
- helping patients who have difficulties with a specific card or communicative move.

3.6 PATIENT SELECTION

ILAT's most researched form, CIAT, has been tested in randomised controlled trials (RCTs) with patients suffering from chronic aphasia after stroke. It is reasonable to assume (but not proven) that patients with other aetiologies also profit from this SLT method. Most studies so far prove effects at the chronic stage, although encouraging results also come from initial exploratory work at the acute post-stroke stage (Kirmess & Maher, 2010). The group setting used in recent studies is most appropriate for patients with moderate to mild forms of aphasia. Very severe language deficits as seen for example in global or mixed-transcortical aphasia, may be best treated in a one-on-

one or two-on-two fashion initially, with equal patient to therapist interaction (Pulvermüller & Schönle, 1993; Kurland et al., 2012).

Many previous studies were all performed on pre-selected clinical populations, some applying rather strict inclusion and exclusion criteria. In principle intensive forms of action-embedded language therapy should be applicable to most patients able to partake in standard SLT. Other forms of SLT used in previous studies have typically included an unconstrained (total communication) training approach based on patient's functional deficits involving exercises such as naming, repetition and sentence completion (e.g. Pulvermüller et al., 2001) or SLT based on PACE (Davis & Wilcox, 1985) therapy (e.g. Kurland et al., 2012). However the special demands related to the intensity of delivery, the group setting and the multiple simultaneous demands on action, perception, interaction and communication ability, limit to a degree the range of patients who may be able to participate or who may benefit from this form of SLT. Criteria that might lead the therapist, or possibly a consultant neurologist, to discourage participation in ILAT, could include the following:

- chronic heart disease or other illness that may make it difficult to participate in engaging activity for several hours,
- inability to understand the introduction to LAGs and related instructions,
- presence of major perceptual, motor and neuropsychological impairments that make it difficult to perform in LAGs, including severe forms of
    - motor impairments and apraxia,
    - visual processing deficits,
    - planning deficits,
    - learning deficits,
    - memory deficits

- attentional deficits.

This said, it should however be noted that a degree of memory, attention, and motor/apraxia impairment can be tolerated in LAGs and may even be worked upon in the settings described. A patient with aphasia and neglect may not only learn to use words and understand in the LAGs, but also may learn to retain an overview of a spectrum of picture cards and co-players during a LAG. Apraxia of speech certainly does not hinder participation but will indeed be a valuable target of SLT in ILAT context (see Kurland et al., 2012), especially where emphasis is put on phonological minimal pairs or card selection biasing verbal output towards consonant clusters and complex utterances challenging the articulatory system. Verbal working memory training is provided, as increasingly complex utterances need to be kept in mind while card sets are being searched. Due to the high attention demands of ILAT, patients with low attention abilities or with very severely impaired language may find it difficult to follow the intensive schedule. On the other hand, the training of turn-taking provided by LAG participation implies also training of attending to communication partners, visual stimuli, others intervening etc., so that both the focusing of attention as well as divided attention can be trained. Furthermore a minimum level of comprehension is needed in order to be able to participate in the LAGs, although as explained, a good deal of the explanation can be done by modelling and shaping. Although ideally ILAT should be carried out in groups, it is however possible to deliver therapy on a one-to-one basis, which may be better suited for severely impaired patients, as mentioned before.

Previous research has shown that patients with different forms of aphasia and different levels of language impairments participating in the same group can benefit from ILAT. ILAT offers possibilities to introduce rules to titrate different difficulty levels for individual players in the same game. Therefore therapy groups can indeed consist of patients with different abilities and impairments. Certainly it will be easier and more efficient to conduct ILAT with a more homogenous patient group (e.g., with moderately impaired patients all suffering from agrammatism), if this happens to be possible. Important complications of mixed ability groups are the possibilities that patients with more severe language problems may sometimes cause less severely impaired patients to become frustrated with the slow pace, whereas severe patients in the context of much better performers might become unnecessarily frustrated with their comparatively low rate or level of success and progress. It is therefore desirable to group patients with similar aphasia severity into the same group, although there are options for balancing demands.

3.7 EVALUATION OF PROGRESS IN LANGUAGE-ACTION GAMES

When taking notes during LAGs, it is important to focus on the evaluation of each individual patient's speech acts. In this context, it has proved to be useful to take notes, in the form of a protocol, of:

a) date, number of game, round, and speech act/turn
b) type of LAG (e.g. "request" or "planning")
c) progression level imposed by materials (simple objects, coloured object arrangements, actions etc.) and rules for each player (use of politeness form, full sentences, etc.)
d) speech act (or attempt) type (requesting, rejecting, accepting, clarifying)
e) utterance type (full sentence, politeness, target word, description of target)

f) appropriateness of speech act (fully functional (3), functional but with minor delay or error (2), still with minor functional contribution (1), not functional at all (0))

A scoring sheet can be used to systematically note the progression of games/ levels (as indicated under a-c) and to evaluate each patient's performance (as indicated under d-f), and in order to plan the next session. An annotated example of how a speech act would be scored using these criteria can be found in Appendix 2. It has proven to be very helpful to videotape or voice record sessions for the purpose of transcribing and evaluating relevant communicative sequences later on, particularly when no co-therapist is available during the therapy. The evaluation of communicative acts after each therapy session will help to monitor the progress for each individual patient and will help the therapist to adjust rules or materials for the next session (see Section 1.3 on focussing for more details). As the therapy proceeds, it is important for the therapists to introduce new rules and constraints and to refine existing rules, referring to notes and any recordings taken.

3.8 SPECIFIC FEATURES OF LAGS

In all LAGs exemplified here, two identical sets of cards are distributed evenly between players, so that each player has 6 to 12 cards in front of her/him. As the first step of each round, one player selects a card from their set and holds it in their hand. Please note again that the simultaneous use of motor and verbal action (holding the card in the hand and speaking) is a crucial element of ILAT. Next the player performs the key speech act, or makes an attempt at performing it. A different participant can then respond to the initial verbal action, for example by passing the picture with the requested object or by agreeing to participate in the proposed action and passing the corresponding card. Note again that passing a card is a nonverbal action into which speech acts are embedded and that this serves as a check for successful communication. After one successful round of communication, the object-requesting or action-proposing player puts aside the matching pair of picture cards. For each player, the aim of the game is to get rid of his or her cards by having them put aside after participating in as many as possible successful communications.

ILAT can be used to practise different kinds of key speech acts, for example REQUESTING an object and PROPOSING an activity, as well as parts of speech (nouns and verbs). In what follows, the rules of ILAT will be illustrated through practical examples of the REQUEST and PLANNING LAGs. The two games follow a similar language-action structure (see Figures 3.2 and 3.3), but importantly encompass different kinds of speech acts, both of which are important for day-to-day communication. Therefore the therapeutic aims of each game are explained to highlight the differences between them. Example transcripts have been taken from therapy sessions with two non-fluent aphasic patients (patients 1 and 2 from Section 4.2.1). The example transcripts will be used to illustrate possible moves, including speech acts from the different players (PA, PB, etc.) Please note numbers in brackets indicate the length of pauses (in seconds) during speech.

3.8.1 Object Request Lag

Therapeutic Aim: To learn to participate in REQUEST dialogues. This means to reliably make REQUESTS using a range of verbal utterances, to appropriately respond to REQUESTS by HANDING OVER objects (cards), or to REJECT the request, or, in case of doubt and difficulty, to work towards CLARIFYING the request. Here words, phrases and syntactic structures of various degrees of difficulty are practised. The use of successful verbal requests results in acquiring pairs of cards with the same objects

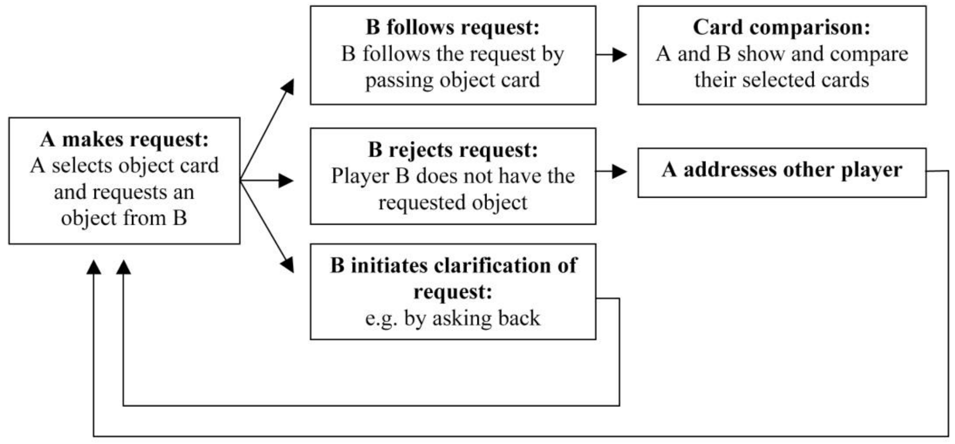


Figure 3.2. Request an object game. This decision tree illustrates the possible moves and relevant speech acts during a "request an object" game.

depicted on them. Figure 3.2 illustrates the sequence structure of the REQUEST LAG, indicating its possible moves and their possible successions in the game.

Objective of the game for the players: To be the first player to have no cards left to match, either by receiving or passing on matching cards.

Rules of the game:

Requesting an object:

A round of the game begins with the first player, whom is labelled A here for convenience. A selects a card and REQUESTS the corresponding item from a different player, B. Verbal utterances that could be used for successfully making a request range from single words to whole sentences and even more complex forms, for example:

> *Strawberry, red little thing. Would you pass me a strawberry, please?*

Responding to the request:

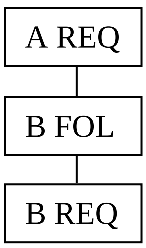
Typically, a request is followed by:

- B FOLLOWING the request by handing over the card with the corresponding object on

- B REJECTING the request by mentioning the unavailability of the requested object card in their set,
- B CLARIFYING the request in case of communication problems.

Following the request: If Player B has identified the requested object and found the corresponding picture card, Players A and B show their cards to each other and to all other players to confirm that the cards match. Player A, who requested the card and received the matching one, may thank B and puts both cards to the side. Player B, the addressee of the previous round, then begins a new round by requesting an item depicted on one of his/her cards. The LAG continues until all cards are matched. This sequence of moves is illustrated by example Transcript 1.

Transcript Example 1 – following a request



A: (Picks up card) Have you a plant, please?

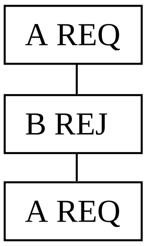
B: Sure, I can certainly give you a plant. (Offers and shows card with plant)

A: Thank you. (Shows his/her card with plant and takes Player B’s card after matching check)

Rejecting the request: If Player B does not have the matching card, they must deny the request (“no”; “sorry, no” or “I do not have this card”). Player A can then address another player with the same request. Note that this feature of the game leads to frequent repetition of successful speech acts and thus contributes to the desirable massing of practice.

Transcript Example 2 – rejecting a request

A: May I please have one large white bottle and two green small bottles?



B: I'd love to give that, but I haven't got it. I'm sorry.

A: Thank you very much.

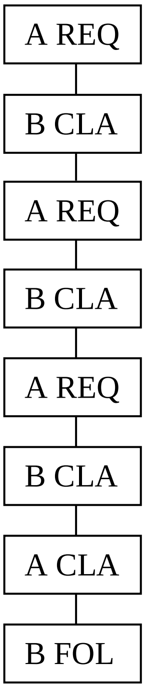
B: That's ok.

A: (to Player C) Would you have one large white bottle and two small green bottles please?

Clarifying the request: During a specific move, there may be times when players either cannot find a suitable target word or phrase to perform the intended speech act, or when more information is needed to make a successful request. In addition, a perfect utterance and unambiguous speech act may be produced by A, but B may not understand appropriately due to comprehension deficits. In these cases, Player B or C (which may be another co-player or the therapist) can query the request, ask Player A to repeat, or encourage Player A to think of alternative ways to communicate what he or she wants B to do. As explained in Section 3.3 (ILAT materials) above, at times different expressions may be equally well suited to achieve communicative success in a particular LAG, whereas at other times more specialisation may be needed in a LAG for example one presenting several different forms of the same item, (e.g. small dogs, ones of different colours). Therapists and players ask and inspire Player A to use alternate expressions and even descriptions of colour, shape or what the object is used for. Clarifications are based on the strategy of systematically exploring the search space based on players' own cards (i.e. "I have two dogs, one is big and one is small"). In general any verbal communication which leads to successful identification of the requested card is actively encouraged and positively reinforced by the therapists' verbal comments and through receiving the pair of matching cards. Unsuccessful attempts should neither be positively rewarded nor punished in any way.

Transcript Example 3 illustrates a complex clarification (or repair) sequence. Here Player A first makes an unsuccessful attempt to request a drill, then clarification questions follow and new attempts at requests are made by A. Later-on a revised description of the desired object “crow hammer … for making holes” leads to the correct assumption on B’s side. Then, B performs another set of clarification moves, asking back whether “power tool” and “drill” is the target of the request and, after agreement on A’s part, hands over the correct card. This sequence provides a quite dramatic demonstration of how the (only partially appropriate) input from different communication partners together with the constraints provided by the LAG can lead to communicative success, even in the absence of canonical utterances.

Example Transcript 3 – Clarifying the request



A: Right, err, do you- err (2s) crow- (3s) crow something, err right,

B: What colour is it Player A?

A: Its blue, blue on one side and red at the back and red at the front, and its clo- crow hammer, crow hammer, (2s) hammer. Have you got it?

B: Does it have one handle or two handles?

A: Err no-not really. Not really a handle.

B: It hasn’t got a handle?

A: Well (1s) err (1s) it’s red on one side and red at the back and the front and call- It’s called something like a crow hammer. Do you have it (3s) for making holes?

B: Hold on, is it a power tool?

A: Yes, yes.

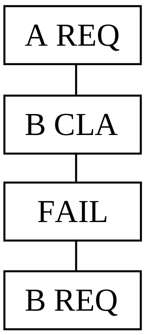
B: Oh I think I have it. I think I know. A drill? (Player shows card)

A: Yes a drill. Thank you (Player shows card and takes it after matching check)

Detection of failure

a. Unsuccessful request: At times in a specific move, it may become clear that an unsuccessful request has occurred. The primary diagnostic here is the mismatch between cards shown by Players A and B. Upon comparing their cards, A, B and the other players will realise the problem. In this situation, A and B take back their own card. After the unsuccessful round, A has lost the right to initiate a new round; Player B goes on to start a new round by selecting a new card and by requesting the depicted object.

Example Transcript 4 – detection of failure



A: Chair with umm a, a (7s) in front of it, it's right, it's in front of it

B: Sorry?

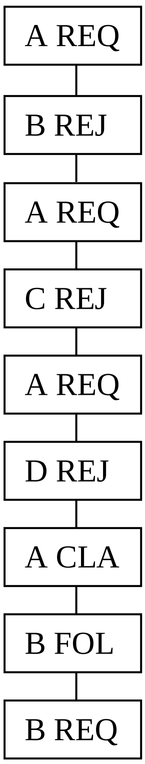
A: Chair with an apple, oh, no, a cushion (6s) in front of it, in front of it, under- underneath it

B: Underneath the chair? (B shows card with cushion on the floor but in front of the chair)

A: No, no, that's the front one, the one benea- beneath it (A shows card with cushion directly under chair. Card mismatch and A and B each take back their own cards and Player B begins new round)

b. *Unsuccessful comprehension:* Communication failure is very obvious in this kind of LAG when all players reject a given request. The transcript below illustrates such a "general" failure, followed however by a repair sequence initiated by A, who interestingly, adds new information thus making a redundant request. A now specifies the requested objects by two attributes "brown bottle" and "with white label", which leads to success. The new round will be initiated by Player B, who has handed over the requested item.

Example Transcript 5 – detection of failure



A: Could I have one brown bottle please?

B: One bro-own bottle. I'm afraid I can't give you any brown bottle

A: Ok, Player C would you have one brown bottle please?

C: No, I'm afraid I haven't got one.

A: Oh, Player D would you have one brown bottle please?

D: I'm afraid to say it but I don't have it either.

A: Ok, somebody has the brown bottle with a label- I'll just do a general one then. One brown bottle with a white label on it.

B: Ah, I have that

A: May I have it please?

B: Yes, thank you (Player B shows card)

A: Yes, thank you very much. (Player A shows card and takes the pair after confirming that they match)

3.8.2 Action Planning Lag

Therapeutic Aim: To learn to participate in interactive PLANNING of future activities, by PROPOSING joint activities, and by responding to such proposals by ACCEPTING them, by REJECTING them, or by CLARIFYING the proposal. This game is played with cards depicting actions; these define the activities to be proposed and the activities

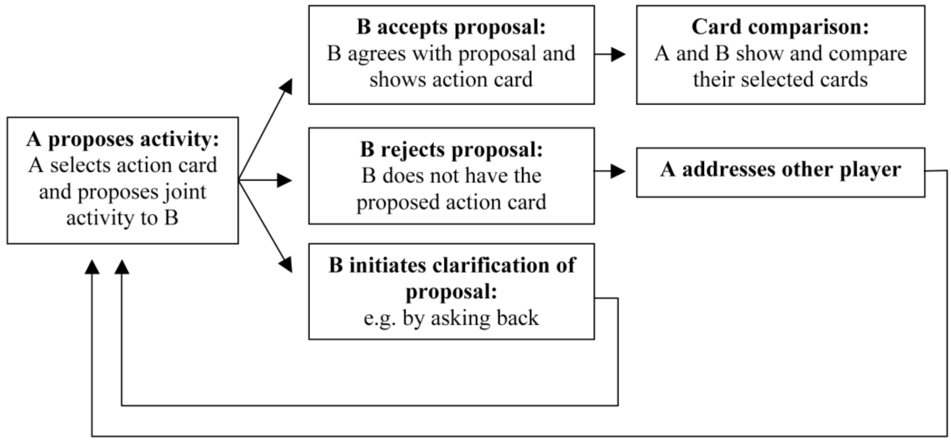


Figure 3.3. Planning an activity game. This decision tree illustrates the possible moves and subsequent speech acts during a "plan an activity" game.

a player can agree to participate in. The use of successful speech acts (activity planning with a co-player) results in acquiring, and putting aside, pairs of these action cards. Figure 3.3 illustrates the possible moves and subsequent steps of the game.

Objective of the game for the players: To be the first player to have no cards left, either by receiving or passing on cards.

Rules of the Game

Proposing an activity

A round begins with Player A picking up a card and proposing the depicted action as a joint activity. A range of length of utterances can be used. Examples of which are:

> *Hiking; play chess; why don't we watch TV; you know what? We should rent a boat*

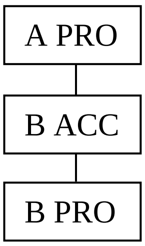
Responding to the proposal

Typically the proposal is followed by:

- B ACCEPTING to join the proposed activity and handing over the corresponding card,
- B REJECTING the proposal by mentioning that the he/she is not able to participate (owing to unavailability of the matching card),
- B CLARIFYING the proposal in case of communication problems.

Accepting the proposal to join an activity: If Player B has the corresponding action picture card, s/he agrees to join the proposed activity. Upon checking the cards match, Player A then takes both cards and puts them aside. Player B then begins a new round by selecting a card from his/her set and by proposing the depicted action as joint activity. Transcript Example 6 illustrates a successful round of the PLANNING game, which however, starts with an unsuccessful attempt at making a request, followed by a repair sequence over which relevant information (that “stick”, “hole” and “ball” are part of the activity) is produced step by step, to incrementally frame the to-be-proposed target activity (playing golf).

Transcript Example 6 – accepting proposal to join activity



A: Can you help me with umm, would you like to play umm. I’ve lost it

B: You can describe it, A.

A: (4s) long stick with two people and a hole and a stick with a hole on the end of it. Umm (2s) I can’t see what else is there?

B: So maybe you could tell me what we could do with the stick?

A: Umm it’s two sticks with a ball and long, a long stick and ball; and a long, umm a ball that you hit?

B: So you hit a ball?

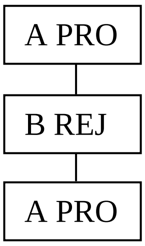
A: Yes, with the long (1s) stick

B: I think I know. Would you like me to play golf with you? (Player A offers card and B also shows card, which matches)

A: Oh, yes. (Player A takes both cards upon confirmation of match).

Rejecting the proposal: If Player B does not have the matching card, he/she should deny the request to participate in the activity. Player A then makes the same proposal to a different player.

Example Transcript 7 – rejecting proposal



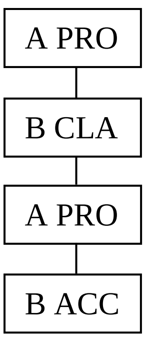
A: B, would you like to join me walking the dog tomorrow?

B: No, I think my dog just want to stay in-indoors

A: Ah, ok. Well then C would you like to join me walking the dog?

Clarifying the proposal: If clarification is needed during a move, Player B can request more information or ask A to repeat the proposal. Again clarification moves are made based on players' own cards. Note that in example Transcript 8, the target activity is "sending out a letter, with a stamp on it". Due to word finding difficulties, the proposal to "lick a stamp" is made initially. Only when A specifies further that the proposed activity relates to an "envelope", the target activity can be selected uniquely among its alternatives in the game.

Example Transcript 8 – clarification of proposal



A: Err, please lick (2s) a stamp for me

B: Stamp for you?

A: Mmm-

B: I've got something licking-

A: Yes? What sort of licking is that?

B: (4s) umm

A: Envelope?

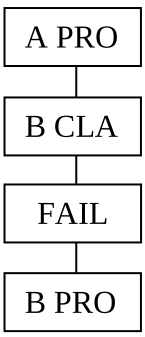
B: Ah yes, lick an envelope (Player B shows card)

A: Great, thanks. (Player A shows card then receives both cards, which match)

Detection of failure

a. Unsuccessful proposal: The unsuccessful outcome of a round is evident when, upon comparing cards, players realise they do not match. Here, Player A and B each take back their own card and Player B begins a new round by proposing an activity depicted on a card in his/her set.

Example Transcript 9 - unsuccessful proposal



A: Umm (2s) right (2s) umm I have here a (3s) hmm a (2s) big long rope and attached to that I've got some err (3s) climbing frame, climbing frame and I'd like to know would you like to please (1s) the (2s) the climbing frame, the (2s) rope and me

B: So you're planning a climbing activity tomorrow and are asking if I would like to join you climbing a wall? Yes?

A: Yes, yes that's right

B: I'm very happy to join in (shows card depicting the activity "climbing indoors")

A: Oh, no. (Shows card depicting the activity "abseiling down a building")

3.9 SUMMARY

This chapter has focused on the practical procedures involved in ILAT and its main variant, CIAT. The underlying principles of ILAT include the use of an intensive schedule, a language-action context for communication and the employment of a range of modelling, focussing and shaping techniques along with explicit rule introduction. Whereas CIAT had exploited one form of communicative interaction (REQUESTING OBJECTS), one more language-action game (PROPOSING ACTIONS) has been highlighted. In the next chapters, the clinical, communicative and neuroimaging results will be discussed from 14 patients who underwent two weeks of therapy following the ILAT methods described here.

CHAPTER 4: THE EFFECTS OF INTENSIVE LANGUAGE ACTION THERAPY ON LANGUAGE PERFORMANCE IN CHRONIC APHASIA: AN EMPIRICAL STUDY

PART 1: STANDARDISED CLINICAL ASSESSMENT

4.1 INTRODUCTION

As outlined in previous chapters, Intensive Language Action Therapy (ILAT) is an intensive form of SLT which aims to implement three principles guided by research from neuroscience and linguistics: massed practise, use of language in an action embedded context, and the focussing of patient's language (see Chapter 1). ILAT's most researched form, CIAT, has thus far been tested in patients suffering with chronic aphasia, and compared with standard SLT (Pulvermüller et al., 2001) and extended forms of PACE therapy (Davis and Wilcox, 1985), using an unconstrained, total communication approach (e.g. Maher et al., 2006; Kurland et al., 2012). Patients suffering with chronic PSA have demonstrated considerable gains in language and communication following ILAT. For those patients who made initial improvements following therapy, stable gains were reported for all patients after 1 month (Maher et al., 2006), 3 months (Faroqi-Shah & Virion, 2009; Breier et al., 2007), and 6 months (Barthel et al., 2008; Meinzer et al., 2005). However loss of initial improvement has also been reported in single subjects (Kurland et al., 2012) and in one third of patients after 3 months (Breier et al., 2009; see Chapter 2).

The present study further explored the efficacy of ILAT, using the extended materials recently developed for English speaking aphasia patients (see Section 3.3; Difrancesco et al., 2012). This extended set targets the practise of a broader spectrum of communication types and speech acts. Patients suffering from chronic aphasia underwent intense training using the methods described in Chapter 3. Training included the original REQUEST LAG described by Pulvermüller et al. (2001), in which patients are able to practise the use of nouns in a behaviourally relevant context where the aim of the game is for players to REQUEST objects. In the present study however, patients also participated in the PLANNING LAG (Difrancesco et al., 2012) in which players can practise the use of verbs in the context of planning activities with other co-players.

4.2 METHOD

4.2.1 Participants

Fourteen patients with chronic (at least one year post-stroke) aphasia underwent two weeks of ILAT. All patients presented with a language impairment following a single stroke affecting the territory of the left middle cerebral artery. This was assessed by reference to medical records and structural magnetic resonance imaging (MRI) scans where available. Only patients who were native monolingual speakers of English before their stroke were included. None of the patients had severe sensory, perceptual or cognitive deficits. Left- handed patients (as assessed by the Edinburgh Handedness Inventory; Oldfield, 1971) and patients with additional neurological diagnosis were not included. Additionally patients with severe comprehension deficits and therefore those not able to fully engage in therapy were excluded. These criteria were assessed at a pre-screening session where an information sheet (Appendix 3) and consent form (Appendix 4) was read through with patients and where possible a friend or relative. Patients were also shown a visual timeline of the study protocol (Appendix 5). The study was approved by the Cambridgeshire Local Research Ethics Committee.

Patients were recruited via local self-help groups in the Cambridgeshire area through leaflet distribution (Appendix 6) and through an advert (Appendix 7) on university websites and websites run by people with aphasia. Table 4.1 shows the age, sex, handedness, duration of aphasia in months, origin of aphasia, and lesion site of each patient.

4.2.2 Procedure

4.2.2.1 ILAT

Patients participated in ILAT in groups of two or three patients per group along with a therapist, plus an additional co-therapist who either participated in LAGs or scored communicative performance of patients (see Difrancesco et al. (2012) for information on the role of a co-therapist). Therapy was delivered for approximately three hours per day over ten consecutive weekdays, following the rules and procedures described in Chapter 3. Briefly, patients participated in LAGs where the aim was to gain pairs of cards by verbally REQUESTING objects from or PLANNING activities with co-players. The type of language used by patients was guided through materials employed in LAGs, modelling of speech by therapists and through explicit rules, to ensure patient's communicative abilities were challenged (Difrancesco et al., 2012).

4.2.2.2 Assessment of Language Abilities

Language abilities were assessed in the week immediately preceding and the week immediately following the two weeks of ILAT. Performance was assessed on the following subsections of the Boston Diagnostic Aphasia Battery (BDAE, Goodglass & Kaplan, 1972): auditory comprehension, including the word comprehension, word comprehension by categories, and the semantic probe subtests; syntactic processing, including the touching A with B, reversible possessives and the embedded sentences subtests; and the Boston Naming Test (BNT). The Token Test (TT), a subtest of the Aachen Aphasia Battery (De Renzi & Vignolo, 1962) was also administered at each

Table 4.1.

