

**Attention system function and motor impairment following  
cerebrovascular accident: Examining hemispheric differences.**

**& Research Portfolio**

**Volume One  
(Volume Two bound separately)**

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## **Chapter One**

### **Small-scale Service Evaluation Project**

#### **Traumatic Events as Precipitators of Referral to an Urban Clinical Psychology Service.**

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Prepared in accordance with guidelines for contributors to *Health Bulletin* (Appendix 1.1)

2700 words

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## ABSTRACT

### *Aims*

To examine the frequency and demographics of referrals citing precipitant traumatic experience, to a Clinical Psychology service in an area of South Glasgow.

### *Design*

Retrospective review of a random sample of case notes drawn from the total population of a one year period of referrals.

### *Setting*

Department of Clinical Psychology, Southern General Hospital, 1345 Govan Road, Glasgow G51.

### *Subjects*

Referral letters and case notes of a random sample of 160 patients, referred to the current department of clinical psychology between 1.4.1999 and 31.3.2000.

### *Results*

26.2% of the current sample of referrals contained reference to a trauma, related, in the referrer's letter to the current problem. 33.7% of referrals assessed by psychologists were deemed to have an aetiologically significant trauma. The concordance between referrer and assessing psychologist was 91.7% for identification of traumatic history, although psychologists identified trauma significantly more frequently. PTSD, as diagnosed by the referrer, accounted for 5% of referrals. However trauma was deemed significant in a wide range of other disorders. Assault was the most frequent trauma type referred to (20% of all traumas). When broken down into sub-types, sexual assault was the single most frequently occurring trauma (11.9% of all traumas). Traumatization failed to predict attendance at first appointment offered. Deprivation category predicted referral to the current service but did not predict traumatization.

### *Conclusions*

Even in the absence of a diagnosis of PTSD, traumatic events can be seen to precipitate the need to access mental health services. As the current service receives many such referrals, the importance of knowledge of work with victims of trauma is emphasised. Accurate prevalence rates within the service would be aided by clinicians feeding back diagnoses of patients seen. Responsibility for the allocation of post-traumatic referrals should also rest with a clinician with interest in and experience of work with the victims of trauma. As the presentations of disorder following trauma vary widely, appropriate treatment streams are advocated.

## INTRODUCTION

The recognition of psychological morbidity following a traumatic event has followed a fluctuating course in the history of psychiatry (van der Kolk *et al.* 1996). The introduction of the formal diagnosis of Post-traumatic Stress Disorder (PTSD) into the psychiatric nomenclature in 1980 has led to a vast literature on the ways people react to overwhelming experiences. In addition, the treatment of individuals with psychological morbidity following trauma has also progressed greatly as a result (Roth and Fonagy 1996).

Post traumatic stress disorder (PTSD) is defined in DSM-IV (American Psychiatric Association 1994) as the development of a characteristic set of symptoms after exposure to an event perceived as threatening the life or physical integrity of the self or another person. The stressor event must be one outside of the range of normal human experience and the individual's reaction to the event must involve intense fear, helplessness or horror. Lifetime prevalence rates in previous studies of the general population have ranged from 1% (Helzer *et al.* 1987) to 9.2% (Breslau *et al.* 1991). This is presumably due to the differing risk factors in terms of exposure to traumatic events in different populations.

The estimation of the prevalence of mental disorder in the population has long posed a significant problem for mental health professionals. Information on prevalence of a type of disorder is crucial in terms of service planning for the highlighted mental health problems (Peck and Shapiro 1990). Therefore an aim of the present study was to examine the frequency of referrals citing traumatic events as causative to the focal problem.

It has become clear that PTSD is not the only form of psychopathology that follows traumatic events (Brom *et al.* 1992). Problems co-morbid with PTSD and simple non-recognition of PTSD cloud the clinical picture of this disorder (Keane and Wolfe 1990). Solomon and Davidson (1997) report, in a literature review, that over 80% of persons with PTSD suffer from secondary psychiatric disorders. It is thus possible that many patients with traumatic events in their history may present with 'other' disorders, yet have post-traumatic symptomatology.

In a study of the prevalence of 'post-traumatic disorders' or disorders of adjustment following traumatic events, Brom *et al.* (1992) found that 18% of psychiatric outpatient referrals showed clinically significant signs of such disorders. This represents a significant proportion of the referral population studied. The authors of this report conclude that post-traumatic symptomatology such as intrusive re-experiencing of the event, avoidance and hyperarousal are phenomena that most mental health professionals are confronted with on a regular basis.

Risk factors in exposure to traumatic events are dependent on social and economic factors (Roth & Fonagy 1996). The area of current focus (South Glasgow; G41, G51, G52 and G53) is largely an area of high social deprivation (Carstairs and Morris 1990). An hypothesis of the current study is, therefore, that individuals from areas of high social deprivation will be over-represented in the traumatised population.

Under-recognition of the effects of trauma is a problem noted previously (Keane and Wolfe, 1990). Referrer recognition of post-traumatic psychological morbidity can thus be seen as centrally important to the current project. The in-depth systematic interview allowed by psychological assessment may be seen to be more likely to elucidate

traumatic events linked to the onset of the index problem. This hypothesis will also be examined, by assessing concordance between the frequencies of referral agent's, and psychologist's, trauma references. In addition, as we are explicitly examining 'psychological disorder following trauma' we will also examine the practicality of allocation of individuals to appropriate services dependent on severity of symptomatology and therefore need.

Following from the previous relevant research, as outlined, in addition to clinical observation, research questions were posed as follows:

- i. What are the relative proportions of problem type referred to the present department during the period 1.4.1999 to 31.3.2000?
- ii. With what frequency is reference to traumatic events made in referrals to the present Department of Clinical Psychology?
- iii. Are those referrals containing reference to traumatic events less likely to be eventuated? (i.e. Are individuals with trauma related problems less likely to attend first appointment offered?)
- iv. Is reference to trauma in the referral letter related to specific demographic characteristics?

## PROCEDURE

The research project sought to audit referrals to the Department of Clinical Psychology, Southern General Hospital, Glasgow.

a.) A retrospective random sample was drawn from the previous year's referral totals. The referral population for the year 1.4.1999 to 31.3.2000 totalled 491 individuals. Of this number a random sample of 160 cases (32.6% of the referral population) was drawn from the total annual referral population. Due to case note availability it was necessary to randomly select 176 patient identifiers to give a sample of 160 cases. The factors that led to case notes being inconvenient were vault storage (n=10) and current use by another service (n=6). It is not thought that this introduced any systematic bias in terms of the individual case notes made unavailable in this way. Randomisation was carried out using a 'random case selection' procedure within the Statistics Package for the Social Sciences (SPSS) version 9.0 for Windows.

b.) Demographic information on this sample was taken from the Referral Database.

c.) The cases notes of individuals randomly drawn from the total population were examined to gain the following data points:

1. Reason for referral / Provisional diagnosis.
2. Presence of referral agent reference to a *clear and identifiable traumatic event* in aetiological relation to the index problem. Traumatic events were defined in terms of an event which was deemed to constitute a threat to personal integrity or the integrity of others. Five categories were explicitly sought; *assault, sexual assault, experience of man-made accident, second order trauma* (witnessing death or threat to the physical integrity of others) or *other trauma* (threats to personal physical integrity not accounted for by these preceding).
3. Presence of reference to a *clear and identifiable traumatic event* in aetiological relation to the index problem by the assessing psychologist.
4. Type of trauma identified (See categories in 2. above and Doherty, 1998).
5. Attendance at first appointment.

Data were analysed using the Statistics Package for the Social Sciences.

## RESULTS

The referral population for the year 1.4.'99 to 31.3.'00 was 491 individuals. The following analyses are based on a random sample of 160 cases drawn from this total figure (32.6%). The initial assessment letters of 101 individuals (63.1% of sample) were also available for analysis of concordance of trauma identification.

### *Demographic Characteristics of the Referral Population*

#### Age and Gender:

The mean age of referral to the present service was 36.39 years, ranging from 17 to 64 years. There were no significant differences between males and females in age at referral (See Appendix 1.2). 56.25% of the referral population were female and 43.75% male.

#### Social Deprivation:

Deprivation Categories (dep.cat.s) give an index of 'material deprivation' for the post-code sector of an individual's address. Material deprivation is considered an important predictor of various health indices (Carstairs and Morris 1990). In the current sample there exists a positive correlation between the total populations of the dep.cat.s in the catchment area of the department (referrable populations) and the number actually referred (Pearson  $r = .878$ ,  $p < .01$ ). See Table 1 and Figure i, below. A two (referrals, referrable population) by five (dep.cat.s) chi-square was run to ascertain whether the referrals from each category were proportional to the size of the populations within that dep.cat. This analysis indicated that referrals significantly deviate from frequencies predicted by population size. ( $\chi^2 = 14.85$ ,  $df = 4$ ,  $p < .01$ ). From analysis of the Figure ii (below) it is apparent that this results from proportional under-referral from dep.cat. 4 areas, and proportionally higher frequency of referral from dep.cat. 7 areas. Thus proportionally higher numbers of referrals are received from the most highly deprived areas in the catchment area.

[Insert Table 1. here]

[Insert Figure i. here]

### *Reasons for Referral (Research question i.)*

The department received referrals for a wide range of problem types during the period assessed. The most frequent referral was for problems related to anxiety (36.2%). Thereafter in frequency (as shown in Figure ii) followed depression and depressive symptomatology (17.4 %), mixed anxiety and depression (13.8%), emotional problems unspecified (9.4%), eating disorders (5%), PTSD (5%), substance abuse (4.4%), anger management problems (4.4%), OCD (2.5%), Sexual dysfunction (2.5%) and requests for psychological testing (1.3%). (See Appendix 1.3. for all referred problem types and presently employed collapsed groups.)

[Insert Figure ii here]

*Referral Agent and Psychologist references to a clear and identifiable traumatic event in aetiological relation to the index problem. (Research question ii. )*

Clear and identifiable trauma was referred to as aetiologically important in 26.2 % of the sample. Of those seen by a clinical psychologist, reference to trauma in assessment letters was 33.7%. Table 2 shows this breakdown.

[Insert Table 2 here]

#### *Concordance of Referral Agent Psychologist Reference to Trauma*

The concordance of referral agent and psychologist's reference to trauma was 91.7% for positive identification of trauma related to presentation (see Table 3).

[Insert Table 3 here]

A two by two cross-tabulation of Agency (Referrer, Psychologist) by Reference Status (Trauma, No Trauma), using McNemar's test of significance of difference for dependent samples was carried out (McNemar 1969 in Hinkle *et al* 1998). This showed that significant differences exist (McNemar's  $\chi^2 = 7.14$ ,  $df = 1$ ,  $p < .01$ ) such that psychologists make more references to trauma in terms of aetiology.

#### *Type of Trauma Referred to*

There was a wide variety of traumatic events referred to by referrers and as elicited by the assessing psychologist. The most frequently referred to grouping was assault, accounting for 20% of references to trauma. The single most commonly referred to event was sexual assault, accounting itself for 11.9% of references. The breakdown of trauma types is graphically represented in Figure iii. (Appendix 1.4.1).

[Insert Figure iii here]

#### *Attendance at First Appointment (Research question iii.)*

68.5% of those for whom data was available, attended their first appointment. It had been hypothesised that those with a history of trauma would be less likely to attend, however this was not found to be the case in the present sample. A cross-tabulation of referral agent reference to trauma and attendance at first appointment did not reveal a significant relationship ( $\chi^2 = .732$ ,  $df = 1$ , n.s.). Thus 'traumatised' individuals, as a group, are not more likely to fail to attend. See Figure iv. (Appendix 1.4.2).

[Insert Figure iv here]

*Trauma Reference by Demographic Characteristics (research question iv.)*

**Trauma reference by Gender:**

24.3% of males referred had histories of trauma compared with 27.8% of females. (See Appendix 1.4.3). Gender did not predict reference to trauma in the referral letter. ( $\chi^2 = .248$ ,  $df = 1$ , n.s.)

**Trauma reference by Deprivation Category:**

It has been shown above that referral frequency is influenced by the deprivation category of the individual's post-code. It was also hypothesised that referrals from areas of greater social deprivation would be more likely to contain reference to trauma. Figure v shows the relative frequency of trauma reference against total referrals from each deprivation category. (See Appendix 1.4.4). A two (trauma references, total referred) by five (deprivation categories areas within catchment) chi-square was carried out. This showed that the distribution of trauma references across deprivation categories within the current sample was not significantly different from that expected by chance ( $\chi^2 = 1.123$ ,  $df = 4$ , n.s.).

## CONCLUSIONS AND RECOMMENDATIONS

33.7% of the current sample were found by assessing psychologists to have histories of traumatisation believed to be aetiological in terms of the focal problem. The implications of this level of traumatisation in terms of service design and service-related research will now be discussed.

Clinicians working in this area will see many individuals for whom a trauma is implicated in their presentation. Secondary traumatisation in clinicians may also be an issue for future research within the service.

The current rate of referral of diagnosed PTSD was 5%. This is similar to the 4.7% prevalence found by Doherty (1997) in Glasgow's East Sector. Referrers in the current study linked trauma to presentation in 26.2% of cases. It was not possible to compare this figure with previous service evaluations and thus it is necessary for future research to ascertain whether this apparently high level is unusual. This would be important in terms of service provision given proposed local variation in terms of risk of experiencing a trauma (Breslau *et al.* 1991).

The design of the current study allowed us to ascertain the prevalence of PTSD only as diagnosed by the referrer. As this diagnosis was often tentative, this points towards the need for clinicians to feed back diagnoses of patients seen to a central database, thus allowing more accurate recording.

Roth and Fonagy (1996) argue, in relation to diagnosed PTSD, that "effective treatments appear to involve relatively complex combinations of treatment methods which may be best administered at service units specialising in this type of disorder" (Roth and Fonagy 1996, p.169). In the absence of a specialist unit it may be possible for a clinician to co-ordinate the necessary elements of a designated trauma-related treatment service within the context of the current service. This may be put in place by identification of a member of staff with a specific interest in assessing *possible* cases of PTSD, treating if appropriate and liaising with other services where necessary. Other than PTSD however, traumatic events are seen to be aetiological in a *variety* of presentations and trauma is deemed a significant factor in approximately one third of present referrals. Streams of *trauma type* expertise within this service are also advocated, for example a stream may specialise in assault related symptoms and a second in post sexual assault morbidity. It may also be possible that sub-threshold PTSD and partial PTSD would be suitable for group approaches to treatment. A *post-traumatic* assessment service might therefore serve to direct cases into the appropriate stream of the service.

The concordance of referrer and psychologist identification of trauma is acceptable at 91.7%. This indicates that the majority of cases involving trauma can be identified from referral letters and importantly shows primary referrer awareness of traumatisation. Therefore where the experience of trauma may have a bearing on treatment this can be reliably inferred from the referral letter. Thus screening of these referrals may allow their treatment by the identified clinician. As over 80% of persons with PTSD have been found to suffer from other psychiatric disorders (Solomon & Davidson 1997) it is argued that it is likely that a significant number of patients presenting with other focal problems, may also have symptomatology of PTSD. Screening may also be important in identifying this comorbid population.

## LIMITATIONS

The present study is limited by a number of factors. Firstly information was gleaned initially from referral letters. As such the majority of cases did not have definitive diagnoses of their mental health problem at the time of referral.

From the current design it was difficult to ascertain the length of time between traumatisation and presentation and thus this was not targetted as a research question. As traumatic events may have different manifestations dependent on whether they are distal or close in time, the length of time since traumatisation would be a useful data point in future projects.

The present study was carried out for audit purposes. Thus the referral patterns and prevalence of the disorders of focus pertain only to the area and service studied. It would be useful to ascertain whether similar findings hold in sample of community mental health team referrals

Data were drawn from a database of referrals and clinical case notes allowing retrospective analyses only. Prospective study of the effects of traumatic events would add much to our understanding of the course of post traumatic psychological morbidity. The service-related aim of such research would be to ascertain the proportion of 'at risk' populations requiring mental health care services in the aftermath of trauma. It is suggested that identifying a population of 'at risk' individuals, such as attenders at Accident and Emergency departments following incidents such as assaults or road traffic accidents, would be a useful methodology in this regard.

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Tables – to be inserted in the text as indicated

Table 1. Deprivation category by frequency of referral and total population.

Depcat <sup>1</sup>	Frequency	Ref.% <sup>2</sup>	Total Population within Catchment <sup>3</sup>	Pop.% <sup>4</sup>
1	0	0.0	No postcode sectors identified	-
2	9	5.6	4938	6.1
3	0	0.0	No postcode sectors identified	-
4	30	18.8	24496	30.2
5	26	16.3	10872	13.4
6	41	25.6	21534	26.6
7	54	33.8	19191	23.7
	160	100.0	81031	

<sup>1</sup> Increasing deprecats indicates increasing deprivation <sup>2</sup> Percentage of Sample of those Referred

<sup>3</sup> Taken from the Census 1991. <sup>4</sup> Percentage of Total Population within Catchment.

Table 2: Trauma Reference by Referral Agents and Psychologists

Status	Referrer Frequency (n = 160)*	Percent	Psychologist Frequency (n = 101)*	Percent
No Trauma Reference	118	73.8	67	66.3
Trauma Reference	42	26.2	34	33.7
Total	160	100.0	101	100.0

\* Numbers used in analyses differ due to availability of initial assessment letters.

Table 3: Cross-tabulation of Referral Agent and Psychologist reference to trauma.

		Psychologist		Total	
		No Trauma	Trauma		
Referrer	No Trauma	Count	65	12	77
		% within Referrer	84.4% <sup>1</sup>	15.6% <sup>2</sup>	100.0%
	Trauma	Count	2	22	24
		% within Referrer	8.3% <sup>2</sup>	91.7% <sup>1</sup>	100.0%
Total		Count	67	34	101
		% within Referrer	66.3%	33.7%	100.0%

<sup>1</sup> Percent concordance (based on those for whom an assessment letter was available, n= 101)

<sup>2</sup> Percent discordance i.e. a reference to trauma by psychologist not referred to by the referrer, or reference to trauma by referrer not thought linked to the index problem in the psychologist's formulation.

Figures – to be inserted in the text as indicated

Figure i: Sample Referrals by Dep.Cat. against Referrable Population of each Dep.Cat within the department's catchment area.

