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Running head: Neglect & Spasticity

Patients with hemi-spatial neglect are more prone to limb

spasticity, but this does not prolong their hospital stay

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26 Abstract

- 27 **Objective:** To determine whether stroke patients who suffer from hemi-spatial
- 28 neglect tend to stay in hospital longer because they are prone to limb spasticity.
- 29 **Design:** Retrospective analysis of in-patient medical notes.
- 30 **Setting:** In-patient neuro-rehabilitation unit of a regional UK teaching hospital
- 31 Participants: All 106 patients admitted to the neuro-rehabilitation unit between
- 32 2008-2010 who had suffered a stroke, as confirmed by CT or MRI.
- 33 **Intervention**: Not applicable.
- 34 Main Outcome Measures: Statistical coincidence of hemi-spatial neglect and
- 35 spasticity; Length of hospital stay.
- 36 **Results:** Chi-square analyses indicated that individuals with left neglect were nearly a
- 37 third more likely to develop spasticity than those without neglect (87% vs. 57%),
- 38 while nearly one half of those with left-sided spasticity showed neglect (44% vs.
- 39 13%). Individuals with neglect stayed in hospital 45 days longer than those without
- 40 neglect, but the presence/absence of spasticity did not affect length of stay.
- 41 **Conclusions:** The results provide the first statistical evidence that neglect and limb
- spasticity tend to co-occur post-stroke, though it is only the former that significantly
- prolongs stay. Diagnostic value aside, these results are important because they tell us
- 44 that the treatment of neglect should not be overshadowed by efforts to reduce co-
- 45 morbid spasticity. Despite its poor prognosis, hemi-spatial neglect continues to
- 46 receive little targeted therapy in some units.

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48 Key words: inattention; hemiplegia; stroke; outcome.

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51 List of Abbreviations

- 52 LOS: Length of stay
- 53 UK FIM+FAM: United Kingdom version of The Functional Independence Measure
- and Functional Assessment Measure
- NPDS: Northwick Park Dependency Scale
- 56 MAS: Modified Ashworth Scale
- 57 NIHSS: National Institutes of Health Stroke Scale
- 58 ADLs: Activities of Daily Living

Hemi-spatial neglect is a debilitating, attentional disorder that can occur in the absence of primary sensory or motor loss¹. Individuals with 'neglect' fail to acknowledge or respond to visual information presented on the side of space opposite their brain lesion, and as such struggle with many daily routines, often bumping into obstacles, becoming lost, and failing to notice people on the affected side. Prevalence is hard to estimate because diagnostic criteria differ, but the most conservative estimate indicates that over half of those who suffer a cerebral stroke will show moderate to severe hemi-spatial neglect in the acute phase, with over 20% continuing to show stable impairment beyond three months¹. The condition is over twice as common following a right hemispheric versus left hemispheric stroke so tends to present on the left-side of space².

Unfortunately, the presence of neglect is strongly associated with poor general functional outcome from stroke. Individuals with neglect (regardless of severity) typically require additional weeks in hospital (118days vs. 78days)³ needing nearly twice as many hours of physiotherapy and occupational therapy, and are more prone to falls and persistent urinary incontinence⁴. Patients with neglect at hospital admission score significantly lower on measures of functional independence both during hospital stay and 12-18 months after leaving⁵⁻⁷. Those who still show neglect on simple bedside tests two months after admission have a higher risk of functional worsening at 1year follow-up.

The aim of the present study was to further investigate the poor prognosis associated with hemi-spatial neglect. Unsystematic observations made during our routine assessment indicate that neglect often co-occurs with unilateral limb spasticity.