Clinical and sociodemographic data of 14 patients who participated in two weeks of ILAT.

P	Age (at therapy)	Sex	Handedness	Duration of Aphasia (months)	Etiology	Lesion site
1	40	Female	Right	26	Aneurysm - subarachnoid haemorrhage	Left posterior communicating artery - Left Sylvian fissure
2	73	Female	Right	22	CVA	Left middle cerebral artery
3	65	Male	Right	80	CVA	Posterior left hemisphere - Left parietal-occipital
4	74	Male	Right	127	CVA	Left MCA territory
5	40	Female	Right	19	Left temporal intracranial haemorrhage	Left MCA territory
6	69	Male	Right	25	CVA	Left MCA territory
7	48	Male	Right	17	CVA	Left MCA territory
8	72	Male	Right	32	CVA	Left MCA territory
9	60	Female	Right	137	CVA	Left MCA territory
10	26	Female	Right	165	Left intracranial haemorrhage	Left fronto-parietal
11	41	Male	Right	19	CVA	Left fronto-parietal
12	76	Male	Right	234	Haemorrhage	Left inferior frontal gyrus
13	54	Male	Right	20	CVA	Left MCA territory
14	59	Male	Right	104	CVA	Left MCA territory
Average	**56.93**			**73.36**		

CVA – cerebrovascular accident; MCA – middle cerebral artery testing session to assess patient's abilities to follow simple to complex commands to touch and handle tokens of different colours, shapes and sizes. In addition, the Communicative Activity Log (CAL, Pulvermüller et al., 2001; Pulvermüller & Berthier, 2008) was completed at each time point, one by patients and another by a close relative. The CAL is an 18-item questionnaire which provides information on communication in everyday life situations. Higher ratings reflect increased frequency and better quality of communication.

4.3 RESULTS

4.3.1 Boston Diagnostic Aphasia Examination

Table 4.2 shows no apparent change in scores for the auditory and syntactic subtests of the BDAE. Paired samples t-tests confirmed no significant differences in the auditory comprehension, $t(13) = 1.94$, $p = .075$, or syntactic processing, $t(13) = 0.24$, $p = .814$ subsections before and after the two weeks of therapy for the group as a whole.

Interestingly, as illustrated in Figure 4.1, a paired samples t-test showed a significant increase in number of items correctly named on the BNT after therapy, compared to before, $t(13) = 3.85$, $p = .002$.

Table 4.2.

Average pre- and post- therapy scores (SD) from the BDAE auditory comprehension, including the word comprehension, word comprehension by categories, and the semantic probe subtests; and syntactic processing, including the touching A with B, reversible possessives and the embedded sentences subtests.

	Pre-testing		**Post-testing**	
Auditory Comprehension	84	(0.67)	85.36	(0.86)
Syntactic Processing	18.79	(1.44)	18.57	(1.70)

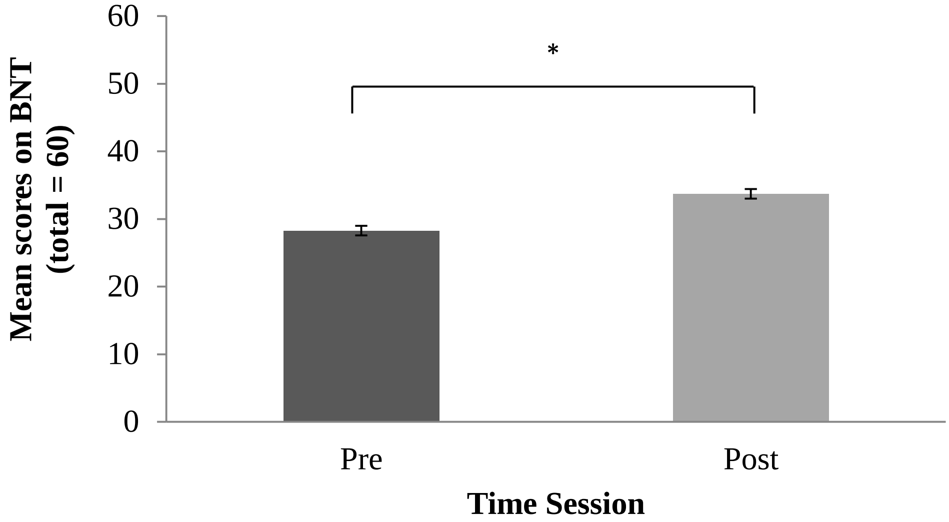


Figure 4.1. Average pre- and post-therapy scores for the number of correct items named on the Boston Naming Test. Error bars represent standard error[1]. * = $p < .05$.

4.3.2 Token Test

A paired samples t-test showed a significant decrease in the number of mistakes made on the TT after therapy, compared to before, $t(13) = 2.20$, $p = .046$ (Figure 4.2).

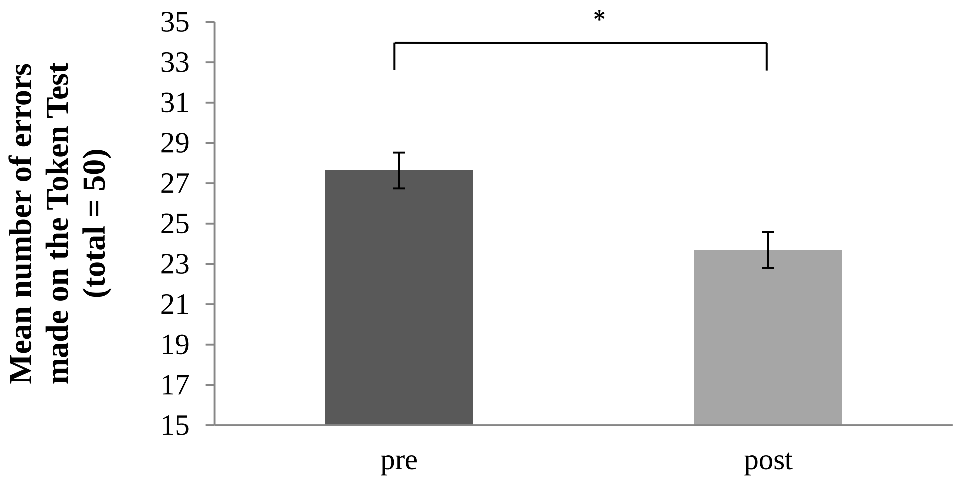


Figure 4.2. Average pre and post therapy scores for number of errors on the Token Test. Error bars represent standard error. * = $p < .05$.

[1] Error bars throughout the thesis are adjusted to reflect between condition variance suitable for repeated measures comparisons (Cousineau, 2005).

4.3.3 Communicative Activity Log

All ratings appeared to show improvements in patients' quality and amount of communication after therapy, for both self and relative rated scores (Figure 4.3). A paired samples t-test showed self-rated scores were significantly higher for quality of communication (available from 11 patients) following the two weeks of therapy, $t(10) = 2.86$, $p = .017$. There was however no change in scores in the self-ratings for amount of communication (available from 14 patients) $t(13) = 1.44$, $p = .175$.

Relative ratings of communication in the weeks following therapy were available for 11 out of the 14 patients who participated. Improvements in everyday communication scores also appear to be reflected in the relative-ratings (Figure 4.3). Similarly to the self-ratings however, a paired sample t-test showed no change in scores for amount of communication following therapy, $t(8) = 0.98$, $p = 0.354$. However ratings for the quality of communication only approached significance for the relative ratings, $t(8) = 2.07$, $p = .072$. Interestingly, a Pearson's correlation showed a significant positive correlation between the CAL relative ratings and the self-ratings, $r(34) = .673$, $p < .001$.

4.4 DISCUSSION

Over 10 days of ILAT, the BNT subsection of the BDAE, used as a standardised clinical measure, yielded significant improvements in naming objects in the group of patients. Furthermore patients as a whole made fewer errors on the TT in the post-therapy testing session. In addition, CAL self-ratings and therapist-ratings indicated the beneficial effect of ILAT, particularly in terms of quality of communication. The significance criterion was reached for the self-ratings in the quality of communication scale, although a numerical improvement was visible on all ratings obtained.

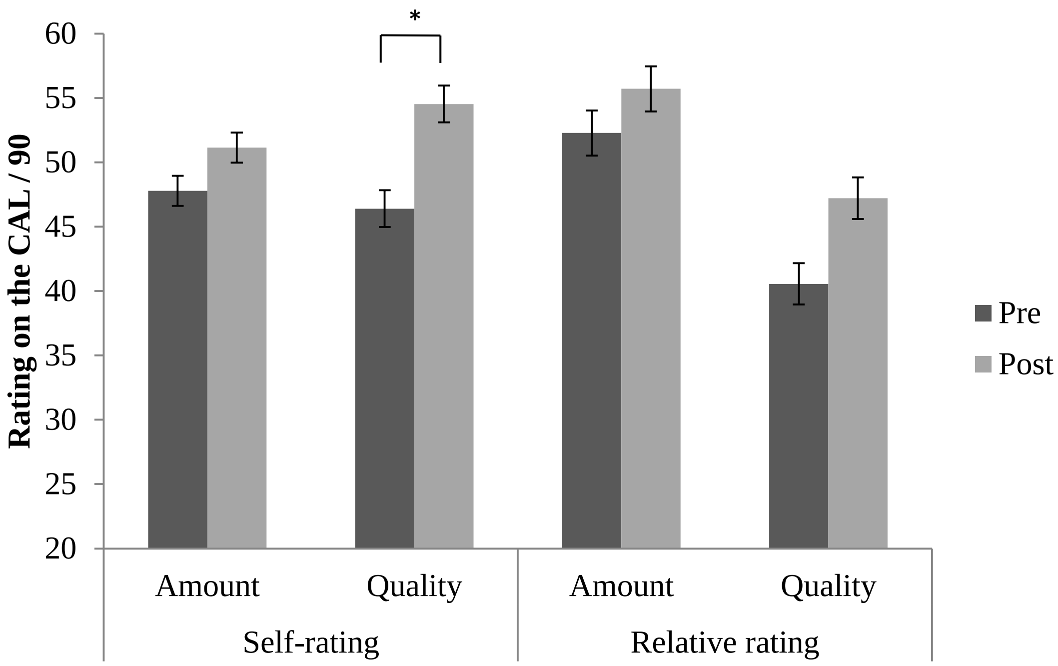


Figure 4.3. Average self- and therapist-rated scores on the amount and quality of communication scales of the Communicative Activity Log (Pulvermüller et al., 2001) recorded before and after the therapy. Higher ratings indicate better communication. * = $p < .05$.

The lack of effects in the auditory comprehension and syntactic processing subtests of the BDAE should not be over-interpreted. A lack of statistical power may explain the absence of significant results in these subtests. First, only a subset of the whole was included in this battery. Similarly to previous findings, individual subtests of aphasia batteries do not always show significant gains in group or individual scores (Faroqi-Shah & Virion, 2009; Goral & Kemplar, 2009; Kurland et al., 2012). Second, most patients had moderate to mild aphasia and many clinical tests lack sensitivity in the upper range of aphasic performance. Third, confrontation naming in the BNT included items which were untreated during therapy and therefore show evidence of generalisation in the gains patients made. The positive results yielded in the BNT are also supported by the improvements in the TT. This assesses patients' abilities to comprehend and follow simple to complex commands involving tokens of different shapes, colours and sizes. Gains in naming and in the TT are in line with previous studies where similar improvements in these particular tasks were found in patients with chronic aphasia who underwent ILAT (Faroqi-Shah & Virion, 2009; Maher et al., 2006; Meinzer et al., 2004; Pulvermüller et al., 2001).

Ratings of communication effectiveness and amount, assessed by the self-rated and therapist-rated CAL, tended to show improvements after therapy. However significant differences were only shown in the quality of communication scale for self-ratings. Taking a positive attitude, there is evidence for improvement in patients, along with a significant correlation between self- and therapist-ratings. Importantly, the communicative improvement indicated in CAL results is paralleled by improvements in the BNT and TT, thus providing some cross-validation of the improvements over testing procedures.

In line with previous research these results indicate that ILAT can lead to significant improvements of language and communication on different measures, ranging from clinical tests to ratings of everyday communication. Although the present results do not unambiguously demonstrate dramatic effects, they add to a growing body of reports on therapy related improvements over ILAT application. These results also indicate that when assessing the effects of ILAT, it is advisable for clinicians not only to assess language functions with clinical tests, but to use communicative rating scales too.

CHAPTER 5: THE EFFECTS OF INTENSIVE LANGUAGE ACTION THERAPY ON LANGUAGE PERFORMANCE IN CHRONIC APHASIA: AN EMPIRICAL STUDY

PART 2: COMMUNICATION ANALYSIS

5.1 INTRODUCTION

In Chapter 4, the beneficial effects of Intensive Language Action Therapy (ILAT) were shown in a group of patients with chronic aphasia. Here and elsewhere however, it has been documented that clinical assessments are not always sufficient in identifying changes in test-retest language assessments (Faroqi-Shah & Virion, 2009; Goral & Kemplar, 2009; Pulvermüller et al., 2001; Szaflarski et al., 2008), particularly so in less severe patients, who may perform near ceiling on some subtests of aphasia batteries (Difrancesco et al., 2012). Furthermore previous reviews of ILAT have highlighted the importance of investigating alternative outcome measures to assess gains made in therapy (Meinzer, Rodriguez & Gonzalez-Rothi, 2012). This includes measuring success on untreated items to assess possible generalisation.

It may be useful to explore the relationship between performance on clinical assessments and performance in terms of communication success during therapy, when patients engage in the various LAGs that form ILAT. For example, although no significant improvement was reported in the auditory comprehension subtests of the Boston Diagnostic Aphasia Examination (BDAE, Goodglass & Kaplan, 1972; see section 4.3.1), patients did make gains on the Token Test (TT, De Renzi & Vignolo, 1962), a task which requires comprehension of simple to complex commands. During this test, patients are asked to point to or handle tokens of different colours, sizes and shapes. It would therefore be of interest to investigate whether there is a relationship between a change in scores on the standardised TT and either overall comprehension performance during LAGs or specifically during LAGs involving colours, sizes and prepositions. An understanding of which clinical assessments may best detect changes in higher ability patients with aphasia is essential for intervention studies.

In addition to being able to demonstrate improvements on standard clinical assessments, it is important to understand how individual patients succeed in the various LAGs. Understanding a patient's capability in using a particular type of language is vital in order to be able to successfully challenge them through the introduction of new materials or rules (see Chapter 3). Equally if a patient is severely struggling with a specific LAG, it is important that they do not become too frustrated. Moreover assessing performance across the full set of materials utilised in ILAT will be valuable for a full understanding of a patient's language capabilities following therapeutic intervention. Particularly for ILAT where patients engage in different kinds of speech acts, practising object-related nouns and action-related verbs, standard language assessments may not be sufficient to detect differences in changes relating to use of specific types of language (i.e. nouns vs. verbs). In Chapter 4, the study utilised the new extended set of materials described by Difrancesco et al. (2012), which included a set of cards depicting actions. This set was used in order for patients to be able to practise using verbs in a behaviourally relevant context (i.e. where they planned an activity with a co-player). In the standard assessments in Chapter 4, no conclusions were drawn regarding changes in player's use of verbs.

To address these issues, a measure of communicative performance during LAGs was recorded. Communicative performance refers to how patients succeed in performing speech acts such as requesting, informing and planning, and how they succeed in understanding these linguistic actions. Previous studies have explored detailed analysis of speech production and comprehension during therapy. Pulvermüller & Schönle (1993) documented improvements on both accuracy and response time (RT) measures over a therapy interval of several weeks in a single patient with severe chronic PSA. Furthermore Difrancesco et al (2012) illustrated improvements in RT measures in two mildly impaired patients. Interestingly there was little change in the pre and post-scores for subtests of the BDAE, yet the analysis of RTs throughout therapy indicated these patients became quicker at making and responding to requests, indicating improvement.

This chapter will investigate the communicative performance of six patients who underwent ILAT as part of the study in Chapter 4, by analysing the RT measures and accuracy rates during LAGs. In addition to these two measures, the complexity index (CI) will be introduced and utilised. The CI was created in order that the type of language patients use can be analysed. An important issue was highlighted in the previous chapter in relation to scores on the Communicative Activity Log (CAL, Pulvermüller et al., 2001). An increase in *quality* of communication was reported, in the absence of an increase in *amount* of communication. Therefore absence of change in the amount or accuracy of communication in a particular patient should not necessarily imply there has been no improvement in that patient. Of equal importance is whether quality of communication improves in patients, in addition to or in place of increases in quantity.

5.2 METHOD

5.2.1 Participants

Six patients (1 female) with chronic post-stroke aphasia were selected from the group of 14 patients who participated in Part 1 of this project (Chapter 4). Due to the time

Table 5.1.

Clinical and demographic data of six patients whose therapy sessions were recorded for communication analysis.

P	Age (at therapy)	Sex	Handedness	Duration of Aphasia (months)	Etiology	Lesion site
1	65	Male	Right	80	CVA	Posterior left hemisphere - Left parietal-occipital
2	74	Male	Right	127	CVA	Left MCA territory
3	40	Female	Right	19	Left temporal intracranial haemorrhage	Left MCA territory
4	69	Male	Right	25	CVA	Left MCA territory
5	48	Male	Right	17	CVA	Left MCA territory
6	72	Male	Right	32	CVA	Left MCA territory
Average	**61.33**			**50.00**		

CVA – cerebrovascular accident; MCA – middle cerebral artery consuming nature of communicative analysis, recordings were taken from only a subset of the whole group. Table 5.1 shows the demographic and clinical profile for each patient (details of inclusion/exclusion criteria are detailed in section 4.2.1).

5.2.2 Procedure

Ten sessions of therapy were delivered employing the rules of ILAT and utilising the full set of materials described in Chapter 3. In each therapy session, patients engaged in either the REQUEST or PROPOSAL LAGs. The first and last 3-5 of each LAG (i.e. the REQUEST LAG and the PLANNING LAG) of the two weeks of therapy were chosen for evaluation, or "test sessions". In addition, the preposition REQUEST LAG was recorded separately as this LAG employed cards depicting two or more objects in various locations and thus required the use of more complex language. Table 5.2 presents a summary of language performance measured by clinical assessments before and after the 10 days of therapy.

5.2.2.1 Analysis of Communicative Performance

Changes in production of and understanding speech acts within the LAGs, was evaluated using a conversation analysis technique (for similar methods, see Pulvermüller & Roth, 1991; Pulvermüller & Schönle, 1993, Difrancesco et al., 2012). Each test session was video and voice-recorded and later analysed in order for speech- and comprehension-performance to be scored. Scoring was based on accuracy, RT and complexity of speech acts and comprehension using the following criteria. RT data was acquired by inputting each recording into Audacity (Audacity Team, http://audacity.sourceforge.net/) and separating it into each patient's spoken output and response to speech.

Table 5.2.

Results of clinical language tests administered before and after ten day therapy interval for six patients.

	BDAE						**TT**		**CAL - self ratings**				**CAL - relative ratings**			
	Auditory Comprehension		*Syntactic Processing*		*BNT*		*(number of errors)*		*Amount*		*Quality*		*Amount*		*Quality*	
	Before	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*
1	84	80	25	25	43	48	5	5	36	45	47.5	59.5	58.5	58.5	65.5	61.5
2	85	86	22	20	12	23	17	14	37	55	30	49	49	56.5	46	53.5
3	84	85	22	18	37	35	30	19	67	60	66	57.5	70	58	34	42
4	81	85	15	21	13	19	31	33	47.5	32.5	46	51	54	-	25	-
5	85	87	11	12	12	24	41	35	38	31	26	24	58	49	25	21
6	81	84	16	9	36	32	48	38	15	18	-	-	10	31	6	15
Mean	83.33	84.50	18.50	17.50	25.50	30.17	28.67	24.00	40.08	40.25	43.10	48.20	49.92	50.60	33.58	38.60
SD	1.86	2.43	5.32	5.96	14.63	10.57	15.68	13.30	16.97	15.94	15.94	14.22	20.75	11.60	20.40	20.15

BDAE (Boston Diagnostic Aphasia Battery; Goodglass & Kaplan, 1972) – Auditory comprehension composite score include word comprehension, word comprehension by categories, and semantic probe subtests; Syntactic processing composite score includes touching A with B, reversible possessives and embedded sentences subtests; BNT – the Boston Naming Test. TT (Token Test - a subtest of the Aachen Aphasia Battery; De Renzi & Vignolo, 1962). CAL (Communicative Activity Log; Pulvermüller et al., 2001; Pulvermüller & Berthier, 2008).

5.2.2.1.1 Speech Production

Spoken output was evaluated as to whether it was sufficient to uniquely identify the target object in the context of the given LAG. Such unique identification could be provided by a best-fit target word, a multi-word expression, a suboptimal description leading to communicative success, or a full sentence. If a player used a misleading object or action name or description, the speech act was scored as unsuccessful. In addition, the rules and constraints of each round had to be followed in order for a speech act to be considered functional. This applied for the type of LAG (REQUESTING or PLANNING) and other explicit linguistic constraints such as the use of politeness forms and full sentences. If a patient self-corrected their speech act, this was accepted as a successful response. Furthermore if the target was reached through prompting from the therapist (as frequently occurred in the most severe patients), this was scored a successful request, providing the struggling patient did not answer with any misleading information. However if a therapist or other player initiated a repair sequence from an unclear or misinformed request, and only after this sequence communicative success was achieved, this was scored as unsuccessful. RTs were measured from the point in time when a patient picked up the card to when they started to pronounce a critical word or phrase which led to communicative success, i.e. to their card being identified by co-players.

5.2.2.1.2 Speech Comprehension

Passing the correct card or accurately rejecting a request was taken as criteria for successful comprehension. Unsuccessful comprehension was scored if a player passed an incorrect card or rejected a card they held in their set (although this information was not always available in the LAG, video recordings allowed for accessing it.) All comprehension events were scored as successful or unsuccessful except the last request of the game, as there was only a single card left. RTs were measured from the onset of the critical word (object or action) to when the patients selected the correct card from their set or explicitly rejected the request. For the evaluation of RTs, only comprehension of the first request in each move was included.

5.2.2.1.3 Complexity Index

The complexity scale used to analyse speech acts reflects the level of spontaneous language, appropriate descriptions and grammatical correctness of output in LAGs. Speech acts were coded on the CI if output included some but not necessarily all of the criteria stated below:

1. Patients:

   - struggle to use any appropriate language and are able to answer only to specific questions from other players in a yes/no manner

2. Patients:

   - spontaneously use single words or broken sentences, perhaps with additional inappropriate language

   - respond to specific questioning with words

   - need prompting from therapists/ other players

3. Patients:

   - use appropriate phrases

   - are successful in speech acts through prompting by therapists

4. Players:

   - use little irrelevant language and need little prompting from others

   - use phrases and descriptions

   - use simple, perhaps phrases but not whole sentences, such as “walk the dog”

- full ungrammatical sentences

5. Players:

   - use full grammatical sentences

   - gives all information needed to make a successful request (i.e. shape, size, number etc)

5.3 RESULTS

The total number of trials evaluated across all players was 1226. There were 592 speech production trials (mean = 49 per patient) and 738 speech comprehension trials (mean = 53 per patient).

5.3.1 Speech Production

5.3.1.1. Accuracy

Group analysis: Figure 5.1 shows although there was a numerical increase in the number of successful speech acts for the REQUEST LAG, preposition LAG and PLANNING LAG, paired samples t-tests conducted on the proportion of correct responses across the group of 6 patients showed a significant increase for the REQUEST LAG only, t (5) = 3.01, p = .030. There was no change across the group in proportion of correct speech acts for either the preposition LAG, t (5) = 2.09, p = .091, or the PLANNING LAG t (5) = 1.67, p = .155.

Individual analysis: Chi-square tests conducted on the proportion of correct speech acts in each patient indicated a range of patterns across the group. Two patients showed a significant change in accuracy of REQUESTS following therapy. Patient 5 had an increase from 54% correct responses to 66% correct speech acts, $X^2 = 12.90$, $df = 1$, $p < .001$. In addition, patient 6 showed a change in accuracy of speech acts with an increase

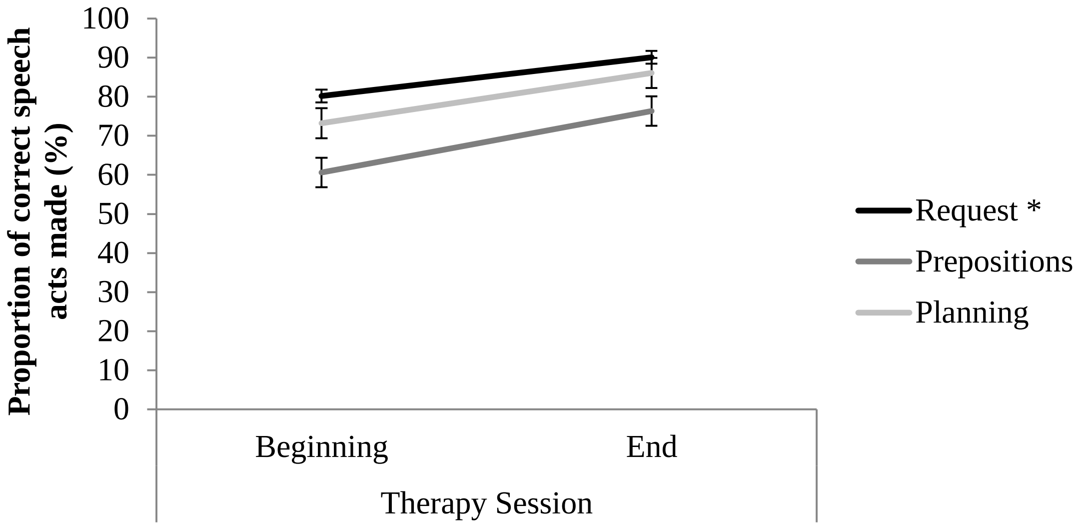


Figure 5.1. Average proportion of correct speech acts for REQUEST LAG, preposition REQUEST LAG and the PLANNING LAG. Error bars represent standard error. * = $p < .05$.

from 75% to 87% correct speech acts, $X^2 = 3.92$, $df = 1$, $p < .05$. For more complex speech acts which required the use of prepositions, only patient 3 showed a significant increase, from 63% to 100% following therapy, $X^2 = 4.5$, $df = 1$, $p < .05$. Finally, in the PLANNING LAG, only patient 2 showed a significant change in accuracy, from 38% to 86%, $X^2 = 18.86$, $df = 1$, $p < .001$.

5.3.1.2 Response Time Measure

Group analysis: Figure 5.2 shows a decrease in the time taken to produce speech acts in each of the three LAGs. However paired samples t-tests conducted on averages for the group again showed a significant decrease in time for the REQUEST LAG only, $t(5) = 2.62$, $p = .047$. There was no change in the average time taken to produce speech acts for either the preposition LAG, $t(5) = .57$, $p = .592$, or the PLANNING LAG $t(5) = 2.15$, $p = .084$.