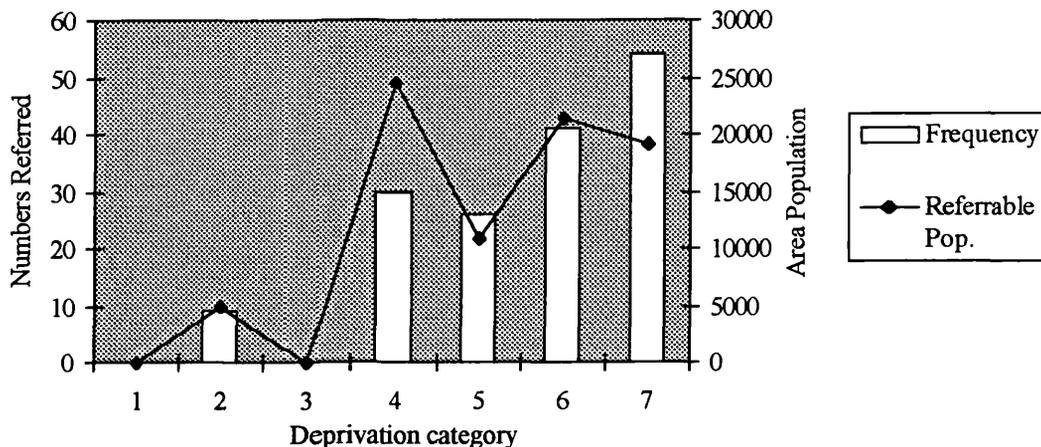
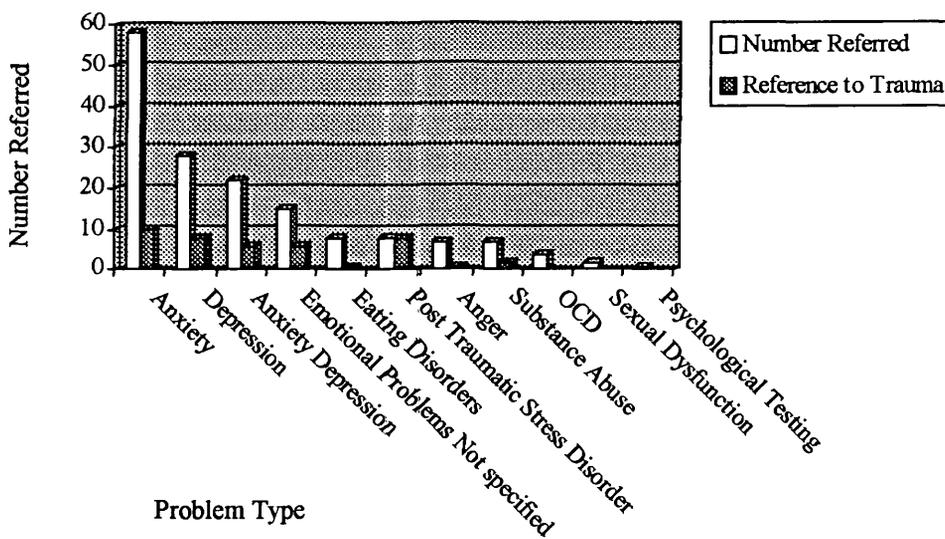


Figure ii. Problem type (Grouped) by Frequency and Percent (Based on Referral Agent description)<sup>2</sup>



<sup>2</sup>See Appendix 1.3 for full referral problem descriptions

Figure iii: Trauma Type by Frequency of Reference by Referrer.

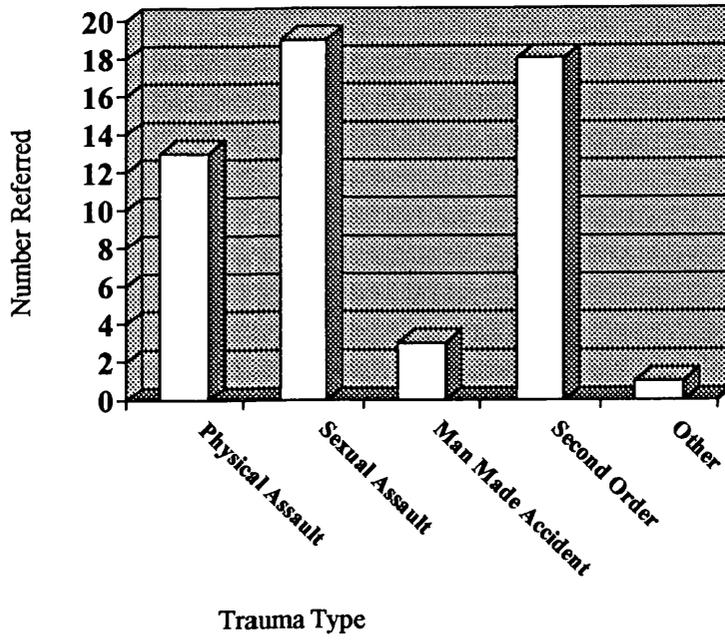
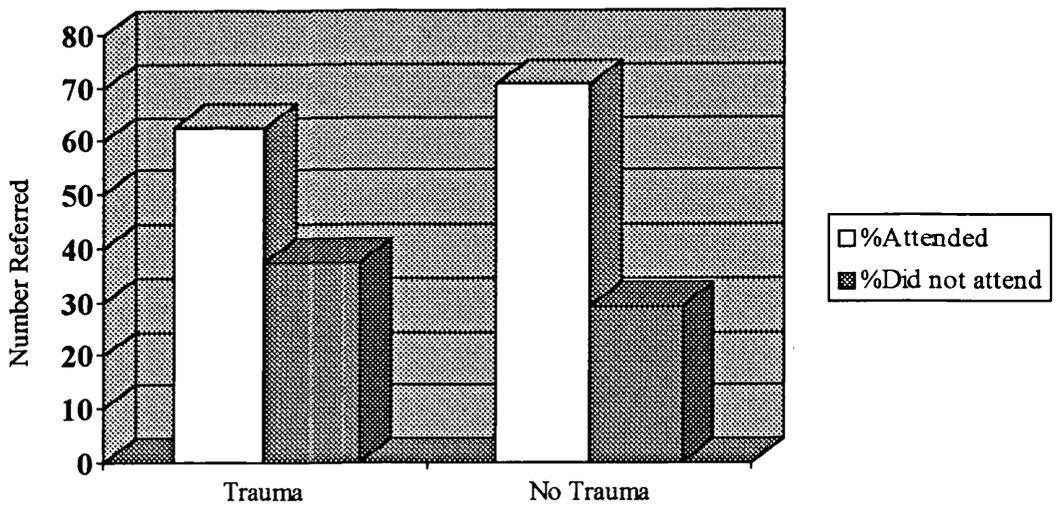


Figure iv: Attendance by Referral Reference to Trauma



## Chapter Two

### Systematic Literature Review

#### **Attention system function and motor impairment following cerebrovascular accident: Examining hemispheric differences.**

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Submitted in accordance with notes for contributors to the *Neurpsychologia* (Appendix 2.1)

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## **Abstract**

**Background:** Motor deficits of the upper and lower limbs are common following unilateral stroke, contributing to the level of disability which this condition causes. Motor dysfunction has been found to be over-represented in right hemisphere stroke patients. Attentional deficits are also more common following damage to the right hemisphere. The right lateralised systems subserving sustained attention, visual attention and attention to the left side of the body are theorised to relate closely to motor areas, in that limb movement requires to be directed in three dimensional space, a function which the attention system subserves. An interconnected neurotransmitter system (noradrenaline), which is right hemisphere dominant, is proposed to mediate the function of the attentional network. Damage to a part of the network may thus explain the common pattern of symptoms following right hemisphere stroke, including hemiplegia, hemi-anaesthesia and hemi-neglect, in addition to the observation of poor sustained attention. The theoretical model subsuming the above findings (as proposed by Rizzolatti & Camarda 1988, Posner 1993, Robertson 1999) currently directs promising experimental approaches to the rehabilitation of impairment following stroke. The model suggests differences in motor recovery between left and right brain injured stroke patients. Studies addressing this hypothesis will be systematically reviewed in the current paper.

**Objectives:** To assess a theoretical model which states that variables of sustained attention and visuo-spatial attention modulate motor impairment following stroke due to lesions in right hemisphere lateralized attention systems. This model suggests differential motor outcome following left or right hemisphere cerebrovascular accident.

### **Search strategy for identification of studies**

Electronic searching of the electronic databases; MEDLINE, EMBASE, CINAHL, PsychInfo and the Cochrane Library via the OVID gateway facility ([http://gateway\\_di.ovid.com](http://gateway_di.ovid.com)). Hand search of journals Clinical Rehabilitation and Stroke.

### **Selection Criteria**

The inclusion criteria were that studies should focus on differential Motor function outcome following cerebrovascular accident (CVA), in relation to the following variables: i. side of lesion, ii. impairment of attention iii. visual neglect.

### **Methods for the Review**

Study quality was assessed using the Scottish Intercollegiate Guideline Network (SIGN) checklists for systematic literature review (SIGN, 2001). See Appendix 2.2.

### **Main Results**

There were equal numbers of studies reporting functional differences between left and right CVA groups as finding in favour of the null hypothesis. Examining findings by study level of evidence and sample size revealed that differences between left and right CVA groups obtained in methodologically superior studies. There was unequivocal evidence that visuospatial deficits were significantly associated with motor or functional outcome.

### **Reviewers Conclusions**

The findings of the review provide further supportive evidence for the hypothesis that left hemiplegia represents a special case in recovery from stroke. However the effect seems to be small and as such may not have particular implications for rehabilitation services. The main findings support the hypothesis that visuo-spatial factors can be identified which have significant potential for reducing the effectiveness of rehabilitation. The area of research

reviewed is limited by lack of acceptance of standard measures and approaches. The current review of studies suggested methodological refinements and hypotheses to be tested in future research.

## **Background**

Cerebrovascular accident (CVA) is the leading cause of disability in developed countries (Stineman, Maislin, Fiedler & Granger, 1997). Persisting motor impairment results in disability in more than half of those who suffer a CVA (Stineman *et al* 1997). The total number of survivors with persisting disability has risen with increased survival following the pathological cerebro-vascular event (Stroke Unit Trialist's Collaboration, 2001). Hemiparesis is the most common deficit after stroke affecting more than 80% of survivors acutely and more than 40% chronically (Gresham, Duncan, Stason *et al* 1995).

Motor impairment following stroke rarely occurs in isolation from other symptoms (Sterzi, Bottini, Celani, Righetti, Lamassa, Ricci, & Vallar 1993). Sterzi and colleagues (1993) describe a constellation of symptoms frequently co-occurring with hemiplegia including visual hemi-neglect and hemi-anaesthesia. In the examined cohort, motor impairment was more common in right hemisphere damaged patients. Similarly and importantly, contralesional sensory inattention and somatosensory problems were also more common in right hemisphere damaged patients (Sterzi *et al* 1993).

An explanation of the association of motor-problems and hemi-inattention has been proposed in terms of the anatomy of these functions (Sterzi *et al* 1993). Posner and colleagues (for example Posner, Inhoff, Friedrich & Cohen 1987) have identified regions of the right hemisphere which play important roles in the maintenance and direction of attention. The cortical areas responsible are interconnected by noradrenaline circuits (Oke, Keller, Mefford & Adams 1978). Greater visuo-spatial difficulties following right hemisphere damage (Bisiach Capitani, Luzzati & Perani 1981) may thus represent selective disruption of these right hemisphere attentional systems. Thus impaired awareness of contralesional space may present primarily as a motor problem (Sterzi *et al* 1993)

Functional recovery following stroke has been associated with various prognostic indicators. The identification of prognostic indicators allows targeted interventions toward the impairment which appears to be hampering recovery. (Denes, Semenza, Stoppa & Lis 1982, Paolucci, Antonucci, Guariglia, Magnotti, Pizzamiglio and Zoccolotti 1995, Saeki, Ogata, Okubo, Takahashi, Hoshuyama, 1993) .

Unilateral visual neglect has been identified as an important predictor of functional recovery following stroke (Kinsella & Ford 1980, Denes *et al.* 1982, Kotila *et al* 1984, Friedman 1992, Gialanella & Mattioli 1992, Jehkonen *et al* 2001). This syndrome is heterogeneous in nature but most commonly follows from damage to the right posterior parietal cortex (Bisiach *et al* 1981). The use of techniques to rehabilitate visual neglect has also been found to significantly improve functional recovery following stroke (Paolucci *et al* 1995). The converse relationship has also been demonstrated such that contralesional limb activation appears to reduce the symptoms of visual neglect (Robertson, Hogg & McMillan, 1998; Samuel, Louis-Dreyfus, Kaschel, Makiela, Troubat, Anselmi, Cannizzo & Azouvi 2000).

Other attentional deficits following right hemisphere damage include impairments of attention to the space occupied by the body, peri-personal space (Robertson & North 1992) and sustained attention or vigilance (Robertson, Manly, Beschin, Daini, Haeske-Dewick, Homberg, Jehkonen, Pizzamiglio, Shiel, Weber 1997). These functions are conceptualised as related but dissociable (e.g. Robertson 1999).

To summarise, visual neglect predicts variance in functional outcome following stroke (e.g. Denes *et al* 1982). In turn, sustained attention has been found to be a marker for visual neglect (Robertson *et al* 1997). The resulting anatomically driven model (Posner 1993) suggests that sustained attention, visuo-spatial attention and motor control functions are related right hemisphere functions.

This model (Posner, 1993, Robertson *et al* 1997) is the basis for current experimental rehabilitation strategies (e.g. Robertson, Hogg & McMillan, 1998). However it is based on findings of hemispheric difference in outcome which have not been reviewed to date. The present paper attempts to provide a systematic review of the literature concerning difference in functional motor outcome after left or right hemisphere CVA, and thus examine the hypothesised links between lateralised attentional functions and motor impairment following CVA.

## **Objectives**

The current review had three broad objectives:

- a. To assess the methodological quality of studies addressing the issues of differential motor outcome following left and right hemisphere stroke and differential outcome related to attentional deficits.
- b. To assess the importance of hemisphere of lesion in predicting motor outcome following stroke.
- c. To assess the degree of relation of functional outcome to visuo-spatial difficulties following unilateral CVA.

## **Criteria for considering studies for this review**

### **Types of Studies**

Case control and cohort studies examining the relationship between hemisphere damaged and motor outcome following CVA.

Case control and cohort studies focusing on differential motor outcome following CVA attributed to the presence of a cognitive or perceptual symptom or cluster of symptoms.

Correlation studies attempting to demonstrate a relationship between cognitive or perceptual assessment scores and motor impairment following stroke.

## **Types of Participants**

Any patients admitted to a acute or post acute facility who had suffered a stroke which resulted in a unilateral hemiplegia. The time elapsed between neurologic event and outcome assessment was noted but not used as an exclusion criterion.

## **Types of Prognostic Indicator**

The studies reviewed focus on the effects of unilateral cerebrovascular accident. The participants of included studies had sustained ischemic (thrombotic and embolic) infarctions, cerebral haemorrhages, sub-arachnid haemorrhages, and intracranial haemorrhages. Infarction was the most frequent stroke type, occurring in approximately 85% of the combined samples.

The main prognostic indicator of interest was hemisphere lesioned by the unilateral CVA. Clinical observation and CT were both acceptable as methods of demonstrating this.

The presence of visual neglect was the second prognostic indicator of interest as this was frequently included as a variable in studies examining the role of side of weakness in predicting outcome.

## **Types of Outcome Measures**

Studies reporting outcome on measures of motor function were included. Studies reporting outcome in terms of ability to perform activities of daily living (ADL) were also included. Reduced disability may also be expected to follow from improved motor and/or cognitive function, so disability measures cannot taken as proxies for motor function measures in that learned adaptations may also lead to reduced disability. Thus the variables can be dissociated. The measures reported in the reviewed studies are reported in the section on Description of the Studies below.

## Methods of the Review

### Search Strategy for Study Identification

The OVID system ([http://gateway\\_di.ovid.com](http://gateway_di.ovid.com)) allowed electronic searching of the databases MEDLINE (1966 to 2002 week 3), EMBASE (1980 to 2002 week 20), CINAHL (1982 to 2002 week 5) and PsychInfo (1984-2002 week 4). A separate pilot search of the Cochrane Library revealed that this was not an appropriate source of relevant articles. (The search history is shown in Table 1). The reference section of papers elicited in this way were also searched for relevant trials.

A hand search of the Journal *Stroke* (Vol.23, 1992 to Vol. 31 2000) and *Clinical Rehabilitation* (Vol. 1 1987-Vol.16 2002) was also carried out. This hand search did not elicit further relevant articles which is taken as evidence that the strategies used in the electronic database search were effective (see Table 1, Search History).

Information on currently active research was not included in the review. Unpublished manuscripts or reports submitted for higher degrees were included in the search space insofar as they are referenced by several of the above databases. However no studies in this form met criteria for inclusion in the review.

[Insert Table 1 here]

### Selection of Trials

Included studies focused on side of lesion as a predictive factor in outcome following unilateral CVA. Studies also examining visuospatial variables as associated with functional outcome following stroke were also selected.

Studies were examined by the author who assessed eligibility and methodological quality. Meta-analyses or systematic reviews have yet to be completed in this area to the knowledge of the author. One narrative review (Jongbloed 1986) was located, containing reference to six studies apparently relevant to the current review [Adams, (19?? [sic]); Andersen, Hanvik & Brown (1950); Boureston (1967); Denes *et al* (1982); Kotila, Waltimo, Niemi, Laaksonen, Lempinen (1984); Wade, Langton-Hewer & Wood (1984)]. The methods and findings of Jongbloed's (1986) review, with regard to side of stroke, were imprecisely reported and therefore the studies included were sought in original. This was possible for Denes, Semenza, Stoppa & Lis (1982); Kotila, Waltimo, Niemi, Laaksonen, Lempinen (1984); Wade, Langton-Hewer & Wood (1984) which all met entry criteria for this review. It was not possible to locate Adams, (19?? [sic]), Andersen, Hanvik & Brown (1950) and Boureston (1967).

Case-control or cohort-studies, quasi randomised control trials, quasi-experimental, naturalistic case studies and case series designs are included.

## **Assessment of Methodological Quality**

Study quality was assessed using the Scottish Intercollegiate Guideline Network (SIGN) checklists for systematic literature review (SIGN 2001, See Appendix 2.2). These tools allow each study to be rated on key methodological issues and yields a 'level of evidence' score. There are four categories with a further three sub-divisions in the top two evidence categories. The classification is shown in Table 2.

Following the methodology suggested by SIGN (2001), the internal validity of the studies was examined in terms of: randomisation procedures; assessment practices; reliability and validity of measures employed; equality of groups in terms of initial impairment and disability; and analyses carried out. Studies were described in terms of: patient characteristics; sample size; measures used; scale and direction of effect; reports of certainty of findings; and characteristics of the setting of the study. This description along with the assessment of internal validity permitted a rating based on assessment of success in reducing bias; persuasiveness of the methodological and statistical information presented; and relevance of the finding in terms of the current population.

[Insert Table 2 here]

## **Methods of Analysis**

Given the diversity of a. types of relationship reported and b. statistics reported it was considered inappropriate to extract effect sizes from the studies. Therefore effects of interest were tabulated by study level of evidence and sample size. This allowed qualitative conclusions to be drawn on the probability that the variables of interest were predictive of motor and functional outcomes after CVA.