Controversy remains over the precise definition of spasticity⁸, though a relatively broad, practical characterization has been forwarded by members of the SPASM consortium who describe it as disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles⁹. As far as we are aware, the concurrence of neglect and spasticity has yet to be formally estimated. However, if there is a strong association then it is possible that the especially poor outcomes associated with neglect are partly attributable to the co-presence of spasticity. On the other hand, although it is known that motor impairment can increase length of stay and reduce functional independence¹⁰, few studies have looked specifically at spasticity. Of those that did, it was not established whether the extended stay could instead be attributed to co-morbid neglect.

In the following sections we report the effects of hemi-spatial neglect and spasticity on the length of time patients remained within the in-patient stroke service of a regional, UK teaching hospital. We chose length of stay as the main study variable because this has been taken as an accurate marker of general functional outcome, has widely understood implications for both hospital and post-discharge resource utilization, and can be obtained accurately and easily. In the first instance, we wanted to confirm our informal observation that the co-incidence of spasticity and neglect is positively associated. In the second instance, we sought to determine whether the detrimental effect of neglect on length of stay increases when spasticity is co-present. To help clarify any significant relationship between these two impairments, a variety of other factors that have also been shown to impair outcome were examined. These

were motor flaccidity¹¹, age⁵, gender¹², hemianopia¹⁰, depression¹³ and neuroanatomical lesion site¹⁴.

Methods

Participants

Data were collected retrospectively from the medical records of 106 stroke patients admitted between 2008-2010 to the East Kent Hospitals in-patient neuro-rehabilitation unit, UK. The unit admits patients directly from the acute stroke wards of three nearby hospitals, and has a catchment population of approximately 800,000. Most patients admitted have few pre-morbid complications, significant psychological issues and difficult familial circumstances that do not allow their rehabilitation goals to be met via early, supported discharge.

All cases of strokes were confirmed via radiological report (CT and/or MRI). With the exception of those who presented with only subarachnoid hemorrhage or who either died before discharge (n=4) or self-discharged prematurely (n=4), every stroke patient admitted to the neuro-rehabilitation unit and whose medical record was available was included in the study. The demographic and clinical characteristics of the sample are presented in Table 1. The mean LOS was 100 days (s.d = 70), considerably longer than that in most US units. The mean UK FIM+FAM¹⁵ score, a measure of global disability and more specific cognitive and psychosocial independence (see below), was 118/210 at admission and 158/210 at discharge. The mean NPDS score¹⁶, a measure of nursing support (see below) was 30 (high dependency: 2 helpers needed for most care activities) at admission and 17 (medium dependency: 1 helper needed for most care activities) at discharge.

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The study received approval from the local research ethics committee before proceeding.

Table 1 about here

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Assessments

(1) Initial assessment of hemi-spatial neglect was attempted within 7 days of acute admission and was based on the NIH stroke scale¹⁷. Following transfer from the acute stroke ward to the neuro-rehabilitation unit, all patients (regardless of whether neglect was suspected) received a more thorough attentional evaluation via the Rivermead Perceptual Assessment Battery¹⁸. The results of the Rivermead assessment were used to confirm the presence/absence and laterality of visual neglect. Specific scores from the Rivermead were not always documented in patients' notes, so only the presence/absence and laterality of neglect were recorded for study purposes. Patients diagnosed with neglect received no targeted therapy, however, they were made continually aware of their impairment via frequent prompting by the occupational therapists and nurses during activities of daily living and mobility training. (2) Muscle tone was assessed using the MAS¹⁹ with a score of 1 denoting spasticity and 0 (together with muscle floppiness) denoting flaccidity. Specific MAS scores were not always available so only the presence/absence of spasticity, rather than severity, was recorded. Assessment was frequently carried out by neurophysiotherapists and the consulting physician, and for study purposes, patients were classified as spastic irrespective of when, during their stay, symptoms developed. Recordings were made of which side of the body was affected, along with whether the