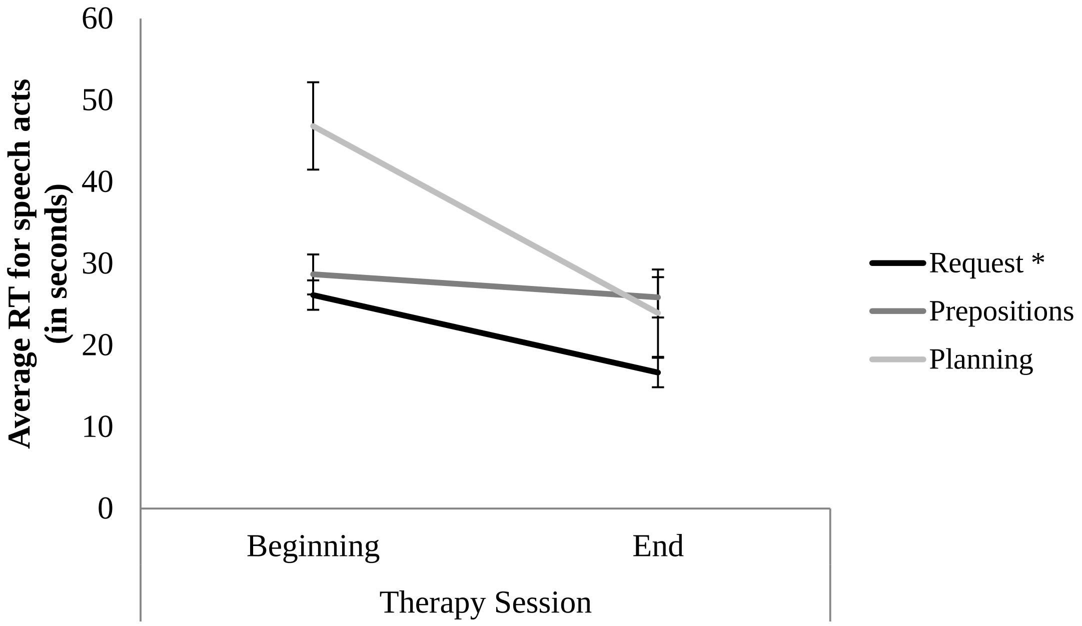


Figure 5.2. Average time taken (response time, RT) for speech acts in the REQUEST LAG, preposition REQUEST LAG and the PLANNING LAG. Error bars represent standard error. * = $p < .05$.

Individual Analysis: Table 5.3 presents the average time taken (in seconds) for each patient across the three recorded LAGs (REQUESTS, prepositions and PLANNING). Independent samples t-tests were conducted on the RTs for individual speech acts. The time it took from selecting the card to producing the critical word or phrase during REQUESTS was significantly less at the end of therapy than the beginning for patient 4, t (30) = 2.86, p = .008; patient 5, t (47) = 2.05, p = .046; and patient 6 t (52) = 2.12, p = .041. RTs for the preposition LAG were significantly decreased at the end of therapy for patient 1 only, t (11) = 2.50, p = .029. At the end of therapy, time taken for speech acts was significantly less for the PLANNING LAG for patient 3, t (11) = 4.16, p =.001; patient 4, t (9) = 2.41, p = .039 and patient 5, t (19) = 2.31, p = .032.

Table 5.3.

*Average time taken in seconds (SD in brackets) from selecting a card to producing the target word or phrase for each of the six patients. Scores reported at the beginning and end of therapy for the REQUEST LAG, prepositions REQUEST LAG and the PLANNING LAG. * = significant decrease in average RT, p<.05.*

	REQUEST LAG					**Preposition LAG**					**PLANNING LAG**				
Patient	*Beginning*		*End*			*Beginning*		*End*			*Beginning*		*End*		
1	8.11	(7.58)	10.29	(8.2)		22.58	(15.87)	10.92	(7.11)	*	12.15	(15.6)	5.84	(2.77)	
2	27.56	(39.36)	23.58	(28.08)		36.98	(47.41)	29.07	(19.48)		51.84	(43.56)	37.70	(45.67)	
3	18.71	(9.6)	14.22	(7.07)		32.07	(29.04)	16.50	(6.73)		42.81	(21.85)	14.52	(6.11)	*
4	45.62	(31.96)	23.96	(12.74)	*	31.12	(28.47)	25.13	(10.48)		95.29	(91.22)	25.28	(15.93)	*
5	26.73	(29.45)	13.58	(12.43)	*	27.93	(18.68)	39.27	(30.32)		48.75	(33.28)	24.34	(20.45)	*
6	30.07	(28.43)	14.37	(25.88)	*	21.33	(10.24)	34.26	(26.61)		30.27	(29.34)	35.90	(32.52)	

In summary, for speech production, communicative performance in the REQUEST LAG demonstrated group improvements in both the accuracy and speed of speech acts. Single-subject analysis of performance also indicated improvement on at least one type of LAG in each patient.

5.3.2 Complexity Index (CI)

Inter-Rater Scoring: 83 recordings of spoken output, taken from the REQUEST LAGs, the prepositions LAG and the PLANNING LAG were scored on the CI by a second rater. 73.5% of the trials were scored the same and 100% of trials were scored within 1 point of the CI across the two raters.

Group analysis: Figure 5.3 shows an increase in scores on the CI across the group for each of the three LAGs. Paired samples t-tests confirmed there were significant increases on this scale for the REQUEST LAG, t (5) = 3.84, p = .012; the preposition LAG, t (5) = 2.87, p = .035; and the PLANNING LAG t (5) = 5.08, p = .004.

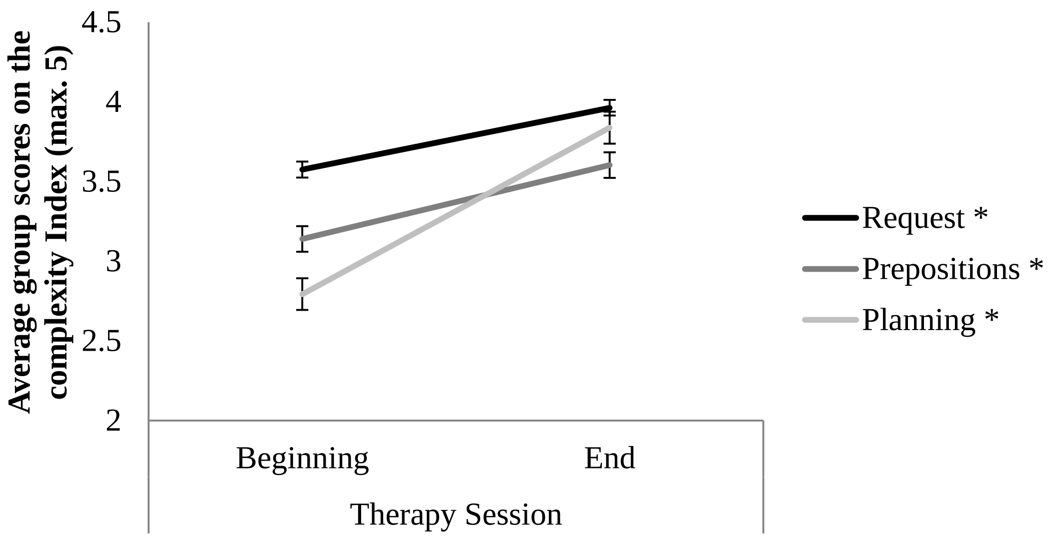


Figure 5.3. Average group scores on the Complexity Index for speech acts in the REQUEST LAG, preposition REQUEST LAG and the PLANNING LAG. Error bars represent standard error. * = $p < .05$.

Table 5.4.

*Average scores at the beginning and end of therapy on the Complexity Index (SD in brackets) for each of the six patients. Scores reported for the REQUEST LAG, the prepositions LAG and the PLANNING LAG. * = significant increase in average CI, p<.05.*

	REQUEST			**Prepositions**			**PLANNING**		
Patient	*Beginning*	*End*		*Beginning*	*End*		*Beginning*	*End*	
1	4.61 (0.49)	4.69 (0.53)		4.31 (0.75)	4.73 (0.59)		4.33 (0.49)	4.73 (0.46)	*
2	3.35 (0.92)	3.51 (1.03)		2.83 (0.41)	3.17 (0.75)		2.00 (0.58)	3.14 (0.77)	*
3	4.06 (0.57)	4.36 (0.50)		3.25 (0.46)	3.73 (0.46)	*	3.64 (0.50)	4.08 (0.28)	*
4	1.64 (0.49)	2.27 (0.59)	*	2.25 (0.50)	3.33 (0.52)	*	1.70 (0.67)	3.00 (0.79)	*
5	4.00 (0.93)	4.68 (0.63)	*	4.00 (0.45)	3.86 (0.38)		2.69 (0.85)	4.25 (1.00)	*
6	3.79 (1.18)	4.27 (1.05)		2.20 (0.84)	2.80 (0.45)		2.40 (0.97)	3.83 (1.03)	*

Individual Analysis: Table 5.4 presents the average complexity scores for each patient across the three recorded LAGs (REQUESTS, prepositions and PLANNING). Independent samples t-tests conducted on the complexity scores for the REQUEST LAG indicated higher scores at the end of therapy for patients 4, t (35) = 3.52, p =.001; and 5, t (47) = 3.01, p = .004. Scores for the CI also increased for the preposition LAG in patient 3, t (21) = 2.40, p = .026; and patient 4, t (8) = 3.29, p = .011. At the end of therapy, CI scores were significantly higher in the PLANNING LAG for all patients: patient 1, t (35) = 2.51, p = .017; patient 2, t (25) = 4.34, p < .001; patient 3, t (15) = 2.58, p = .021; patient 4, t (25) = 4.34, p < .001; patient 5, t (27) = 4.45. p < .001; and patient 6, t (20) = 3.34, p = .003.

5.3.3 Speech Comprehension

5.3.3.1 Accuracy

Group Analysis: When analysing comprehension of speech acts, a slight increase in the number of correct responses was noticeable across the group for the REQUEST LAG, preposition LAG and PLANNING LAG, see Figure 5.4. However paired samples t-tests conducted on the proportion of correct responses failed to confirm significant changes over the therapy period: REQUEST LAG, t (5) = 0.70, p = .513; preposition LAG, t (5) = 0.46, p = .668, PLANNING LAG t (5) = 0.39, p = .711.

Individual analysis: Similarly, Chi-square tests conducted on the proportion of correct responses to speech acts in each patient indicated very little change across the therapy interval. Only patient 1 showed a change in accuracy for comprehension, in the prepositions LAG, averaging at 55.6% accuracy at the beginning of therapy and 100% accuracy at the end of therapy, $X^2 = 4$, $df = 1$, $p < .05$.

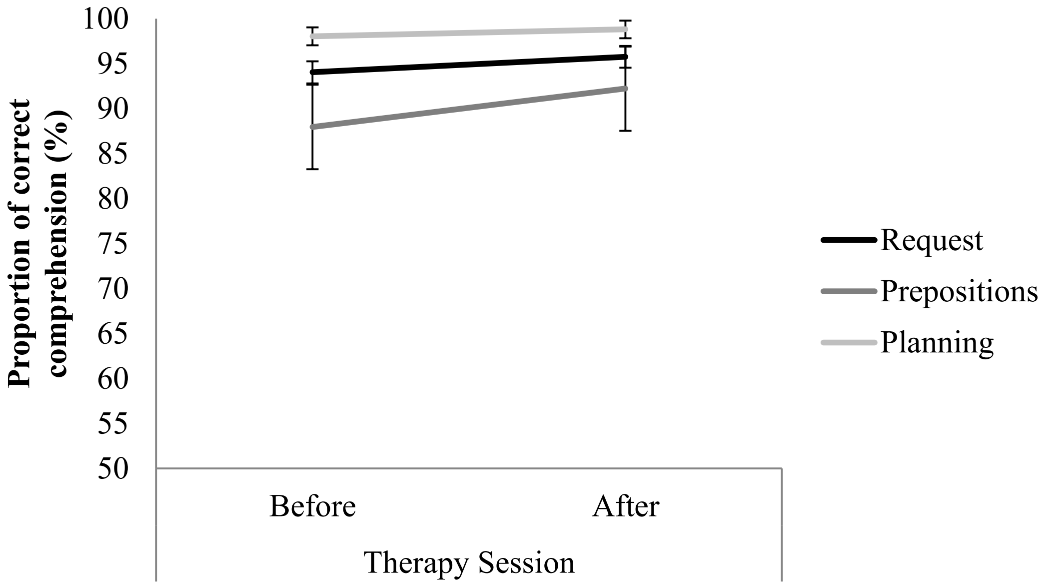


Figure 5.4. Average proportion of correct comprehension of speech acts for REQUEST LAG, preposition REQUEST LAG and the PLANNING LAG. Error bars represent standard error.

However as Table 5.5 illustrates, the average comprehension accuracy was above 80% for all but this one LAG at the beginning of therapy, and therefore near ceiling in all patients, leaving little room for improvement.

5.3.3.2 Response Time Measure

Group analysis: Figure 5.5 shows a decrease in the time taken to comprehend speech acts in the REQUEST LAGs and the PLANNING LAG, but a slight increase in RT for the prepositions LAG. Paired samples t-tests conducted on averages for the group confirmed changes in the PLANNING LAG only, t (5) = 3.04, p = .029. There was no change in the average time taken to comprehend speech acts for either the REQUEST LAG, t (5) = 1.06, p = .338, or the prepositions LAG t (5) = 0.39, p = .713.

Table 5.5.

*Proportion of correct responses to speech acts at the beginning and end of therapy for each of the six patients. Scores reported for the REQUEST LAG, the prepositions LAG and the PLANNING LAG. * = significant change in proportion of correct responses, p<.05.*

	REQUEST		**Prepositions**			**PLANNING**	
Patient	*Beginning*	*End*	*Beginning*	*End*		*Beginning*	*End*
1	100.0	100.0	55.6	100.0	*	100.0	92.9
2	98.0	100.0	100.0	94.4		100.0	100.0
3	87.5	100.0	83.3	100.0		100.0	100.0
4	94.7	88.9	100.0	87.5		100.0	100.0
5	100.0	100.0	88.9	71.4		94.4	100.0
6	84.0	85.7	100.0	100.0		93.8	100.0

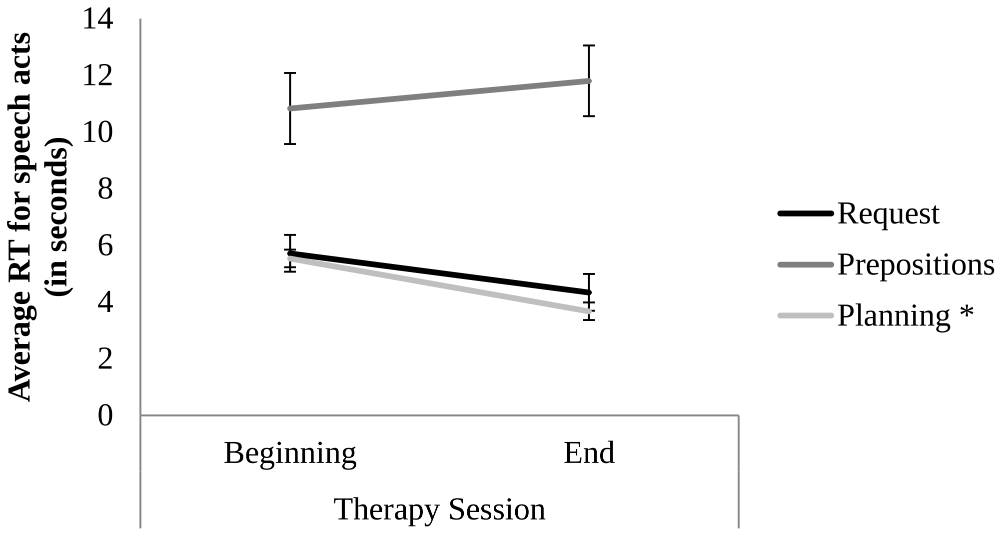


Figure 5.5. Average time taken (response time, RT) for comprehension of speech acts in the REQUEST LAG, preposition REQUEST LAG and the PLANNING LAG. Error bars represent standard error. * = $p < .05$.

Individual Analysis: Table 5.6 presents the average time taken (in seconds) from onset of the target word or phrase to when the correct card was selected or the request was explicitly rejected, for each patient across the three recorded LAGs (REQUESTS, prepositions and PLANNING). Independent samples t-tests demonstrated a significant decrease during REQUEST LAGs for patient 2, t (37) = 3.64, p = .001; patient 4, t (27) = 2.17, p = .039; and patient 6 t (13) = 2.31, p = .038. There were no changes in the time it took to comprehend speech acts for any patients during the preposition LAG. Furthermore, despite the significant group decrease in RT for the PLANNING LAG, there were no significant changes in individual analysis for this LAG.

In summary, when analysing comprehension of speech, performance gains across the group were seen only by a decrease in the speed of comprehension during the PLANNING LAG. Only one patient made gains on accuracy of responses to speech acts, but three out of the six patients demonstrated faster responses to speech towards the end of therapy.

5.3.4 Correlation Between Communicative Performance and Clinical Language Measures

Correlation analyses were carried out in order to identify possible relationships between the scores in the clinical language assessments and the measures of communicative performance during LAGs. Changes in raw scores from the Boston Naming Test (BNT) were correlated with the changes in accuracy of spoken output from the REQUEST LAG, and with changes in scores on the CI, also from the REQUEST LAG. No correlation ($p > .05$) was found for either the change in accuracy ($r = -.105$) or change in CI scores ($r = -.439$).

In the clinical assessments of comprehension reported in Chapter 4, it was noted that there was no significant improvement in the auditory comprehension subtests of the BDAE (see section 4.3.1). In contrast an overall decrease in errors made was reported on the TT, which involves having to touch and move tokens of different shapes, sizes and colours. Therefore, changes in raw scores on the TT were correlated with the changes in accuracy of comprehension in all REQUEST LAGs, and then specifically with LAGs involving shapes, sizes and prepositions. No correlation ($p > .05$) was found for the change in accuracy in LAGs involving shapes, sizes and prepositions ($r = .062$). Interestingly however, a correlation that approached significance ($p = .06$) was found between a decrease on scores in the TT and an increase in accuracy across comprehension scores in general ($r = .783$). Although some r-values reported for correlations between clinical measures and scores in comprehension and speech output are high, none of the correlations reached statistical significance.

Table 5.6.

*Average time taken in seconds (SD in brackets), for each patient, from onset of target word or phrase to selecting a card or rejecting the request. Scores reported at the beginning and end of therapy, for the REQUEST LAG, the prepositions LAG and the PLANNING LAG. * = significant decrease in average RT, p<.05.*

	REQUEST					**Prepositions**				**PLANNING**			
Patient	*Beginning*		*End*			*Beginning*		*End*		*Beginning*		*End*	
1	4.53	(2.71)	4.69	(2.96)		11.66	(7.99)	10.97	(8.77)	7.40	(4.76)	4.25	(2.17)
2	2.76	(1.18)	5.48	(4.23)	*	4.55	(1.98)	5.76	(5.00)	3.40	(0.60)	4.31	(3.31)
3	5.30	(3.13)	5.70	(3.20)		33.32	(17.67)	24.45	(25.47)	6.20	(2.30)	3.82	(2.37)
4	4.58	(1.76)	3.13	(1.78)	*	4.99	(0.00)	6.57	(5.62)	5.50	(3.55)	2.85	(0.88)
5	8.96	(14.18)	3.04	(1.00)		7.60	(1.96)	10.01	(4.78)	5.92	(5.66)	3.25	(0.86)
6	8.15	(6.02)	3.98	(1.96)	*	2.85	(0.00)	13.06	(12.49)	4.77	(2.40)	3.54	(0.80)

5.4 DISCUSSION

Over and above the improvement on clinical language tasks reported in Chapter 4, the detailed evaluation of communicative performance provided evidence for more efficient use of different speech acts during therapy as well as some evidence for an increase in comprehension success over the treatment interval. Interestingly, gains were seen in both the REQUEST LAG, originally described by Pulvermüller et al. (2001) and the PLANNING LAG, which included a new set of items requiring patients to plan an activity with another player (Difrancesco et al., 2012). Whereas the analysis of the latency and accuracy of speech *production* showed significant improvements towards the end of therapy in five out of the six patients, compared with pre-therapy scores, the analysis of *comprehension* performance was less clear, particularly in terms of accuracy rates. The lack of an accuracy effect for comprehension however can be explained by the ceiling effect apparent both in the clinical assessments of auditory comprehension and in performance at the beginning of therapy.

It could be argued that RT measure can only provide weak evidence for the efficacy of a particular intervention, as, for example, speeding could be due to the learning of LAG rules and may not necessarily reflect increased communicative skills. However the results reported here also demonstrate gains in the accuracy of speech acts. Critically, these communicative improvements were shown in 'test sets' of cards, which included novel items not previously trained in the therapy sessions, thus demonstrating a non-trivial, generalising effect of treatment.

Furthermore an effect due only to learning is predicted to be strong during the first sessions, but reduced or absent as soon as patients become used to the interaction games. In a recent report, analysis of communication performance was reported in two patients who participated in ILAT as part of the study in Chapter 4 (Difrancesco et al., 2012). Here, it was reported that the patients picked up the LAG rules quickly and were well familiar with the methods after three sessions, so that any LAG familiarisation effect should be specific to the initial therapy segment. However, speech act production latencies improved constantly over the training interval, even with a tendency towards greater improvement in the second half of the therapy period than in the first. This pattern argues against the LAG learning possibility.

The results presented are also in line with previous reports where similarly detailed analyses of speech production and comprehension have been described. Here improvements were documented in a single patient with severe chronic PSA, who underwent less intensive communicative aphasia therapy with LAGs. Gains were made on both accuracy and RT measures over a therapy interval of several weeks (Pulvermüller & Schönle, 1993).

Finally in addition to RT and accuracy measures, the CI was also utilised in the present study. The CI was created to reflect the level of spontaneous language, appropriate descriptions and grammatical correctness of output in LAGs. Results from this analysis demonstrate clear improvements in the complexity of speech in each patient. Although the CI is a subjective measure of communicative performance, a selection of trials rated by a second therapist showed high inter-rater scores. These findings are interesting, particularly in light of the similar results reported in the previous chapter in relation to scores on the CAL. Here ratings indicated that despite an absence of change in the amount of communication, an increase was noted in the quality of patient's communication following therapy. Taken together, these findings highlight the importance of a full assessment of patient's communicative performance following therapy, including the quality of patient's language.

Aside from the CAL, the clinical assessments reported in Chapter 4 were quantitative measures of language performance. From these, the BNT and the TT showed the clearest improvement in the group of patients studied. To explore the relationship between clinical assessments and communicative performance during LAGs, the scores from the BNT and TT were correlated with performance in speech output and comprehension, respectively. A correlation which neared significance was seen only between a decrease in errors on the TT and overall change in accuracy of comprehension. It is interesting that a second correlation found no relationship between change in performance during LAGs specifically requiring the use of prepositions and colours; and improvement in the TT, a test which requires patients to touch and move tokens of different colours and sizes. However the analyses in this chapter were carried out only on a subset of patients described in Chapter 4 and therefore the correlation analysis lacked power. Future trials of ILAT should aim to explore the relationship between clinical assessments and communicative performance in a larger group of patients undergoing intervention. However it is positive that even within the small group of 6 patients, a relationship was seen between these two measures.

Taken together, these results indicate that, when assessing the effect of ILAT, it is advisable for clinicians not only to assess language functions with standardised clinical tests, but to use communicative rating scales and more detailed analysis of communicative and comprehension performance (Pulvermüller & Schönle, 1993; Pulvermüller & Roth, 1991). Particularly the latter not only provides a vast amount of information about changes in communication due to treatment, but is also helpful, or possibly indeed necessary, for planning and delivering the most appropriate LAGs with materials most relevant for a particular patient. In evaluation of communicative performance, latencies of crucial speech act production and comprehension during

LAGs, and the complexity of patient's speech acts seem to be particularly sensitive to detecting therapy-related changes.

CHAPTER 6: THE EFFECTS OF INTENSIVE LANGUAGE ACTION THERAPY ON LANGUAGE PERFORMANCE IN CHRONIC APHASIA: AN EMPIRICAL STUDY

PART 3: FMRI CORRELATES OF AUDITORY LANGUAGE COMPREHENSION IN AN AMBIGUITY RESOLUTION TASK

6.1 INTRODUCTION

Understanding the processes that contribute to the recovery of language function following a stroke is of importance in guiding and evaluating rehabilitation methods. Non-invasive brain imaging techniques such as functional Magnetic Resonance Imaging (fMRI) allow for the identification of changes which may occur in the brain following intervention and the conditions under which this reorganisation occurs. In this chapter, results from behavioural language tasks are presented alongside imaging data from a group of patients with chronic aphasia, who underwent fMRI scanning immediately before and after two weeks of Intensive Language Action Therapy (ILAT).

Following initial spontaneous repair of neural tissue in the acute aphasia phase (Berthier & Pulvermüller, 2011; Klebic et al., 2011), further behavioural and neuronal changes have been shown to occur following SLTs, particularly when delivered over a prolonged or intensive period (Basso & Macis, 2011; Ciceroni et al., 2005; Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005; Richter et al., 2008; Szaflarski et al., 2008). The fact that these changes occur in chronic patients in whom spontaneous recovery is assumed to have finished suggests that it is likely the result of intervention. As discussed in Chapter 2, investigation of cortical reorganisation following ILAT has thus far demonstrated variable results. Although both the left and right hemispheres appear to contribute to recovery from aphasia (Brier et al., 2006; Kurland et al., 2012; Pulvermüller et al., 2005), the most efficient recovery may occur when reintegration of spared left hemisphere (LH) regions is possible (Breier et al., 2006; Breier et al., 2009; Meinzer et al., 2008; Richter et al., 2008).

In the current chapter, a semantic ambiguity task was used to investigate therapy-related cortical reorganisation following ILAT in a group of patients with aphasia. Previously this paradigm has demonstrated reliable activation in patient populations and in single-subject comparisons (Coleman et al., 2007). Understanding natural speech involves comprehending the meaning of individual words and appropriately combining those to form sentence meaning. Previous research supports the idea that speech comprehension is a hierarchical process, where non speech-specific sounds are processed in primary auditory areas and more complex speech processing extends through temporal regions to inferior posterior temporal areas and to the inferior frontal cortex (Rodd et al., 2005). For patients suffering LH damage following a stroke, impairment to these frontal and posterior temporal regions can result in comprehension deficits (Bates et al., 2003).

A more substantial load is placed on neural systems when sentences include ambiguous words, which have more than one meaning, for example ‘pen’. The relative frequencies of the different meanings of ambiguous words (known as dominance) can either be balanced between two alternative meanings or biased towards a specific meaning. For example, a pen can mean a writing implement or enclosure for an animal. It is possible to constrain the interpretation of this word to the subordinate meaning “enclosure” by placing it in the context of the sentence “a pen was used by the farmer to enclose the stock before he moved them to the market”.

Previous imaging studies demonstrate that regions in the bilateral inferior frontal gyrus (IFG) and left posterior inferior temporal regions are recruited when healthy volunteers listen to sentences containing biased ambiguous words (Rodd et al., 2005; Zempleni, Renken, Hoeks, Hoogduin & Stowe, 2007). Patients with damage to these LH regions appear to be impaired at resolving lexical ambiguities. When processing short sentences containing biased ambiguous words, two patients with damage specifically to the Left IFG (LIFG), but who presented with no residual comprehension problems were slower at resolving the lexical ambiguities compared to both healthy controls and a patient with non-LIFG damage (Vuong & Martin, 2011). Furthermore results from previous studies show that patients with non-fluent aphasia resulting from LH damage were unable to select the contextually appropriate meaning of ambiguous words, such that appropriate and inappropriate meanings were selected equally following a constraining sentence (Grindrod & Baum, 2003). These findings suggest the LH and the LIFG in particular are critical in processing lexical ambiguities.

Two experiments are presented in this chapter. The first explored whether patients with chronic aphasia were able to resolve lexical ambiguities, through a forced choice behavioural task, where the appropriate meaning of spoken sentences containing ambiguous words, must be identified. The second experiment investigated therapy-related changes in the neural activation following ILAT in a group of patients with aphasia, who underwent fMRI scanning before and after two weeks of intervention.