## **Description of the Studies**

A total of 14 studies were identified by July 2002. Descriptive information on these 14 studies was taken from the published reports. Among the included studies there was 1 narrative review (Jongbloed 1986). There were 6 case-control studies (Andrews 1982, Blanc-Garin 1994, Buonocore 1990, Chen-Sea 1993, Denes 1982, Feigenson 1977) - where cases were defined as either a. right hemisphere involvement or b. presence of a prognostic sign and controls were other stroke patients. There were seven cohort studies (Granger 1992, Kotila 1984, Mills 1983, Saeki 1993, Sanchez-Blanco 1999, Sterzi 1993 and Wade 1984).

### ***Types of relationship***

Within the reviewed studies 5 studies showed that side of lesion predicted functional/motor outcome (Blanc-Garin 1994, Buonocore 1990, Denes 1982, Granger 1992, Sterzi 1993). 10 studies showed that measures of visual attention predicted motor or functional outcome (Blanc-Garin 1994, Chen-Sea 1993, Denes 1982, Feigenson 1977, Jongbloed 1986, Kotila 1984, Sanchez-Blanco 1999, Sterzi 1993, Wade 1984). 2 studies reported no relationship between either side of lesion or presence of visuo-spatial difficulties and outcome (Andrews 1982, Saeki 1993).

## *Settings*

All 14 studies examined outcome of CVA patients following inpatient care. 5 studies (Blanc-Garin 1994, Feigenson 1977, Saeki 1993, Sanchez-Blanco 1999, Wade 1984) recruited patients who had received care in specialist rehabilitation units or stroke units. 1 study (Denes 1982) recruited patients from a Hospital Specialised for the care of older adults. 8 studies (Andrews 1982, Buonocore 1990, Chen-Sea 1993, Granger 1992, Jongbloed 1986, Kotila 1984, Mills 1983, Sterzi 1993) recruited from general medical facilities. Organised dedicated inpatient care of stroke survivors has previously been shown (in a meta-analysis) to reduce the odds of death or institutionalised care and dependency at final review (Kalra, 1994, Stroke Unit Trialists' Collaboration, 2001). Potential biases associated with these samples are discussed below.

## *Study Populations*

Table 3 below describes the samples of the individual studies included in the review. Most indices were extractable from the published reports. Notably, this was not possible for Andrews 1982, due to very poor description of the procedure of the study. In addition, Jongbloed 1986 presented a narrative review of studies but did not present information on the populations of the included studies.

[Insert Table 3 here]

(i) *Samples*: The total mean sample size was 725.46. (s.d. 2158.57) However this is skewed by the very large database analysis by Granger 1992. Removing this sample n reduces the mean to 127.17 (s.d. 80.75). The median sample size was 124.

(ii) *Age*: The mean age of study participants was 64.25 (s.d. 5.62). This is a relatively young total sample. For example it is outside of the modal Scottish age range of CVA incidence of 70-74 years (Scottish Executive Information and Statistics Department 2000).

(iii) *Gender*: The mean percentage of males among the sample was 56.77 (12.96). This is reflective of gender differences in the incidence of stroke in the age group of the total sample (e.g. Scottish Executive Information and Statistics Department 2000).

(iv) *Stroke characteristics*: The mean percentage of infarction among the stroke samples was 83.81 (17.68). This reflects the frequency of infarction in the general stroke population. Percentages of other subtypes of stroke were not calculated as the style of reporting was heterogeneous.

(v) *Comparability of source populations*: The study of attention problems following stroke presents specific methodological problems. The symptom clusters with which post CVA patients present are heterogeneous and vary greatly in severity. For example, the presence or absence of neglect is correlated with the presence of sustained attention difficulties (Robertson *et al* 1997), although the symptoms are dissociable. Therefore to differentiate groups on the presence of a specific attentional difficulty risks the possibility that the groups will differ on other capacities not assessed within the study. A requirement for matching is suggested. However study design usually includes matching only on gross severity indices only if at all. The methodological task of matching on certain neuropsychological test performance is posited to be difficult if not impossible given the range and severity spectrum of post CVA presentations.

(vi) *Time since stroke onset*: The mean time from stroke onset to outcome assessment was 127 days (s.d. 122).

### ***Outcome Measures***

(i) *Motor Function*: Brunnstrom Test (Brunnstrom 1974): Chen-Sea 1993, Saeki 1993; Allovon and Miard Scales (Allovon & Minard 1985): Blanc-Garin 1994; Functional Ambulation Classification (Holden, Gill, Magliozzi, Nathan & Piehl-Baker 1984): Sanchez-Blanco 1999; Oxford Scale (Bamford, Sandercock & Dennis 1988): Sterzi 1993; Bisiach Faglioni Assessment (Bisiach & Faglioni 1974): Denes 1982; Visual Simple Reaction Time: Buonocore 1990, Non standardised assessment protocol: Feigenson 1977, Kotila, 1984, Sterzi 1993, Mills 1983.

(ii) *Disability*: Barthel Activities of Daily Living Index (Mahoney & Barthel 1965): Saeki 1993, Sanchez-Blanco 1999, Wade 1984; Functional Independence Measure (Keith *et al* 1987): Granger 1992 Klein Bell Activities of Daily Living (Klein & Bell 1979): Chen-Sea 1993; Allovon and Miard Scales: Blanc-Garin 1994; DeLagi Activities of Daily Living (Delagi *et al* 1960): Denes 1982; Discharge disposal: Granger 1992; Non standardised assessment protocol Feigenson 1977, Kotila 1984. Not specified: Andrews 1982, Jongbloed 1986, Mills 1983.

### ***Prognostic Measures***

(i) *Hemisphere Damaged*: Observation of laterality of weakness of acute onset lasting more than 24 hours comprised the modal assessment of laterality of cerebral damage. Confirmation of laterality of damage by tomographic methods (computerized tomography, magnetic resonance imaging, positron emission tomography) was reported in 5 studies (Blanc-Garin 1994, Chen-Sea 1993, Feigenson 1977, Kotila 1984, Sterzi 1993). None of the studies including tomographic analysis reported excluding patients on the basis of this assessment. Therefore it is not felt that this biased findings in the studies not employing such assessment.

(ii) *Visuospatial Attention*: The presence of neglect was identified most frequently using stimuli cancellation tests: Letter cancellation (Weintraub & Mesulam 1985) was used by Blanc-Garin 1994. Chinese Word Cancellation Test (Chen-Sea, 1991) was employed by Chen-Sea 1993. The Confrontation Test was used by Sterzi 1993, while Clockface copying was used by Kotila 1984. Copying Crosses Test (De Renzi & Faglioni 1967) was used by Denes 1982. A Line cancellation test (Albert 1969) was employed by Saeki 1993. Feigenson 1977 used a non standard test.

## Methodological Quality

The methodological quality of tests was evaluated according to SIGN (2001) guidelines. Tables 4 and 5 contain the level of evidence assigned to each study (in terms of statistical analyses and findings respectively). Important methodological issues (which contributed to the level of evidence assigned) are described in the following section under group equality, assessment blindness, assessment validity and reliability, percent of participants included in the analysis and provision of uncertainty indices.

### *Group Equality<sup>2</sup>*

8 studies carrying out group comparisons reported indices of equality. Andrews 1982, Feigenson 1977, Wade 1984 ensured equality on age and gender. Buonocore 1990 ensured equality on age and gender, stroke lesion site and time since CVA. Chen-Sea 1993 matched for age, education and duration post CVA onset. Denes 1982 controlled for severity of lesion. Granger 1992 used a very large dataset which made matching unnecessary. Sterzi 1993 reported group equality in terms of frequency of excluded patients.

3 studies (Blanc-Garin 1994, Jongbloed 1986, Mills 1983) did not report on group equality. Jongbloed 1986 reviewed previous research and did not report on attempts to match. Blanc-Garin 1994 defined her groups on the basis of a factor analysis thus making group equality on variables unrelated to the hypotheses difficult to demonstrate.

Matching was not appropriate in the 3 cases of Kotila 1984, Saeki 1993, Sanchez-Blanco 1999 who attempted to build predictive models for samples as a whole.

### *Assessment Blindness*

As side of weakness is a highly salient feature of patients post stroke, adequate concealment of patients' group membership was not possible in any of the included studies.

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<sup>2</sup> *Randomisation*

The included studies assessed the effect of side of hemiplegia or weakness on various outcome measures. Studies are therefore naturalistic quasi experimental and discussion of randomisation is inappropriate. The remainder of the quality rating headings below reflect the fact that much of the methodological criteria for assessing Randomised Control Trials is inappropriate for studies as reviewed here.

### *Assessment reliability and validity*

Motor function was specifically assessed in 11 of the 14 studies. 10 studies (Chen-Sea 1993, Saeki 1993; Blanc-Garin 1994, Sanchez-Blanco 1999, Sterzi 1993, Denes 1982) measured motor outcome using assessments with published reliability or validity co-efficients. 4 studies (Feigenson 1977, Jongbloed 1986, Kotila, 1984) failed to give adequate information on the reliability or validity of measures used

Disability was assessed in 12 of 14 studies (not in Buonocore 1990, Sterzi 1993). 7 Studies (Blanc-Garin 1994, Chen-Sea 1993, Denes 1982, Granger 1992, Saeki 1993, Sanchez-Blanco 1999, Wade 1984) measured disability using assessments with published reliability or validity co-efficients. 5 studies (Andrews 1982, Feigenson 1977, Jongbloed 1986, Kotila 1984, Mills 1983) failed to give adequate information on type of measure employed or its reliability or validity.

### *Percentage of participants included in the analysis*

The rate of inclusion of recruited participants in the post-intervention analysis was high. The mean percentage was 88.67% (s.d: 11.18), ranging from 53.33 % (Denes 1982) to 100 % (Andrews 1982, Buonocore 1990, Granger 1992, Mills 1983).

### *Statistical Analysis*

There was a great deal of variation in terms of the statistical analyses used in the various studies. The modal principal analysis was examination of difference between groups (n=9), using a variety of statistics including ANOVA, t-Test and Chi-Square. Regression was employed in 2 studies and correlation in 1 study. 1 study was a review in which no statistical analysis was used. Table 4 shows the statistical analyses employed in terms of quality of reporting and how successful the authors dealt with possible confounding variables.

[Insert Table 4 here]

The same data processing methods were used for cases and controls in all studies where this was relevant (n=12). Uncertainty indices (e.g. confidence intervals) were provided in only 3 studies (Buonocore 1990, Sanchez-Blanco 1999, Sterzi 1993). However this was not deemed appropriate in a further 3 studies (Blanc-Garin 1994, Jongbloed 1986, Mills 1983).

### *Homogeneity across multiple sites*

11 of the included studies reported findings from single sites only. The 3 studies which drew participants from multiple sites (Granger 1992, Jongbloed 1986, Sterzi 1993) did not report an index of homogeneity across sites

## **Results - Methodology**

### *Minimisation of bias*

The included studies generally failed to explicitly report how potential biases were minimised. Examination of the studies in terms of known correlates of the prognostic and outcome measures allowed assessment of how well the studies were designed to minimise bias (see Table 6). Two studies (Buonocore 1990, Granger 1992) received a SIGN ratings (SIGN 2001) of ++, the highest rating of methodological rigour in minimising bias within the included study designs (see Table 2). 8 of the studies (Blanc-Garin 1994, Chen-Sea 1993, Denes 1982, Granger 1992, Kotila 1984, Sanchez-Blanco 1999, Sterzi 1993, Wade 1984) received SIGN ratings of +. 4 studies (Andrews 1982, Feigenson 1977, Mills 1983, Saeki 1993) received ratings of –.

### *Levels of evidence*

The methodological quality of the studies reviewed was generally high as shown in Table 5. However all of the studies were either case-control or cohort, therefore their corresponding level of evidence was confined to the range of 2++ to 4. 2 studies were rated as 2++, 8 studies were rated as 2+ and 4 studies were rated as 2 –.

[Insert Table 5 here]

### *Relevance of studies to target population*

14 of the 14 studies reviewed were deemed relevant to the population of interest (stroke survivors with hemiparetic impairment). The number of exclusion criteria reported in these studies was quite low. Cases were selected on the basis of motor impairment following CVA (Blanc-Garin 1994, Buonocore 1990, Chen-Sea 1993) or else were sequences of patients from stroke units. (Denes 1982, Granger 1992, Sanchez-Blanco 1999, Saeki 1993, Sterzi 1993, Wade 1984). Mills (1983) recruited participants entering a rehabilitation centre with “moderate motor involvement” They excluded those with serious co-morbid medical problems and those who did not complete their rehabilitation treatment. This study thus represents the largest number of exclusion criteria, thus putting into question its relevance to the prognosis of stroke survivors generally. Saeki 1993 recruited patients with a mean age of 55 which is significantly younger than the mean age in other studies. The remaining samples are thought to be relevant to the general stroke population in terms of their demographics.

## **Results - Findings**

### *Effects found*

The findings of the included studies are described here and summarised with regard to key study descriptors in Table 6 below.

1. Andrews 1982 found no relationship between severity of motor impairment, functional outcome or sensory loss and laterality. A methodologically poor study, the authors failed to report measures or statistics used.

2. Buonocore 1990 found that patients with right hemisphere cerebrovascular accidents (RCVA) showed longer visual simple reaction times than those following left cerebrovascular accidents (LCVA) ( $p < 0.05$ ).
3. Blanc-Garin 1994 used a variation of factorial analysis (multiple correspondence analysis) to identify two courses of recovery trajectory; a 'functional lag' group characterised by a discrepancy between motor and functional recovery and a 'consistent recovery' group. Chi square analysis of group membership showed RCVA patients were significantly over-represented in the functional lag group ( $\chi^2 = 7.47$ ,  $p < 0.01$ ).
4. Chen-Sea 1993 found that hemi-inattentive patients were poorer than non-lateralized inattentive patients and those with normal attention on ADL performance score ( $F = 31.4$ ,  $p = 0.0064$ ). They also found that hemi-inattentive patients scored significantly lower than the other groups on a measure of motor function ( $F = 9.75$ ,  $p = 0.0002$ ). The study did not report analyses by lesion side.
5. Denes 1982 found that RCVA tended to recover motor function to a lesser degree than LCVA ( $F = 2.90$ ,  $df = 1.46$ ,  $p < 0.10$ ). This study also found that RCVA patients improved significantly less than LCVA on an ADL metric ( $F = 10.52$ ,  $df = 1.46$ ,  $p < 0.005$ ). After partialling out concomitant variables a regression analysis revealed that visual hemineglect was the only significant coefficient of ADL improvement ( $\beta = 0.846$ ,  $p < 0.05$ ).
6. Feigenson 1977 found that severe perceptual dysfunction (grouping the variables; denial, neglect, disorders of body image, visuo-spatial difficulties and left-right disorientation) adversely affected ADL, ability to walk and discharge disposition (home or continued care). No differentiation on the basis of side of lesion was reported.
7. Granger 1992 found that RCVA patients improved less during rehabilitation than those following a LCVA.
8. Jongbloed 1986 reviewed studies up to that point and concluded that hemisphere of lesion did not predict functional outcome. The author also concluded that visuospatial neglect did predict functional outcome.
9. Kotila 1984 found the presence of visuospatial difficulties in 39/65 and 25/61 patients at 3 and 12 months respectively. 24/39 and 18/25 were independent in activities of daily living (ADL). Patients without visuospatial deficits were more often independent in ADL (24/26 and 35/36 at 3 and 12 months respectively,  $p < 0.01$ ). However when discriminated by side of lesion the groups were not significantly different on outcome ADL.
10. Mills 1983 found no differences between left and right CVA patients on measures of ADL, perception/information processing. But for RCVA perception/information processing correlated significantly with mobility ( $r = .28$ ,  $p < .02$ ).
11. Saeki 1993 found that four variables significantly contributed to rehabilitation effectiveness: Lack of motivation, urinary incontinence, age and delay from CVA onset to rehabilitation. However this study had two potential confounds discussed below. Visual neglect did not enter the regression equation but tended to reduce the effectiveness by 9%. (Regression co-efficient  $r = -9.4$ ,  $p < 0.09$ ).

12. Sanchez-Blanco 1999 found that 11 day classification of patients according to whether motor impairment obtained solely (M) or in addition to sensory difficulties (MS) and sensory difficulties and hemianopsia (MSH) significantly predicted independence in ADL at six months. (The relative risk of achieving independence (sic) in ADL of M with respect to MSH (95% confidence intervals) was 6.02 (2.13-16.97),  $p < 0.001$ )

13. Sterzi 1993 found that a RCVA group had a greater frequency of motor deficits ( $p = 0.0044$ , odds ratio=3.39, 95%CI=1.34-9.65) visual half field deficits ( $p=0.0098$ , odds ratio=2.99, 95%CI=1.19-7.74) and position sense difficulties ( $p=0.044$ , odds ratio=1.79, 95%CI=0.97-3.31).

14. Wade 1984 found that RCVA patients had greater frequency of spatial disorders (no statistics reported). Assessing RCVA patients only, those with spatial disorders were more likely to die in the 1<sup>st</sup> six months ( $p < 0.05$ ) suggesting greater severity of stroke. They also had lower Barthel ADL scores on discharge ( $p < 0.05$ ). The RCVA and LCVA groups were equivalent on follow-up measures of ADL and Motor Function.

[Insert Table 6 here]

#### ***Findings by study level of evidence and sample size***

The level of evidence of each study's findings were estimated by assessing the methodological rigour and sample size (see Table 5).

#### ***Side of lesion***

Functional differences between left and right CVA groups were apparent in 5 studies out of a total of 10 where this was examined (4 studies examined influence of lateralised attention deficits only): Buonocore 1990, Blanc-Garin 1994, Granger 1992, Denes 1982, Sterzi 1993, (total  $n = 8350$ ). There were no statistically significant differences in function between left and right CVA patients in 5 studies where this was examined: Andrews 1982, Jongbloed 1986, Kotila 1984, Mills 1983, Wade 1984 (total  $n = 553$ ). The total  $n$  for studies failing to report a difference was lower than in those reporting difference (omitting Jongbloed 1986 due to unreported sample sizes). Studies reporting a difference were rated as being of higher level of evidence than those failing to report a difference [2(2++); 3(2+) versus 3(2-); 2(2+) respectively]. More recent studies also appeared more likely to report functional differences.

This finding is at odds with the results of a previous review. Jongbloed 1986 stated for example that "there is general agreement that there is no relationship between hemisphere of stroke and function on discharge". However the conclusions of this narrative review are based on 4 studies published between 1950 and 1984. She also failed to report on the methodological quality of the studies. Two of the four studies she included as representing 'general consensus' (Wade 1984, Kotila 1984) were rated as SIGN (2001) 2+ level of evidence. Two others (Boureston 1967, Anderson *et al* 1950) were not available to the current author and the methodological quality could not be rated.