- upper or lower limbs (or both) were implicated. The condition was comprehensively
- managed using Botulinum injection or intra-thecal Baclofen pump.
- 160 (3) Hemianopia was assessed via the NIHSS using visual confrontation testing.
- 161 (4) Depression was assessed via the Beck Depression Inventory²⁰, and indicated if the
- individual scored 14 or more.
- 163 (5) Lesion laterality and lobular distribution was confirmed by either CT (65 patients),
- or MRI (11 patients) or both (28 patients) and classified according to hemisphere and
- 165 cortical lobe(s).
- 166 (6) ADLs were measured using the NPDS and UK version of the FIM+FAM
- administered within the neurorehabilitation unit at admission and discharge. The
- NPDS is a 4 to 6 point 23 item composite measure of nursing dependency,
- specifically designed for use with in-patient neurological rehabilitation. Patients can
- score a minimum of 0 and maximum of 100. The UK version of the FIM+FAM was
- developed specifically for use in brain injury, and compared to the NPDS focuses less
- explicitly on nursing need and time and more on the ability to carry out certain
- activities of daily living. The measure has two components, the FIM, a 7 point 18
- item scale, which focuses on physical and cognitive disability, and the FAM, a 7 point
- 175 12 item scale, which focuses on psychosocial issues. Patients can score a minimum of
- 176 30 and maximum of 210.
- 177
- 178 Statistical Analyses
- Pearson's Chi-square (χ^2) was applied to test for significant associations between
- hemi-spatial neglect and other observed co-morbidities. Multiple linear regression
- analysis was then used to determine significant predictors of LOS. LOS was defined

as the period between initial admission to the acute stroke ward and subsequent discharge from the specialist in-patient neurorehabilitation unit. Prior to this analysis, a natural log transformation was applied to the LOS data to reduce positive skew. Separate univariate analyses were then carried out for each predictor variable; left neglect, spasticity, spastic side (left vs. right), age (<60years vs. >60years), flaccidity, hemianopia, depression, lesion site (occipital, temporal, parietal, frontal), and gender. Given the a priori hypotheses, neglect and spasticity were automatically carried forward into the multiple linear regression while only those other variables that were statistically significant (α =0.05) when interrogated individually were added. Only age met this criterion.

Initial inspection of the data indicated that there were twice as many cases of left neglect (31 cases) than right neglect (15 cases). Given this uneven weighting, it made little sense to analyze both forms of neglect as a single variable. This was because any significant effect could reflect trends within the left neglect group alone. Cases of right neglect were therefore excluded from analyses, though summary data of the entire sample (n=106) are presented in both Table 1 and Table 3b.

Results

Missing data are summarized in Table 2.

Table 2 about here

Factors associated with the presence of left neglect

In line with the hypothesis, chi-square analysis indicated that the presence of left neglect and spasticity was positively associated ($\chi^2 = 8.6(1)$, ϕ -coefficient =.307, p<0.01) (see Table 3a). 87% (27/31 patients) of patients with left neglect had

spasticity, compared to only 57% (34/60) of patients who did not have neglect. Further interrogation revealed that all those with left neglect who showed spasticity suffered from left, as opposed to right, spasticity. In those who did not have neglect, 11 showed left spasticity, 19 showed right spasticity and 4 showed both. In those patients with spasticity, 44% (27/61) showed left neglect. All 27 of these patients presented with left-sided spasticity. Only 13% (4/30) of patients without spasticity showed left neglect.

Left neglect was also significantly associated with several other factors. 37% of patients with neglect suffered from hemianopia, compared to 9% of patients without neglect ($\chi^2 = 8.1(1)$, ϕ -coefficient = .326, p<0.01). At an anatomical level, 71% of patients with left neglect showed damage to the right parietal lobe compared to only 38% of those without neglect ($\chi^2 = 6.8(1)$, ϕ -coefficient = .313, p<0.01). Right frontal lobe damage was also more prominent in the neglect sample ($\chi^2 = 7.6(1)$, ϕ -coefficient = .332, p<0.01); 71% of patients with neglect suffered frontal damage compared to 35% of those without neglect. Finally, 38% of neglect patients showed right temporal lobe damage, compared to 15% of those without neglect ($\chi^2 = 4.8(1)$, ϕ -coefficient = .262, p<0.05).