6.2 METHODS

6.2.1 Participants

A subset of ten patients (3 female, mean age 54.5 years, SD = 15.9 years) were selected from Part 1 of this project (Chapter 4). The average time since stroke in this subgroup was 77 months. The same inclusion/exclusion criteria detailed in section 4.2.1 also applied here. Following the first two groups of patients from Chapter 4 who underwent testing, it was noticed that due to tiredness after the scanning sessions, patients found it difficult to provide responses in a post-scanning task which measured whether they had successfully disambiguated sentences heard in the scanner. Therefore an additional ambiguity resolution task was created for the remaining ten patients to assess their ability to resolve ambiguities.

6.2.2 Aphasia Therapy and Behavioural Improvement

Participants received ILAT for three hours per day over 10 consecutive weekdays using the methods described in Chapter 3. Language performance, as documented by standardised aphasia tests and self-rated questionnaires, improved over the 10 days of therapy. In the complete group of 14 patients described in Chapter 4, the clearest improvements between pre- and post-therapy sessions could be seen in the Boston Naming Test (p = .002; BNT, a subtest of the Boston Diagnostic Aphasia Battery, BDAE; Goodglass & Kaplan, 1972) and in a decrease in the number of errors made in the Token Test (p = .046; De Renzi & Vignolo, 1962), which assesses patients' abilities to follow commands (see Chapter 4 for detailed results and discussion).

6.3 EXPERIMENT 1 – AMBIGUITY RESOLUTION TASK

6.3.1 Method

6.3.1.1 Materials

36 high-ambiguity and 36 low-ambiguity sentences (from Vitello, Devlin & Rodd, 2012) spoken by a native English female speaker were presented to the patients. The high ambiguity sentences contained an ambiguous word which was disambiguated in the sentence, towards the subordinate frequency meaning of the word (i.e. 'the students

believed the *plant* should never have been built). Each high ambiguity sentence was matched to a low ambiguity sentence for syntactic structure, number of syllables, number of words, sentence duration, target and disambiguating word length, target word frequency and log frequency, disambiguating word frequency, and the number of senses for the disambiguating word. The number of senses for target words in ambiguous and unambiguous sentences was significantly different. Low ambiguity sentences contained minimally ambiguous words (i.e. 'the students believed the *hill* could never have been climbed'). The duration of the sentences ranged from 2.21s to 2.29s long.

For each sentence, two probe words were generated. Probe words for the high ambiguity sentences were a related probe (i.e. for the above ambiguous example- *manufacture*) which was related to the meaning of the ambiguous word as disambiguated in the sentence, and an irrelevant probe (i.e. *bush*) which was related to the irrelevant, dominant meaning of the ambiguous word. Probe words for the low ambiguity sentences were a related probe (i.e. *valley*), which was related to the sentence meaning, and an unrelated probe (i.e. *dollar)* not related to the sentence meaning. Probe words were matched across conditions for length, frequency and log frequency. Probes were also matched across conditions for their semantic relatedness to the sentence (rated on a 7-point scale).

6.3.1.2 Procedure

All stimuli were presented using E-prime Professional 2.0 (Psychology Software Tools, Pittsburgh). A cross in the centre of the screen indicated the beginning of a trial. Patients were instructed to press any key on a button box to begin a trial when they were ready. Each sentence was heard one at a time, followed by a 2000ms pause. After the presentation of each sentence, the two probe words were visually presented. In addition, patients also heard the two probe words spoken by a native English male speaker. Patients were instructed to decide which of the two words best fit with the meaning of the sentence and to press a button on the left or right which corresponded to a probe word on the left or right of the screen. Patients were given three trials not included in the main task as a practice run.

The 36 items from each condition were split into two equal runs, each including 18 pairs of matched high- and low-ambiguity sentences. The two runs were also matched for number of syllables per sentence, duration, rated naturalness and dominance scores of the ambiguous word. Patients received one run at each of two time sessions, pre- and post-therapy. The runs were counterbalanced across the two sessions.

6.3.2 Results

A repeated measures analysis of variance (ANOVA) showed patients were significantly more accurate at selecting the correct probe word for low- compared to high-ambiguity sentences (F (1, 9) = 45.375, p < .001, η_p^2 = .834; see Figure 6.1). There was no difference in the number of correct answers across the two sessions (F (1, 9) = .878 p = .373, η_p^2 = .089) and there was no interaction between the factors of session and sentence type (F (1, 9) = 1.552, p = .224, η_p^2 = .147). One-sampled t-tests demonstrated that patients correctly chose the relevant probe words for high ambiguity sentences significantly more than chance level at both the pre- (t (9) = 14.048, p < .001) and post-therapy (t (9) = 22.422, p < .001) testing sessions. This suggests patients were able to extract the correct meaning from both high and low ambiguity sentences and choose the appropriate related word whilst ignoring an irrelevant probe word, but that this was easier when the sentences contained no ambiguous words. This pattern remained the same after the two weeks of therapy.

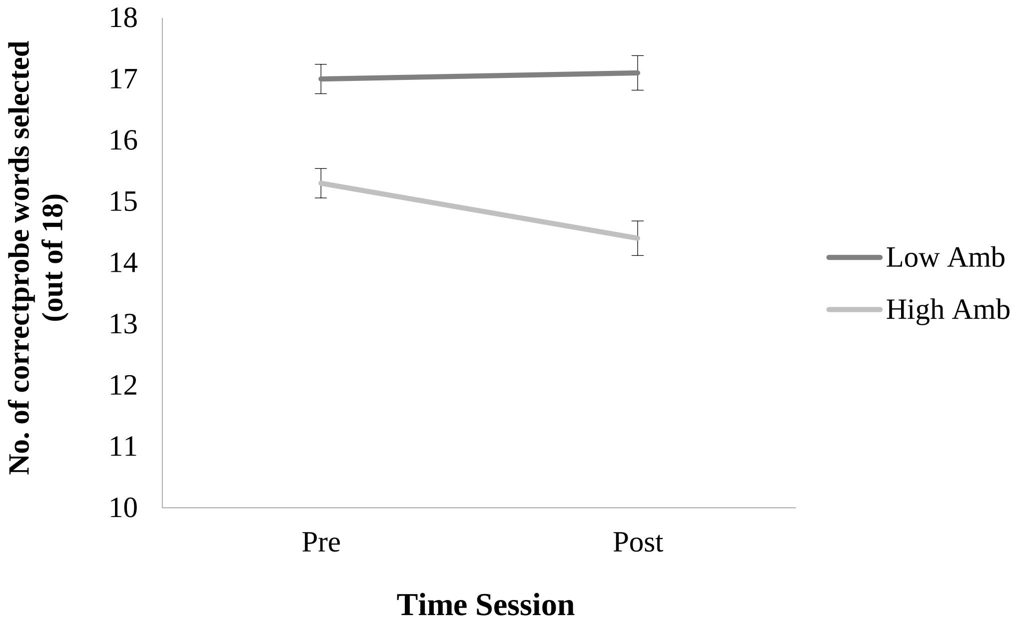


Figure 6.1. Number of correct probe words selected for low ambiguity and high ambiguity sentences across two time sessions (pre and post therapy). Error bars represent standard error.

6.4 EXPERIMENT 2- fMRI INVESTIGATION OF AUDITORY LANGUAGE COMPREHENSION

6.4.1 Method

6.4.1.1 Participants

Eight (1 female, mean age 63.4 years, range 41 – 76) right-handed patients, from the same population as Experiment 1 of this chapter, also underwent an fMRI scan at each testing session. Table 6.1 shows the demographic and clinical data for each patient. In addition to satisfying the inclusion criteria described in Chapter 4, patients were excluded from this part of the study if they had a pacemaker or any other metallic objects permanently attached to the body (i.e. surgical clips), were wheelchair bound or suffered from claustrophobia. Table 6.2 presents the results from the clinical aphasia tests administered before and after the 10 days of therapy.

Table 6.1.

Neurological and demographic data of eight patients who underwent fMRI scanning.

P	Age (in years, at therapy)	Sex	Handedness	Duration of Aphasia (months)	Etiology	Lesion site
1	74	Male	Right	127	CVA	Left MCA territory, extending from left frontal to left occipital and parietal area
2	69	Male	Right	25	CVA	Left MCA territory, in LIFG, with additional small lesion in left IPC
3	48	Male	Right	17	CVA	Left MCA territory, extending from LIFG to STG
4	72	Male	Right	32	CVA	Left MCA territory, extending from left frontal to posterior STG and parietal area
5	60	Femal e	Right	137	CVA	Left MCA territory, extending from left frontal to left temporal and IPC
6	41	Male	Right	19	CVA	Left SFG extending posteriorly to left IPC, with additional lesion in left ITG
7	76	Male	Right	234	Haemorrhage	Small lesion in posterior LIFG, extending to insula
8	59	Male	Right	104	CVA	Left MCA territory, extending from LIFG to left temporal and IPC
Average	**63.38**			**88.88**		

CVA – cerebrovascular accident; IPC – inferior parietal cortex; ITG – inferior temporal gyrus; LIFG – left inferior frontal gyrus; MCA - middle cerebral artery; SFG – superior frontal gyrus; STG – superior temporal gyrus.

Table 6.2

Results of clinical language tests administered before and after ten day therapy interval for eight patients who underwent scanning.

	BDAE						**TT**	
	Auditory Comprehension		*Syntactic Processing*		*BNT*		*(number of errors)*	
Patient	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*
1	85	86	22	20	12	23	17	14
2	81	85	15	21	13	19	31	33
3	85	87	11	12	12	24	41	35
4	81	84	16	9	36	32	48	38
5	83	80	18	16	26	27	15	18
6	80	81	16	14	8	14	49	38
7	88	90	21	22	48	48	16	17
8	82	86	15	15	48	51	35	30
Mean	83.13	84.88	16.75	16.13	25.38	29.75	31.50	27.88
SD	2.70	3.23	3.54	4.58	16.69	13.31	14.16	9.96

BDAE (Boston Diagnostic Aphasia Battery; Goodglass & Kaplan, 1972) – Auditory comprehension composite score include word comprehension, word comprehension by categories, and semantic probe subtests; Syntactic processing composite score includes touching A with B, reversible possessives and embedded sentences subtests; BNT – the Boston Naming Test. TT (Token Test - a subtest of the Aachen Aphasia Battery; De Renzi & Vignolo, 1962).

6.4.1.2 Materials

The stimuli used were taken from Rodd et al. (2005) and consisted of 2 speech conditions (high-ambiguity and low-ambiguity sentences) and a signal correlated noise (SCN) condition, each with 57 items. High ambiguity sentences contained two ambiguous words which were disambiguated in the sentence (i.e. 'there were *dates* and *pears* in the fruit bowl'). Low ambiguity words contained minimally ambiguous words (i.e. 'there was *beer* and *cider* on the kitchen shelf'). The duration of the sentences ranged from 1.2s to 4.3s long and the two conditions were matched for number of syllables, duration, rated naturalness and imageability.

57 sentences not used in either speech condition but matched for number of syllables, number of words and physical duration were converted to SCN (Mummery, Ashburner, Scott & Wise, 1999). These items have similar amplitude envelopes to the original speech but they are not intelligible. SCN was used as a comparison to control for activity related to lower level auditory processing. An additional 57 silent trials were included to allow for comparisons between low-level SCN activation and silent rest periods.

6.4.1.3 Procedure and fMRI Acquisition

A sparse imaging technique was used to minimise interference from scanner noise (Hall et al., 1999). Participants heard a single sentence or an SCN equivalent in a nine second silent period before a two second scan. As in previous studies using the same paradigm (Rodd et al., 2005), the timing of stimulus onset was altered for each sentence or noise condition, in order that the midpoint of each stimulus was temporally aligned with a point 5s before the midpoint of the subsequent scan (i.e. 5s into the 9s silent period).

This ensured the haemodynamic response from processing the sentences was at the approximate maximum peak at the time of the scan.

The 57 trials for each speech and SCN condition were split into three sessions of 76 scans/trials which included 19 items per condition in addition to 19 silent trials. Items from each condition were equally distributed across the three scanning runs and pseudo-randomised to ensure that every condition occurred equally often after each of the others. One of the three scanning runs was to be delivered at each of three time points; pre-therapy, post-therapy and at a 6 month follow up. However due to time constraints and high dropout rates in patients at the follow up scan, only the pre- and post-therapy scans were included in analysis. The order of the runs was counterbalanced across the scanning sessions.

All images were acquired on a Siemens 3T Tim Trio scanner (Siemens Medical Solutions, Camberley, UK) with a 12-channel head coil. Echo planar image volumes were acquired over a 12 minute session. Each volume consisted of 32 slices, each 3mm thick, with an interslice gap of 0.75mm and in-plane resolution of 3mm. FOV= 192mm x 192mm; Total TR = 11s (TE = 30ms, acquisition time = 2s). A T1-weighted structural image was acquired for each patient using an MPRAGE sequence (TR=2250ms, TE=2.99 ms, flip angle=9°, FOV=256 mm×240 mm×160mm, voxel size=1 mm× 1mm×1mm).

6.4.1.4 fMRI Analysis Methods

fMRI data were pre-processed and analysed using Statistical Parametric Mapping software (SPM5, Wellcome Department of Imaging Neuroscience, London, UK). Pre-processing steps included realignment, coregistration, spatial normalisation of the functional images to a standard EPI template and spatial smoothing using a Gaussian kernel of 10mm. At the first level, a General Linear Model was generated that modelled each session with three columns: SCN, low, and high ambiguity, in addition to six movement regressors (of no interest).

For each of two time periods, pre- and post-therapy and for a post>pre contrast, three comparisons were conducted. Firstly, general *acoustic processing* was assessed by comparing responses for SCN (i.e. non-speech) to silent rest. The second contrast assessed *speech specific processing* by comparing responses for SCN with the average of the speech conditions (high- and low-ambiguity sentences). Finally an *ambiguity response* was assessed by comparing high ambiguity to low ambiguity sentences. This final contrast allowed for identification of higher-level processing of the semantic aspects of speech.

For the first and third of these contrasts, i.e. to assess *acoustic processing* and the *ambiguity effect*, comparisons were first conducted at the whole brain level to identify peaks of activation across the brain. Regions of interest (ROIs) analyses were then conducted individually using the Marsbar toolbox (Brett, Anton, Valabregue & Poline, 2002, http://marsbar.sourceforge.net/). MarsBar averages across all voxels within an ROI to identify if that area is more active for one condition than another. Using these analyses allowed for identification of more subtle effects that may have been obscured by the need to correct for the whole brain volume.

For the second contrast, to identify areas involved in *speech processing*, small volume corrections were applied to whole brain level comparisons of speech compared to SCN, on an individual basis. Applying a small volume correction allows identification of voxels that are more active for speech stimuli than SCN within a pre-defined area. Peaks of activation within this area can be identified, even if the rest of the region is not active.

ROIs for each of the three contrasts were defined from regions of activation in healthy volunteers (data taken from Rodd et al., 2005) and included areas in both the left and right hemispheres. These regions were transformed so that the LH regions were identical to those in the Rodd et al. (2005) data. However the right hemisphere (RH) regions included a reflection of the left activation plus the RH areas identified from the Rodd et al. (2005) data. Lesioned tissue, identified using the Automatic Lesion Identification (ALI) procedure (Section 6.4.2.2), was then excluded from each ROI on a subject by subject basis so as to ensure that activation was examined within intact tissue only.

For two patients (patients 7 and 8 in Table 6.1), issues with the timing offset recorded by E-prime during the pre-therapy scanning session meant the data was unable to be used for further analysis. Therefore only the data from the six remaining patients was further analysed.

6.4.1.5 Post Scanning Word Association Task

Following the fMRI scan, patients participated in a word association task as a measure of whether they had successfully disambiguated sentences heard in the scanner. The stimuli for the word association task consisted of 76 ambiguous words: 38 primed words, from the sentences heard in the scanning session; and an additional 38 ambiguous words taken from one of the other two sets of high-ambiguity sentences to act as control unprimed words. Patients heard the ambiguous words one at a time, spoken by a native English female speaker, and words were repeated if necessary. Patients were instructed to say the first word that came to mind that was related to the word they had just heard.

Previous research has shown that just a single presentation of an ambiguous word in context is enough to bias a listener's interpretation of that word towards the intended sentence meaning (Rodd, Cutrin, Kirsch, Millar & Davis, 2013). As the sentences were biased towards the subordinate meaning of the ambiguous words, it was expected patients would only provide the subordinate and therefore consistent meaning to primed ambiguous words if they successfully disambiguated, and extracted the correct sentence meaning.

6.4.2 Results

6.4.2.1 Post Scanning Word Association Task

Four out of the eight patients who were scanned were able to respond to the word association task at both the pre- and post-therapy testing sessions. Due to tiredness after the pre-therapy scanning session, two further patients were able to provide responses at the post-therapy session only. In addition, one patient who was not scanned but was exposed to the same sentences was able to provide a fifth full set of responses at both pre- and post-therapy sessions. All responses were coded according to whether they were consistent with the meaning from the sentence heard in the scanner or another meaning. For example, the word *pears* was disambiguated in the sentence 'there were dates and *pears* in the fruit bowl' and therefore responses such as pears-apple or pears-fruit were coded as 'consistent', whereas responses such as pairs-two were coded as 'inconsistent'. Words which were ambiguous in their meaning were coded as errors and excluded.

Figure 6.2 shows the proportion of correct responses for primed and unprimed words. A mixed measures ANOVA showed no differences in the number of consistent responses given for primed and unprimed words (F (1, 10) = .020, p = .889, η_p^2 = .002). There was also no difference in the number of consistent answers given in the pre- and post-therapy testing sessions (F (1, 10) = .291, p = .602, η_p^2 = .028) and no interaction between the factors of session and word type (F (1, 10) = 1.662, p = .226, η_p^2 = .143). As patients provided the same number of consistent answers for primed words and unprimed words, this suggests they may not have been able to disambiguate the words they heard in order to successfully extract sentence meaning. Alternately it could have been that patients were able to extract sentence meaning at the time of hearing the sentences, but this did not influence their interpretation of the ambiguous words after a short period of time. This will be discussed along with results acquired from fMRI scanning in Section 6.5.

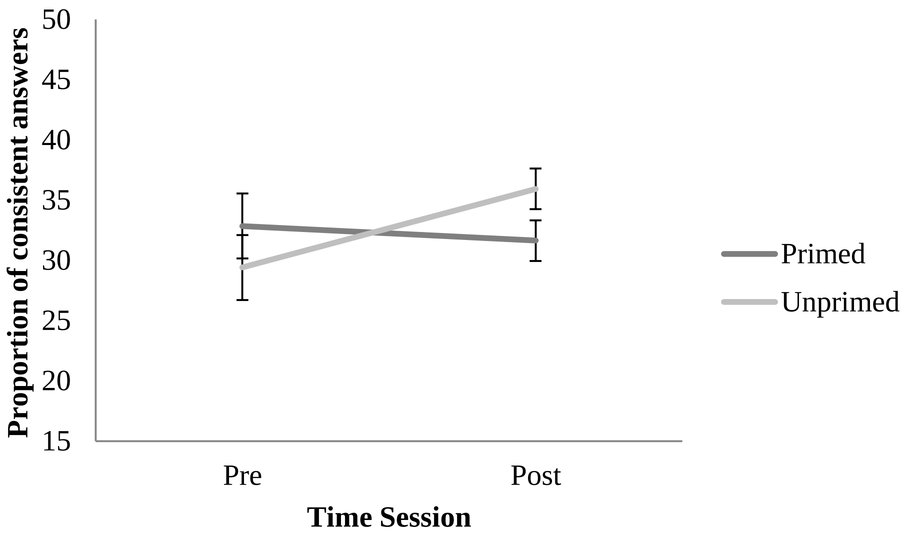


Figure 6.2. Proportion of consistent answers given for primed and unprimed ambiguous words at the pre- and post-therapy testing sessions. Error bars represent standard error.

6.4.2.2 Lesion Identification

A lesion map identifying the sites of major damage in each patient's brain was obtained using the ALI toolbox (Seghier, Ramlackhansingh, Crinion, Leff & Price, 2008). This method involves augmenting the standard generative model for unified segmentation (as implemented in SPM5) with an empirical prior for a "lesioned tissue class" that is optimised iteratively. Segmentations from a group of age matched neuro-typical individuals (60 individuals, mean=61, min=43, max=75 years) were then used with a fuzzy clustering procedure to identify outlier grey and white voxels to identify lesioned tissue for each patient. For one patient, the ALI was unable to segment the structural MRI to include the additional 'lesion' class at the default threshold probability of .0333. Therefore for this individual the probability threshold for identifying abnormal voxels was lowered to 0.26.

Individual binary lesion images from the six patients entered into the fMRI analysis were combined to give a lesion probability map, showing the extent and overlap of lesions across the group (Figure 6.3).

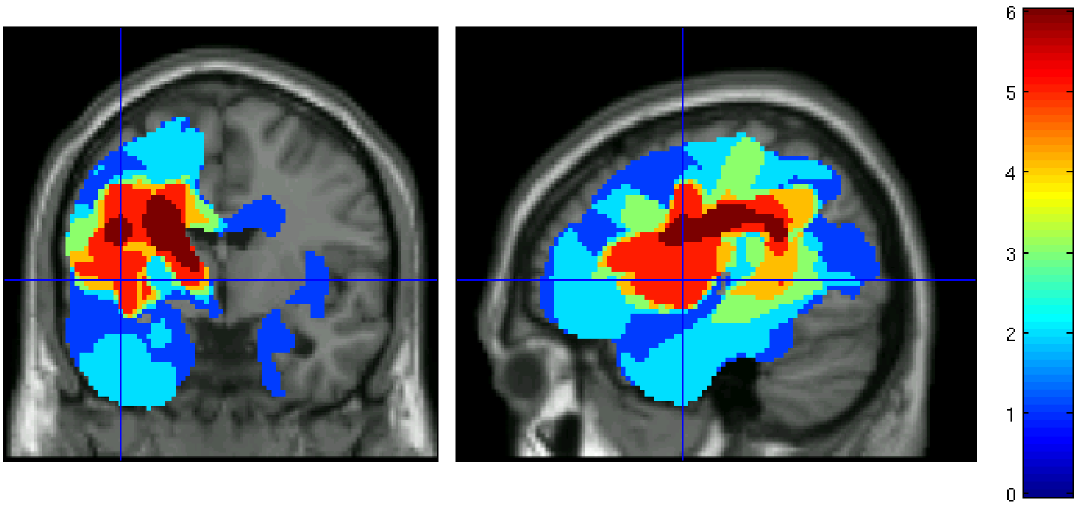


Figure 6.3. Lesion overlap map for 6 patients. Colour indicates the number of patients with damage at each voxel (maximum of 6).

Common to the majority of patients (number in brackets) was damage to left-hemisphere regions around and extending from the Sylvian fissure, including the inferior (n=4) and middle (n=2) frontal gyrus, inferior (n=2) and superior (n=5) temporal gyrus, inferior parietal areas (n=4), hippocampus (n=2) and left insula (n=3). The damage also extended to white matter, following the curve of the arcuate fasciculus (AF, n=6), a white matter tract which functionally connects inferior frontal with inferior parietal and temporal regions. This tract has been implicated in previous studies of analysis of lesions in stroke patients with comprehension deficits (Bates et al., 2003). In patient 1, the ALI also identified extended ventricles in the RH and lesioned tissue in parts of the occipital lobe.

6.4.2.3 Activation for Acoustic Processing (Contrast SCN>Silent baseline)

Low level processing of auditory stimuli was assessed by comparing responses for SCN to silent rest. In healthy controls, this contrast produced activation in auditory areas, surrounding Heschl's gyrus (Rodd et al., 2005).

6.4.2.3.1 SCN>Silent Baseline – Individual Analyses of Whole Brain Activity

Pre and Post Testing Sessions: All patients showed anatomically appropriate responses in the low-level comparison both pre- and post-therapy when corrected for multiple comparisons at the whole brain level ($p < .05$ Family Wise Error correction (FWE); Figure 6.4). For one patient (patient 4), evidence of anatomically appropriate activation was seen only when the statistical threshold was lowered to $p < .001$, uncorrected. Within the group, the neural responses were variable. Two patients (patient 2, bilaterally and patient 3 in the LH only) showed activation comparable to that of the healthy controls seen in Rodd et al. (2005), whereas in three patients activation was limited

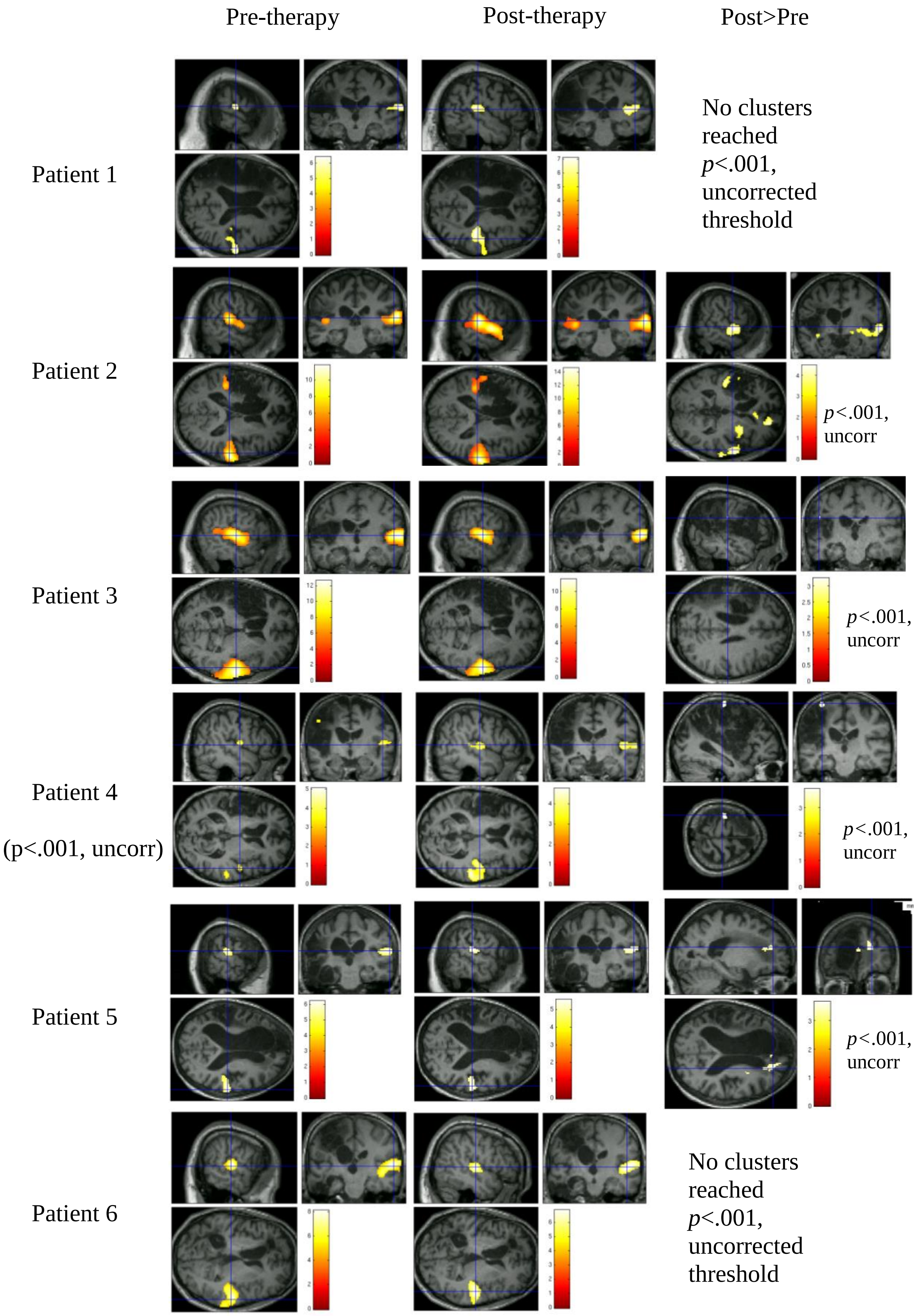


Figure 6.4. Haemodynamic responses for SCN compared to a silent baseline at pre-therapy and post-therapy scanning sessions, and a post>pre comparison. (All comparisons above a threshold of $p < .05$ FWE corrected, unless otherwise stated).