### *Visuospatial deficits*

Visuospatial deficits were significantly associated with motor or functional outcome in 10 studies out of a total of 12 where this was examined (2 studies examined side of lesion alone, see Table 5): Blanc-Garin 1994, Chen-Sea 1993, Denes 1982, Feigenson 1977, Jongbloed 1986, Kotila 1984, Mills 1983, Sanchez-Blanco 1999, Sterzi 1993, Wade 1984 (total n = 1371). There were no statistically significant associations in 2 studies: Andrews 1982, Saeki 1993, (total n = 259). The total n for studies reporting a relationship was higher than those failing to report a relationship (omitting Jongbloed 1986). Studies reporting a difference were rated as being of higher level of evidence than those failing to report a difference [7(2+); 3(2-) *versus* 2(2-) respectively].

## Discussion

The studies in the present review proved difficult to compare. Different measurement tools, different means of describing the variables used (e.g. scores on validated measure, presence or absence of a sign, categorisation or diagnosis) contributed to the difficulty in comparison.

From examination of the measures used in assessing outcome it is apparent that there is little consensus on which measures are standard. Many of the early studies use non-standardised or tools accepted by local clinician consensus. Research in this area would greatly benefit from comparable measures and thus comparable findings across studies. Examination of the modal assessment tools used is perhaps relevant, although the wide variety of tools employed is acknowledged. The Barthel Index (Mahoney & Barthel 1965) was the most frequently employed measure of disability in the studies included (n=3). The Brunnstrom Arm Recovery Stage (Brunnstrom 1974) was the most frequently employed measure of motor impairment (n=2).

The methods of ascertainment of the presence of visuospatial difficulties differed greatly across studies. Studies aiming to specifically ascertain the presence of visuo-spatial neglect generally used valid methods which is reflected in the level of evidence rating assigned. In those studies rated as relatively methodologically poor (e.g. Andrews 1982, Feigensen 1977, Mills 1983) there was an absence of relationship between laterality and motor/ADL function. As these studies were criticised on operationalisation of variables this lack of finding may reflect lack of sensitivity of measures employed. For example Mills 1983 used a case review methodology so that patients were not assessed to specifically answer the research question. The estimates of presence or absence of functional problems were thus based on gross therapist opinion rather than specific reported measures.

There was a great deal of variability in the reported rate of occurrence of unilateral spatial neglect in the samples included in this review. This is an issue addressed by Bowen, McKenna & Tallis (1999). In a systematic review of the frequency of unilateral visual neglect after stroke Bowen *et al* (1999) report their main finding as the impossibility of deriving a reliable estimate of the frequency of neglect. The reasons they posited included (i.) the study of different populations, using different sampling methods and different selection and exclusion criteria; (ii.) differences in reporting lesion location; (iii.) the assessment of abilities at differing times post CVA and (iv.) the fact that different assessment tools provide different rates of unilateral spatial neglect. The difficulties identified by Bowen *et al* (1999) also seem to apply to the heterogeneity of the current sample of studies.

## **Reviewers Conclusions**

There were similar numbers of studies supporting functional differences between left and right CVA groups (n=5) and finding group equivalence (n=5). Studies reporting a difference were rated as being of higher level of evidence and were more recent than those failing to report a difference. It is therefore concluded that there seems to be support for the hypotheses that RCVA patients have poorer prognosis for the recovery of functional abilities although the difference may require relatively high power to detect.

Visuospatial difficulties were significantly related to poorer motor/functional outcome in the majority of studies where this was examined. It was not possible to derive a reliable quantified estimate of the relationship between visuo-spatial attention and functional recovery given the heterogeneity of abilities assessed, operationalisation of these variables and methods of reporting the statistics employed. However the findings seem to support the hypothesis that visuo-spatial factors can be identified which have significant potential for reducing the effectiveness of rehabilitation. Understanding the extent to which such factors reduce effectiveness is important in planning stroke rehabilitation programmes.

## **Limitations of the Present Review**

The limitations of the present study should be acknowledged. Only data from published studies were used in the review. For treatment effectiveness studies a publication bias may be expected in that studies reporting positive findings are more likely to be published. This bias is thought to be reduced in the present review, based as it is on observations of frequency of deficits and their inter-relationships.

The studies located using the current search criteria (Table 1) specifically addressed side of lesion or presence of visuo-spatial difficulties as factors affecting ADL or motor outcome. It is possible that studies addressing other aspects of stroke recovery or treatment may have reported findings related to this review but which were not reported in the abstract. These potential findings would thus not be available to the search tools used.

The mean age of study participants was relatively young compared with statistics on the incidence and prevalence of stroke. This poses problems in terms of generalisation of the review findings. However this is a reflection of a general limitation of stroke research in that the common use of age exclusion criteria (of 70 or 75 years) excludes a large proportion of the population, as the mean age range of new stroke cases is within the 70-75 year range. (Scottish Executive Information and Statistics Department 2000).

## **Implications for Practice**

Sanchez-Blanco 1999 used a syndromic classification system developed by Reding & Potes (1988). This system distinguishes patients with motor impairment alone (M) from those with a. additional sensory difficulties (MS) b. additional sensory difficulties and hemianopsia (MSH). They found that assessment and categorisation at 11 days post CVA predicted functional independence at 6 months. They present their methodology as a practical approach to

the functional prognosis which is understandable to the patient and his or her relatives in that it quantifies the help or assistance required in walking and coping with day to day chores.

This type of syndromic classification may be criticised methodologically however in terms of aggregating a large number of variables with their group definitions, thus blurring the explanatory power of individual variables which may be relevant to the process of rehabilitation. The syndromic classes of M, MS and MSH suggest progressively greater territory across the categories. For example the categories might equate to motor area involvement only (M), motor and sensory motor/parietal involvement (MS), and motor area, sensory area and posterior visual areas (MSH). Thus the classes may be regarded as shorthand, easily assessibles indices of lesion size. Despite these concerns on what the classes represent, their practical use has been evidenced (Reding and Potes 1988, Sanchez-Blanco 1999) and it is concluded that further study of the clinical use of such classifications is warranted.

## **Implications for Research**

### *Methodology*

The review supported the hypothesis that RCVA patients have poorer prognosis for the recovery of functional abilities although the difference may require relatively high power to detect. Future studies should thus be longitudinal and prospective in nature and employ a large sample size (n=200 approximately). These suggestions might be operationalised by systematically assessing patients on standardised tools at fixed assessment points as part of routine clinical assessment in a stroke unit for example. In this way relatively large samples may be recruited over a period of years effectively and in a cost efficient manner.

Sample selection may be a universal problem in stroke research given the heterogeneity of the CVA population. Entry criteria are either operationalised according to the hypothesis advanced or in terms of convenience; in both cases heterogeneity will obtain. Blanc-Garin (1994) proposed a possible methodological solution to inter-patient difference. The reported study involved measurement of behavioural variables (impairment and recovery of motor capacity, functional abilities, walking and activities of daily living) in addition to visual attentional variables. Impairment and recovery variables were then entered into a factorial analysis (multiple component analysis). This process identified groups of patients defined by different relationships between impairment and disability. A group was defined by consistency of recovery of activities of daily living and motor function (consistent recovery group) and a second group was defined by a lag in recovery of activities of daily living in respect of motor function (functional lag group). The analysis then involved assessing the distribution of visual attentional variables within these groups. Blanc-Garin's (1994) 'functional lag' group, 'lagged' in walking and daily life activities in respect of basic motor function abilities. This is similar to the concept ("he does but can he?") expressed by Andrews and Stewart (1979). Given the heterogeneity of initial impairments and recovery rate in stroke, this methodology may lower the risk of Type I error in the pursuit of hypothesised differences between groups on behavioural variables. This would also allow broader selection of patients for research, describing the population more realistically in so doing. It has not been possible to locate critiques of the methodology employed although it may be that possible statistical criticisms could be made, the present writer is not aware of these.

The study by Saeki and colleagues (1993) contains logical errors which serve as important caveats. They found that 'poor motivation'; urinary incontinence; age and 'delay from CVA onset to rehabilitation' significantly contributed to rehabilitation effectiveness. However, poor motivation is defined as 'insufficient or poor participation and accomplishment in the rehabilitation training activity'. The definition used ensures the relationship they effort to demonstrate. The authors also noted that the longer the delay between stroke and admission to the rehabilitation service, the less the improvement. However this follows from the known natural history of recovery. Recovery is fastest soon after stroke and declines thereafter (e.g. Wade, Wood & Langton-Hewer, 1985). Therefore, if the first assessment is delayed, there is less scope for recovery. The results therefore cannot be used to support earlier rehabilitation.

The findings of the current review suggest that year of publication may have an effect on the determination of functional difference by laterality of stroke. The care of stroke patients has advanced a great deal in recent years (Stroke Unit Trialists' Collaboration 2001). One aspect of this apparent improvement in care is the move to providing care in an organised inpatient unit to meet the specific needs of CVA patients. A recent meta-analysis has shown that those treated in organised 'Stroke Units' are more likely to survive, regain independence and return home than those cared for in general medical wards (Stroke Unit Trialists' Collaboration 2001). Amelioration of care, and subsequent increased independence overall, may also be more likely to highlight those that do not benefit so much from the rehabilitation stay. This hypothesis remains untested however.

### ***Measures***

Examination of the measures used in assessing outcome revealed little consensus on which measures are standard. Many of the early studies use non-standardised or tools accepted by local clinician consensus. Research in this area would greatly benefit from comparable measures and thus comparable findings across studies.

Measurement of motor function is highlighted as crucial to research examining the influences of laterality or attention on stroke outcome. All of the studies (attempting to do so) measured motor function in terms of strength and ability to position the affected limb. This traditional and easily administered assessment has practical advantages and is the current assessment of choice. It is proposed however that a measure of use of the affected limb in unit time may be a better estimate of real-life functional *activity* rather than point-in-time *ability*, and may therefore be of more relevance to rehabilitation (Uswatte, Miltner, Foo, Varma, Moran, & Taub, 2000). advances in accelerometer technology (allowing measurement of the acceleration of a limb in space) and computational treatment of the output allows valid and reliable measurement in this domain (Uswatte *et al* 2000). A lack of functional use may then be targetted for specific interventions designed to increase the probability of arm use with the device also measuring treatment effects (e.g. Robertson, North & Geggie 1992; Taub, Uswatte & Pidikiti 1999).

The assessment of functional disability may also impact on the apparent influence of side of lesion. For example Woo and colleagues (1999) published findings which indicate that the National Institutes of Health Stroke Scale (NIHSS) may favour left hemisphere strokes. They selected patients with left and right hemisphere CVA and matched for NIHSS score. They found that those with right hemisphere lesions had statistically greater lesion than those with left hemisphere CVA. This carries the suggestion that stroke scales may generally focus more on

observable difficulties such as language impairment leading to poor sensitivity to visuospatial disorders. This possibility warrants further study. Conversely it is also suggested that a good relationship of lesion volume and scores achieved on such 'general' measures may also increase their validity.

### **Potential Conflict of Interests**

No potential conflict of interests was identified. No commercial party having a direct financial interest in the results of the review has or will confer a benefit on the author or organisation with which the author is associated.

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### **Blanc-Garin 1994**

Blanc-Garin, J. (1994) Patterns of Recovery Following Stroke: *Neuropsychological Rehabilitation*, 4 (4) 359-385.

### **Buonocore 1990**

Buonocore, M., Casale, R., Arrigo, A., (1990) Psycho-motor skills in hemiplegic patients: reaction time differences related to hemispheric lesion side. *Neurophysiologie Clinique* 20, 203-206.

### **Chen-Sea 1993**

Chen-Sea, M., Henderson, A., Cermak, S. (1993) Patterns of visual spatial inattention and their functional significance in stroke patients. *Archives of Physical Medicine and Rehabilitation*, 74, 355-360.

### **Denes 1982**

Denes, G., Semenza, C., Stoppa, E., & Lis, A. (1982) Unilateral spatial neglect and recovery from hemiplegia: A follow-up study. *Brain* 105, 543-552

### **Feigenson 1977**

Feigenson, J.S., Fletcher, H., McDowell, M.D., Meese, P., McCarthy, M.L. Greenberg, S. (1977) Factors influencing outcome and length of stay in a stroke rehabilitation unit. 8 (6), 651-656.

### **Granger 1992**

Granger, C.V., Hamilton, B.B., Fiedler, R.C. (1992) Discharge outcome after stroke rehabilitation. *Stroke*, 23, 978-982.

### **Kotila 1984**

Kotila, M., Waltimo, O., Niemi, M.L., Laaksonen, R., Lempinen, M. (1984) The profile of recovery from stroke and factors influencing outcome. *Stroke*, 15 (6) 1039-1044.

### **Jongbloed 1986**

Jongbloed, L. (1986) Prediction of function after stroke: A critical review. *Stroke* 17, 765-776.

### **Mills 1983**

Mills, V.M., DiGenio, M. (1983) Functional differences in patients with left or right cerebrovascular accidents. *Physical Therapy*, 63 (4), 481-485

### **Saeki 1993**

Saeki, S., Ogata, H., Okubo, T., Takahashi, K., Hoshuyama, T. (1993) Impact of factors indicating a poor prognosis on stroke rehabilitation effectiveness. *Clinical Rehabilitation*, 7: 99-104.

### **Sanchez-Blanco 1999**

Sanchez-Blanco, I., Ochoa-Sangrador, C., Lopez-Munain, L., Izquierdo-Sanchez, M., Feroso-Garcia, J. (1999) Predictive model of functional independence in stroke patients admitted to a rehabilitation programme. *Clinical Rehabilitation*, 13: 464-475.

### **Sterzi 1993**

Sterzi, R., Bottini, G., Celani, M.G., Righetti, E., Lamassa, M., Ricci, S. & Vallar G. (1993) Hemianopia, hemianaesthesia and hemiplegia after right and left hemisphere damage. A hemispheric difference. *Journal of Neurology, Neurosurgery and Psychiatry* 56, 308-310.

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**Tables:** To be inserted in text as indicated

**Table 1** Results of searches of MEDLINE, EMBASE, CINAHL, PsychInfo and the Cochrane Library via the OVID gateway facility ([http://gateway\\_di.ovid.com](http://gateway_di.ovid.com)).

<i>Step</i>	<i>Search word / Instruction</i>	<i>Matches</i>	<i>Titles/Abstracts retrieved</i>	<i>Total Studies included</i>
1	hemiplegia or hemiparesis	17914		
2	#1 or stroke	112401		
3	#2 and outcome	10487		
4	#3 and attention	271	271	
5	#3 and neuropsychological	184	184	
6	stroke or head injury	119967		
7	#6 and side of lesion	133	133	
8	#6 and side and motor	486		
9	#6 duplicates removed	302	302	
10	attention or side or lateral	677306		
11	#10 and stroke and motor	96	96	
12	side of damage or lesion) and motor	443		
13	#12 duplicates removed	264	264	
14	attention and motor impairment	837		
15	#6 and #14	42	42	
16				14

**Table 2** SIGN Levels of Evidence (SIGN 2001)

<i>Level</i>	<i>Description of Criteria</i>
1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1	Meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
2++	High quality systematic reviews of case-control or cohort studies
	High quality case-control or cohort studies with a very low risk of confounding bias, or chance and a moderate probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding bias, or chance and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Table 3 Sample descriptions of studies included in the review

	<i>First Author</i>	<i>Year</i>	<i>Number</i>	<i>Mean Age</i>	<i>Gender</i>	<i>Stroke characteristics</i>	<i>Time Outcome (days)</i>	<i>CVA-</i>
1.	Andrews	1982	135	?	?	?	365	
2.	Blanc-Garin	1994	79	61.7	53.5%male	100% infarct	27.5	
3.	Buonocore	1990	20	60.9(12.8)	85%male	100% infarct	107	
4.	Chen-Sea	1993	64	57.1(9)	72% male	48.4% infarct	'sub-acute'	
5.	Denes	1982	48	61.4	?	?	53.5	
6.	Feigenson	1977	248	67	50% male	89.2% infarct	81	
7.	Granger	1992	7905	70.7	48.2%male	?	54	
8.	Jongbloed	1986	33 studies	?	?	?	?	
9.	Kotila	1984	154	61	54.5%male	79% infarct	365	
10.	Mills	1983	102	67.7 (10.8)	38.2% male	100% infarct	100	
11.	Saeki	1993	124	55	60% male	?	67	
12.	Sanchez-Blanco	1999	92	67 (10)	64.1% male	76% infarct	150	
13.	Sterzi	1993	298	74	49% male	77.9% infarct	30	
14.	Wade	1984	162	67.5	50%male	?	'sub-acute'	
	<i>Total mean</i>		<i>725.46</i>	<i>64.25</i>	<i>56.77</i>	<i>83.81</i>	<i>127.27</i>	
	<i>(Total s.d.)</i>		<i>(2158.57)</i>	<i>(5.62)</i>	<i>(12.96)</i>	<i>(17.68)</i>	<i>(122.76)</i>	

Table 4 Statistical Analysis: Level of evidence in terms of analysis and dealing with confounders

	<i>Study</i>	<i>Analysis Type</i>	<i>C.I.?</i>	<i>Goodness of Fit?</i>	<i>Correction for Multiple Tests?</i>	<i>Confounders identified?</i>	<i>Confounder Details</i>	<i>Level of evidence</i>
1	Andrews 1982	Group comparison ( $\chi^2$ )	No ( $\chi^2$ )	n/a ( $\chi^2$ )	n/a ( $\chi^2$ )	No	Gross measures summing various functions	2-
2	Blanc-Garin 1994	Group comparison, Correlation	n/a (r)	n/a (r)	n/a (r)	Yes		2+
3	Buonocore 1990	Group comparison (t)	Yes	n/a	n/a (2 comparisons)	Yes		2++
4	Chen-Sea 1993	ANOVA	No	n/a	Yes	Yes		2+
5	Denes 1982	ANOVA	No (t)	Yes	Yes	Yes		2+
6	Feigenson 1977	Descriptive analysis	No	No	n/a	No	Group differentiation? Outcome clarity?	2-
7	Granger 1992	Group comparison (SNK)	No	n/a	Yes	Yes		2++
8	Jongbloed 1986	Review	n/a	n/a	n/a	n/a		2-
9	Kotila 1984	Group comp. ( $\chi^2$ )	No	No	No	Yes		2+
10	Mills 1983	Correlation	n/a (r)	n/a (r)	No	No	No index of stroke severity eg. lesion size	2-
11	Saeki 1993	Regression	No	Yes	n/a	No	i. Motivation con. w/ recovery. ii. Time to rehab con. w/ severity	2-
12	Sanchez-Blanco 1999	Regression	Yes	Yes	n/a	Yes		2+
13	Sterzi 1993	Group comparison ( $\chi^2$ )	Yes	n/a	n/a	Yes		2+
14	Wade 1984	Group difference	No	n/a	No	Yes		2+