The statistical association between neglect and depression was borderline significant ($\chi^2 = 3.9(1)$, ϕ -coefficient =.205, p=0.05), whereby 45% of patients with neglect were classified as depressed compared to 25% of those without neglect.

Tables 3a and 3b about here

229 Predictors of Length of Stay

The regression analysis indicated that the presence of hemi-spatial neglect and age independently predicted LOS (see Table 4). Patients with neglect stayed 45 days

longer than those without neglect (130 days vs. 85 days). Patients younger than 60 years stayed an average of 39 days longer those above 60 years (126 days vs. 87 days). Importantly, the presence/absence of spasticity did not predict LOS (105 days vs. 108 days). The explanatory power of the model was unaffected when the interaction between neglect and spasticity was added, accounting for only an extra 0.5% of the variance (p=0.43).

Table 4 about here

Activities of Daily Living (ADL)

Although patients with left neglect and spasticity did not stay any longer than patients with only neglect, it is possible that the former were nevertheless discharged with a lower ADL score. We therefore compared FIM+FAM and NPDS scores between the two groups at discharge. An independent samples t-test showed no difference in FIM+FAM discharge scores between those only with neglect (140/210) versus those with neglect and spasticity (145/210) (t=0.13 (d.f.=12), p>0.05). We also found no statistical difference in NPDS score (neglect =19.0, neglect+spasticity =20.0) (t=0.2 (d.f.=22), p>0.05). Both scores fall within the 'medium dependency' range, characterized by the need for one person to assist with most care activities.

Discussion

This study was motivated by two aims; (1) to validate our informal observation that neglect patients have a higher likelihood of showing limb spasticity, and (2) to determine whether co-morbid spasticity partly explains why neglect patients tend to stay longer in hospital¹⁻⁷. The data confirmed a significant association between left neglect and spasticity; over three quarters of patients with left-sided neglect had a left

spastic limb, while only one half of those without left neglect showed spasticity. Patients with left neglect stayed in hospital for an average of 45 days longer than those who did not have neglect. However, the co-presence of spasticity did not prolong the stay of neglect patients. Spasticity also failed to affect LOS in patients without neglect.

From a diagnostic perspective, the high coincidence of neglect and spasticity is important because in some units neglect diagnosis relies heavily on the visual tests performed as part of the NIHSS. While these tests usually catch severe cases of inattention, more mild cases can be overlooked if the patient is immobile or situated within a structured environment. Mild to moderate neglect can also be masked by hemianopia or simply given less priority than more grossly observable or manageable deficits such as hemiplegia and speech and language impairment. Yet even those mild cases of neglect that manifest in relatively subtle ways, such as when the individual is confronted with a novel or challenging situation or when salient stimuli appear in the ipsilesional field, significantly impair general functional recovery³. Given our finding that approximately one in two patients with left-sided spasticity will show neglect, it would therefore seem sensible to conduct a mandatory, detailed screen for neglect in all who present with left limb spasticity post-stroke.

Why do neglect and spasticity co-occur? One clue may arise from the cortical proximity of processes associated with lateralized visual attention and motor control. Many of these regions are perfused by the middle cerebral artery, so would be jointly affected by infarcts within its lower sections. Against this explanation is our failure to find a common lesion site in those with neglect and spasticity. That said, neglect and

spasticity can each arise from a variety of lesion distributions so it is possible that the two conditions do share a common anatomical pathology but that this is masked by the many ways in which it can manifest. A more speculative explanation is that neglect and spasticity can co-occur following dysfunction within the subcortical reticular activating system. Mesulum and others have strongly linked attentional arousal with elevated activity within the ascending pathways of the system and proposed that neglect may arise when this activity becomes chronically depressed²¹. By contrast, descending projections from other nuclei within the reticular formation are known to modulate muscle tonus and activity²² and have been associated with increased muscle rigidity when damaged²³. Theoretically, reticular dysfunction could therefore contribute to both neglect and spasticity.