(patients 1, 4 and 5, see Figure 6.4). Only one (patient 2) out of the six patients showed statistically reliable activation in the LH in addition to that in the RH.

Post>Pre comparisons: Although no activation was statistically reliable for the post > pre comparison for any patients at a threshold of $p<.05$ FWE corrected, activation was seen in four out of the six patients (patient 2, 3, 4 and 5) at a lower threshold of $p<.001$, uncorrected. However in patients 3 and 4 this activation was minimal, and in patient 5, activation was not in anatomically appropriate regions (see Figure 6.4).

6.4.2.3.2 SCN>Silent Baseline - ROI Analysis in Individuals

Figure 6.5 illustrates individual ROIs defined by activation in healthy volunteers (top row), for sound compared to rest (in Rodd et al., 2005), excluding lesioned tissue.

Pre and Post Testing Sessions: All patients showed statistically reliable activation within the RH ROI (Table 6.3). In line with the whole brain activation maps, patient 2 also produced reliable activation in the LH ROI at both pre- and post-therapy testing sessions, at a corrected threshold ($p <.05$ FWE).

Post>Pre comparisons: The activation from the post-therapy session evoked in patient 2 was statistically stronger than in the pre-therapy session in both the left and right hemisphere ROIs (see Table 6.3). Patient 5 also showed activation in the LH ROI in the post-therapy session, at a lower statistical threshold ($p <.001$).

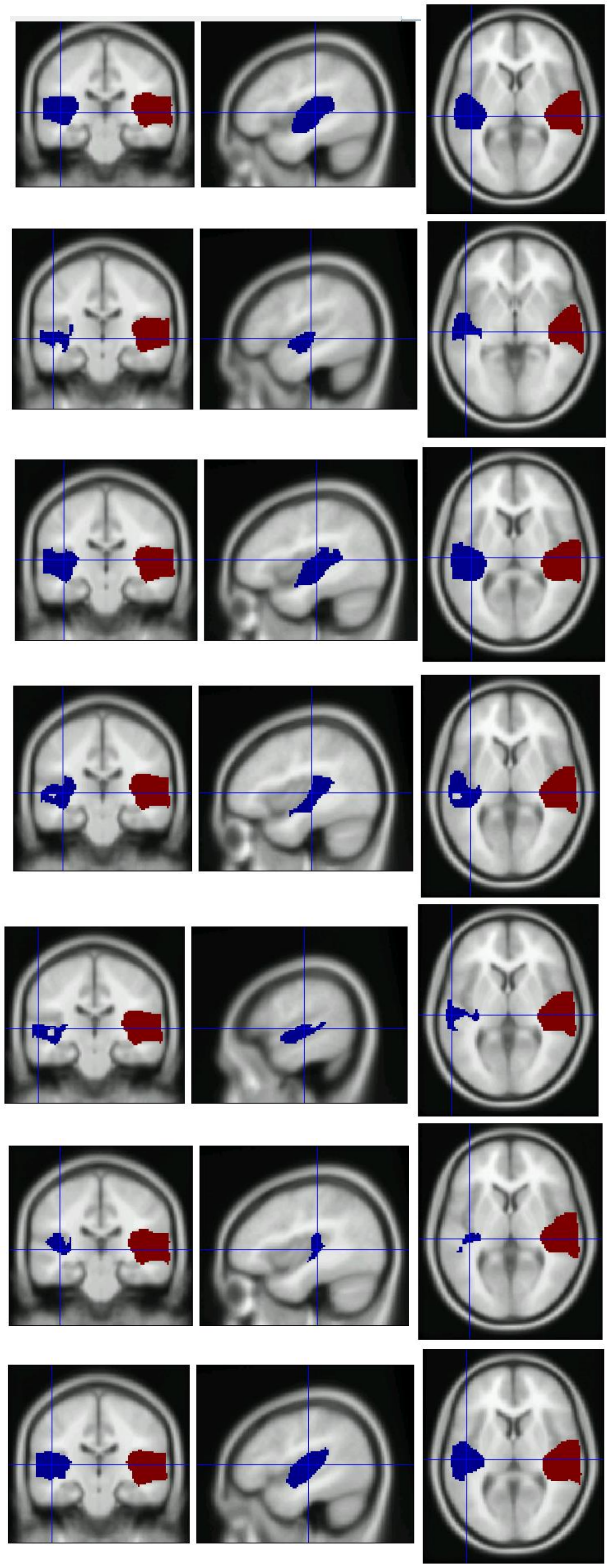


Figure 6.5. Region of interest maps from healthy volunteers defined by contrast SCN>silent baseline taken from Rodd et al. (2005) excluding lesioned tissue within each individual. (Blue – left hemisphere ROI; red – right hemisphere ROI).

Table 6.3.

*Results comparing SCN to a silent baseline pre, post and post >pre therapy within an ROI in the left hemisphere and the right hemisphere. ROIs defined by healthy volunteers from contrast SCN>silent baseline from Rodd et al., (2005) excluding lesioned tissue within each individual. (P values reported at p<.001, uncorrected, ** = p <.05 FWE corrected).*

	LH					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.41	0.133	0.30	0.216	-0.11	0.585
Patient 2	0.38	0.004**	0.80	0.000**	0.42	0.019**
Patient 3	0.03	0.394	-0.14	0.920	-0.17	0.883
Patient 4	-0.55	0.913	0.28	0.241	0.83	0.073
Patient 5	0.35	0.216	0.76	0.036*	0.41	0.249
Patient 6	0.11	0.289	0.06	0.391	-0.05	0.573

	RH					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.58	0.002**	0.78	0.000**	0.20	0.228
Patient 2	0.70	0.000**	1.29	0.000**	0.60	0.010**
Patient 3	0.81	0.000**	0.59	0.000**	-0.23	0.939
Patient 4	0.47	0.039**	0.54	0.017**	0.07	0.409
Patient 5	0.73	0.001**	0.88	0.000**	0.14	0.321
Patient 6	0.87	0.000**	0.73	0.000**	-0.14	0.690

6.4.2.3.3 SCN>Silent Baseline – Group Analysis

Contrast values for each individual in the left and right hemisphere at the pre- and post-therapy sessions were extracted from the ROI analysis and entered into a 2x2 repeated measures ANOVA so as to examine effects present across the group of subjects.

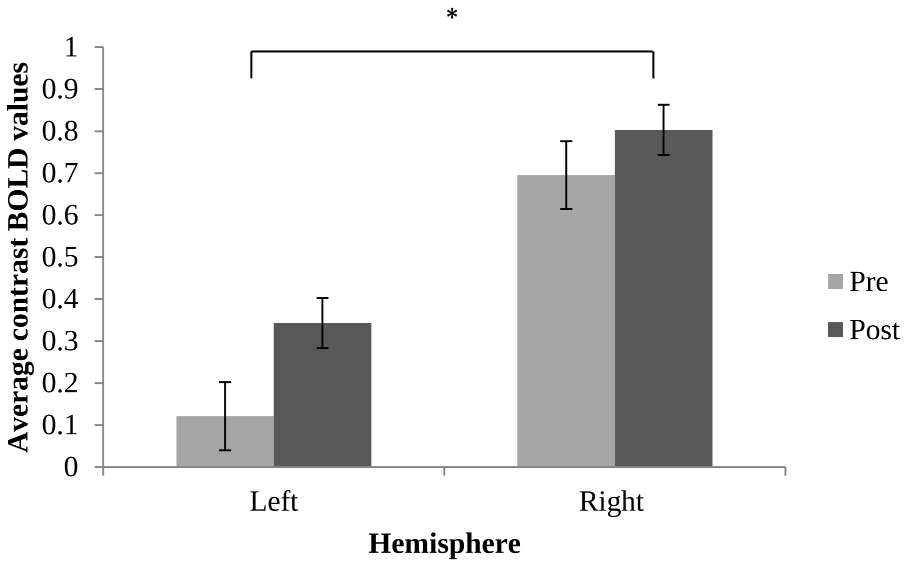


Figure 6.6. Average contrast values for 6 patients in the left and right hemisphere ROIs pre- and post-therapy for SCN compared to silent baseline. ROIs were defined by healthy volunteers from contrast SCN>silent baseline from Rodd et al. (2005), excluding lesioned tissue within each individual. (* = $p < .005$).

Figure 6.6 shows that across the group, there was significantly more activation in the RH than the left (F (1, 5) = 35.039, p = .002, η_p^2 = .875). There was no difference in contrast values between the two time sessions (F (1, 5) = 1.905, p = .226, η_p^2 = .276), and no interaction between the factors of hemisphere and time (F (1, 5) = .552, p = .491, η_p^2 = .099).

In summary, for processing of acoustic stimuli, patient 2 showed an increase in neural activation to non-speech sounds at the post-therapy testing session but no overall group effect was found. In addition, despite there being intact tissue in the LH in some of the patients, on the whole the RH ROI was activated more than the left.

6.4.2.4 Activation for Speech Processing (Contrast Speech>SCN)

Speech specific responses were assessed by comparing responses for SCN with the average of the speech conditions (high- and low-ambiguity sentences). Small volume

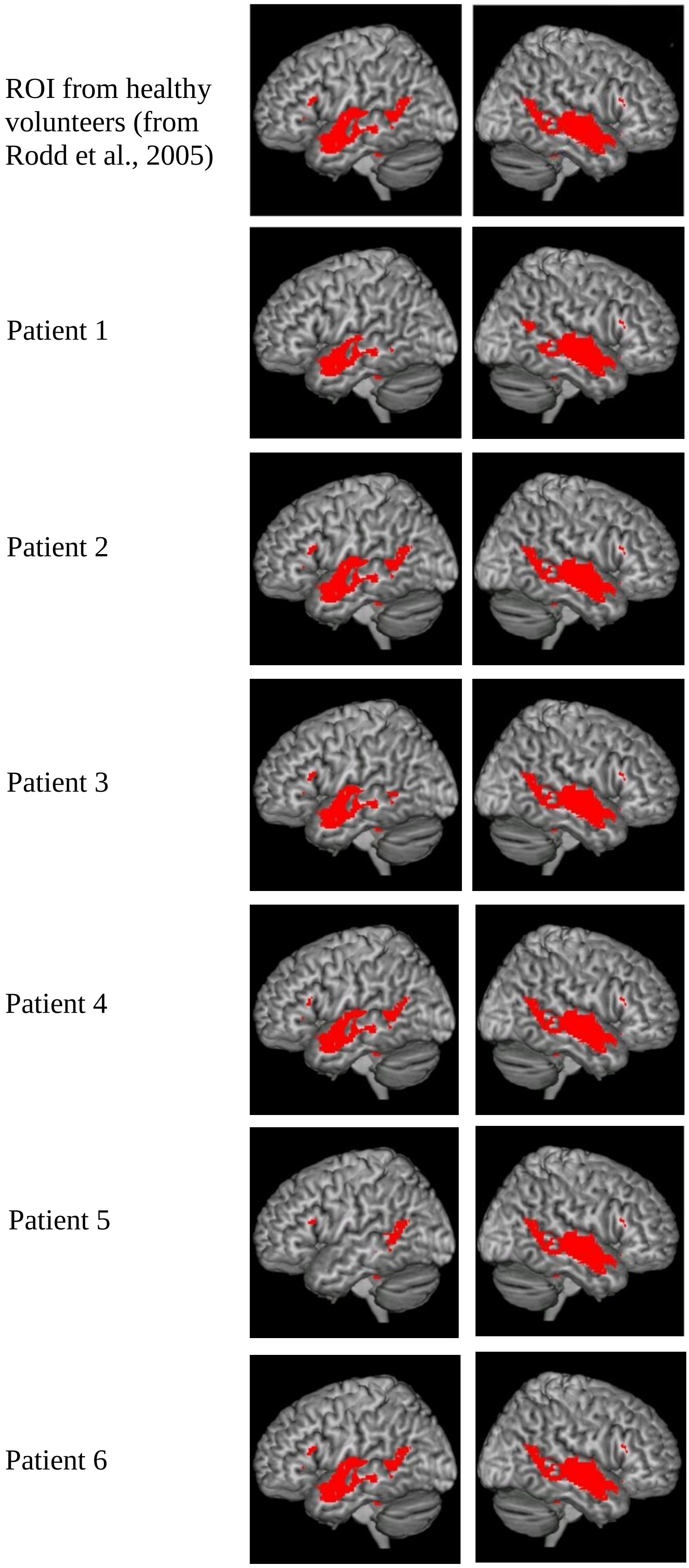


Figure 6.7. Region of interest maps from healthy volunteers defined by contrast speech>SCN taken from Rodd et al. (2005), excluding lesioned tissue within each individual.

corrections were applied on an individual basis and were defined as described in section 6.4.1.4 The ROI included an area centred on the superior temporal sulcus, extending to anterior and posterior middle temporal gyrus and additionally included a portion in the IFG, bilaterally, but excluded lesioned areas (Figure 6.7).

6.4.2.4.1 Speech>SCN – Individual Analyses using Small Volume Corrections

Pre and Post Testing Sessions: Figure 6.8 shows activation maps after the small volume corrections were applied in the left and right hemispheres for individual patients. Three out of the six patients showed significant activation in temporal lobe for speech sounds compared to low-level noise in the pre- and post-therapy sessions (Table 6.3). Two patients (patients 2 and 3) showed significant bilateral activation in middle and superior temporal gyrus, extending to temporal poles (TP). One patient (patient 6) showed extensive activation in the LH only, in the middle temporal gyrus (MTG) extending to the middle TP. Patient 1 also showed a small activation cluster in the MTG in the post-therapy scanning session, significant only at a lower threshold of $p < .001$, uncorrected.

Post>Pre comparisons: There were no significant activation clusters for the post>pre speech vs. sound comparison for any of the patients.

6.4.2.4.2 Speech>SCN – Group Analysis

Whole brain level comparisons for the speech vs. sound contrast for each patient were then entered into a 2^{nd} level random effects analysis. An explicit mask was applied to this contrast so that only the area defined from activation from healthy volunteers (taken

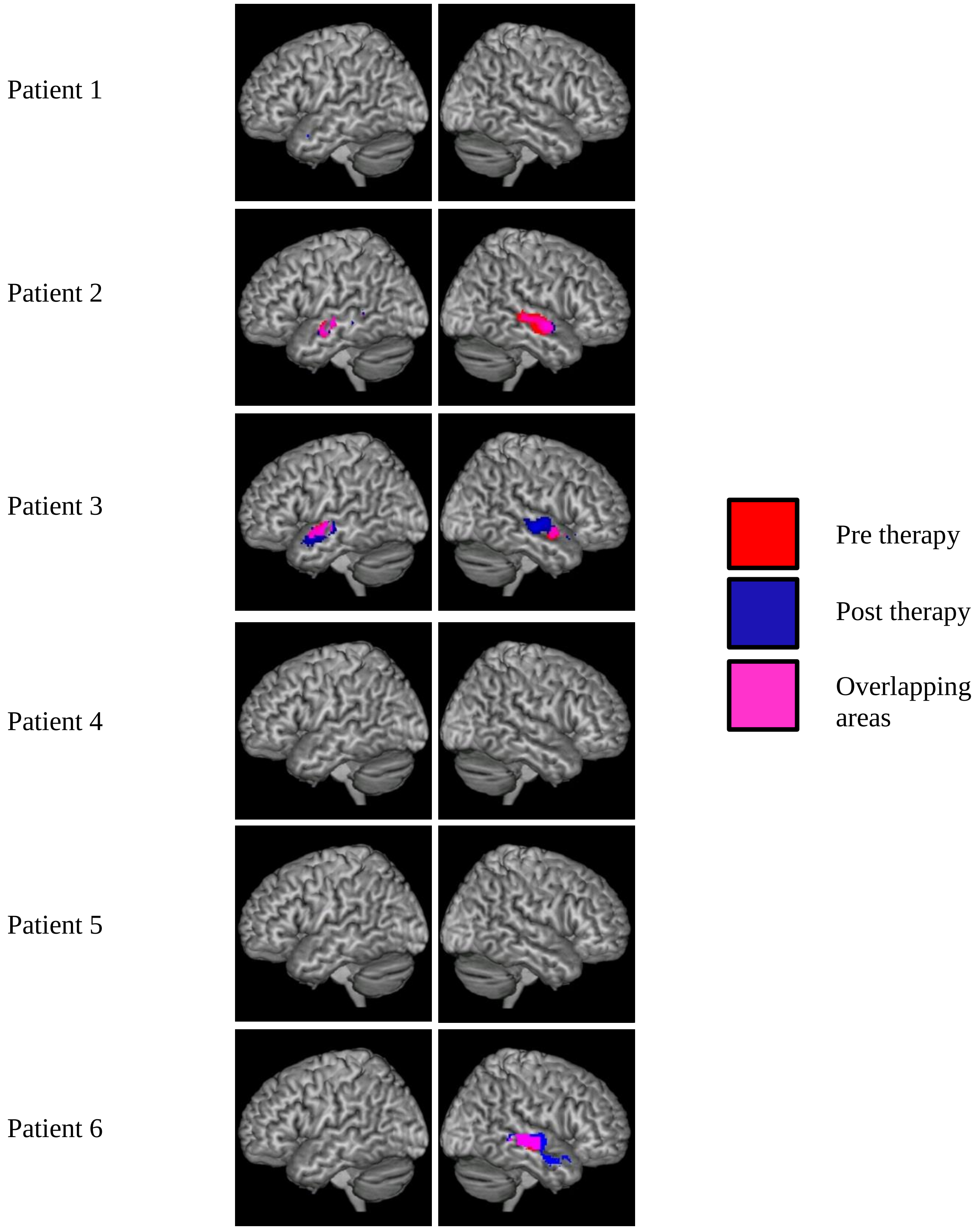


Figure 6.8. Results from small volume corrections for contrast speech > SCN in the left hemisphere and the right hemisphere for each patient. Small volume correction was conducted using ROIs in Figure 6.7.

Table 6.4.

*Speech versus SCN: small volume corrected activation peaks for individual patients (p<.001 uncorrected, or ** for p<.05 FWE corrected). Additional peaks within a single activation cluster are indented, following the most significant peak from each cluster.*

	Pre therapy						**Post therapy**					
				co-ordinates						co-ordinates		
		P (uncorrected)	Z-score	*x*	*y*	*z*		*P* (uncorrected)	Z-score	*x*	*y*	*z*
Patient 1							L MTG	0.000	3.87	-54	8	-22
Patient 2	L MTG	0.000**	7.26	-58	-10	-10	L Middle TP	0.000**	6.67	-60	-10	-10
	Post L MTG	0.000**	5.19	-52	-38	0	R MTG	0.000**	6.10	62	-4	-10
	R MTG	0.000**	6.44	58	-28	0	R MTG	0.000**	5.26	58	-26	-2
	R MTG	0.000**	5.94	62	-12	-10	R STG	0.000**	4.51	66	-12	-2
							L MTG	0.000**	5.49	-54	-36	-2
							L MTG	0.000	4.32	-62	-42	0
Patient 3	L MTG	0.000**	6.18	-60	-6	-6	L MTG	0.000**	6.79	-60	-10	-6
	L TP	0.000	4.53	-58	2	-8	L MTG	0.000**	5.73	-58	2	-12
	R TP	0.000**	5.95	60	4	-8	R STG	0.000**	6.27	64	-14	-4
	R MTG	0.000**	4.62	48	-28	-2	R STG	0.000**	5.74	48	-28	2
	R TP	0.000	3.92	54	12	-12	R TP	0.000**	5.47	60	2	-8
							R TP	0.000**	4.76	50	18	-14
							R TP	0.000	4.55	50	22	-12
								0.000	4.5	-14	-48	4
Patient 6	R MTG	0.000**	6.66	54	-36	-2	R MTG	0.000**	7.12	54	-34	-2
	R MTG	0.000**	6.53	60	-22	-6	R MTG	0.000**	6.38	58	-20	-6
							R Middle TP	0.000**	5.39	52	10	-24

MTG - middle temporal gyrus; STG – superior temporal gyrus; TP – temporal pole

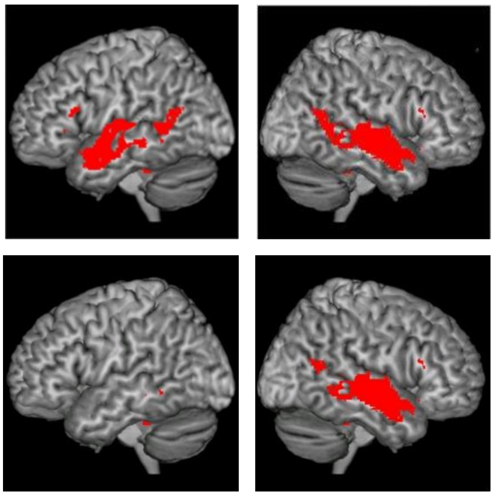


Figure 6.9. Region of interest maps in the left and the right hemispheres. (1) ROI from healthy volunteers defined by contrast speech>SCN in Rodd et al. (2005). (2) ROI from Speech>SCN contrast in healthy participants excluding the combined lesioned area from the 6 patients, entered into the 2nd level analysis.

from Rodd et al., 2005) excluding any areas of lesioned tissue found across any of the patients, was included in the analysis (Figure 6.9). Although no results reached significance at a corrected threshold, there were activation clusters in the RH at an uncorrected threshold of $p < .001$ in both testing sessions, in middle and superior temporal gyrus, extending to temporal pole (Figure 6.10, Table 6.4). There were no significant changes in activation clusters across the two time sessions.

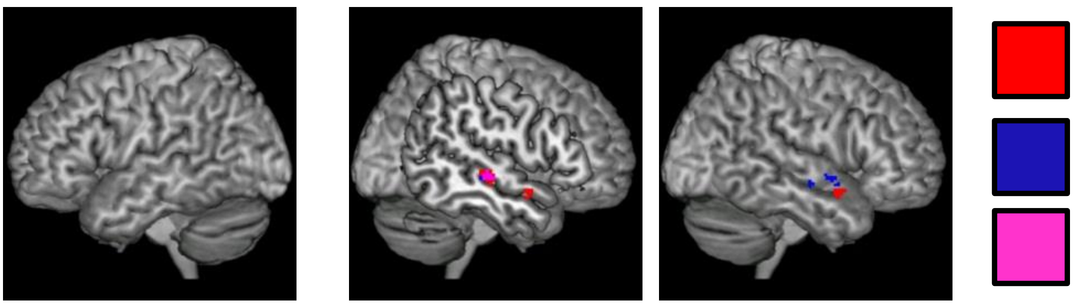


Figure 6.10. Results from a 2nd level group analysis using a small volume correction for the comparison of speech>SCN pre and post therapy in the (a) left hemisphere and (b) right hemisphere. Small volume correction includes ROI as defined in Figure 6.9 (bottom row).

Table 6.5.

Speech versus SCN: small volume corrected activation peaks from a 2nd level group analysis (p<.001 uncorrected). Additional peaks within a single activation cluster are indented, following the most significant peak from each cluster.

	Pre therapy						Post therapy					
				co-ordinates						co-ordinates		
		P (uncorrected)	Z-score	*x*	*y*	*z*		*P* (uncorrected)	Z-score	*x*	*y*	*z*
Group	R Middle TP	0.000	4.18	56	6	-16	R MTG	0.000	3.60	52	-20	-4
	R MTG	0.000	3.78	44	-40	-6	R MTG	0.001	3.27	58	-12	-10
	R MTG	0.000	3.67	46	-44	2	R TP	0.001	3.28	56	4	-10
	R MTG	0.000	3.67	52	-20	-4	R STG	0.001	3.16	60	-2	-4
	R STG	0.000	3.50	58	-12	-2						

MTG – middle temporal gyrus; STG – superior temporal gyrus; TP – temporal pole

In summary, there were no changes in activation that reached statistical significance across the two time sessions for either individual patients, or across the group. Evidence for response to speech stimuli in the same areas activated by healthy controls however, was seen individually in 3 patients, 2 of whom showed bilateral activation. Furthermore, anatomically similar activation to controls was seen across the group of patients in right temporal regions.

6.4.2.5 Activation for Ambiguity Response (High Ambiguity>Low Ambiguity)

Higher-level processing of the semantic aspects of speech was assessed by comparing sentences which were harder to comprehend as they contained ambiguous words (such as pears/pairs; night/knight) to simpler, unambiguous sentences. In healthy volunteers, this ambiguity response produced activation in left posterior inferior temporal lobe as well as in bilateral IFG (Rodd et al., 2005). Activation in these areas in patients could imply higher level semantic processing.

6.4.2.5.1 High Amb>Low Amb –Individual Analyses of Whole Brain Activity

At the whole brain level, there were no significant clusters for any patients when corrected for multiple comparisons. However due to the subtle differences between the high and low ambiguity sentence types and because there were a smaller number of scans for this comparison, the power of this contrast was weaker than of the other two comparisons.

6.4.2.5.2 High Amb>Low Amb – ROI Analysis in Individuals

Figure 6.11 illustrates individual ROIs defined by activation in healthy volunteers for high ambiguity compared to low ambiguity (in Rodd et al., 2005), excluding lesioned tissue (method in Section 6.4.1.4).