Table 5 effects of interest found by study level of evidence

	<i>Study</i>	<i>Level of evidence</i>	<i>Sample size</i>	<i>Were there differences between L / R CVA groups?</i>	<i>Did Visuospatial problems predict function?</i>
1.	Andrews 1982	2-	135	No	No
2.	Blanc-Garin 1994	2+	79	Yes	Yes
3.	Buonocore 1990	2++	20	Yes	N/A
4.	Chen-Sea 1993	2+	64	N/A	Yes
5.	Denes 1982	2+	48	Yes	Yes
6.	Feigenson 1977	2-	248	N/A	Yes
7.	Granger 1992	2++	7,905	Yes	N/A
8.	Jongbloed	2-	?	No	Yes
9.	Kotila 1984	2+	154	No	Yes
10.	Mills 1983	2-	102	No	Yes
11.	Saeki 1993	2-	124	N/A	No
12.	Sanchez-Blanco	2+	92	N/A	Yes
13.	Sterzi 1993	2+	298	Yes	Yes
14.	Wade 1984	2+	162	No	Yes

Table 6 Studies included in the review by study type, sample, relationship examined and findings

<i>Author / Year</i>	<i>Study Type</i>	<i>Population</i>	<i>Intervention / prognostic variable</i>	<i>Relevant Outcomes measured</i>	<i>Findings</i>
1 Andrews 1982	Prognostic factor /Outcome study	135 Stroke patients (survivors at 12 months)	Right vs. left hemisphere stroke damage	Power loss, ADL* Disability	No sig. diffs. between groups
2 Blanc-Garin 1994	Prognostic factor /Outcome study	79 stroke patients (27.5 days post stroke)	Right vs. left hemisphere stroke damage	Motor function, ADL.	RCVA <LCVA (Consistent Recovery).
3 Buonocore 1990	Between groups quasi experimental study	20 stroke patients (107 days post stroke)	Right vs. left hemisphere stroke damage	Visuo-motor function	RCVA <LCVA (Reaction Time)
4 Chen-Sea 1993	Prognostic factor /Outcome study	64 stroke patients (sub-acute)	Hemi-inattention	ADL, Motor function	VSD** predicted ADL+Mot.
5 Denes 1982	Prognostic factor /Outcome study	48 stroke patients (53.5 days post stroke)	Right vs. left hemisphere stroke damage.	ADL, Motor function	RCVA <LCVA
6 Feigenson 1977	Prognostic factor/ Outcome study	248 stroke patients (72 days post stroke)	Right vs. left hemisphere stroke damage	Walking, ADL, Discharge disposition	VSD predicted ADL
7 Granger 1992	Prognostic factor/ Outcome study	7905 stroke patients (54 days post stroke)	Right vs. left hemisphere stroke damage	ADL, (and change), Discharge disposition	RCVA <LCVA (ADL change)
8 Jongbloed 1986	Narrative Review	33 studies 1950-1986.	Right vs. left hemisphere stroke damage Hemi-inattention	ADL	VSD predicted ADL
9 Kotila 1984	Prognostic factor /Outcome study	Stroke patients (survivors at 12 months)	Hemi-inattention	ADL	VSD predicted ADL
10 Mills 1983	Prognostic factor / Outcome study	102 stroke survivors with moderate motor involvement	Right vs. left hemisphere stroke damage	ADL	VSD predicted ADL
11 Saeki 1993	Prognostic syndrome / Outcome study	124 stroke survivors at 67 days post CVA	General prognostic factors including neglect	ADL, Motor function	No sig. predictors of interest
12 Sanchez-Blanco 1999	Prognostic syndrome / Outcome study	92 stroke survivors at 150 days post CVA	Presence of sensory and hemianopsic symptoms	ADL.	VSD predicted ADL
13 Sterzi 1993	Prognostic factor /Outcome study	298 stroke patients (30 days post stroke)	Right vs. left hemisphere stroke damage	Motor function, Position Sense	RCVA <LCVA (Motor, VSD)
14 Wade 1984	Prognostic factor /Outcome study	162 stroke patients (sub-acute)	Right vs. left hemisphere stroke damage	ADL, Arm function, Walking ability	VSD =lower discharge ADL

\* Activities of Daily Living \*\* Visuospatial Difficulties

**Chapter 3**

**Major Research Project Proposal**

**Attention system function and motor impairment following cerebrovascular accident: Examining hemispheric differences.**

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Submitted 14.12.01

2200 words

## INTRODUCTION

Cerebrovascular accident (CVA) is the leading cause of disability in developed countries (Stineman, Maislin, Fiedler & Granger, 1997). Persisting motor impairment results in disability in more than half of those who suffer a CVA (Stineman *et al* 1997). Despite the widespread use of various techniques in the rehabilitation of hemiplegia, the literature as reviewed by Duncan (1997) is equivocal on the value of physical rehabilitation of motor problems in sub-acute patients.

Motor impairment following stroke rarely occurs in isolation from other symptoms (Sterzi, Bottim, Celani, Righetti, Lamassa, Ricci, & Vallar 1993). Sterzi and colleagues (1993) describe a constellation of symptoms frequently co-occurring with hemiplegia including visual hemi-neglect and hemi-anaesthesia. In the examined cohort, motor impairment was more common in right hemisphere damaged patients. Similarly and importantly, contralesional sensory inattention and somatosensory problems were also more common in right hemisphere damaged patients (Sterzi *et al* 1993).

An explanation of the association of motor-problems and hemi-inattention has been proposed in terms of the anatomy of these functions (Sterzi *et al* 1993). Posner and colleagues (for example Posner, Inhoff, Friedrich & Cohen 1987) have identified regions of the right hemisphere which play important roles in disengaging visual attention from current focus (posterior parietal area) and in maintaining attention (activity focused on right frontal areas). Greater visuo-spatial difficulties following right hemisphere damage may represent disruption of the attentional system subserving shift to contralesional space and that subserving attention to left personal space respectively. However this in itself does not account for the preponderance of motor impairment following right hemisphere damage relative to left (Sterzi *et al* 1993), as motor control for the left side of the body is not significantly lateralised to the right. It has been proposed that left motor problems may often be related to the phenomenon of left personal neglect, wherein the patient has reduced awareness of the contralesional side of the body (Robertson & North 1992). Thus impaired attention to contralesional space may present primarily as a motor problem (Sterzi *et al* 1993)

Functional recovery following stroke has been associated with various prognostic indicators. The identification of prognostic indicators allows targeted interventions toward the impairment which appears to be hampering recovery. Research in this domain suggests that successful rehabilitation of factors prognostic of poor outcome facilitates functional improvement (Paolucci *et al* 1996).

Unilateral visual neglect has been identified as an important predictor of functional recovery following stroke (Kinsella & Ford 1980, Denes *et al.* 1982, Kotila *et al* 1984, Friedman 1992, Gialanella & Mattioli 1992, Jehkonen *et al* 2001). This syndrome is heterogeneous in nature but most commonly follows from damage to the right posterior parietal cortex (Bisiach Capitani, Luzzati & Perani 1981). Conversely, the use of techniques to rehabilitate visual neglect has also been found to significantly improve functional recovery following stroke (Paolucci *et al* 1996). The converse relationship has also been demonstrated. Contralesional limb activation appears to reduce the symptoms of visual neglect (Robertson, Hogg & McMillan, 1998; Samuel, Louis-Dreyfus, Kaschel, Makiela, Troubat, Anselmi, Cannizzo & Azouvi 2000).

Work on the rehabilitation of visual neglect has resulted in a useful fractionation of the neglect syndrome. Hemi-inattention may thus manifest as neglect for extra-personal space or for personal space (e.g. Robertson & North 1992). It is proposed that these functions are dissociable. Personal attention appears related to the direction of limb movement in peri-personal space, while extra-personal visual attention facilitates the direction of whole body movement in space (Robertson & North 1992). Personal neglect may thus be more related to motor impairment than visual inattention. However, to the knowledge of the current writer, this remains to be directly tested experimentally.

The neural systems underpinning visuo-spatial attention are related to systems subserving sustained attention systems both anatomically and functionally (Posner & Dehaene 1994). The frontal sustained attention system is argued to modulate the activity of the posterior parietal spatial attention systems (Posner 1993). This action is argued to be mediated by interconnections involving right hemisphere dominant noradrenaline circuits (Oke, Keller, Mefford & Adams 1978).

Robertson and colleagues (1997) reported that auditory sustained attention was a marker for unilateral spatial neglect (Robertson, Manly, Beschin, Daim, Haeske-Dewick, Homberg, Jehkonen, Pizzanuglio, Shiel, Weber 1997). This further supports the close links between sustained attention and visuo-spatial attention. Their study also included measures of range and strength of movement (Motoricity Index - Wade & Langton-Hewer, 1987), as well as for personal neglect and visual neglect. Moderate to high correlations were reported (a) between patients' sustained attention scores and capacity for contralesional movement; (b) between patients' personal neglect scores and Motoricity scores; and (c) between visual neglect scores and Motoricity scores. The relative importance of these variables in predicting variance in the motor measure was not reported.

Techniques to improve sustained attention have been shown to lead to significant reduction of neglect phenomena (Robertson *et al* 1995). The functional relatedness of the sustained attention system and visuo-spatial attention system has also been demonstrated such that children with attention deficit hyperactivity disorder omitted significantly more left stimuli than age and education matched controls in letter cancellation tasks (Sandson *et al* 2000).

To summarise, visual neglect predicts variance in functional outcome following stroke (e.g. Denes *et al* 1982). In turn, sustained attention has been found to be a marker for visual neglect (Robertson *et al* 1997). Posner's (1993) anatomically driven model suggests that sustained attention, visuo-spatial attention and motor control functions are related right hemisphere functions. Thus, the laterality of lesion location in terms of predicting outcome is important.

The model subsuming these relations (Robertson 1999) is the basis for current experimental rehabilitation strategies (e.g. Robertson, Hogg & McMillan, 1998). This model suggests that visuo-spatial attention function and sustained attention function will predict motor function in right hemisphere-damaged CVA patients.

In conclusion, studies to date have focused on the association of visual hemi-neglect and functional outcome. To our knowledge, the importance of visual hemi-neglect in predicting motor function variance remains unexamined relative to sustained attention and attention for personal space. The current proposed study aims to test the hypothesis that sustained attention, hemi-neglect and motor function combine to statistically discriminate patients

with damage to the right hemisphere systems proposed to be involved. This will contribute to theoretical knowledge on the inter-relationships of the attentional systems and their association with motor impairment and disability.

## PROPOSAL

To assess limb impairment and disability in a sample of patients who have been hospitalised following first episode CVA. Tests sensitive to visual neglect, personal neglect and a test of sustained attention will be administered to delineate their association with each other and with the motor function and disability outcome variables. Following the findings of Sterzi *et al* (1993) and the theoretical work of Posner (1993) and Robertson (1999) it is an aim of the study to replicate the finding that, on tests of neglect (personal and visual), right hemisphere CVA patients will be more impaired than left hemisphere patients. Sustained attention will also be expected to differ between groups with less impaired scores obtaining in the left hemisphere group. Furthermore sustained attention and neglect and severity of motor impairment will significantly predict side of lesion in a logistic regression analysis. This will examine the existence of a relationship between the hypothesised right hemisphere systems of sustained attention, visuo-spatial attention and systems underpinning limb movement.

Posner's (1993) anatomically driven hypothesis suggests a possibility that the inter-relationship of attentional and motor functions as manifested in CVA patients is an artefact of damage compromising multiple, potentially independent, right-hemisphere functions. Lateralised damage may thus account for the apparent relationships between the attentional systems discussed. A test of this model would entail assessing whether a left lateralised function predicts motor impairment variance in left hemisphere damaged patients. It is thus hypothesised that verbally mediated attention (as measured using the left-damage-sensitive Verbal Fluency Test - Tucha, Smely & Lange, 1999; Keller & Sutton, 1991; Ramier & Hecaen 1970) will be associated with left hemisphere involvement but will not predict contralesional severity of motor impairment.

Pre-morbid abilities and post CVA deficits are heterogeneous. A small battery of neuropsychological tests will be therefore be administered to describe participants. Side of lesion will be confirmed by computerized tomography scan information.

## AIMS

1. To examine theoretically predicted associations between tests sensitive to neglect (line bisection, star cancellation), and sustained attention (elevator tone counting test) in predicting functional impairment following stroke. The study thus seeks to evidence the model of attention system influence on motor function that forms the theoretical basis of experimental rehabilitation strategies (Robertson *et al* 1997; Robertson 1999).
2. To test the model of association of spatial and non-spatial attentional systems further by assessing whether a test of verbally mediated attention (Verbal Fluency Test) adds to the explained variance in motor impairment following stroke. The design therefore allows a test of a model of hemispheric organisation of sustained attention and visuo-spatial attention systems (Posner 1993).

## HYPOTHESES

- i. Deficits in visuo-spatial attention and sustained attention will predict greater severity of motor impairment in right hemisphere stroke patients.
- ii. Deficits in verbally mediated attention will be associated with left hemisphere damage but will not predict impairment in left hemisphere damaged patients.
- iii. Sustained auditory attention will significantly correlate with scores achieved on tests of visuo-spatial attention.

## DESIGN

A two sample design will be used. Patients will be categorised as left or right hemisphere damaged as a result of CVA. Statistical difference will be examined between groups on motor function, sustained attention, visuo-spatial attention, variables previously associated with poor prognosis. Subsequently the optimum logistic regression model explaining variance in group membership will be derived.

## PARTICIPANTS

Participants will be male or female patients aged 16 to 75 who have received specialised inpatient care for right hemisphere stroke and will be subsequently deemed medically stable. Patients who have been evaluated as suitable for entry to rehabilitation programmes will be included. This exclusion criterion will control for the possibility of globally poor scores obscuring the presence of a relationship between the variables of interest. Participants with severe receptive aphasia will be excluded due to the possibility that they may be unable to give informed consent or understand test instructions.

The natural history of recovery following stroke suggests a rapid improvement in function in the first thirty days, followed by a slowing of functional improvement thereafter (e.g. Wade, Wood & Langton-Hewer 1985). Patients thirty days following stroke and less than one year post-stroke will be included.

No identified published study reported differences in severity of motor impairment between left and right brain injured groups. As such, a direct power calculation for discriminating left and right hemisphere stroke patients was not possible.

An estimate of sample size was arrived at by focusing on the relationship between sustained attention and visual neglect symptomatology (hypothesised in my current proposal to be correlated) a sample size of 21 would yield a power of 0.8. (Based on Robertson, Manly, Besehin *et al* 1997). As this study examined right hemisphere damaged patients only the current sample will recruit a similar number of left hemisphere patients. The sample size will be rounded to a more conservative 50.

## PROCEDURE

Participants will be identified through acute stroke services and community rehabilitation teams serving Glasgow South. Patients with right hemisphere strokes will then be contacted, provided with information on the study and asked to participate. Participants will be assessed by the researcher during pre-arranged hospital or home visits.

Assessment data to be collected is outlined under measures below. Total data collection time per patient (including tests for neuropsychological description) is estimated at one hour.

## ASSESSMENT MEASURES

### *Variables related to hypotheses*

1. Visual neglect — Star cancellation and line bisection sub-tests from the Behavioural Inattention Test (Wilson, Cockburn & Halligan 1988).
2. Personal neglect measures — hair combing task, razor/powder compact task (e.g. Robertson, Hogg & McMillan 1998) and Scale for Personal Neglect (Bisiach *et al.* 1986)
3. Sustained attention measure — Elevator tone counting from the Test of Everyday Attention (Robertson, Ward, Ridgeway and Nimmo-Smith 1994): This measure can be administered at various volumes to correct for patients' auditory acuity.
4. Verbal fluency measure — F.A.S. test (Benton & Hamsher 1989).
4. General disability measures — Modified (5 level scoring) Barthel Index (Shah, Vanclay & Cooper 1990, after Mahoney & Barthel 1965)
6. Hemiplegia measure — Motoricity Index. (Wade & Langton-Hewer, 1987; Collen & Wade 1990)

## Neuropsychological description measures

1. Visuo-Spatial Ability — Rey Figure (Copy) This is a measure of the participants ability to perceive and copy a complex figure (Meyers & Meyers, 1995).
2. Language — Revised Token Test (parts 1 and 5): To screen for comprehension deficits (De Renzi & Faglioni 1978).
3. Memory — Prose Passage recall sub-test of the Adult Memory and Information Processing Battery: A verbal memory index (Coughian & Hollows 1985).  
Rey Figure Recall (Meyers & Meyers, 1995): A visual memory test wherein the participant recalls the figure previously copied (above).
4. Executive Function — Hayling Sentence Completion Test: A verbal test of the patients ability to inhibit over-learned associations in the generation of responses (Burgess & Shallice 1997)
5. Mood — Wimbledon Self Report Scale (Coughlan & Storey, 1988)
6. Pre-morbid Intellectual Functioning — National Adult Reading Test (Nelson & Willison, 1991, Crawford, 1992)
7. Presence of shoulder pain (Roy *et al*, 1995)
8. Awareness of functional impairment (Gialanella & Mattioli 1992)

## *Demographic information* (to be drawn from medical notes)

Age; Gender; Time since stroke; Time to attain continence (as index of stroke severity); Location of lesion (from patient diagnosis).

## ANALYSIS

The proposed design will allow discriminative analysis of the predictors by group. The discriminating variables will be entered in to a logistic regression analysis with group as dependent variable.

The data will be analysed using SPSS version 9.0 for Windows. Data will be stored on a password-protected personal computer. Information containing patient identifiers will be kept in accordance with the Data Protection Act.

## TIMETABLE

The Research Ethics Committee of the South Glasgow University Hospitals NHS Trust approved the methodology of this proposal in November 2001. Data collection will begin after protocol approval and is expected to be completed by July 2002.

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## **Chapter 4**

### **Major Research Project Report**

#### **Attention system function and motor impairment following cerebrovascular accident: Examining hemispheric differences.**

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Prepared in accordance with guidelines for contributors to *Neuropsychologia* (Appendix 3.1)

8000 words

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## ABSTRACT

Background studies to date have found that visual hemi-neglect hampers functional recovery following stroke. The neglect syndrome, more common following right hemisphere damage, has been conceptualised as impairment of dissociated visuo-spatial systems directing attention to the left side of the body, peri-personal and extra personal space which underpin the direction of contra-lesional limb movement. Correlations between sustained attention impairments, neglect, and motor impairment have also been demonstrated. The current study aimed to assess the importance of visual hemi-neglect in predicting motor function variance relative to sustained attention and attention for personal space, thus testing the hypotheses: (i) that visuo-spatial attention and sustained attention are lateralised functions such that they will differentiate groups of patients defined by side of hemiplegic weakness. (ii.) That sustained attention, hemi-neglect and motor function will combine to discriminate groups defined by unilateral damage. And (iii) that sustained attention deficits are markers for visual neglect. To attempt to control for the effect of gross lateralised damage, it was also hypothesised that verbally mediated attention (as measured using the left-damage-sensitive Verbal Fluency Test) - will be associated with left hemisphere involvement but will not predict contralesional severity of motor impairment. Logistic regression modelling and correlation analyses were employed. The results from the generated models indicate that visual neglect in combination with attention to the impaired side of the body and verbally mediated attention (verbal fluency) differentiated left and right hemiplegia patients. Motor impairment and sustained attention did not enter the model differentiating side of lesion as expected. A second logistic regression showed that high levels of motor function are differentiated from poor motor function by a combination of sustained attention and attention to the impaired side of the body. Sustained attention was not correlated with visual neglect. Visual hemi-neglect was significantly negatively correlated with motor function, change in motor function since stroke and disability. The findings are discussed in terms of previous research, study limitations and implications for future research.