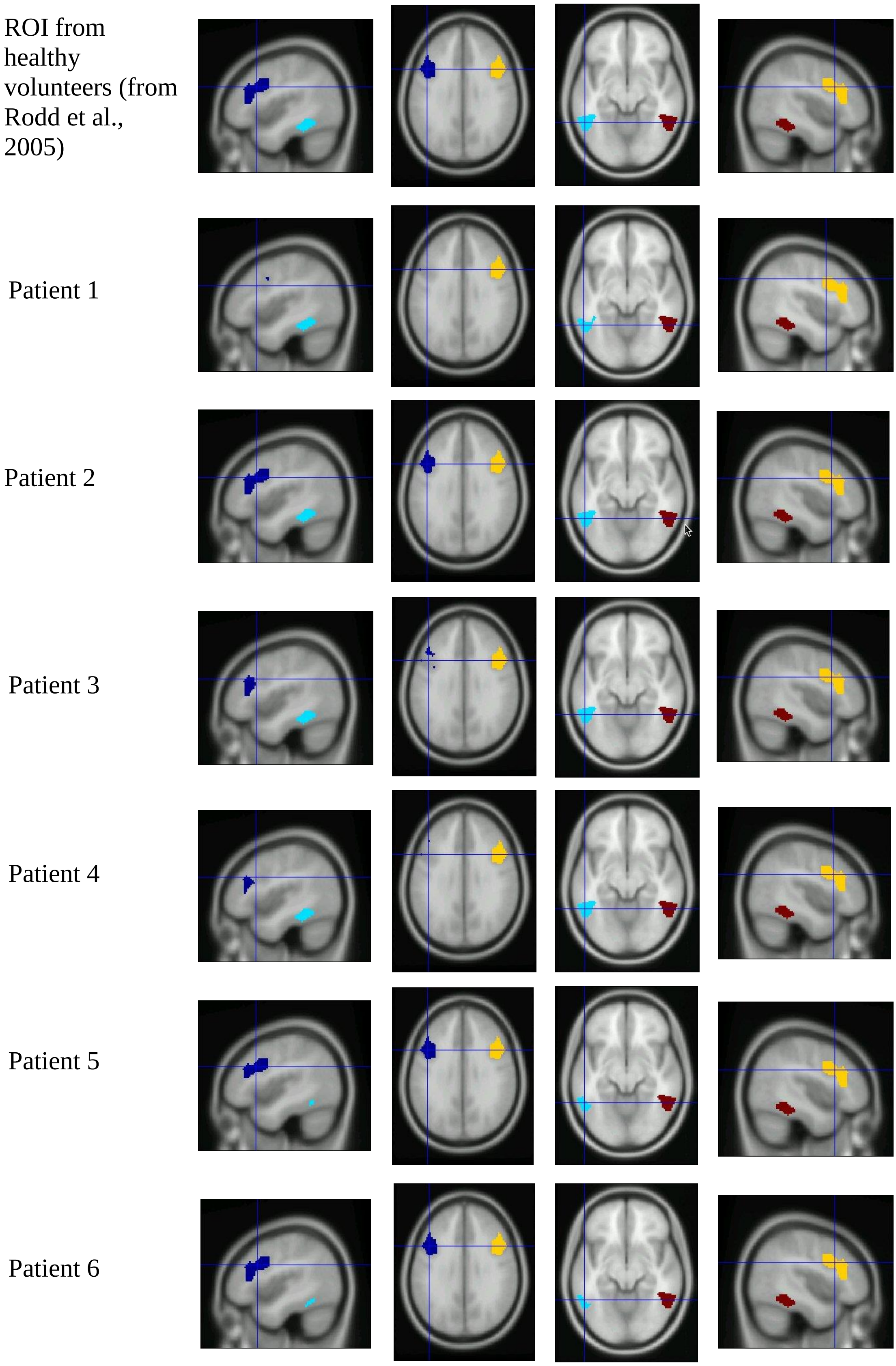


Figure 6.11. Region of interest maps from healthy volunteers defined by contrast high ambiguity sentences>low ambiguity sentences (taken from Rodd et al., 2005), excluding lesioned tissue within each individual. (Dark blue – left frontal ROI; light blue – left temporal ROI; yellow – right frontal ROI; red – right temporal ROI).

Pre and Post Testing Sessions: Table 6.5 shows the ROI analysis for individual patients. There was more activation for high ambiguity compared to low ambiguity sentences in the left inferior frontal ROI for patient 1 in the pre-therapy session. Patient 3 also showed an ambiguity response in the post therapy session, for both left inferior frontal ROI and the right inferior frontal ROI. Each of these contrasts however only approached significance ($p < .1$). Higher activation for high-ambiguity sentences in the ROIs defined is in line with results from healthy volunteers which suggest these regions are recruited when listening to complex sentences which include ambiguous words.

Post>Pre comparisons: Patient 3 showed a change in activation across sessions that approached significance in the right inferior frontal ROI ($p = .061$). As table 6.5 shows, there was significantly more activation for patient 3 for high ambiguity compared to low ambiguity sentences in the right frontal ROI post-therapy, where there was no difference in the pre-therapy session.

Two patients showed a change in the right temporal ROI, which approached significance for patient 3 ($p = .072$) and reached significance for patient 4 ($p = .02$). Interestingly however, these changes were due to a decrease in activation for low-ambiguity sentences, rather than an increase in activation for high-ambiguity sentences. In the pre-therapy session, these patients showed more activation for low ambiguity sentences compared to high ambiguity sentences. This is in contrast to the results from healthy volunteers which suggest the inferior temporal ROI is more active for high compared to low ambiguity sentences.

Table 6.6.

*Results comparing high ambiguity sentences to low ambiguity sentences pre, post and post>pre therapy, within four ROIs, in the left inferior frontal, left temporal, right inferior frontal and right temporal cortex. ROIs were defined by healthy volunteers from contrast high ambiguity>low ambiguity from Rodd et al., (2005) excluding lesioned tissue within each individual. (P values reported at p<.001, uncorrected, †= p reported at <.05 FWE corrected; * = contrasts which approached significance, ** = significant contrasts).*

	Left Frontal ROI					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.38	0.055*	0.22	0.178	-0.15	0.676
Patient 2	-0.21	0.784	-0.33	0.894	-0.12	0.624
Patient 3	0.00	0.513	0.20	0.095*	0.20	0.169
Patient 4	-0.46	0.859	-0.09	0.583	0.37	0.266
Patient 5	0.29	0.111	-0.05	0.577	-0.34	0.843
Patient 6	0.03	0.461	-0.49	0.939	-0.52	0.876

	Left Temporal ROI					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.06	0.416	-0.04	0.557	-0.11	0.599
Patient 2	-0.01	0.515	0.06	0.372	0.07	0.399
Patient 3	0.00	0.509	0.18	0.112	0.18	0.188
Patient 4	-0.27	0.933	-0.01	0.511	0.27	0.146
Patient 5	-0.09	0.636	-0.01	0.521	0.08	0.416
Patient 6	-0.28	0.935	-0.31	0.955	-0.03	0.543

	Right Frontal ROI					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.13	0.295	0.18	0.233	0.05	0.442
Patient 2	-0.14	0.718	-0.14	0.713	0.01	0.493
Patient 3	-0.14	0.773	0.28	0.075*	0.42	0.061*
Patient 4	-0.26	0.828	-0.05	0.568	0.22	0.288
Patient 5	-0.20	0.777	0.08	0.375	0.28	0.222
Patient 6	-0.22	0.824	-0.34	0.929	-0.12	0.644

	Right Temporal ROI					
	Pre therapy		Post therapy		Post>Pre	
	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)	Contrast value	*P* (uncorrected)
Patient 1	0.31	0.117	-0.02	0.533	-0.33	0.813
Patient 2	0.05	0.359	0.10	0.229	0.05	0.396
Patient 3	-0.17	0.916*	0.08	0.244	0.25	0.072*
Patient 4	-0.57	0.997**	0.02	0.461	0.59	0.020** (0.078†*)
Patient 5	0.06	0.396	0.00	0.500	-0.06	0.575
Patient 6	-0.36	0.987	-0.24	0.937	0.12	0.298

6.4.2.5.3 High Amb>Low Amb – Group Analysis

Contrast values for each of the two ROIs (frontal, temporal) in the left and right hemisphere at the pre- and post- therapy scanning sessions were extracted from the ROI analysis and entered into a 2x2x2 (region, hemisphere, time) repeated measures ANOVA in order to identify consistent effects across the group of subjects (Figure 6.12). Across the group, there was no main effect of hemisphere (F (1, 5) = .346, p = .582, η_p^2 = .065), time session (F (1, 5) = .459, p = .528, η_p^2 = .084) or region of activation (F (1, 5) = .012, p = .919, η_p^2 = .002). However there was a significant interaction between scanning session and hemispheres (F (1, 5) = 8.349, p = .034, η_p^2 = .625). At the pre-therapy session, there was no significant difference in contrast values between the right and left hemisphere (t (11) = 1.207, p = .253). However the RH was significantly more active for high ambiguity sentences than the LH in the post therapy testing session (t (11) = 2.212, p = .049).

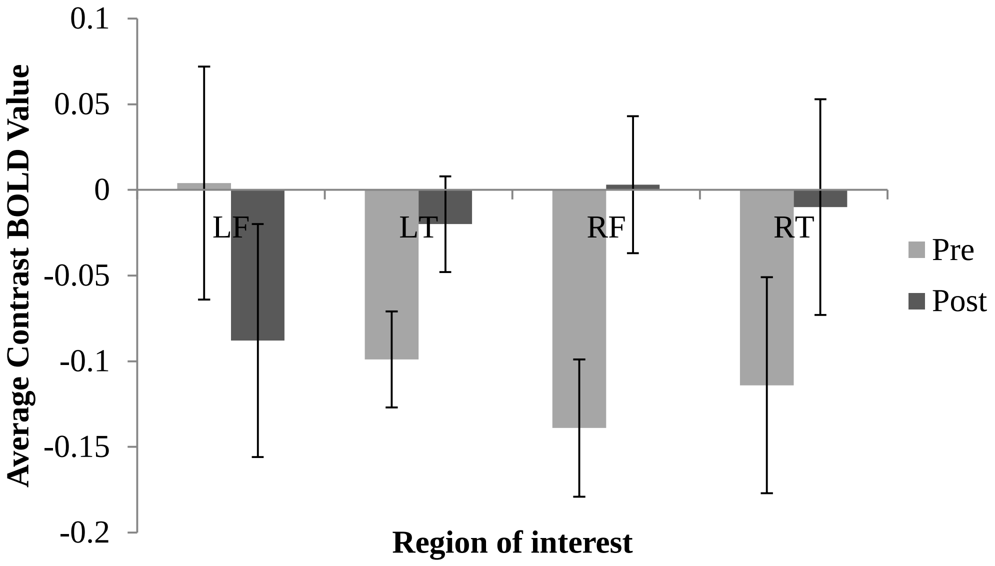


Figure 6.12. Average contrast values for 6 patients in the left inferior frontal, left temporal, right inferior frontal and right temporal ROIS, pre- and post-therapy for the ambiguity comparison. ROIs were defined by healthy volunteers from contrast high ambiguity>low ambiguity from Rodd et al., (2005), excluding lesioned areas in each individual.

In summary, two patients showed evidence of a change in neural activation across time in the RH, one of whom showed a significant change in both right frontal and right temporal areas. No overall group effect was found for a change across time. However as a group, patients activated the RH ROIs significantly more than the left in the post-therapy testing session.

6.4.2.6 Correlation Analyses for Ambiguity Response and Behavioural Changes

Correlation analyses were carried out in order to identify possible relationships between the changes in neural activation that occurred across the two time sessions and the changes in behavioural measures. Changes in activation within each of the four ROIs in the ambiguity comparison were correlated with the changes in raw scores from the BNT (from Chapter 4). No correlations (*p> .05)* were found in any of the four ROIS: left inferior frontal *(r = -.192);* left temporal *(r = -.544)*; right inferior frontal *(r = -.043)*; right temporal *(r = -.571).* Although r-values are high, correlations did not reach significance. However due to the small number of patients in this comparison, the power of this correlation was considerably weak and therefore the lack of results should not be over-interpreted. It is interesting that patient 3, who showed an ambiguity effect in the post-testing session in bilateral inferior frontal regions and increases in the ambiguity effect in both RH ROIs, also demonstrated an increase in their BNT score of >2 SD (gender, age, and education adjusted). When comparing pre- and post-therapy scores, previous literature (Maher et al., 2006) has used a change of ≥2 *SD* to indicate a critical change. This suggests a significant improvement in naming performance for patient 3, which coincides with changes in neural activation for the ambiguity response in the RH.

6.5 DISCUSSION

In this study, a hierarchical fMRI method was used to measure auditory, speech and semantic responses in patients suffering from chronic aphasia following a single stroke. Patients were tested at two time sessions, once immediately before and once immediately after two weeks of ILAT, in order to identify any therapy-induced neural changes. Despite the small number of participants, evidence of a change in neural activation following therapy was seen in some individuals. Due to the limited patient numbers and small number of scans, particularly in the ambiguity contrast, some analyses are reported at the $p<.001$ uncorrected threshold and therefore all interpretations have been considered with caution. One patient showed an increase in bilateral activation to SCN stimuli following therapy. In addition, two patients showed evidence of a change in activation to ambiguous sentences in the RH following therapy. Across the group, the RH was significantly more active than the left during ambiguity processing, following therapy.

Analysis of the neural responses of separate testing sessions showed a range of patterns across the patients. All patients showed anatomically appropriate activation to auditory stimuli, comparable to that of healthy volunteers from Rodd et al. (2005) in both the pre- and post-therapy testing sessions. This activation however was predominantly restricted to the RH. Three patients showed significant responses to speech stimuli comparable to that of healthy controls (Rodd et al., 2005) and two patients' also demonstrated appropriate responses to speech stimuli which included ambiguous words and were therefore more difficult to process. Group analyses also indicated a trend in that the RH (usually unaffected in aphasia) is more active during processing of auditory and speech stimuli than the LH. This was true for both the pre- and post-therapy testing sessions.

Changes following ILAT

No overall group changes were found when contrasting pre- and post-therapy neural activation for either auditory or speech processing. When processing more complex sentences which contained ambiguous words however, the patient group tended to recruit the RH more than the LH following therapy. Before intervention there was no difference in neural activation between the right and left hemispheres. The small changes across the group of patients are less clear than those seen in previous research where two weeks of ILAT resulted in improvements in behavioural outcomes in a group of patients, alongside changes in language-specific neural activation (Breier et al., 2009; Kurland et al., 2012; Pulvermüller, Hauk, Zohsel, Neininger Mohr, 2005). However, as only the data from 6 patients were available for analysis, there was limited power in group comparisons.

Nonetheless, the paradigm employed here also allows for analysis on a single subject level. Previous research (Davis et al., 2007; Coleman et al., 2007) and findings reported here demonstrate consistent neural activation in single-subject analysis, which is comparable to activation seen in a group of healthy volunteers (Rodd et al., 2005). On a single subject level, one patient (patient 2) showed a bilateral increase in neural activation to non-speech sounds following therapy. Furthermore although patients 3 and 4 showed no increase in speech-specific activation following therapy, there was evidence of a change in neural activation in the more complex processing of sentences which contained ambiguous words. Small changes, which approached significance, were seen in the RH temporal regions in both patients, and the right inferior frontal area in addition for patient 3.

Changes in the RH temporal areas followed an unexpected pattern, whereby during the pre-therapy scan, both patients 3 and 4 showed significant activation in the opposite direction to the ambiguity contrast. That is, higher activation was seen for unambiguous sentences than ambiguous sentences. This is in contrast with previous findings where healthy volunteers typically recruit the inferior posterior temporal region when processing ambiguous sentences (Rodd et al., 2005). Although the change in neural activation seen in the right temporal regions was due to a reduction in activation for unambiguous sentences, rather than an increase in activation for ambiguous sentences, this change is nonetheless in the appropriate direction, partly supporting the idea of stronger and more appropriate neural activity during language processing following intensive therapy.

The exploratory nature of analyses in this thesis allowed for comparisons of data to identify possible relationships between different measures of therapy outcome. The changes in clinical and neural activation in patient 3 were interesting in particular. This patient showed significant extensive bilateral activation for speech processing both pre and post-therapy, comparable to that of healthy volunteers (in Rodd et al., 2005), suggesting some level of intact processing of language. In addition to the decrease in low ambiguity sentences discussed in the right temporal ROI, patient 3 also demonstrated an increase in activation induced by ambiguous sentences following therapy in the right Inferior Frontal ROI. Furthermore activation was seen in the LIFG, which neared significance in the post-therapy session but not the pre-therapy session.

Both bilateral inferior frontal regions and inferior temporal regions have previously been identified as crucial in resolving lexical ambiguities and therefore involved in the complex processing of semantic linguistic information (Rodd et al., 2005; Zempleni et al., 2007). Higher activation in these areas following two weeks of ILAT therefore supports the idea that massed practise of behaviourally relevant language may aid recovery after stroke (Pulvermüller et al., 2001). Supporting these findings is an accompanying change in patient 3's behavioural language output following therapy, where an increase of more than 2 SDs was seen in the post-therapy testing session on the BNT (see Chapter 4). The behavioural and neuronal changes seen in this patient were seen in the chronic post-stroke phase (beyond 1 year) and therefore are unlikely to be due to spontaneous recovery (Berthier & Pulvermüller, 2011) and likely to be the result of intensive intervention. Although these results are small, they are in line with previous findings that show improvement in language outputs alongside neural changes in patients with chronic aphasia following ILAT (Kurland et al., 2012; Meinzer et al., 2008; Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005).

Consistent with findings in the single-subject analysis where a post-therapy increase in RH activation was seen, patients as a group, also tended to activate the RH significantly more than the left after therapy, when processing ambiguous sentences. These results are in line with previous literature suggesting the RH plays a role in recovery of language (Berthier et al., 2011; Saur et al, 2006).

Conversely, the data appear to be in contrast with findings from Richter et al. (2008), where strong pre-therapy RH activation which decreased following ILAT was found to correlate with therapy success. However as Breier et al. (2009) report, RH regions may be recruited immediately following therapy, but without the reintegration of LH regions also, gains made in communication may not be stable. Efficient recovery from aphasia appears to be most stable when spared LH regions are re-recruited (Breier et al., 2009; Meinzer et al., 2008), in addition to the RH for a bilateral contribution to language processing (Brier et al., 2006; Kurland et al., 2012; Pulvermüller, Hauk, Zohsel, Neininger & Mohr, 2005). As the planned six month follow up testing sessions were unable to take place, the stability of recovery from ILAT in the group of patients presented here cannot be commented on. However although the results presented indicate that the RH was recruited more so than the left for language processing, single-subject analyses also revealed significant clusters of activation in the LH, supporting the notion that bilateral hemisphere recruitment during language processing may help to aid recovery from aphasia.

Pre and post-therapy scanning sessions

In addition to the changes found across the two time sessions, results from pre- and post-therapy testing sessions taken separately show evidence of intact linguistic processing and support behavioural findings that resolving lexical ambiguities is possible for patients with LH damage. Although the extent and strength of activation for acoustic stimuli was variable, all patients showed reliable activation in anatomically appropriate regions in the RH, comparable to that of healthy controls (Rodd et al., 2005). Only one patient (patient 2) showed reliable LH activation for this contrast in addition to the right. These results imply basic auditory processing is intact. In addition a group analysis confirmed there was more activation in the RH compared to left. This is consistent with the fact all patients presented with LH damage and little or no damage to the RH (see figure 6.3 for patient lesion-map).

Three out of the six patients showed anatomically appropriate activation for the mid-level contrast comparing speech to non-speech stimuli, in single-subject analysis. For two of these patients (patients 2 and 3), this activation was similar to that of healthy volunteers (Rodd et al., 2005), with extensive bilateral activation in MTG that extended to the temporal poles. One further patient (patient 6) showed fairly extensive activation but in the RH only. Interestingly, despite only patient 2 showing LH activation for acoustic stimuli, both patients 2 and 3 recruited the LH when processing sentences. Therefore despite damage to the LH following a stroke, it continues to a play a critical role in linguistic processing. Unlike healthy controls in Rodd et al. (2005) however, none of the patients activated the left inferior frontal regions for processing of speech-specific stimuli. Furthermore across the group as a whole, clusters of activation for speech stimuli were seen in the RH only, in middle and superior temporal regions. These results fit with the pattern of activation already discussed, suggesting the RH is more active for auditory language processing in patients with aphasia.

Previous research has demonstrated that healthy participants activate bilateral IFG and left posterior inferior temporal regions when processing sentences which contain ambiguous words (Rodd et al., 2005). The results presented here demonstrate that two out of the six patients showed activation which reached near significance in the LIFG, similar to healthy volunteers (Rodd et al., 2005). One of these patients, patient 3, also showed near significant activation in the Right IFG (RIFG) in the post-therapy testing session. This patient demonstrated significant bilateral activation when comprehending speech stimuli.

Lack of significant activations found on an individual basis for the ambiguity contrast should however not be over interpreted. Due to the subtle differences between the high and low ambiguity sentence types and because there were a smaller number of scans for this comparison, the power of this contrast was considerably weaker than of the two lower-level comparisons. Activation comparable to that of controls (from Rodd et al., 2005) for processing non-speech and speech stimuli suggests the preceding stages of speech comprehension are indeed intact in this group of patients. On average the group tended to show overall more responses to unambiguous sentences than ambiguous sentences in the areas where healthy volunteers show the opposite effect. This might suggest patients with aphasia are unable to resolve ambiguity resolution or failed to try to resolve the more complex sentences. This will be discussed in relation to behavioural data from a forced-choice ambiguity resolution task and the post-scanning word association activity.

Can patients with aphasia resolve lexical ambiguities?

Two behavioural experiments were presented in this chapter, which investigated whether patients with aphasia were able to comprehend complex sentences in order to resolve lexical ambiguities. In experiment 2, ambiguous words were presented within a sentence which constrained meaning to one sense, the subordinate meaning. Following the presentation of these sentences in the scanner, patients then underwent a word association task which included primed targets (ambiguous words heard during the presentation) and unprimed targets (ambiguous words not heard). Data from healthy individuals shows that typically, listeners are biased towards retrieving the dominant meaning of ambiguous words (Rodd et al., 2013). However following just one presentation of the ambiguous word in its subordinate meaning context is enough to bias listeners towards the subordinate meaning. In a word association task, words generated for primed targets were more consistent with sentence meaning and therefore the subordinate sense, compared to unprimed targets (Rodd et al., 2013). In contrast, the data presented here showed the words patients generated were no more consistent with the sentence meaning for primed compared to unprimed targets.

Grindrod and Baum (2003) suggest that after hearing a sentence with an ambiguous word, patients with left-hemisphere damage activate both the appropriate and inappropriate meanings of the ambiguous word. The findings here could be interpreted in this way; once both meanings are activated following the presentation of an ambiguous word, patients are unable to select the appropriate meaning and therefore are unable to provide more answers that are consistent with sentence meaning.

However the results from the ambiguity resolution task in Experiment 1 contrast with this interpretation. Here, patients appear to be able to use sentence context to disambiguate and select the appropriate meaning whilst ignoring the inappropriate sense. Furthermore these results fit with Vuong and Martin's (2011) findings that patients are able to disambiguate following the presentation of a sentence constraining the words meaning. This study also showed that patients with LH damage are significantly slower than healthy controls and a patient with left-parietal damage at doing so.

There are a number of possible reasons for the contrast in the two behavioural tasks. First, ambiguous words from the word association task were presented in their constraining sentences during a scanning session. During scanning, sentences were presented consecutively and contained two ambiguous words. It is possible that if patients are in fact delayed in their ability to disambiguate, as Vuong and Martin (2011) suggest, they may have struggled to disambiguate the two ambiguous words before the next sentence was presented. In contrast during the ambiguity resolution task, patients heard one sentence presented on its own and were given as much time as needed to disambiguate and select the appropriate meaning before the next sentence (and therefore the next ambiguous word) was heard. It would be interesting in future testing to include the recording of latency of responses during a similar ambiguity resolution task. This would be useful in identifying whether it is possible for patients with aphasia to disambiguate in the time given during scanning runs.

Understanding how patients are able to disambiguate would also help to interpret the findings from the imaging data which appear to show that as a group, patients do not recruit the same cortical areas as healthy volunteers (in Rodd et al., 2005) during the processing of lexical ambiguities. It is possible that due to the task, the patient group were unable to disambiguate during the scanning sessions. Alternatively it is possible patients simply did not attempt to disambiguate during the scans. When faced with a forced choice alternative as in Experiment 1, selecting the appropriate meaning was more critical than in the passive listening task experienced in Experiment 2, when ambiguous words were heard during a scanning run. Finally it is possible that during the scanning run, patients were able to disambiguate the sentences heard, but that this did not affect their bias in retrieving meanings of ambiguous words at a later time.

Rodd et al. (2013) report that following the presentation of the ambiguous word in its subordinate meaning context biases healthy listeners towards the subordinate meaning. As no behavioural data were taken during the scanning session, it is difficult to infer whether or not patients were indeed disambiguating. It would be interesting to apply a similar passive listening and word-association task outside the scanner, in order to identify whether simply hearing an ambiguous word within a constraining sentence biases patients' retrieval. It is worth noting patients were often tired after being in the scanner and only 4 out of the 8 patients originally scanned were able to provide answers to the word association task at both pre and post-therapy time points. This tiredness could have impacted on patient's abilities to provide appropriate responses.

Taking into account the tasks explored in this chapter and previous research, it is likely patients with chronic aphasia are able to resolve lexical ambiguities; however they may be delayed in doing so. For this reason, the type of task employed may be critical to both success in disambiguating, and in being able to detect areas in the brain recruited for this process. Patients with LH damage may require longer to process lexical ambiguities (Vuong & Martin, 2011) and may perform best in an on-line, rather than passive listening task.

Conclusions

In this chapter, results from behavioural language tasks were presented alongside neuroimaging data from a group of patients with aphasia who underwent fMRI scanning before and after two weeks of ILAT. The paradigm reported, investigating hierarchical language processing and comparisons to data from healthy individuals (Rodd et al., 2005) provides a useful tool for assessing levels of language processing in patients with aphasia. Further investigation of the implications of LH damage in the ability to resolve lexical ambiguities, including a higher number of scans for the more subtle ambiguity contrast, would allow for interesting pre- and post-therapy comparison data on a single subject basis. A robust imaging technique would mean being able to identify changes and draw more concrete conclusions about neural activation following a particular intervention.

One limitation of this experiment is that no control group of untreated patients who underwent the same scanning protocols was included to control for scanning repetition effects. However, previous reports have shown stability in activation across test-retest sessions in healthy controls within a 2-week interval (Meinzer et al., 2006), and in patients with aphasia who underwent a baseline scan three weeks before the pre-therapy scan (Breier et al., 2009). Although the present results must be considered with caution, they are in line with previous reports demonstrating therapy related neural changes with ILAT application. The present findings indicate the important role of the RH in compensation of some function from the LH, following a stroke.

CHAPTER 7: SUMMARY AND CONCLUSIONS

Intensive Language Action Therapy (ILAT) is a relatively new form of SLT employed to aid patients suffering with aphasia. Despite increasing interest in ILAT, this thesis provides the first detailed guidance in how to run ILAT and how to adjust this intervention to the wide spectrum of deficits patients with aphasia suffer. Sections of Chapter 3 were presented in a recent publication which fully described the underlying principles of ILAT and provided samples of therapy elements from two types of LAGs (Difrancesco et al., 2012). Considering the many recent trials of ILAT (or one of its variants –CIAT; Pulvermüller et al., 2001; CILT; Maher et al., 2006; Meinzer et al., 2005) reviewed in Chapter 2, these detailed explanations are important in highlighting how each of the principles of ILAT are applied practically to ensure appropriate implementation of this intervention.

In this thesis clinical, communicative and neuroimaging data were presented from 14 English speaking patients, who underwent two weeks of therapy utilising ILAT methods. In addition to the original *request* LAG outlined by Pulvermüller et al. (2001), patients also engaged in the *planning an activity* LAG, described in Chapter 3. This new LAG extends the type of language that patients use during therapy, as it requires that players practise action-related verbs as well as object-related nouns from the original ILAT protocol. In this group of 14 patients, significant behavioural improvements were seen in standardised clinical aphasia tests. As a whole, the patients became significantly more accurate in both measures of spoken output and comprehension following ILAT therapy. Furthermore, after the two-week intervention, patients rated their quality of communication in everyday life as higher than at the start.

In addition to the positive results from standardised tests, a novel measure of communicative performance described in Chapter 5 also highlighted the gains made throughout the two weeks in 6 of the 14 patients. Recordings from LAGs during therapy demonstrated faster speech production and comprehension over the two weeks of therapy. Furthermore, the complexity of patient's speech, as recorded on the newly developed *complexity index* seemed particularly sensitive to detecting therapy-related changes in communication. These results highlight the importance of measuring therapy efficacy not only on functional clinical tests, but alternative measures of communication, both within therapy and in everyday language use.

The final part of this thesis was undertaken in order to augment understanding of how the brain adapts in recovery from aphasia. A subset of the 8 patients who participated in ILAT also underwent a functional Magnetic Resonance Imaging (fMRI) scan in the weeks immediately before and after therapy. Neural activation induced during a language comprehension task was recorded in each of these sessions, which allowed for investigation of hierarchical language processing, assessing brain responses to a noise condition, to spoken sentences and to sentences which contained ambiguous words and therefore were more difficult to process. The results demonstrated that patients with aphasia tended to recruit the right hemisphere more than the left hemisphere during language processing. Following ILAT, changes were seen in neural activation induced by high ambiguity sentences in the right hemisphere and in the left inferior frontal region in one patient. Although these results were drawn with caution due to limited power of the MRI study, they are in line with previous research that indicates RH contributions to recovery from aphasia.

Future research investigating the effects of ILAT should address the issues raised by the present study. First, observations of the changes in clinical data and brain activation indicated a link between measures of therapy outcome. Of particular interest were the changes seen within the RH following therapy. More power in experiments using functional imaging would allow further exploration of these findings. Recruiting a higher number of patients would allow for more rigorous testing of the relationship between brain activation and clinical therapy outcome measures across the group. In addition, including the full set of ambiguity trials in each scanning run would provide more power in single subject analyses. This would allow for pre- and post-therapy comparisons within each patient and the possibility of identifying particular patterns of results, for example based on demographic data.

Second, future trials of ILAT should aim to include a follow up testing session, for example 3 or 6 months post-therapy. The results presented here demonstrate that following two weeks of ILAT, where patients made improvements in clinical measures of language performance, the RH was recruited more so than the LH during a language task. Previous research (Breier et al., 2009) however suggests that although the RH plays an important role in recovery from stroke, reintegration of the LH may result in more stable, long-term recovery. Including a 6 month follow up session would allow investigation of how neural activity is related to changes in clinical and behavioural outcomes over a longer period of time and whether initial post-therapy gains made by patients who recruit the RH are stable over a period where patients receive no therapy.

Finally, a shortcoming of this project was that no control group of patients who underwent the same testing and scanning protocols but with no intervention was included. Previous research comparing two forms of therapy has shown stronger and faster improvements in patients treated with ILAT (Maher et al., 2006; Kurland et al., 2012). Similarly, previous studies have reported stability in neural activation across test-retest sessions in healthy controls (Meinzer et al., 2006) and patients with aphasia

(Breier et al., 2009). However future studies should aim to include a second group of patients treated with a different form of intensive therapy, in order that stronger conclusions regarding the efficacy of ILAT can be drawn.

The present results add to a growing body of reports on therapy-induced behavioural and neural changes following ILAT. Importantly, all the patients in this group were classed as suffering with chronic aphasia (at least 1 year post-stroke), with an average time since stroke of 73 months. Therefore improvements in language function, alongside neural reorganisation in the brain are unlikely to have occurred due to spontaneous recovery and are likely the result of intensive intervention, specifically combining communicative language therapy with action performance.

REFERENCES

Aten, J. L., Caligiuri, M. P., & Holland, A. L. (1982). The efficacy of functional communication therapy for chronic aphasic patients. *Journal of Speech and Hearing Disorders, 47 (1)*, 93-96.

Audacity Team (2008). Audacity (Version 2.0.0) [Computer software]. Retreived from http://audacity.sourceforge.net/

Barrós-Loscertales, A., González, J., Pulvermüller, F., Ventura-Campos, N., Bustamante, J. C., Costumero, V., … Ávila, C. (2012). Reading salt activates gustatory brain regions: fMRI evidence for semantic grounding in a novel sensory modality. *Cerebral Cortex, 22 (11),* 2554-2563. doi: 10.1093/cercor/bhr324.

Barthel, G., Meinzer, M., Djundja, D., & Rockstroh, B. (2008). Intensive language therapy in chronic aphasia: Which aspects contribute most? *Aphasiology, 22 (4),* 408-421. doi: 10.1080/02687030701415880.

Basso, A., & Macis, M. (2011). Therapy efficacy in chronic aphasia. *Behavioural Neurology, 24 (4),* 317-325. doi: 10.3233/BEN-2011-0342.

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesion-symptom mapping. *Nature Neuroscience, 6 (5),* 448-450. doi: 10.1038/nn1050.

Berthier, M. L. (2005). Poststroke aphasia: Epidemiology, pathophysiology and treatment. *Drugs & Aging, 22 (2),* 163-182. doi: 10.2165/00002512-200522020-00006.

Berthier, M. L., Garcia-Casares, N., Walsh, S. F., Nabrozidis, A., Ruíz de Mier, R. J., Green, C., … Pulvermüller, F. (2011). Recovery from post-stroke aphasia: Lessons from brain imaging and implications for rehabilitation and biological treatments. *Discovery Medicine, 12 (65),* 275 – 289.

Berthier, M. L., Green, C., Lara, J. P., Higueras, C., Barbancho, M. A., Davila, G., & Pulvermüller, F. (2009). Memantine and constraint-induced aphasia therapy in chronic poststroke aphasia. *Annals of Neurology, 65 (5),* 577-585. doi: 10.1002/ana.21597 .

Berthier, M. L., & Pulvermüller, F. (2011). Neuroscience insights improve neurorehabilitation of poststroke aphasia. *Nature Reviews Neurology, 7 (2),* 86-97. doi: 10.1038/nrneurol.2010.201.

Bhogal, S.K., Teasell, R., & Speechley, M. (2003). Intensity of aphasia therapy, impact on recovery. *Stroke 34 (4)*, 987-993. doi: 10.1161/01.STR.0000062343.64383.D0.

Branigan, H. P., Pickering, M. J., & Cleland, A. A. (1999). Syntactic priming in written production: Evidence for rapid decay. *Psychonomic Bulletin & Review, 6 (4),* 635-640. doi: 10.3758/BF03212972.

Breier, J. I., Juranek, J., Maher, L. M., Schmadeke, S., Men, D., & Papanicolaou, A. C. (2009). Behavioral and neurophysiologic response to therapy for chronic aphasia. *Archives of Physical Medicine and Rehabilitation, 90 (12),* 2026-2033. doi: 10.1016/j.apmr.2009.08.144.

Breier, J. I., Maher, L. M., Novak, B., & Papanicolaou, A. C. (2006). Functional imaging before and after Constraint-Induced Language Therapy for aphasia using magnetoencephalography. *Neurocase, 12 (6),* 322-331. doi: 10.1080/13554790601126054 .

Breier, J. I., Maher, L. M., Schmadeke, S., Hasan, K. M., & Papanicolaou, A. C. (2007). Changes in language-specific brain activation after therapy for aphasia using magnetoencephalography: A case study. *Neurocase, 13 (3),* 169-177. doi: 10.1080/13554790701448200.

Brett, M., Anton, J., Valabregue, R., & Poline, J. (2002). Region of interest analysis using an SPM toolbox. Presented at the 8th International Conference on Functional Mapping of the Human Brain, 2nd- 6th June, Sendai, Japan. Available on CD-ROM in *NeuroImage, 16,* 2.

Cherney, L., Patterson, J., Raymer, A., Frymark, T., & Schooling, T. (2008). Evidence-based systematic review: Effects of intensity of treatment and Constraint-Induced Language Therapy for individuals with stroke-induced aphasia. *Journal of Speech, Language and Hearing Research, 51 (5),* 1282-1299. doi: 10.1044/1092-4388(2008/07-0206).

Cicerone, K. D., Dahlberg, C., Malec, J. F., Langenbahn, D. M., Felicetti, T., Kneipp, S., … Catanese, J. (2005). Evidence-based cognitive rehabilitation: Updated review of the literature from 1998 through 2002. *Archives of Physical Medicine and Rehabilitation, 86 (8),* 1681 – 1692. doi: 10.1016/j.apmr.2005.03.024.

Coleman, M. R., Rodd, J. M., Davis, M. H., Johnsrude, I. S., Menon, D. K., Pickard, J., D., & Owen, A. M. (2007). Do vegetative patients retain aspects of language comprehension? Evidence from fMRI. *Brain, 130 (10),* 2494-2507. doi: 10.1093/brain/awm170.

Coltheart, M. (1981). The MRC psycholinguistic database. *The Quarterly Journal of Experimental Psychology Section A, 33 (4),* 497-505. doi: 10.1080/14640748108400805.

Cousineau D. (2005). Confidence intervals in within-subject designs: A simpler solution to Loftus and Masson's method. *Tutorials in Quantitative Methods for Psychology, 1 (1),* 42–45.

Davis, M. H., Coleman, M. R., Absalom, A. R., Rodd, J. M., Johnsrude, I. S., Matta, B. F., … Menon, D. K. (2007). Dissociating speech perception and comprehension at reduced levels of awareness. *Proceedings of the National Academy of Sciences of the United States of America, 104 (41),* 16032-16037. doi: 10.1073/pnas.0701309104.

Davis, G. A., & Wilcox, M. J. (1985). *Adult aphasia rehabilitation: Applied pragmatics*. San Diego: College-Hill Press.

De Renzi, A., & Vignolo, L. A. (1962). Token test: A sensitive test to detect receptive disturbances in aphasics. *Brain: A Journal of Neurology, 85 (4),* 665-678. doi: 10.1093/brain/85.4.665.

Difrancesco, S., Pulvermüller, F., & Mohr, B. (2012). Intensive Language Action Therapy (ILAT): The Methods. *Aphasiology, 26 (11),* 1317-1351. doi: 10.1080/02687038.2012.705815.

Elman, R. J., & Bernstein-Ellis, E. (1999). The efficacy of group communication treatment in adults with chronic aphasia. *Journal of Speech, Language, and Hearing Research, 42 (2),* 411-419.

Engelter, S. T., Gostynski, M., Papa, S., Frei, M., Born, C., Ajdacic-Gross, V., … Lyrer, P. A. (2006). Epidemiology of aphasia attributable to first ischemic stroke: Incidence, Severity, Fluency, Etiology, and Thrombolysis. *Stroke, 37 (6),* 1379 – 1384. doi: 10.1161/01.STR.0000221815.64093.8c.

Fadiga, L., Craighero, L., Buccino, G., & Rizzolatti, G. (2002). Speech listening specifically modulates the excitability of tongue muscles: a TMS study. *European Journal of Neuroscience, 15 (2),* 399-402. doi: 10.1046/j.0953-816x.2001.01874.x.

Faroqi-Shah, Y., & Virion, C. R. (2009). Constraint-induced language therapy for agrammatism: Role of grammaticality constraints. *Aphasiology, 23 (7-8),* 977-988. doi: 10.1080/02687030802642036.

Gainotti, G. (2000). What the locus of brain lesion tells us about the nature of the cognitive defect underlying category-specific disorders: A review. *Cortex, 36 (4)*, 539-559. doi: 10.1016/S0010-9452(08)70537-9.

González, J., Barros- Loscertales, A., Pulvermüller, F., Meseguer, V., Sanjuán, A., Belloch, V., & Ávila, C. (2006). Reading *cinnamon* activates olfactory brain regions. *NeuroImage, 32 (2),* 906-912. doi: 10.1016/j.neuroimage.2006.03.037.

Goodglass, K., & Kaplan, E. (1972). *Assessment of aphasia and related disorders*. Philadelphia: Lea and Febiger.

Goral, M., & Kempler, D. (2009). Training verb production in communicative context: Evidence from a person with chronic non-fluent aphasia. *Aphasiology, 23 (12),* 1383-1397. doi: 10.1080/02687030802235203.

Grindrod, C. M., & Baum, S. R. (2003). Sensitivity to local sentence context information in lexical ambiguity resolution: Evidence from left- and right-hemisphere-damaged patients. *Brain and Language, 85 (3),* 503-523. doi: 10.1016/S0093-934X(03)00072-5.

Hall, D. A., Haggard, M. P., Akeroyd, M. A., Palmer, A. R., Summerfield, A. Q., Elliott, M. R., … Bowtell, R. W. (1999). “Sparse” temporal sampling in auditory fMRI. *Human Brain Mapping, 7 (3),* 213 – 223. doi: 10.1002/(SICI)1097-0193(1999)7:3<213::AID-HBM5>3.0.CO;2-N.

Hauk, O., Johnsrude, I., & Pulvermüller, F. (2004). Somatotopic representation of action words in human motor and premotor cortex. *Neuron, 41 (2)*, 301-307. doi: 10.1016/S0896-6273(03)00838-9.

Hebb, D. O. (1949). *The organisation of behavior: A neurophysiological theory*. New York: Wiley.

Heiss, W. D., & Thiel, A. (2006). A proposed regional hierarchy in recovery of post-stroke aphasia. *Brain and Language, 98 (1),* 118-123. doi: 10.1016/j.bandl.2006.02.002.

Huber, H., Poeck, K., Weniger, D., & Willmes, K. (1983). *Aachener Aphasie Test.* Göttingen: Hogrefe.

Kelly, H., Brady, M. C., & Enderby, P. (2010). Speech and language therapy for aphasia following stroke. *Cochrane Database of Systematic Reviews, Issue 7.* doi: 10.1002/14651858.CD000425.pub2.

Kemmerer, D., Rudrauf, D., Manzel, K., & Tranel, D. (2012). Behavioral patterns and lesion sites associated with impaired processing of lexical and conceptual knowledge of actions. *Cortex, 48 (7),* 826-848. doi: 10.1016/j.cortex.2010.11.001.

Kempler, D., & Goral, M. (2011). A comparison of drill- and communication-based treatment for aphasia. *Aphasiology, 25 (11),* 1327-1346. doi: 10.1080/02687038.2011.599364.

Kiefer, M., Sim, E.J., Herrnberger, B., Grothe, J., & Hoenig, K. (2008). The sound of concepts: Four markers for a link between auditory and conceptual brain systems. *The Journal of Neuroscience, 28 (47),* 12224-12230. doi: 10.1523/JNEUROSCI.3579-08.2008.

Kirmess, M., & Maher, L. M. (2010). Constraint induced language therapy in early aphasia rehabilitation. *Aphasiology, 24 (6-8),* 725-736. doi: 10.1080/02687030903437682.

Klebic, J., Salihovic, N., Softic, R., & Salihovic, D. (2011). Aphasia disorders outcome after stroke. *Medical Archives, 65 (5),* 283 - 286. doi: 10.5455/medarh.2011.65.283-286.

Kolk, H., & Heeschen, C. (1990). Adaptation symptoms and impairment symptoms in Broca's aphasia. *Aphasiology, 4 (3)*, 221-231. doi: 10.1080/02687039008249075.

Kurland, J., Pulvermüller, F., Silva, N., Burke, K., & Andrianopoulos, M. (2012). Constrained versus unconstrained intensive language therapy in two individuals with chronic, moderate-to-severe aphasia and apraxia of speech: Behavioral and fMRI outcomes. *American Journal of Speech-Language Pathology, 21 (2),* S65-S87. doi: 10.1044/1058-0360(2012/11-0113).

Maher, L. M., Kendall, D., Swearengin, J. A., Rodriguez, A., Leon, S. A., Pingel, K., … Gonzalez Rothi, L. J. (2006). A pilot study of use-dependent learning in the context of constraint induced language therapy. *Journal of the International Neuropsychological Society, 12 (6),* 843-852. doi: 10.1017/S1355617706061029.

Meinzer, M., Djundja, D., Barthel, G., Elbert, T., & Rockstroh, B. (2005). Long-term stability of improved language functions in chronic aphasia after constraint-induced aphasia therapy. *Stroke, 36 (7),* 1462-1466. doi: 10.1161/01.STR.0000169941.29831.2a.

Meinzer, M., Elbert, T., Wienbruch, C., Djundja, D., Barthel, G., & Rockstroh, B. (2004). Intensive language training enhances brain plasticity in chronic aphasia. *BMC Biology, 2:* 20. doi: 10.1186/1741-7007-2-20.

Meinzer, M., Flaisch, T., Breitenstein, C., Wienbruch, C., Elbert, T., & Rockstroh, B. (2008). Functional re-recruitment of dysfunctional brain areas predicts language recovery in chronic aphasia. *NeuroImage, 39 (4),* 2038-2046. doi: 10.1016/j.neuroimage.2007.10.008.

Meinzer, M., Flaisch, T., Obleser, J., Assadollahi, R., Djundja, D., Barthel, G., & Rockstroh, B. (2006). Brain regions essential for improved lexical access in an aged aphasic patient: A case report. *BMC Neurology, 6 (28).* doi: 10.1186/1471-2377-6-28.

Meinzer, M., Rodriguez, A. D., Gonzalez Rothi, L. J. (2012). First decade of research on constrained-induced treatment approaches for aphasia rehabilitation. *Archives of Physical Medicine and Rehabilitation, 93 (1),* S35-S45. doi: 10.1016/j.apmr.2011.06.040.

Meinzer, M., Streiftau, S. & Rockstroh, B. (2007). Intensive language training in the rehabilitation of chronic aphasia: Efficient training by laypersons. *Journal of the International Neuropsychological Society, 13 (5),* 846-853. doi: 10.1017/S1355617707071111.

Miceli, G., Silveri, M., Villa, G. & Caramazza, A. (1984). On the basis for the agrammatic's difficulty in producing main verbs. *Cortex, 20 (2),* 207-220. doi: 10.1016/S0010-9452(84)80038-6.

Mummery, C. J., Ashburner, J., Scott, S. K., & Wise, R. J. S. (1999). Functional neuroimaging of speech perception in six normal and two aphasic subjects. *Journal of the Acoustic Society of America, 106 (1),* 449 – 457. doi: 10.1121/1.427068.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9 (1),* 97 – 113. doi: 10.1016/0028-3932(71)90067-4.

Pederson, P. M., Vinter, K., & Olsen, T. S. (2004). Aphasia after stroke: Type, severity and prognosis. The Copenhagen Aphasia Study. *Cerebrovascular Diseases,17 (1),* 35 – 43. doi: 10.1159/000073896.

Pulvermüller, F. (1999). Words in the brain's language. *Behavioral and Brain Sciences, 22 (2),* 253-336. doi: 10.1017/S0140525X9900182X.

Pulvermüller, F. (2001). Brain reflections of words and their meaning. *Trends in Cognitive Sciences, 5 (12),* 517-524. doi: 10.1016/S1364-6613(00)01803-9.

Pulvermüller, F. (2005). Brain mechanisms linking language and action. *Nature Reviews Neuroscience, 6 (7)*, 576-582. doi: 10.1038/nrn1706.

Pulvermüller, F. (2010). Brain embodiment of syntax and grammar: Discrete combinatorial mechanisms spelt out in neuronal circuits. *Brain and Language, 112 (3)*, 167-179. doi: 10.1016/j.bandl.2009.08.002.

Pulvermüller, F., & Berthier, M. L. (2008). Aphasia therapy on a neuroscience basis. *Aphasiology, 22 (6),* 563-599. doi: 10.1080/02687030701612213.

Pulvermüller, F., & Fadiga, L. (2010). Active perception: sensorimotor circuits as a cortical basis for language. *Nature Reviews Neuroscience, 11 (5)*, 351-360. doi: 10.1038/nrn2811.

Pulvermüller, F., & Hauk, O. (2006). Category-specific conceptual processing of color and form in left fronto-temporal cortex. *Cerebral Cortex, 16 (8)*, 1193-1201. doi: 10.1093/cercor/bhj060.

Pulvermüller, F., Hauk, O., Nikulin, V. V., & Ilmoniemi, R. J. (2005a). Functional links between motor and language systems. *European Journal of Neuroscience, 21 (3),* 793-797. doi: 10.1111/j.1460-9568.2005.03900.x.

Pulvermüller, F., Hauk, O., Zohsel, K., Neininger, B., & Mohr, B. (2005b). Therapy-related reorganization of language in both hemispheres of patients with chronic aphasia. *NeuroImage, 28 (2),* 481-489. doi: 10.1016/j.neuroimage.2005.06.038.

Pulvermüller, F., Kiff, J., & Shtyrov, Y. (2012). Can language-action links explain language laterality?: An ERP study of perceptual and articulatory learning of novel pseudowords. *Cortex, 48 (7),* 871-881. doi: 10.1016/j.cortex.2011.02.006.

Pulvermüller, F., Neininger, B., Elbert, T., Mohr, B., Rockstroh, B., Koebbel, P., & Taub, E. (2001). Constraint-Induced therapy of chronic aphasia after stroke. *Stroke, 32 (7),* 1621-1626. doi: 10.1161/01.STR.32.7.1621.

Pulvermüller, F., & Roth, V. M. (1991). Communicative aphasia treatment as a further development of PACE therapy. *Aphasiology, 5 (1),* 39-50. doi: 10.1080/02687039108248518.

Pulvermüller, F. & Schönle, P. W. (1993). Behavioral and neuronal changes during treatment of mixed transcortical aphasia: A case study. *Cognition, 48 (2)*, 139-161. doi: 10.1016/0010-0277(93)90028-T.

Pulvermüller, F., Shtyrov, Y., & Ilmoniemi, R. J. (2003). Spatiotemporal dynamics of neural language processing: an MEG study using minimum-norm current estimates. *NeuroImage, 20 (2),* 1020-1025. doi: 10.1016/S1053-8119(03)00356-2.

Richter, M., Miltner, W. H. R., & Straube, T. (2008). Association between therapy outcome and right-hemispheric activation in chronic aphasia. *Brain, 131 (5),* 1391-1401. doi: 10.1093/brain/awn043.

Rizzolatti, G., & Sinigaglia, C. (2010). The functional role of the parieto-frontal mirror circuit: Interpretations and misinterpretations. *Nature Reviews Neuroscience, 11 (4),* 264-274. doi: 10.1038/nrn2805.

Robey, R. R. (1998). A meta-analysis of clinical outcomes in the treatment of aphasia. *Journal of Speech, Language and Hearing Research, 41 (1),* 172 – 187.

Rodd, J. M., Cutrin, B. L., Kirsch, H., Millar, A., & Davis, M. H. (2013). Long-term priming of the meanings of ambiguous words. *Journal of Memory and Language, 68 (2),* 180-198. doi: 10.1016/j.jml.2012.08.002.

Rodd, J. M., Davis, M. H., & Johnsrude, I. S. (2005). The neural mechanisms of speech comprehension: fMRI studies of semantic ambiguity. *Cerebral Cortex, 15 (8),* 1261 – 1269. doi: 10.1093/cercor/bhi009.

Sarno, M. T., & Levita, E. (1979). Recovery in treated aphasia in the first year post-stroke. *Stroke, 10 (6),* 663 – 670. doi: 10.1161/01.STR.10.6.663.

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., & Weiller, C. (2006). Dynamics of language reorganization after stroke. *Brain, 129 (6),* 1371- 1384. doi: 10.1093/brain/awl090.

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime user's guide.* Pittsburgh: Psychology Software Tools Inc.

Seghier, M. L., Ramlackhansingh, A., Crinion, J., Leff, A. P., & Price, C. J. (2008). Lesion identification using unified segmentation-normalisation models and fuzzy clustering. *NeuroImage, 41 (4),* 1253-1266. doi: 10.1016/j.neuroimage.2008.03.028.

Szaflarski, J. P., Ball, A. L., Grether, S., Al-fwaress, F., Griffith, N. M., Neils-Strunjas, J., … Reichhardt, R. (2008). Constraint-induced aphasia therapy stimulates language recovery in patients with chronic aphasia after ischemic stroke. *Medical Science Monitor, 14 (5),* CR243-CR250.

Taub, E. (2004). Harnessing brain plasticity through behavioral techniques to produce new treatments in neurorehabilitation. *American Psychologist, 59 (8),* 692-704. doi: 10.1037/0003-066X.59.8.692.

Taub, E., Crago, J.E., & Uswatte, G. (1998). Constraint-induced movement therapy: a new approach to treatment in physical rehabilitation. *Rehabilitation Psychology, 43 (2),* 152-170. doi: 10.1037/0090-5550.43.2.152.

Taub, E., Uswatte, G., & Elbert, T. (2002). New treatments in neurorehabilitation founded on basic research. *Nature Reviews Neuroscience, 3 (3),* 228-236. doi: 10.1038/nrn754.

Taub, E., Uswatte, G., & Pidikiti, R. (1999). Constraint-induced movement therapy: A new family of techniques with broad application to physical rehabilitation- A clinical review. *Journal of Rehabilitation Research and Development, 38 (3),* 237-251.

Tranel, D., & Kemmerer, D. (2004). Neuroanatomical correlates of locative prepositions. *Cognitive Neuropsychology, 21 (7),* 719–749. doi: 10.1080/02643290342000627.

Tsumoto, T. (1992). Long-term potentiation and long-term depression in the neocortex. *Progress in Neurobiology, 39 (2),* 209-228. doi: 10.1016/0301-0082(92)90011-3.

Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology, 76 (20),* 1726 – 1734. doi: 10.1212/WNL.0b013e31821a44c1.

Vitello, S., Devlin, J. T., & Rodd, J. M. (2012). TMS to pars triangularis affects the semantic processing of sentences. Poster presented at the Neurobiology of Language Conference, San Sebastian, Spain, 25th – 27th October.

Vuong, L. C., & Martin, R. C. (2011). LIFG-based attentional control and the resolution of lexical ambiguities in sentence context. *Brain & Language, 116 (1),* 22-32. doi: 10.1016/j.bandl.2010.09.012.

Watkins, K. E., Strafella, A. P., & Paus, T. (2003). Seeing and hearing speech excites the motor system involved in speech production. *Neuropsychologia, 41 (8),* 989-994. doi: 10.1016/S0028-3932(02)00316-0.

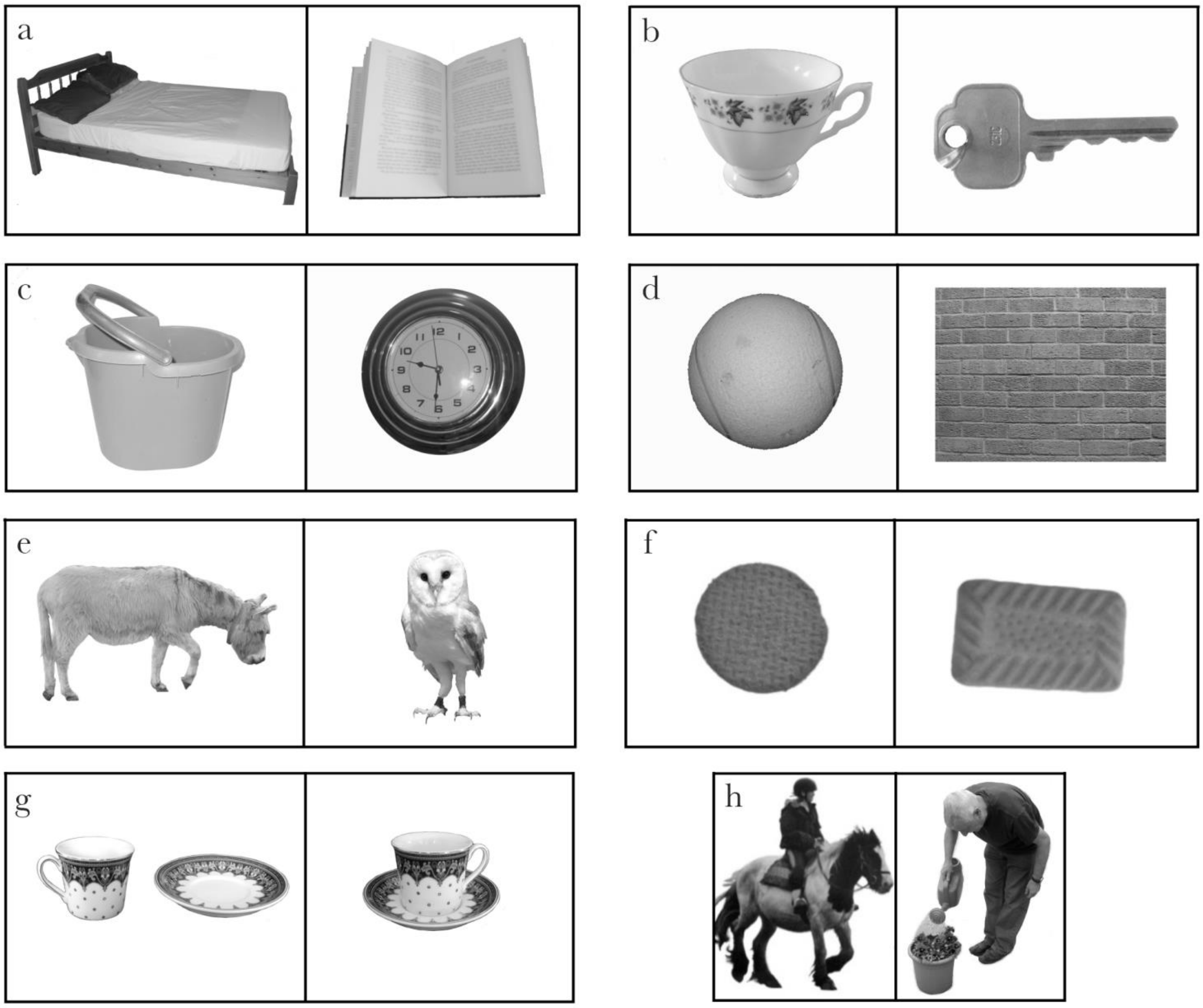
Wittgenstein, L. (1953). *Philosophical Investigations*. Blackwell Publishers, Oxford.