## INTRODUCTION

Cerebrovascular accident (CVA) is the leading cause of disability in developed countries (Stineman, Maislin, Fiedler & Granger, 1997). Persisting motor impairment results in disability in more than half of those who suffer a CVA (Stineman *et al* 1997). Despite the widespread use of various techniques in the rehabilitation of hemiplegia, the literature as reviewed by Duncan (1997) is equivocal on the value of physical rehabilitation of motor problems in sub-acute patients. This suggests that current rehabilitation strategies may be refined to promote greater recovery.

Motor impairment following stroke rarely occurs in isolation from other symptoms (Sterzi, Bottini, Celani, Righetti, Lamassa, Ricci, & Vallar 1993). Sterzi and colleagues (1993) describe a constellation of symptoms frequently co-occurring with hemiplegia including visual hemi-neglect and hemi-anaesthesia. In the examined cohort, motor impairment was more common in patients with right hemisphere damage and resultant left hemiplegia. Similarly and importantly, contralesional sensory inattention and somatosensory problems were also more common in right hemisphere damaged patients and posited to explain the observed poorer motor outcome (Sterzi *et al* 1993).

An explanation of the association of motor-problems and hemi-inattention has been proposed in terms of the anatomy of these functions (Sterzi *et al* 1993). Posner and colleagues (for example Posner, Inhoff, Friedrich & Cohen 1987) have identified interconnected regions of the right hemisphere which play important roles in disengaging visual attention from the current focus (posterior parietal area) and in maintaining attention (activity focused on right frontal areas). Damage of these attentional systems is hypothesised to disrupt the ability to direct attention to the contralesional side of the body or the contralesional side of extra-personal space (Robertson & North, 1992). This phenomenon in turn leads to impairment in ability to direct motor movement (Robertson 1999). Thus impaired attention to contralesional space may present primarily as a motor problem (Sterzi *et al* 1993)

Functional recovery following stroke has been associated with various prognostic indicators. The identification of prognostic indicators allows targeted interventions toward the impairment that appears to be hampering recovery. Research in this area suggests that the successful rehabilitation of factors predicting poor outcome, in turn facilitates functional improvement (Paolucci *et al* 1995).

Unilateral visual neglect has been identified as an important predictor of functional recovery following stroke (Kinsella & Ford 1980, Denes *et al* 1982, Kotila *et al* 1984, Friedman 1992, Gialanella & Mattioli 1992, Jehkonen *et al* 2001). Neglect phenomena are heterogeneous in nature but most commonly follow damage to the right posterior parietal cortex (Bisiach Capitani, Luzzati & Perani 1981). The use of techniques to rehabilitate visual neglect has been found to significantly improve functional recovery following stroke (Paolucci *et al* 1995). The converse relationship has also been demonstrated. Contralesional limb activation appears to reduce the symptoms of visual neglect (Robertson, Hogg & McMillan, 1998; Samuel, Louis-Dreyfus, Kaschel, Makiela, Troubat, Anselmi, Cannizzo & Azouvi 2000). Moreover contralesional limb activation training has been shown to improve hemiplegic limb function in a randomised control trial (Robertson, McMillan, MacLeod, Edgeworth & Brock, In press).

Work on the rehabilitation of visual neglect has resulted in a useful fractionation of the neglect syndrome. Hemi-inattention may thus manifest as neglect for extra-personal space, for personal space or for body space (e.g. Robertson & North 1992). These functions have been shown to be dissociated (Robertson & North 1992). Personal attention appears related to the direction of limb movement in peri-personal space, while extra-personal visual attention facilitates the direction of whole body movement in space (Robertson & North 1992). Neglect of the body may thus be more related to motor impairment than its associate, visual neglect. However, to the knowledge of the current writer, this remains to be directly tested.

The neural systems underpinning visuo-spatial attention are related to systems subserving sustained attention, both anatomically and functionally (Posner & Dehaene 1994). The frontal sustained attention system is argued to modulate the activity of the posterior parietal spatial attention systems (Posner 1993). This action is argued to be mediated by interconnections involving right hemisphere dominant noradrenaline circuits (Oke, Keller, Mefford & Adams 1978).

Auditory sustained attention (vigilance) is a function which can be conceptualised as an organism's preparedness to act in response to an unpredictable target. Thus interconnections with pre-motor and visuo-spatial systems may be expected. This appears to be so. Sustained attention has been shown to depend on right frontal circuits (Wilkins, Shallice & McCarthy, 1986). And Robertson and colleagues (1997) reported that auditory sustained attention was a marker for unilateral spatial neglect (Robertson, Manly, Beschin, Daini, Haeske-Dewick, Homberg, Jehkonen, Pizzamiglio, Shiel, Weber 1997). They also demonstrated moderate to high correlations between: (a) patients' sustained attention scores and contralesional motor function; (b) patients' personal neglect scores and motor function scores; and (c) visual neglect scores and motor function scores. The relative importance of these variables in predicting variance in the motor measure was not reported.

Techniques to improve sustained attention have been shown to lead to significant reduction of neglect phenomena (Robertson *et al* 1995). The functional relatedness of the sustained attention system and visuo-spatial attention system has also been demonstrated such that children with attention deficit hyperactivity disorder omitted significantly more left stimuli than age and education matched controls in letter cancellation tasks (Sandson, Bachna & Morin 2000).

To summarise, visual neglect predicts variance in functional outcome following stroke (e.g. Denes *et al* 1982). In turn, sustained attention has been found to be a marker for visual neglect (Robertson *et al* 1997). Posner's (1993) anatomically driven model suggests that sustained attention, visuo-spatial attention and motor control functions are related right hemisphere functions. Thus, the laterality of lesion location in predicting outcome appears important.

The model subsuming these relations (Robertson 1999) is the basis for current experimental rehabilitation strategies (e.g. Robertson, Hogg & McMillan, 1998, Robertson *et al* (In press)). This model suggests that visuo-spatial attention function and sustained attention function will predict motor function in right hemisphere-damaged CVA patients.

In conclusion, studies to date have focused on the association of visual hemi-neglect and functional outcome. To our knowledge, the importance of visual hemi-neglect in predicting motor function variance remains unexamined relative to sustained attention and attention for personal space. The current study thus aimed to test the hypotheses: (i.) That visuo-spatial attention and sustained attention are lateralised functions such that they will differentiate groups of patients defined by side of hemiplegic weakness; (ii.) that sustained attention, hemi-neglect and motor function will combine to discriminate groups defined by side of hemiplegic weakness and (iii.) that sustained attention deficits are markers for visual neglect.

Posner's (1993) anatomically driven hypothesis suggests the possibility that the inter-relationship of attentional and motor functions as manifested in right hemisphere CVA patients is an artefact of damage compromising multiple, but potentially independent, right-hemisphere functions. Lateralised damage of *adjacent* systems rather than functionally interrelated systems accounting for the apparent relationships between the attentional systems discussed. A test of this alternative model would entail assessing whether a left lateralised function predicts motor impairment variance in left hemisphere damaged patients. It is thus also hypothesised that verbally mediated attention (as assessed using the Verbal Fluency Test which is sensitive to left-damage - Tucha, Smely & Lange, 1999; Keller & Sutton, 1991; Ramier & Hecaen 1970) will be associated with right hemiplegia but will not predict motor impairment. By assessing this model it is hoped to contribute to theoretical work on the inter-relationships of the attentional systems and their association with motor impairment and disability.

## METHODS

### Design

A two-sample between-group design was used. Patients with motor impairment affecting the left side of the body formed group one and those with right motor impairment formed the second. Statistical difference between groups was assessed on motor function, disability, memory, language and attentional measures. Variables demonstrating a bivariate relationship were entered in a logistic regression model. Subsequently the optimum logistic regression model explaining variance in group membership was derived. A second logistic regression examined predictors of motor impairment as a dichotomous variable. Correlation analyses of relationships between variables of interest were also carried out.

### Participants

52 right handed CVA patients with residual motor difficulties participated in the study. Table 1 below shows means and standard deviations of the demographic variables. The mean age was 67.21 (standard deviation: 10.91) with a range of 29 to 87 years. 31 were male and 21 female. All of the participants had been admitted to one of two specialised stroke rehabilitation units and at assessment 13/52 remained inpatients. 39 had been discharged (36 to their own homes, 3 to sheltered accommodation). Only patients thirty days following stroke and less than one year post-stroke were included and the mean time since CVA was 178 (124) days. All participants were medically stable and either currently receiving physiotherapy or had completed a physiotherapy course. 29 had left hemiplegia and 23 had right hemiplegia.

The frequency of different CVA types was as follows: 51.9% had suffered a stroke affecting the middle cerebral artery territory; 29.6% an anterior circulation infarct; 14.8% a parietal infarct; 25.9% a lacunar infarct and 7.4% 'other' stroke types (calculated on the basis of 27 cases for which case-notes were retrieved).

The mean Token Test part 5 score (De Renzi & Faglioni 1978) was 11.23 (3.24) out of a maximum of 13. The entry criteria, which stipulated that all participants have sufficient comprehension to give informed consent, are reflected in these scores. The mean duration of formal education was 11 years (3.03, range: 0-21). The mean (NART) premorbid IQ estimate was 104.33 (12.76, range: 79-128).

### Power

A study reporting differences in *severity* of motor impairment between left and right brain injured groups was not identified. The only comparable analyses of outcome differences after left and right CVA were reported by Denes *et al* (1982) and Sterzi *et al* (1993). The study by Denes *et al* (1982) recruited a sample of 48 patients with hemiplegia yielding a power of 0.89 for their analysis of improvements in disability scores (UCLA Dept. of Statistics, 2001).

Sterzi *et al* (1993) identified proportions of those with motor impairment following left and right hemisphere CVA in

a cohort analysis of 298 patients. They did not attempt to assess severity of impairment however. The analysis revealed that 95% of right CVA patients and 85% of left CVA patients had motor deficits one month following CVA [chi square (1) =3.43,  $p < .01$ , odds ratio=3.39(1.34-9.65)]. However this proportional analysis was not suitable for a post hoc power calculation analysis (UCLA Dept of Statistics, 2001).

Another power calculation (UCLA Dept of Statistics, 2001) was based on the observed correlation between sustained attention and visual neglect in Robertson, Manly, Beschin *et al* (1997). This analysis suggested that the current sample size would yield a power  $\geq 0.8$  with respect to that finding. The current sample size ( $n=52$ ) was also therefore in line with the power analysis of the findings of Denes *et al* (1982).

### **Procedure**

Suitable participants were identified by key staff in acute stroke services and community rehabilitation teams serving South Glasgow. Patients were then contacted, provided with information on the study and invited to participate. Signed informed consent forms were collected before inclusion. Participants were assessed by the researcher during pre-arranged hospital or home visits. The maximum assessment time per participant was one hour and thirty minutes.

## Measures

All patients received a battery of tests of unilateral neglect, sustained attention and fluency as well as tests of motor function and disability. These were chosen based on their brevity, reliability and validity as evidenced by frequent employment in previous research

### *Variables related to hypotheses by functional area measured*

#### Disability (Appendix 3.3)

*Barthel Index* (Mahoney & Barthel 1965) an index of support required across self care areas including feeding, mobility, toileting, bathing, dressing, and continence.

#### Motor Function (Appendix 3.2)

*Motoricity Index* (Wade & Langton Hewer, 1987; Collen & Wade 1990) An assessor rated categorical index of motor impairment relative to defined criteria.

#### Visual Neglect (Appendices 3.4 and 3.5)

*Star Cancellation Test*, measure of visual neglect requiring cancellation of target stars against competing non-targets.

*Line Bisection Test* measure of visual neglect requiring the person to bisect each of three (20cm) lines.

(Both measures are taken from the Behavioural Inattention Test - Wilson, Cockburn & Halligan 1988).

#### Personal Neglect

*Comb Test* (e.g. Robertson, Hogg & McMillan 1998) requires the person to comb their hair as normal with the unimpaired hand. Comb-strokes to the left and right of the midline of the head are recorded and expressed as a proportion of total hair combing strokes.

*Scale for Personal Neglect* (Bisiach *et al.* 1986) requires the person to blind locate the hemiplegic hand with the unimpaired hand. Responses are categorised.

#### Sustained Attention (Appendix 3.6)

*Elevator Counting Test* This requires the person to listen to and count the tones within each of 7 audio presented strings of between 3 and 14 tones with random (3-5secs) intervals (Test of Everyday Attention - Robertson, Ward, Ridgeway and Nimmo-Smith 1994).

#### Verbal Fluency (Appendix 3.7)

*Controlled Oral Word Association (F.A.S. test)* (Benton & Hamsher 1989) requires the person to generate words beginning with F, A and S over each of three one minute periods, avoiding repetition. A test of fluency of rule governed recall and self monitoring. Thought to tap left frontal dysfunction and concomitant executive difficulties.

### *Description measures by function measured*

#### Visuo-Spatial Ability

*Rey Figure (Copy)* This measure of visuo-spatial ability requires the person to copy a complex figure (Rey 1941, Meyers & Meyers 1995).

## Language Comprehension

*Revised Token Test* (parts 1 and 5): This language comprehension test Requires person to respond behaviourally to verbal commands which increase in complexity. (De Renzi & Faglioni 1978).

## Memory

*Prose Passage Recall* This verbal memory index requires the person to recall a verbally presented passage of prose from the Adult Memory and Information Processing Battery: (Coughlan & Hollows 1985).

*Rey Figure Recall* (Rey, 1941, Meyers & Meyers, 1995) This visual memory test requires the participant to recall the previously copied Rey figure after a short delay.

## Pre-morbid Intellectual Functioning

*National Adult Reading Test* (Nelson & Willison, 1991, Crawford, 1992)

## Demographical data

Information on participant age, gender, education, time since CVA were recorded.

Participants were also questioned on the presence of shoulder pain (Roy *et al*, 1995) and incontinence at time of CVA. The latter variable is thought to be an estimate of stroke severity, occurring independently of other neurological and neuropsychological deficits, and predictive of survival and functional recovery (Wade, Wood & Langton Hewer, 1985).

Regarding anosognosia, participants' responses to questions about functional impairment were noted and categorised according to various degrees of awareness of their disability (disability mentioned spontaneously; only after disability specific questions; only after demonstration or complete denial (Gialanella & Mattioli 1992).

## Analysis

The design allowed discriminative analysis of the predictor variables by group. This analysis employed a sensitive level of significance ( $p < .10$ ) to ensure inclusion of variables with non-zero coefficients. The significantly discriminating variables were entered in to logistic regression analyses with (i.) side of weakness and (ii.) motor function as dichotomous dependent variables (Tabachnick & Fidell, 1996). Correlational analyses were also carried out to examine inter-relationships between the variables of interest.

The data were analysed using SPSS version 9.0 for Windows. Data were stored on a password-protected personal computer. Information containing patient identifiers were separated from data sheets and kept in a lockable cabinet.

## Ethical Approval

The study protocol was approved by the Ethics Committee of South Glasgow University Hospitals NHS Trust in November 2001.

## RESULTS

### Demographic information

Demographic information for the whole sample is presented in Table 1 below. The principal grouping variable in this study was side of hemiplegic weakness. Therefore in addition to presenting descriptive statistics for whole group, Table 1 also presents descriptive data on these sub-groups and indicates significant differences on group comparisons. There were no significant group differences on the demographic variables; age ( $t(50) = -.87$ , NS), gender, (Chi-square (1) = .164,  $p=.686$ ), education ( $t(50) = .64$ , NS), days since CVA ( $U(50) = 302.5$ , NS) or pre-morbid IQ estimate ( $t(50) = 0.685$ ,  $p=0.5$ )

### Neuropsychological measures

Measures were administered to describe the current sample. While not directly related to the hypotheses, group differences on these measures were examined with the results also presented in Table 1.

[Insert Table 1 here]

Visuo-spatial ability (Rey Figure – Rey, 1941, Meyers & Meyers, 1995) was assessed in 40 patients, with 12 unable to complete the task due to physical limitations. The mean Rey Copy score was within the normal range of scores for an age matched control group (Meyers & Meyers, 1995). This reflects the fact that as a sample there was a low rate of non-specific visuo-spatial disturbance. Patients with left and right hemiplegia did not differ significantly on this measure ( $t(38) = -.265$ ,  $p=.792$ ). Visual memory (Rey Figure Recall – Rey, 1941, Meyers & Meyers, 1995) did not differ between the groups ( $t(37) = -.026$ ,  $p=.98$ ). The sample mean was normal for a group of similar mean age (Meyers & Meyers, 1995).

Verbal memory (Prose Passage from Coughlan & Hollows, 1985) was the sole descriptive index on which the groups differed significantly. Patients with left hemiplegia achieved higher scores than those with right hemiplegia ( $t(40) = 2.95$ ,  $p<.005$ ). On the Shortened Token Test (De Renzi & Faglioni 1978) of receptive aphasia, the higher scores of the left hemiplegia group approached significance ( $t(50) = 1.79$ ,  $p=.079$ ).

12 patients had initial faecal incontinence (an estimate of stroke severity - Wade, Wood & Langton Hewer, 1985), 6 in each group. The groups did not differ significantly in prevalence of incontinence (Chi square(1)=0.21,  $p=0.65$ ) suggesting equal initial severity of stroke. The groups also failed to differ on presence of shoulder pain (Chi square(1)=.71,  $p=.40$ ) and on their awareness of functional impairment (Chi square(2)=4.06,  $p=0.132$ ).

The distribution of CVA types between left and right hemiplegia groups was not significantly different (Chi-square (4) = .89,  $p=.93$ ). As CVA was described in terms of the territory affected by CVA this suggests that there was no significant difference in terms of territory affected between groups defined by side of weakness.

### Variables related to the hypotheses (See Table 2 below)

The means and standard deviations of variables related to the hypotheses are presented in Table 2. This table also indicates the variables that differed significantly between left and right hemiplegia groups.

[Insert Table 2 here]

On the Line Bisection Test (Wilson, Cockburn & Halligan 1988) left hemiplegic patients deviated to the right significantly more in their estimation of the midpoint ( $t(50)=2.45$ ,  $p=0.018$ , 95% C.I.=0.89-8.93). This indicates a greater tendency of left hemiplegic patients to neglect left visual space.

On the Star Cancellation Test (Wilson, Cockburn & Halligan 1988) left hemiplegic patients did not omit significantly more contralesional stars than patients with right hemiplegia ( $t(50)=1.46$ ,  $p=.15$ ). Therefore there was some dissociation in the results of these two measures of neglect.

On the Comb Test (e.g. Robertson, Hogg & McMillan 1998) patients with left hemiplegia directed a significantly lower proportion of total comb-strokes towards the weak side ( $t(50)=-3.196$ ,  $p=.002$ ), indicating that they are, on this measure, more likely to neglect the affected side of body space. The between group differences on the Bisiach Scale for Personal Neglect (Bisiach *et al.* 1986) were not significant (Chi square(1)=2.92,  $p=0.087$ ).

The FAS Verbal Fluency Test (Benton & Hamsher 1989) was administered to 45 patients (86.54% of the sample), 7 patients, all with right hemiplegia, were unable to complete this test due to severe word production difficulties. The mean FAS performance was in the unimpaired range in terms of fluency and the sample showed few deficits in monitoring. Left hemiplegic patients scored significantly higher than those with right hemiplegia ( $t(43)=4.14$ ,  $p=.001$ ).

The mean Elevator Tone Counting score (Robertson, Ward, Ridgeway and Nimmo-Smith 1994) for the whole sample was 5.80(1.77) out of a total of 7 target strings. Patients with left or right sided weakness did not significantly differ on this measure of sustained attention ( $t(49)=1.36$ ,  $p=.179$ ). This was contrary to hypothesised laterality of this function.

The mean Barthel Index score (Mahoney & Barthel 1965) indicated that, on average, patients required assistance in four of the assessed areas of function (see Appendix 3.3 – Barthel Index). Patients with left hemiplegia did not differ from those with right hemiplegia in severity of disability ( $t(50) =-1.257$ ,  $p=.269$ ), contrary to hypothesised differences in outcome.

The mean (s.d.) Motoricity Index score (Wade & Langton Hewer, 1987) for the whole group (148.37 (44.74) / 198 max.) reflected the relatively high impairment of the sample. There were no significant difference between left and

right hemiplegic patients on severity of motor impairment ( $t(50)=-.863$ ,  $p=.392$ ), again contrary to expected differences in outcome.

An initial severity of motor impairment was not available. Therefore an estimate of recovery was attempted by expressing degree of deviation from normal motor function in terms of time since CVA,

i.e.  $(\text{Maximum Motoricity Score} - \text{Actual Motoricity Score}) / \text{Time since CVA}$ . This metric also failed to differentiate left and right hemiplegic patients ( $t(50)=1.20$ ,  $p=.236$ ).

#### **Associations with dichotomous variables: i. Side of Hemiplegia, ii. Motor function.**

i. Side of hemiplegia was employed as an outcome variable in the logistic regression analysis. A second dichotomous variable was created from total motoricity score by dividing the groups at the median and this formed the outcome variable for the second regression analysis.

The first procedure in the regression analyses was to define groups based on the dichotomous outcome variables and compare group means of each potential predictor variable. Hosmer & Lemeshow (1989) recommended the use of a sensitive cut-off for statistical significance ( $p<0.10$ ) to ensure inclusion of non-zero coefficients in the subsequent analysis. The results of this procedure are shown in Table 3.

ii. Groups defined on *side of hemiplegia* were significantly different on: (a.) Comb test ( $t(50)=2.25$ ,  $p=.002$ ), such that those with left hemiplegia made fewer comb-strokes on the affected side; and (b.) Line bisection average deviation to L or R ( $t(50)=2.25$ ,  $p=.018$ ), such that those with left hemiplegia deviated to the right in their estimates of the mid-line; (c.) and sustained attention ( $U(50)=231$ ,  $p=.061$ ) such that those with right hemiplegia were more vigilant. Those with left hemiplegia were however significantly higher scorers on (d) the Token test total score ( $U(50)=225$ ,  $p=.016$ ); (e.) FAS total in three minutes ( $t(43)=4.14$ ,  $p=.000$ ); and (f.) FAS total repetitions in three minutes ( $U(43)=181$ ,  $p=.1$ ).

[Insert Table 3 here]

For the second regression analysis independent variables were also subjected to t-tests (or Mann-Whitney U tests as appropriate) to identify variables which differentiated high and low scoring motoricity scores (split at the median score). This dichotomous variable demonstrated significant differences in terms of: (a.) Comb test ( $t(50)=-1.95$ ,  $p=.057$ ); (b.) Line bisection average deviation ( $t(50)=2.34$ ,  $p=.023$ ); (c.) Star cancellation (omissions left,  $t(50)=2.12$ ,  $p=.039$ ); (d.) Star cancellation (omissions right,  $t(50)=1.72$ ,  $p=.092$ ); (e.) Star cancellation (total omissions,  $t(50)=2.30$ ,  $p=.026$ ); (f.) Sustained attention (tone counting,  $U(50)=210$ ,  $p=.018$ ) and (g.) Rey figure ( $U(50)=108$ ,  $p=.016$ ).

## **Predictors of side of hemiplegia**

Following the difference testing analyses a logistic regression analysis was carried out to identify a model that differentiated the groups (taking interactions between the explanatory variables into account). This procedure thus aimed to test the hypothesis that *visual neglect and deficits in sustained attention will predict greater severity of motor impairment for patients following CVA*.

[Insert Table 4 here]

The model shown in Table 4. above subsumed the 'Attention to body-space' variable [Comb-test], mean deviation in mm on the Line Bisection task [LineBis] and Verbally Mediated Attention [FAS Verbal Fluency] and was significant in predicting side of hemiplegia ( $\chi^2 = 26.93, (3), p < .0001$ ). These three variables, dependent to varying degrees on 'attentional' systems, formed a model correctly categorising 80% of the sample (N=45 for this analysis). 76.92% of left hemiplegic patients and 84.21% of right hemiplegic patients were correctly categorised. However contrary to expectation Sustained Attention (as measured by the tone counting test), and motor function were excluded from the model differentiating patients by side of hemiplegia. Thus the finding in this model is that left hemiplegia is associated with impaired attention to the hemiplegic side, deviations to the right on a line bisection task and higher scores on a measure of verbally mediated attention. This is in line with previous research on laterality of attentional systems. However as motor function did not differ between groups the finding only partly supports the model under examination.

A hypothesis of the study stated that '*deficits in verbally mediated attention (as measured by the Verbal Fluency Test) will not predict motor impairment in left hemisphere damaged patients*'. In Table 4. it can be seen that verbally mediated attention did significantly contribute to the regression model differentiating patients by side of hemiplegia as expected, with those with left hemiplegia scoring significantly higher. However severity of motor impairment did not significantly differ between groups and was not significantly correlated with verbal fluency (see Table 6). Therefore, as hypothesised, verbal fluency was impaired by left CVA damage but was unrelated to motor function.

## **Predictors of motor function (as a dichotomous variable formed by splitting at the median)**

Table 3. also shows variables which significantly discriminated between severity of motor impairment as a dichotomous variable. These (highlighted) variables were entered into a second regression analysis, the results of which are shown in Table 5.

[Insert Table 5 here]

Sustained attention, as measured by the Tone Counting Test, and attention to contralesional body space, as measured by the Comb Test, were the only variables, which contributed to the model best predicting severity of motor

impairment. This model was significant ( $\chi^2=14.67, (2), p<.001$ ) relative to a constant only model and the resulting equation correctly categorised 68.63% of the sample (N=51 for this analysis). The regression equation further correctly categorised 61.54% of low scorers and 76% of high scorers. Thus lower motoricity scores were associated with sustained attention impairments and impairments of attention to the hemiplegic side of the body.

### **Correlations among predictor variables**

It was hypothesised *that sustained auditory attention will significantly correlate with scores achieved on tests sensitive to visuo-spatial neglect*. Table 6. shows a correlation matrix for this analysis.

[Insert Table 6 here]

There was good reliability between different tests of visual neglect. Line bisection correlated highly with Star cancellation ( $r=.720, p<.01$ ). Contrary to the hypothesis, sustained attention did not show a significant relationship with any of the measures of visual hemi-neglect in this sample. It is of interest also that there was little association between the measures of visual neglect (Line bisection and Star cancellation) and the measure of attention to lateral personal space (Comb test). This supports the concept of dissociated attentional systems for personal space and near extra-personal space (e.g. Robertson & North, 1992).

Verbally mediated attention (assessed by the Verbal Fluency Test (FAS) correlated positively and significantly with sustained attention (Tone Counting) performance ( $r=.436, p<.01$ ). Impairment on these tasks has been linked to damage to the left and right frontal lobes respectively (Tucha *et al*, 1999; Wilkins, Shallice & McCarthy, 1986). However this positive correlation of performance on the tests perhaps indicates a mutual dependence on processing which is potentially impaired by damage irrespective of lateralisation. This is discussed further below.

Robertson *et al* (1997) only studied patients with left hemiplegia and reported a correlation between sustained attention and visual neglect. A similar analysis was thus carried out for those in this sample with left hemiplegia (see Table 7). This analysis also failed to demonstrate a significant correlation between sustained attention and measures of neglect.

[Insert Table 7 here]

### **Correlations of attentional variables with motor and disability variables**

Previous research has identified that visual neglect predicts poor motor outcome after stroke. Visual neglect scores, as well as attention to body space and sustained attention variables were examined in terms of their inter-relationships. Table 8 below shows the results of these analyses.

[Insert Table 8 here]

In line with previous research (Robertson *et al* 1997), significant negative correlations were observed between Left omissions on the Star Cancellation test and the Motoricity Index ( $r=-.365$ ,  $p<.01$ ); Change in motor function since CVA ( $r=.627$ ,  $p<.01$ ) and the Barthel ADL Index ( $r=.443$ ,  $p<.01$ ). A similar pattern was demonstrated for the Line Bisection measure of neglect (see Table 8).

Attention to body space (Comb Test) was negatively correlated with verbally mediated attention ( $r=-.412$ ,  $p<.01$ ).

While sustained attention did not predict motor function it was found to mark disability, correlating significantly with Barthel Index total ( $r=.443$ ,  $p<.01$ ). Sustained attention was also correlated significantly with verbally mediated attention ( $r=.436$ ,  $p<.05$ ).

## DISCUSSION

The current sample was largely representative of other CVA research samples. Specifically the present participants were compared with those in the study by Robertson *et al* (1997). The current mean Motoricity total for those with left hemiplegia was lower than that in the above study suggesting a sample with relatively high motor impairment. The mean deviation to the right on the line bisection task was also slightly higher reflecting a sample with a relatively high degree of left neglect. Entry criteria for both studies stipulated a maximum time since CVA of one year. In Robertson *et al* (1997) patients were on average 88 (s.d: 97) days post CVA whereas in the current study they were 178 days post CVA (s.d: 125). Thus the current population can be regarded as less well recovered after longer duration post CVA.

This finding of a relatively impaired sample suggests that specific biases due to sampling a database of community resident survivors is unlikely. It had been expected that patients discharged successfully to their own homes would have higher levels of functioning, but this was not the case.

### *Interpretations of the regression modelling*

The first regression analysis showed that side of hemiplegic weakness was best differentiated by combining measures of attention to body-space (Comb Test), visual neglect (Line Bisection task) and verbally mediated attention (FAS Test). These three variables each represent 'attentional' systems, thus supporting findings on the laterality of attentional functions. However, contrary to expectation, sustained attention and motor function were not part of the model differentiating patients by side of hemiplegia. Thus it was found that left hemiplegia was associated with impaired attention to the hemiplegic side, deviations to the right on a line bisection task and higher scores on a measure of verbally mediated attention. This is in line with previous research but only partly supports the current hypothesis.

A hypothesis of the study stated that '*deficits in a verbally mediated test of attention will not predict motor impairment in left hemisphere damaged patients*'. Verbally mediated attention did significantly contribute to the regression model differentiating patients by side of hemiplegia as expected, with those with left hemiplegia scoring significantly higher. However severity of motor impairment was not significantly correlated with performance on the verbally mediated attention task (Verbal Fluency Test). Therefore the finding supports this hypothesis.

The second regression model demonstrated that sustained attention (as measured by the Tone Counting Test) and attention to the impaired side of the body (Comb Test) were the only independent variables predicting category of motor function as a dichotomous variable. Thus lower motoricity scores are associated with sustained attention impairments and impairments of attention to the hemiplegic side of the body.

In summary, the findings from the generated models indicate that visual neglect in combination with attention to the impaired side of the body and verbally mediated attention, but not motor impairment or sustained attention, appear to differentiate left and right hemiplegia patients. High levels of motor function are differentiated from poor motor function by a combination of sustained attention and attention to the impaired side of the body.

#### *Further support for the model arose from the discriminative analyses*

It is informative to compare those variables which significantly differentiated the groups on sensitive ( $p < 0.1$ ) means comparisons (Table 3) with those variables which contributed to the logistic regression equations (Tables 4, 5). Comparing means, side of hemiplegia was differentiated by attention to the impaired side of the body (Comb test), visual neglect (Line bisection), sustained attention (Tone Counting) aphasia (Token test), verbally mediated attention (FAS total) and self-monitoring (FAS total repetitions). Although sustained attention differed significantly between groups, at this sensitive level of significance, it did not enter the logistic regression equation as hypothesised. The token test total score and FAS repetitions also failed to enter but had not been hypothesised to do so. The corollary is that motor function did not differentiate the groups even at this sensitive level. The finding of non-laterality of motor impairment is anomalous and contrary to previous research.

Level of motor function, as a dichotomous variable, was differentiated on the means comparison tests (Table 3) by attention to the impaired side (Comb test), visual neglect (all measures: Line bisection average deviation; Star cancellation - omissions left; Star cancellation - omissions right; Star cancellation- total omissions), sustained attention (Tone Counting) and visuo-spatial ability (Rey figure). Sustained attention (as measured by the Tone Counting Test) and attention to the impaired side of the body (Comb Test) then entered the significant model in the regression analysis (Table 5). Thus their removal from the other variables differentiating the groups revealed that visual neglect measures and visuospatial ability (Rey Figure) failed to enter the regression model. For visual neglect this was contrary to expectation. However, neglect was negatively correlated with motor function in a later analysis, thus providing some support for the model subsuming this relationship (e.g. Posner 1993, Robertson 1999).

### *Poorer left recovery was not observed as hypothesised*

Greater impairment after CVA of the left side relative to the right side was hypothesised but not found in the current study. The hypothesised difference has been previously found in other studies (Blanc-Garin 1994, Buonocore 1990, Denes *et al* 1981, Sterzi *et al* 1993) with other studies supporting the null hypothesis (Andrews 1982, Jongbloed 1986, Kotila 1984, Wade 1984). Furthermore the relationship between motor function and right lateralised attention function has not been reliably demonstrated (Blanc-Garin 1994, Chen-Sea *et al* 1993, Denes *et al* 1982, Feigenson *et al* 1977, Jongbloed 1986, Kotila *et al* 1984, Mills *et al* 1983, Sterzi *et al* 1993).

Possible explanations of the lack of support for this central hypothesis are proposed here. The underlying construct of attentional factors hampering functional recovery may be criticised. It might be argued, for example, that better recovery for the right hand is simply an artefact of a more extensive learning history of right hand use in right handed individuals. Or, at a different level of explanation, that greater volumes and complexities of left cortical areas protect them against damage, and therefore protect right motor function. These arguments are countered in part in that measures of attention differed between groups and these measures predicted motor function in correlation analysis. That is right CVA patients in this study demonstrated higher levels of visual neglect (Line Bisection) and neglect for the impaired side of the body (Comb Test). Low levels of motor function (as a dichotomous variable) were also differentiated by a regression equation involving the Comb Test variable. Thus this attentional variable differentiated both side of lesion and level of motor impairment, implying that the attention deficit is due to lateralised damage and is related to motor function.

Issues of measurement may explain the current lack of finding. Specifically, it is proposed that that current measures of motor function are invalid for assessing real-life motor function. The Motoricity Index (Wade and Langton Hewer 1987), for one example of many similar indices, aims to assess limb positioning and strength. It may be the case that there was no real difference between left and right hemiplegic patients on their ability to position their limb against gravity or resistance. That said there may still exist a difference such that patients with left hemiplegia attend less to the left arm in real life and thus make less functional use of it. Andrews & Stewart (1979) noted that a substantial fraction of stroke patients performed all ADL they were asked to conduct in the clinic better than they did at home. Uswatte, Miltner, Foo, Varma, Moran & Taub (2000) report that many patients can perform laboratory motor tests with the affected arm but report almost zero use of the arm on returning home. Thus the current point-assessment of motor function in terms of strength may be insensitive to the hypothesised interplay of attention and arm use.

### *Correlation analyses confirm some but not all hypothesised relationships*

Contrary to the hypothesised relationship, sustained attention performance was not a marker neglect. This does not support the findings of Robertson *et al* (1997). A methodological difference in the current study may be important in this regard. The Elevator Tone Counting task in the present study consisted of 7 strings of tones to be counted (Robertson *et al* 1994). Robertson *et al* (1997) employed 14 strings of tones making their version presumably more difficult in requiring longer durations of vigilance and thereby more sensitive to impairments of attention.

The tests of visual neglect, star cancellation and line bisection, showed good degrees of reliability, correlating positively and significantly. However, the comb-test did not correlate significantly with either of the tests of visual neglect. This supports the concept of dissociated systems subserving attention to *body space*, and *personal* and *extra-personal space* respectively (Robertson & North 1992). A further test of this hypothesis may obtain in the development of assessments which reliably differentiate groups or subgroups formed by co-occurrence of the various neglect symptoms. It is also speculated that this may contribute to clinical assessment, in that, pinpointing which system is 'neglecting' could inform individual rehabilitation strategies.

Relationships were demonstrated which replicate previous findings. Motor function was significantly correlated with each of the included tests of visual neglect such that increased neglect predicted increased impairment. This is in line with previous reports of both point association of these variables and the effect of neglect on motor recovery (Blanc-Garin 1994, Chen-Sea *et al* 1993, Denes *et al* 1982, Feigenson *et al* 1977, Jongbloed 1986, Kotila *et al* 1984, Mills *et al* 1983, Sterzi *et al* 1993).

Auditory sustained attention was found to be significantly correlated with verbally mediated attention. This may be explicable in that both tests require patients to monitor a stream of stimuli (self generated and external respectively) over time and also require patients to utilise a short term verbal store (to avoid repetition and keep count respectively). This is in line with the assertion that performance on both tests is based upon systems whose function is to bridge 'temporal gaps in the perception – action cycle' (Fuster 1990). Performance on tasks of this type has been relatively reliably localised to dorso-lateral prefrontal cortical systems (e.g. Berman *et al* 1995). However, these tasks are thought to reflect lateralised damage; left hemisphere damage in the case of verbally mediated attention or fluency (Tucha *et al* 1999); and right damage in the case of sustained attention (Wilkins *et al* 1986). Taking this laterality into account, a related explanation may be derived from a working memory theory which posits a system(s) which controls short term information storage independent of hemisphere where this information is stored (Baddeley, 1996). Damage to a component of an attention system so organised may lead to impairment in another component although this has not been directly damaged (Baddeley, 1992, 1993, 1996).

The Line Bisection Test (mean deviation) was also negatively correlated with the Verbal Fluency Test score. This suggests that higher Verbal Fluency Test scores predicted greater contra-lateral visual neglect. This may be regarded as relevant in that poorer verbally mediated attention is predicted by left sided damage while right hemisphere damage was associated with greater contralesional neglect.