Zempleni, M., Renken, R., Hoeks, J. C. J., Hoogduin, J. M., & Stowe, L. A. (2007). Semantic ambiguity processing in sentence context: Evidence from event-related fMRI. *NeuroImage, 34 (3),* 1270-1279. doi: 10.1016/j.neuroimage.2006.09.048.

APPENDICES

APPENDIX 1

EXAMPLES OF MATERIALS FROM ILAT. CARDS DEPICTED FROM EACH OF THE EIGHT CATEGORIES: A) HIGH FREQUENCY; B) MEDIUM FREQUENCY; C) LOW FREQUENCY: D) MINIMAL PAIRS; E) SEMANTIC CATEGORIES – ANIMALS; F) OBJECTS WHICH DIFFER BY ATTRIBUTES: ‘CIRCLE BISCUIT’ AND ‘SQUARE BISCUIT’; G) PREPOSITIONS; H) ACTIONS.


a
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APPENDIX 2

ANNOTATED EXAMPLE OF THERAPY SCORING SHEET

As described in the main text, the progression of the LAG protocol can be organised in the following way:

a) Date/ Number of Game/ Round/ Speech act/turn: Therapy Day 2/ Game 3

b) Type of LAG: Planning

c) Progression level/ Materials: Action set, Materials set 8

Progression level/ Rules: JR: no politeness, full sentences

LS: no politeness, **no** full sentences

In addition to keeping track of the type of game played, each move a player makes can also be recorded and scored. These scores are then used to guide therapists in determining further rules and progression for players. As an example, we will illustrate how a speech act could be scored using example transcript 4 from the main text. In this LAG, the production of explicit action description had been defined as a specific goal for participant A:

> A: "Umm (2s) right (2s) umm I have here a (3s) hmm a (2s) big long rope and attached to that I've got some err (3s) climbing frame, climbing frame and I'd like to know would you like to please (1s) the (2s) the climbing frame, the (2s) rope and me
>
> Co-player: So you're planning a climbing activity tomorrow and are asking if I would like to join you climbing a wall? Yes?
>
> A: Yes, yes that's right

d) Speech Act (or attempt) type: A provides the background knowledge for an action proposal by informing B about the availability of climbing tools by saying "I have here a big long rope and attached to that I've got some climbing frame". A makes an attempt to propose joint climbing by uttering the string "I'd like to know would you like to please the climbing frame, the rope and me".

e) Utterance Type: full sentence to describe climbing tools; string with syntactic deviance and politeness formula for making the proposal.

f) Appropriateness of Speech Act - fully functional (3), functional but with minor delay or error (2), minor functional contribution (1), not functional at all (0): Appropriate performance for providing background knowledge. Nonstandard utterance missing an action-descriptive term used for making a proposal. This is ambiguous and requires clarification. As explicit action descriptors were defined as target of the LAG, the score is 1 (without such a constraint, the score would be 2, as communicative success is reached).

APPENDIX 3

PARTICIPANT INFORMATION SHEET

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Patient Information Sheet

Language therapy and recovery in chronic aphasia

Part 1

We would like to invite you to take part in our research study. Before you decide, we would like you to understand what the study is about and what it involves for you. We will go through all the information with you in detail and answer any questions you may have.

Part 1 of this information sheet will give you some details about the experiment itself and Part 2 gives you more information about how the study is conducted.

The principal aims of this research are to test if patients with aphasia benefit equally well from Intensive Language Action Aphasia Therapy (ILAT), also known as constraint-induced aphasia therapy and intensive conventional speech and language therapy.
We will also look at the brain changes that occur after a two-week period of intensive speech therapy. This will be done by measuring electrical brain activity and blood flow changes in the brain.

i. What is the purpose of this study?

Stroke represents a major health problem worldwide and is a frequent cause of long term disability, often leading to aphasia, a chronic condition where patients have mild to severe speech and language impairments.

Access to treatment for speech and language impairments, especially for chronic patients is very limited due to a number of factors. In this research, we wish to compare the effects a new intensive form of aphasia therapy, ILAT, with the effects of conventional therapy. We will use two brain scanning methods, electroencephalography/magneto-encephalography (EEG/MEG) and functional magnetic resonance imaging (fMRI) to measure brain activity and any changes in the brain due to intensive therapy.

We hope to establish a short term and cost effective aphasia therapy which is easy to administer and could potentially improve the quality of life for many stroke sufferers.

ii. Why have I been invited to take part?

You have been chosen to participate in this study because you are an adult who has suffered a stroke affecting the left side of your brain, resulting in speech and language problems. We will test a maximum of 50 adults who suffer from aphasia in this study. You will also be right handed (you used the right hand for most tasks before the stroke) and you will be a native speaker of English.

You should not take part in the fMRI scans if you have a pacemaker or any other metallic objects which are permanently attached to your body (e.g. surgical clips). You must also consent to remove any metallic objects (e.g. earrings, watches, piercings) during scanning. You will only be scanned if you do not suffer from claustrophobia, severe epilepsy and if you are not wheelchair bound.

iii. Do I have to take part?

Participation in this study is voluntary and you do not have to take part. We will describe each part of the study for you in detail. If you decide to take part, we will ask you to sign a consent form. You can withdraw from participating in this study at any point without giving a reason why and without any penalty. If you choose to withdraw, your data will be destroyed immediately.

iv. What will I be asked to do if I take part?

If you agree to take part in this study, you will participate in the following procedure (please see also visual chart of timeline of research at the end of this information sheet):

You will be invited to come to the Medical Research Council, Cognition and Brain Sciences Unit (MRC-CBU), Cambridge. **You are welcome to bring along a friend/relative to these sessions if you feel more comfortable**. **If you wish, your relative/friend can also assist you with filling out a questionnaire about your use of language in daily activities.**

Day 1:

We will test your handedness with a questionnaire and we will assess your language abilities using a standard test. There will also be a short task on a computer, where your will listen to a number of short sentences and then decide out of two words presented on screen fits best with the meaning of the sentence. This session will last for about an hour. Then, we will ask you to listen to words and nonwords (sound which do not make sense) while your electrical brain activity is measured using EEG/MEG. The recording will take approximately 40 minutes.

Day 2:

On the next day, we will invite you to come back to the MRC-CBU. This time, we will do another language test and we will ask you to fill out a questionnaire about your communication in daily activities. We will also ask you questions about whether you have any metallic objects implanted, such as a pacemaker. We will need this information before we ask you to participate in fMRI scanning. The language task and questionnaires will take approximately 30 minutes.

We will then ask you to participate in fMRI brain scanning. During brain scanning, we will ask you to listen to words and nonwords and to a story. After a break, we will ask you to silently read words which will come up on a screen. If for any reason you may be unable to be scanned, we would instead ask you to take part in a short computer task.

During this, you will listen to the same stimuli as those played in the scanner and your task is to judge whether or not what you hear makes sense.

There will be many breaks throughout these testing and scanning sessions. However if you should become too tired over these two days, it is possible to postpone the assessments and computer tasks to a 3rd day.

This procedure will be repeated after termination of the therapy. You will also be asked to take part in a third scanning session. This will be either three months before the start of the therapy or six months after the therapy has ended.

You have the right to withdraw from the study at any point in time without giving reasons why. Although EEG/MEG and fMRI do not cause any harm to the body, it is very important to let us know if you feel any discomfort. We will then stop the scanning immediately.

EEG/MEG testing
EEG/MEG records the small changes in electric/magnetic fields at the surface of the head generated by nerve cell activity inside the brain. In the MRC Cognition and Brain Science unit this technique is regularly used for measuring brain activity related to human perception and cognition. If you agree to take part in this session, you will first be fitted with a cap which has some electrodes positioned on it. This cap is used to pick up the electrical signals your brain is constantly producing. The top of your head will be positioned within a helmet-like device that can measure the very weak magnetic fields that are constantly produced in your brain. Possibly, a few sensors will also be attached to your forehead with tape. This will not cause any discomfort. We will use these sensors to measure the position from your head to the helmet. This preparation will take ca. 30-40 min.

During the recording, you will be seated in a chair while you will hear words and non-words (these are nonsense sounds which are similar to words) but you should try and ignore these. During this task, you will be asked to sit as quietly as possible and to avoid any movements. There will be several breaks during the experiments where you can move. The session will last ca. 30-40 min. This procedure is not painful at all. In case you should feel any discomfort, we will stop the session immediately. Before we measure your brain activity, we will show you how the machine works and you can decide if you would like to participate or not.

fMRI testing
fMRI is a device used by doctors or other medical personnel to map brain activity. An fMRI machine is a big, bed-sized, expensive piece of medical equipment that generates high magnetic fields. To enter the machine, a patient lies on a horizontal bed-like platform which slides into a cylindrical cavity. The patient's head is scanned magnetically from all sides.
(For more information on MRI, please see separate "MRI information" leaflet).

Whilst being scanned, you will be asked to silently read words displayed on a computer screen. All words will be short, common words. After the task, you will be given a recognition test, consisting of a list of words presented previously and new words. This is done to ensure that you were engaged in the task. During this task, you will be asked to lay as still as possible. There will be several breaks during the experiments. There will a long break and after that, you will hear words and non-words. You will be asked to listen to this. After another long break, you will hear a short story. You will be asked to carefully listen to the story. After the scanning, you will be asked a question about this story.

The session will last no longer than an hour and there will be several breaks during this hour. This procedure is not painful at all. In case you should feel any discomfort, we will stop the session immediately.

Aphasia Therapy

You will randomly be assigned to either conventional aphasia therapy or ILAT. Both treatments will consist of 3 hours of therapy per day for 10 consecutive workdays. Both treatments will be delivered in small groups of 3-4 patients with a therapist and co-therapist and will take place at Anglia Ruskin University, Cambridge.

Conventional speech and language therapy will involve training the specific language functions that you have difficulty with (e.g. naming, repetition, sentence completion, etc.).

ILAT will involve card games, such as requesting an object on a card or responding to a request another player makes.

v. Expenses and payments

We will not be able to reimbursed any travel expenses involved in this study and these will need to be paid fully by you.
Complimentary refreshments will be provided for you during all therapy and testing sessions.

You will receive two weeks of speech and language therapy (a total of 30 hours) free of charge. This will either be intensive language action therapy (ILAT) or intensive conventional aphasia therapy.

vi. What will I have to do?

We ask that you are willing and able to participate in approximately 3 hours of therapy a day for 10 consecutive work days. In addition, we ask that you are willing to undergo a series of brain scanning sessions and language assessments in order for us to measure any changes that may occur do to language therapy.

vii. What are the possible disadvantages and risks of taking part?

It may be possible that you get tired and/or get dry eyes during brain scanning sessions. If that happens, please let the researcher know, so that you can have a break or withdraw from the experiment, if necessary.

Agreement to participate in this research should not compromise your legal rights should something go wrong.

viii. What are the possible benefits of taking part?

You will receive two weeks (3 hours per day) of intensive speech and language therapy free of charge. This will either be ILAT or conventional therapy. Both these methods have proven to be effective in improving language abilities in patients with chronic aphasia.
The study will help to further improve existing aphasia treatments and will help to understand how therapy can improve recovery after stroke.

ix. What will happen when the research study stops?

After the study stops, we will analyze the data and will send you a report of the outcome of this research, if you wish.
We will not be able to provide any further therapy sessions after termination of the study, but we hope that the therapy we offer has long-lasting benefits and will improve your quality of life.

If the information in Part 1 has interested you and you are considering participating in our study, please read the additional information in Part 2 before you make any decisions.

Part 2

i. What if relevant new information becomes available?

Sometimes we get new information about the treatment we are studying. If this happens we will tell you and discuss whether you should continue in the study.

ii. What will happen if I don't want to carry on with the study?

If you do decide to take part, you can withdraw from participating in this study at any point without giving a reason why and without any penalty. If you choose to withdraw, your data will be destroyed immediately.

iii. What if there is a problem or something goes wrong?

If you have a concern about any aspect of this study, please speak to the researchers who will do their best to answer your questions (please see contact details below). If any concerns can not be resolved by the research team and in case you may wish to make a formal complaint, please contact Prof. Michael Cole, Director of Research, Anglia Ruskin University, Cambridge. Telephone number: 0845 196 2525. Email address: Michael.Cole@anglia.ac.uk.
Anglia Ruskin University indemnity policies apply for this research project.

iv. Will my taking part in this study be kept confidential?

The data will be confidentially and anonymously stored on a computer and a locked filing cabinet at the Department of Psychology, Anglia Ruskin University and at the Medical Research Council, Cognition and Brain Sciences Unit. You will be assigned a number and your data will be stored without your name. Only the research team will have access to the data. Once the data have been published, they will be destroyed.

v. Involvement of the GP

We will ask your permission to contact your GP to inform him/her about your participation in this study and we will ask him/her to provide information about your stroke and the resulting brain lesion. We will ask for a copy of the referral letter from the hospital and/or neurologist. If an MRI or CT scan is available, we will ask if it was possible to obtain a copy as well. In case your GP charges you a fee for providing this information, we will reimburse the fees up to a maximum of £50.

vi. What will happen to the results of the research study?

We aim to publish results of this study in scientific journals and at research conferences. Please let us know if you wish to receive a copy of the report on this study as well as copies of publications and we will send them to you after termination of the study.

vii. Who has reviewed the study?

Before any research goes ahead, it has to be checked by a Research Ethics Committee. They make sure that the research is fair. This project has been approved by the Cambridgeshire 1 Research Ethics Committee.

viii. Who is conducting the study?

This study is conducted by Dr. Bettina Mohr (Reader in Psychology), Stephanie Difrancesco and Karen Harrington (PhD students) at the Department of Psychology, Anglia Ruskin University and Prof. Friedemann Pulvermüller, Medical Research Council, Cognition and Brain Sciences Unit, Cambridge.

If you would like further information or would like to discuss any aspect of this study, then please contact either of the following:

Dr. Bettina Mohr
Anglia Ruskin University
Department of Psychology
East Road
Cambridge CB1 1PT
Tel: 0845 196 2258
bettina.mohr@anglia.ac.uk

Stephanie Difrancesco
Anglia Ruskin University
Department of Psychology
East Road
Cambridge CB1 1PT
Tel: 0845 196 2794
stephanie.difrancesco@student.anglia.ac.uk

YOU WILL BE GIVEN A COPY OF THIS TO KEEP,
TOGETHER WITH A COPY OF YOUR CONSENT FORM

This is a picture of the EEG/MEG machine which we going to use in our study. All participants will be seated underneath the helmet-like device. The helmet will only surround the head, but does not touch it.

This is a picture of the fMRI scanner which we are going to use in the study. All participants will be placed on the bed-like device during brain scanning.

APPENDIX 4

PARTICIPANT CONSENT FORM

Anglia Ruskin University

stephanie.difrancesco@student.anglia.ac.uk
T: 0845 196 2794
M: 07852 732 680

Patient Identification Number:

CONSENT FORM

Title of Project: **Cortical Reorganisation in Chronic Aphasia**

Name of Participant:

Main investigators and contact details:
Stephanie Difrancesco (Stephanie.difrancesco@student.anglia.ac.uk, 0845-196-2794)
Dr. Bettina Mohr (Bettina.mohr@anglia.ac.uk, 0845-196-2258)
Department of Psychology, Anglia Ruskin University, Cambridge

Members of the research team: Prof. Friedemann Pulvermüller, Karen Harrington

Please initial box

1. I confirm that I have read and understood the information sheet dated 16.12.2011 for the above study. I have had the opportunity to ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reasons, without my legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by members of the research team above. I give permission for these individuals to have access to my records. ☐

4. I agree to my GP being informed of my participation in this study. ☐

5. I agree to take part in the above study. ☐

Data Protection: I agree to the University[1] processing personal data which I have supplied. I agree to the processing of such data for any purposes connected with the Research Project as outlined to me.

Name of participant
(print)………………………….Signed………………..….Date………………

Name of witness
(print)……………………………..Signed………………..….Date…………..

YOU WILL BE GIVEN A COPY OF THIS FORM TO KEEP

If you wish to withdraw from the research, please complete the form below and return to one of the main investigators named above.

Title of Project: **Cortical Reorganisation in Chronic Aphasia**

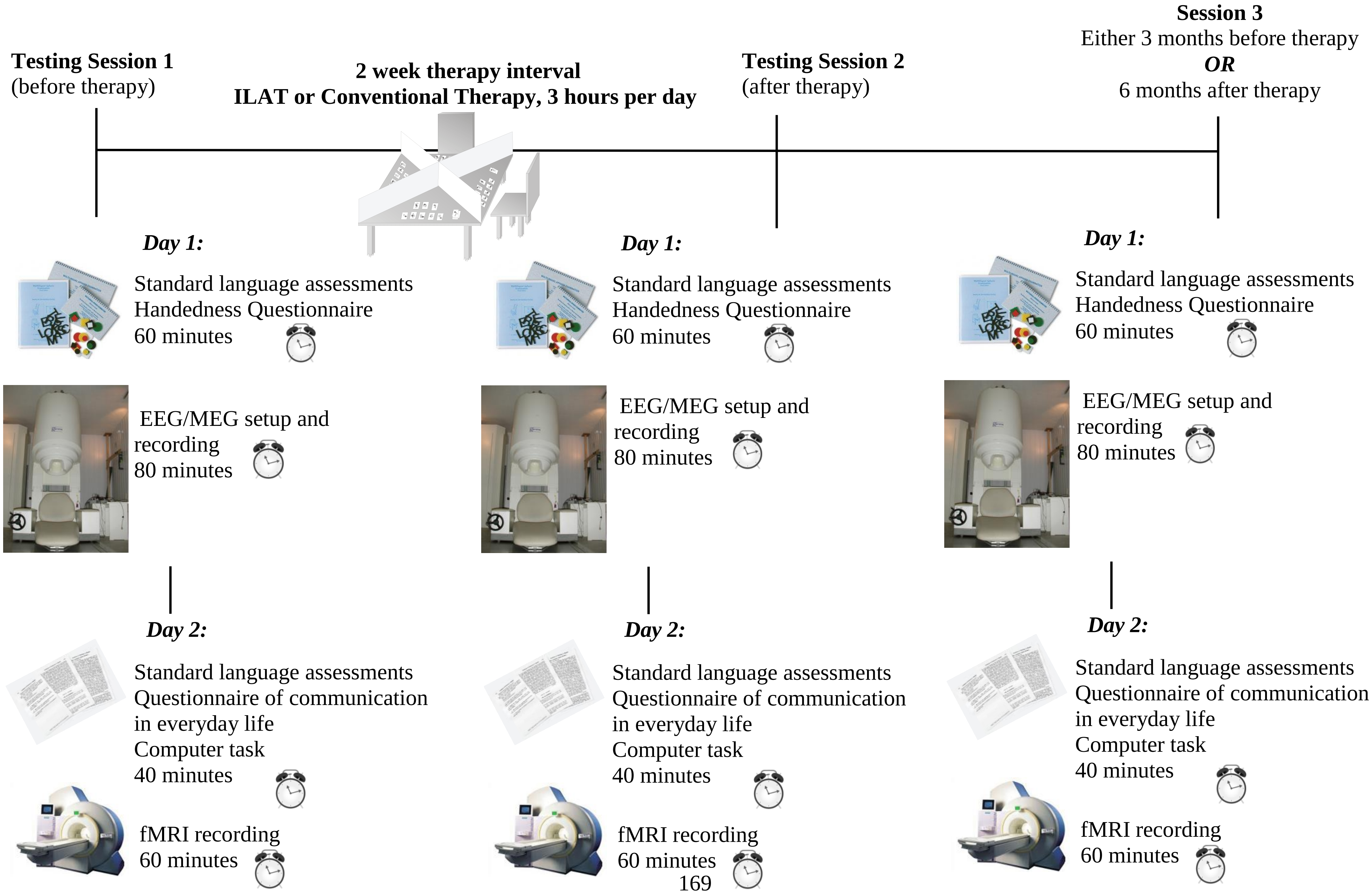
I WISH TO WITHDRAW FROM THIS STUDY

Name: ……………………………………. Date: …..……………..

Signed: ……………………………..….. Date: …………………

APPENDIX 5

VISUAL TIMELINE OF STUDY PROTOCOL


Testing Session 1
(before therapy)
2 week therapy interval
ILAT or Conventional Therapy, 3 hours per day
Testing Session 2
(after therapy)
Session 3
Either 3 months before therapy
OR
6 months after therapy
Day 1:
Standard language assessments
Handedness Questionnaire
60 minutes
EEG/MEG setup and
recording
80 minutes
Day 2:
Standard language assessments
Questionnaire of communication
in everyday life
Computer task
40 minutes
fMRI recording
60 minutes
Day 1:
Standard language assessments
Handedness Questionnaire
60 minutes
EEG/MEG setup and
recording
80 minutes
Day 2:
Standard language assessments
Questionnaire of communication
in everyday life
Computer task
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EEG/MEG setup and
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Day 2:
Standard language assessments
Questionnaire of communication
in everyday life
Computer task
40 minutes
fMRI recording
60 minutes

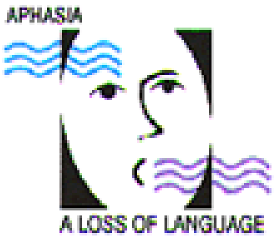
APPENDIX 6

LEAFLET DISTRIBUTED TO SELF-HELP GROUPS

Information about intensive language action aphasia therapy (ILAT)

What is aphasia?

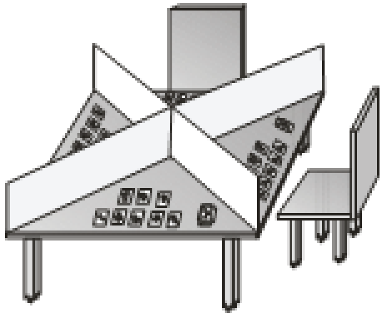
After having a stroke, many people experience problems with speaking and understanding language, as well as with reading and writing. This is called aphasia. Often, these problems improve over time, but many patients experience long-term communication problems- chronic aphasia.



Most patients receive language therapy immediately after having suffered a stroke. Access to language treatment for chronic patients however is very limited, with most people no longer having access to therapy despite having persistent problems with speaking and understanding language.

What is intensive language action aphasia therapy (ILAT)?

ILAT is a relatively new form of language therapy where people with aphasia re-learn to use their remaining language abilities to verbally communicate more efficiently. It is carried out in a group setting of 3-4 patients and 2 therapists with around 3 hours of daily training over a period of two consecutive weeks. The therapy involves card games where players practice communication skills which are relevant for everyday life, such as *making requests* or *planning an activity*.



This is what a typical ILAT setting looks like. Group members sit around a table. They have cards to practice so-called "language games". Barriers are used, so that players can't see other players' cards.

Our research project

We are a team of neuroscientists and psychologists who wish to compare the effects of ILAT with the effects of conventional speech therapy. We are looking at the improvements of language after therapy and we want to know how the brain changes due to therapy.

The research project will last for 6 months, however participation is not continuous over this time. The therapy involves two weeks of intensive ILAT or conventional therapy, administered for around 3 hours per day. In order to measure any changes in language abilities, language tests and brain scanning sessions will be carried out at three points during the study: immediately before and immediately after therapy and six months after therapy has terminated.

Brain scanning (neuroimaging) sessions will involve functional magnetic resonance imaging (fMRI-pictured) and magneto-electroencephalography (EEG/MEG).

Who can participate in the project?

Anybody can participate who:

- has long-term language problems at least one year after stroke (chronic aphasia)
- is willing to participate in speech and language therapy for 3 hours per day for 2 consecutive weeks
- is willing to be tested for speech and language problems before and after the therapy
- is willing to be tested with fMRI and EEG/MEG before and after therapy
- is not wheelchair bound (due to health and safety regulations)
- does not have a pacemaker or any other permanent metallic objects attached to their body (i.e. a surgical clip)
- is a native English Speaker
- was dominantly right-handed before stroke

Where does the project take place?

Therapy sessions, language testing and brain scanning sessions will take place at:

Anglia Ruskin University
East Road
Cambridge

or

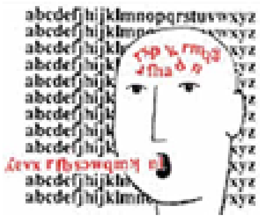
Medical Research Council
Cognition and Brain Sciences Unit
Cambridge.

What do I have to do to participate in the project?

If you would be interested in gaining more information, then please do not hesitate to contact either:

Stephanie Difrancesco
Email:
stephanie.difrancesco@student.anglia.ac.uk
Phone: 07852732680
0845 196 2794
Department of Psychology
Anglia Ruskin University
Cambridge CB1 1PT

Or



Dr. Bettina Mohr
Reader in Psychology
Email: bettina.mohr@anglia.ac.uk
Phone : 0845 196 2258
Department of Psychology
Anglia Ruskin University
Cambridge
CB1 1PT

Research approved by NHS Cambridgeshire 1 Ethics Committee.

We look forward to hearing from you.

APPENDIX 7

ADVERT PUBLISHED ON UNIVERSITY AND APHASIA WEBSITES

Language Therapy and Recovery in Stroke Patients

We are a team of psychologists and neuroscientists from Anglia Ruskin University and the Medical Research Council-Cognition and Brain Sciences Unit (MRC-CBU), Cambridge, investigating the **changes that may occur in the brain following intensive language therapy in stroke patients.**

The principle aims of this research are to scientifically test a short-term form of aphasia therapy- **Intensive Language Action Therapy (ILAT)**, by **comparing the results to** those of **conventional therapy.**

Therapy is carried out in groups **of 3-4 patients and 2 therapists** with around **3 hours of therapy per day for 10 consecutive workdays.** The therapy involves card games where players practice communication skills which are relevant for everyday life, such as *making requests* or *planning activities.*

The study involves participating in **either intensive ILAT or intensive conventional therapy** for 2 consecutive weeks and undergoing a series of **clinical language tests and brain scanning sessions** (EEG/MEG and fMRI) to measure any brain changes due to intensive speech and language therapy.

We are looking for people who suffer with chronic aphasia after stroke to participate in therapy, brain imaging and language assessments.

The study will take place at Anglia Ruskin University, East Road, Cambridge and at the Medical Research Council, Cognition and Brain Sciences Unit, **Cambridge.**

If you would be interested in gaining more information about this study, please do not hesitate to contact either:

Stephanie Difrancesco
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