In summary of our main findings, several of the included attentional variables, including attention to the impaired side of the body (comb-test) differentiated left and right hemiplegia patients, whereas measures of motor function did not. The motor function measure (motoricity) was, however, significantly correlated with measures of neglect (line bisection and star cancellation) in correlation analyses of the whole sample.

### *Implications: Direction of effect*

Motor function was significantly negatively correlated with each of the included tests of visual neglect. This is in line with previous findings suggesting that the presence of neglect predicts poor outcome (Blanc-Garin 1994, Chen-Sea *et al* 1993, Denes *et al* 1982, Feigenson *et al* 1977, Jongbloed 1986, Kotila *et al* 1984, Mills *et al* 1983, Sterzi *et al* 1993). Some of the previous studies (e.g. Blanc-Garin, Denes *et al* 1982, Mills *et al* 1983) employed methodology which enabled the researchers to partial out other variables, allowing in turn the interpretation that neglect hampers recovery, not permissible on simply demonstrating association. Examination of the impact of neglect on observed improvement over time would have been beyond the scope of the current study but would allow stronger interpretation.

The direction of causal relationship between correlated variables is difficult to surmise. However the relationship between visuo-spatial attention and motor function, as evidenced in the correlation observed here, has been argued to be reciprocal in nature. This bi-directionality of effect has been demonstrated previously, in that improvement in attention to left space has been shown to improve motor function (Paolucci *et al*, 1996) and contralesional limb activation reduces neglect (See Robertson 1999). Thus it is argued that the demonstration of correlation here supports this line of experimental work into treatment approaches.

Demonstration of functional association between cortical areas is fundamental to the approach to rehabilitation which has been termed *guided recovery* (Robertson & Murre, 1999). Activation of intact pathways in the damaged system itself or related system can bring about a recruitment of neurons to that function through a process of Hebbian learning, in that *cells which fire together wire together* (Hebb, 1949). Thus correlational analysis of the inter-relationships of functions after brain damage is potentially useful to indicate new treatment approaches.

The Comb Test was predictive of both side of lesion and level of motor impairment in the regression analyses, visual neglect was not predictive on these dichotomies as hypothesised. This suggests that more clinical attention be paid to this difficulty in addition to visual neglect. Visual neglect is easy to assess and observe which may account for the popularity of its use. However the conceptually related but dissociated function, attention to body space, can also potentially hamper limb use.

### *Limitations of the current study*

The current sample was recruited from both inpatient and outpatient populations at the study centres. Sampling issues may have obtained in terms of the patients deemed moribund or otherwise unable to partake by the referrers. It is suggested that those with aphasia (predicted by left sided damage) may have been deemed unsuitable at a higher frequency due to issues of consent than those with right hemisphere damage. Thus more patients with difficulties specific to language and leaving motor less impaired may have been excluded by this criterion. This is also highlighted as a limitation of previous studies excluding on the basis of language screening tests. Cohort studies

where informed assent is sought may solve this problem but also pose ethical dilemmas which at this time remain to be resolved in this area of research.

A potential explanation of the failure to find a difference in motor impairment between left and right hemisphere groups may rest on the power calculation as reported above. No directly comparable study was located and the current sample size was therefore conservatively estimated following the findings of Denes *et al* (1982) in respect of differences in disability scores. The findings of the current study revealed that measures of visual neglect were significantly correlated with the point assessment of motor impairment. Similarly these attentional variables were found to differ between groups defined on side of hemiplegic weakness. This implies in turn that employing a larger sample size (e.g. Sterzi *et al* 1993, n=298) might be more likely to reveal that severity of motor impairment is related to side of hemiplegia. Recruitment of a sample of that size was beyond the scope of the current study. With regard to extending a novel aim of this study in future research, a large sample size would also yield more power in examining the relative *prospective* prognostic value of a.) sustained attention and b.) attention to body space, in predicting the recovery slope of CVA patients.

Some of the measures employed here may be potentially fundamentally criticised in terms of the impact of laterality and inter-manual differences on their performance. Performance with the left hand (the dominant hand impaired after Left CVA) might be argued to be poorer than that of the dominant hand by definition. Some of the central tasks of interest (visual neglect measures, comb test, Rey figure) might therefore be argued to be affected by inter-manual differences in performance. Bush (2000) examined the possibility that constructional task performance would favour those with dominant side intact, controlling for other factors. A sample (n=44) of non brain-injured participants completed the same visuo-spatial task (clock drawing) with left and right hands. Despite qualitative differences (e.g. in quality of lines) there was no difference between hands in total score achieved. While replication in a brain-injured group, perhaps examining further constructional tests would be worthwhile, Bush's (2000) findings support the reliability and specificity of this neglect test in measuring the underlying attentional dysfunction.

Results from this study support the contention that inter-manual differences do not confound the findings. The Comb Test was carried out by those with right hemiplegia using the left hand, arguably the hand more subject to 'bias'. But right hemiplegia patients more approximated 50% attention to each side while those with left hemiplegia tended to neglect the impaired side. Therefore left body neglect is deemed valid and attributed to right hemisphere damage.

Restrictions on patient data available prevented identification of factors affecting prognosis for rehab stay recovery. The units in the study project used various measures of intake motor function and disability and this heterogeneity prevented the use of these assessments in the report.

### *Future research*

Measurement of motor function was highlighted above as critical to research examining the influences of laterality or attention on stroke outcome. A measure of use of the affected limb in unit time may be a better estimate of real-life functional activity and may therefore be of more relevance to rehabilitation (Uswatte *et al* 2000). It is suggested that future research studies employ devices to measure and record the frequency of gross movements in time, which might then be standardised with observer ratings of functional movement. This would allow recording for longer and over a range of tasks impractical for an observer. Accelerometer technology (allowing measurement of the acceleration of a limb in space) and computational treatment of the output appears to allow valid and reliable measurement in this domain (Uswatte *et al* 2000). Research using this methodology might therefore test the basic hypotheses that patients with left hemiplegia or unilateral neglect make less functional use of the impaired arm. If demonstrated this lack of functional use may then be targeted for specific interventions designed to increase the probability of the arm being used (e.g. Robertson, North & Geggie 1992; Taub, Uswatte & Pidikiti 1999).

Sanchez-Blanco and colleagues (1999) examined the use of classifying patients post CVA by syndromes of neurological signs in predicting needs at six months. Using the system of Reding & Potes (1988) patients with motor impairment only formed the first group, those with motor impairment and sensory disturbance formed group two and the third comprised motor and sensory patients with hemianopsia. They found that classifying patients in this way significantly and usefully predicted the extent of assistance required in ADL at six months. While ecologically valid, this approach may be criticised for aggregating variables which alone may have contributed explanatory power. However this *syndromic classification* is not mutually exclusive with the approaches of identifying single variables or related variable groups which appear to hamper recovery. The identification of factors which may inform rehabilitation strategies, as the current project aimed, may also contribute to more accurate prognostic syndromic classifications.

The findings of the present study are relevant to experimental rehabilitation strategies. Contralesion limb activation training (LAT) is an approach wherein the patient's attention is drawn to the impaired limb by a device emitting a semi random tone. Movement of the limb then cancels this tone, providing contingent reinforcement for movement. Robertson *et al* (in press) studied this intervention in the rehabilitation of patients with neglect, the problem for which the strategy was first developed (Robertson, North, & Geggie, 1992, Robertson *et al*, in press). The researchers found that those receiving LAT had significantly better limb function post intervention. Therefore, providing an external cue to overcome impaired attention to the left limb, with contingent reinforcement for movement, improved limb function.

To date LAT has been delivered to patients with visual neglect only, as an adjunct to rehabilitation as usual (RAU). A future study might add LAT to RAU for patients with and without neglect (encompassing neglect for the body). It is hypothesised that patients with neglect gain more from the addition of LAT above RAU. Similarly right hemisphere CVA patients might be expected to benefit more from LAT than those with left hemisphere damage.

The prospects offered by these and similar studies reflect an exciting new realm of rehabilitation research. That is, by identifying impairments in abilities which hamper the recovery of related systems, and by providing supportive interventions for those abilities, improvement in recovery likelihood may be found.

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**Tables** – to be inserted in the text as indicated

Table 1. Descriptive Statistics of Demographic and Neuropsychological-Descriptive Variables

<i>Variable</i>	<i>Sample Mean (N=52)</i>	<i>(Std. Dev.)</i>	<i>Left Hemi Mean (N=29)</i>	<i>(Std. Dev.)</i>	<i>Right Hemi Mean (N=23)</i>	<i>(Std. Dev.)</i>	<i>Group Differences (Left/Right)</i>
Age	67.23	(10.90)	66.05	(10.60)	68.71	(11.33)	t(50) = -.87, NS
Education	11.00	(3.03)	11.24	(2.56)	10.70	(3.57)	t(50) = .64, NS
Days Post CVA	178.37	(124.91)	173.55	(124.84)	184.43	(127.53)	U(50) = 314.5, NS
IQ estimate	104.33	(12.76)	103.24	(14.13)	105.70	(10.95)	t(50) = -.69, NS
Rey Figure copy	28.71 a.	(7.07)	28.48 d.	(6.80)	29.10 f.	(7.71)	U(38) = 178, NS
Rey Figure recall	13.86 b.	(6.11)	13.84 d.	(6.10)	13.89 g.	(6.35)	U(37) = 178.5, NS
Story recall	26.93 c.	(13.50)	32.04 e.	(12.68)	20.74 h.	(12.01)	t(40) = 2.95*
Token Test	20.71 i.	(4.68)	21.72	(3.16)	19.43	(5.91)	U(50) = 224.5*

\* significant at the p<.05 level. a. Max. score=36, N=40 b. Max. score=36, N=39 c. Max. score=50, N=42 d. N=25 e. N=23 f. N=15 g. N=14, h. N=19 i. Max score=23.

Table 2. Descriptive Statistics of variables related to the hypotheses

<i>Variable</i>	<i>Sample Mean (Std. Dev.)</i>	<i>Left Hemi Mean (Std. Dev.)</i>	<i>Right Hemi Mean (Std. Dev.)</i>	<i>Left/ Right Differences†</i>
Motoricity (arm total)	70.00 (24.65)	67.38 (25.59)	73.30 (23.55)	U(50) = 274, NS
Motoricity (leg total)	78.37 (24.30)	76.21 (28.65)	81.09 (17.61)	U(50) = 331, NS
Motoricity total	148.37 (44.74)	143.59 (49.55)	154.39 (38.04)	U(50) = 308, NS
Motricity change‡	.78 (1.38)	.95 (1.70)	.55 (.79)	U(50) = 313, NS
Barthel index total	81.15 (22.13)	78.10 (24.33)	85.00 (18.83)	U(50) = 227, NS
Line bisection (mean deviation)	7.69 (4.97)	8.29 (6.08)	6.93 (3.01)	t(50) = 2.45, *
Star cancellation (omissions left)	2.38 (4.80)	3.24 (5.99)	1.30 (2.36)	t(50) = 1.45, NS
Comb Test (% on weak side)	46.53 (9.07)	43.24 (10.21)	50.69 (5.06)	t(50) = 2.25, *
Sustained Attention	5.80 (1.77)a.	6.11 (1.57)c.	5.43 (1.95)	U(49) = 231, NS
Verbal Fluency (FAS total)	32.04 (12.94)b.	37.88 (12.48)d.	24.05 (8.73)e.	t(43) = 4.14, **
Self monitoring (FAS repetitions)	1.13 (1.60)b.	.77 (1.18)d.	1.63 (1.98)e.	U(43) = 181, NS

\* significant at the p<.05 level. \*\* significant at the p<.01 level. a. N=51, b. N=45, c. N=28, d. N=26 e. N=19.

† Calculated as deviation from normal over time since CVA.

‡ Differences examined using independent sample *t* tests where data were normally distributed or Mann-Whitney U tests if not.

Table 3. Investigation of Associations Between Dichotomous Variables (Side of Hemiplegia and Motor Function) and Demographic and Neuropsychological Variables.

<i>Variable</i>	<i>Side of Hemiplegia</i>	<i>Motor Function</i>	<i>Statistic*</i>
Age	.387	.610	t
Years of education	.524	.469	t
Time Post CVA	.726	.516	U
Comb test % on weak side	.002	.057	t
Motoricity (arm total)	.267	†	U
Motoricity (leg total)	.963	†	U
Motoricity total	.631	†	U
Motricity change from normal over time since CVA	.706	†	U
Line bisection average true deviation to L or R	.018	.275	t
Line bisection average deviation (in mm)	.332	.023	t
Star cancellation (omissions left)	.153	.039	t
Star cancellation (omissions right)	.691	.092	t
Star cancellation (total omissions)	.193	.026	t
Sustained attention (tone counting)	.061	.018	U
Token test total score	.079	.184	U
FAS total in three minutes	.000	.387	t
FAS total repetitions in three minutes	.100	.741	U
Rey figure total score	.804	.016	U
Rey figure recall	.919	.124	U
NART IQ estimate	.496	.789	t
Barthel index total score	.285	†	U

Note: Table 3 *p* values (in bold) are significant at the  $p < 0.10$  level, following Hosmer & Lemeshow, 1989.

\* *p*-values are derived from independent sample *t* tests where data were normally distributed or Mann-Whitney *U* tests if not.

† These variables were excluded as they contributed to (or were closely related to) the definition of the dichotomous variable.

Table 4. Logistic regression predictors of side of hemiplegia, as a dichotomous variable, among independent variables (demographics and variables of interest).

<i>Outcome variable</i>	<i>Log likelihood</i>	$\chi^2$	<i>df</i>	<i>Sig.</i>	<i>% correct L hemi</i>	<i>% correct R hemi</i>	<i>Predictors</i>	<i>Sig.</i>	<i>R</i>
Hemi side	61.29	26.93	3	.0000	76.92	84.21	CombTest	.03	.196
							LineBis.	.04	-.185
							Fluency	.008	-.284

Table 5. Logistic regression predictors of severity of motor impairment, as a dichotomous variable, among independent variables (demographics and variables of interest).

<i>Outcome variable</i>	<i>Log likelihood</i>	$\chi^2$	<i>df</i>	<i>Sig.</i>	<i>% correct Low scores</i>	<i>% correct High scores</i>	<i>Predictors</i>	<i>Sig.</i>	<i>R</i>
Motoricity (Dichot.)	70.68	14.67	2	.0007	61.54	76.00	Sustained		
							Attention	.011	.253
							CombTest	.037	.183

Table 6. Correlations between auditory sustained attention and measures of spatial neglect

	<i>Sustained Attention</i>	<i>Star Cancellation (omissions left)</i>	<i>Line Bisection (average deviation, mm)</i>	<i>Combtest % weak side</i>	<i>Motoricity total</i>	<i>FAS total in three minutes</i>
Sustained Attention	1.000†	-.079†	-.196†	-.040†	.259†	.436**
Star Cancellation (omissions left)		1.000	.720**	-.199	-.474**	-.096
Line Bisection (mean deviation)			1.000	-.168	-.498**	-.248
Combtest % weak side				1.000	.243	-.312*
Motor function (Motoricity)					1.000	.118
Verbal Fluency (FAS)						1.000

N=52 except † N=51; \*\* p < 0.01 (2-tailed); \* p < 0.05 (2-tailed).

Table 7. Correlations between auditory sustained attention and measures of neglect (Left Hemiplegia patients).

	<i>Sustained Attention</i>	<i>Star Cancellation (left omissions)</i>	<i>Line Bisection (mean deviation)</i>	<i>Comb test % on weak side</i>	<i>Motoricity total</i>	<i>Verbal Fluency FAS</i>
Sustained Attention	1.000†	-.106†	-.222†	-.063†	.068†	.408*
Star Cancellation (left omissions)		1.000	.804**	-.118	-.558**	-.264
Line Bisection (mean deviation)			1.000	-.192	-.617**	-.431*
Comb test % on weak side				1.000	.217	-.092
Motor Function (Motoricity)					1.000	.164
Verbal Fluency (FAS)						1.000

N=29 except † N=28; \*\* p < 0.01 (2-tailed); \* p < 0.05 (2-tailed).

Table 8 Correlation matrix of independent variables related to hypotheses

	<i>Comb test % on weak side</i>	<i>Line bisection mean deviation</i>	<i>Star cancellation (left omissions)</i>	<i>Sustained attention</i>
Side of weakness <sup>a</sup>	.412**	-.137	-.201	-.191†
Motoricity (arm total)	.214	-.339*	-.365*	.239†
Motoricity (leg total)	.230	-.573**	-.502**	.235†
Motoricity total	.243	-.498**	-.474**	.259†
Motoricity change <sup>b</sup>	-.039	.629**	.627**	-.125†
FAS Total	-.312*‡	-.248‡	-.090‡	.436*‡
Barthel Index Total	.151	-.406**	-.431**	.443**

N=52, except † N=51, ‡ N=45; \*\* p < 0.01 (2-tailed); \* p < 0.05 (2-tailed).

<sup>a</sup> Left weakness =1, Right weakness =2. <sup>b</sup> Calculated as deviation from normal over time since CVA.

## **Single-case Research Study Abstract**

**Examining the efficacy of contralesional limb activation therapy in the rehabilitation of unilateral hemiplegia and visual neglect:**

**A baseline-intervention study.**

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**270 words**

## ABSTRACT

### Introduction

Sensory inattention and hemiplegia are related phenomena common after right hemisphere CVA. Attentional problems may thus present as motor impairment. A rehabilitation strategy known as limb activation therapy (LAT) was developed for use in the rehabilitation of unilateral visual neglect. A recent (in press) randomised control trial suggests that it may be efficient in rehabilitating unilateral weakness following CVA. During LAT an electronic device draws attention to the contralesional limb by emitting a tone if lack of movement is identified. It has been argued that a positive feedback loop involving neural visuo-spatial attentional systems, personal (body) attentional systems and motor systems explains this phenomenon.

Previous studies of limb activation therapy have focused on its effects on unilateral visual attention deficits. The current study aimed to examine its utility as an adjunctive therapy for a patient with left sided weakness and visual neglect following CVA, thus examining its relative effectiveness in treating motor and attention deficits.

### Procedure

A single-n baseline intervention design allowed examination of treatment response within a patient who presented with left motor impairment and visual neglect. The Motoricity Index (a measure of limb motor function), Star Cancellation Test and Line Bisection Test (Measures of visual neglect) were administered as repeated measures. The hypotheses that limb activation therapy will improve motor function and reduce neglect compared to baseline was examined.

### Results

The results indicate that in this case LAT significantly reduced visual neglect as measured by the Star Cancellation test. This change was not significant on the Line Bisection test. Contrary to the hypothesis arm impairment was not reduced by LAT. However a significant change in the recovery slope was demonstrated.

### Discussion

The results provide partial support for the model linking attentional systems and motor function such that reciprocal improvements obtain after LAT. The results are discussed in terms of models of the mechanism of contralesional limb activation.