Regarding length of stay, the failure of spasticity to exert an effect in those either with or without neglect is perhaps surprising because spasticity reduces the ability to perform various ADLs²⁴. However, very few studies have actually examined the effect of spasticity on LOS. Most have instead examined the more generic effects of 'hemiparesis', 'hemiplegia' or 'motor disability^{5,10,25} that not only encompass spasticity but other motor impairments such as self-reported muscle stiffness, hyperreflexia and clonic beats. For example, of the 77 patients described in one study as hemiparetic, only 20 were classified as spastic²⁴. In those LOS studies that have employed more specific measures of motor impairment, it was unclear whether the patients also had a neglect that could instead account for their prolonged stay. A further consideration is that stroke patients with severe physical disability but intact cognitive function can participate actively in rehabilitation and benefit from an intense and relatively short programme. Post-discharge, while the spastic patient may

lack the ability to physically interact with the environment, there is much provision to help bypass his/her loss; prosthetic aids are available and homes can be adapted to support essential activity. By contrast, such adaptations have proved less effective in compensating for neglect, most likely because the patient lacks the spatial ability, insight and motivation to use them. These differences may partly explain why neglect but not spasticity impacted LOS.

Study Limitations

Several important shortcomings limit the generalizability of our results. The retrospective nature of the study meant that certain outcome measures were not as well-defined as we would have liked. In particular, the severity of neglect and spasticity was not consistently recorded, so it remains unclear whether more severe cases remained in hospital for longer. Although all incidences of spasticity were recorded, other forms of motor impairment that might have contributed to hospital stay were rarely documented in patients' notes. Likewise, although the cortical lobes affected by stroke were clearly reported, the extent and nature of sub-cortical damage was often unreported. Speech and language deficits were also overlooked. To be discharged from the neuro-rehabilitation unit a safe discharge destination must be secured, the patient must have reached a plateau in his/her rate of rehabilitation improvement, and there must be access to community stroke services that can support on-going rehabilitation. These criteria are not only affected by clinical factors, and other indices of clinical progress and patient wellbeing must therefore be sought to corroborate our findings.

We conclude that although individuals with hemi-spatial neglect are especially prone to limb spasticity, it may be the presence of neglect rather than spasticity that keeps them in hospital. This finding underlines the need to carefully assess the attentional capacities of new stroke admissions and develop rehabilitation programmes that are specifically targeted towards neglect. In terms of hospital resource allocation, a sensible next step would be to determine, potentially by means of the Rehabilitation Complexity Scale^{26,} whether the shorter stay of spasticity patients is offset by more intensive use of hospital services. Such an investigation would inform the debate as to whether the focus on spasticity within stroke management is out of step with its impact on patient wellbeing^{25,27}.

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Clinical Characteristics	Incidence	LOS (s.d.)
Gender: male/female	62/44 (58%/41%)	97/104 (61/82)
Age: <60yrs/>60yrs	49/57 (46%/54%)	126/87 (69/69)
Handedness: left/right	96/10 (91%/9%)	102/88 (72/58)
Neglect	46 (43%)	120 (79)
left-side	31 (29%)	130 (85)
right-side	15 (14%)	99 (56)
Spasticity	73 (68%)	105 (78)
left-side	38 (36%)	116 (84)
right-side	31 (29%)	83 (63)
bilateral	4 (4%)	151 (86)
lower limb	4 (4%)	48 (16)
upper limb	39 (36%)	103 (78)
upper and lower limb	29 (27%)	112 (81)
Flaccidity	13 (12%)	119 (47)
Depression	34 (32%)	94 (48)
Hemianopia	17 (16%)	105 (61)
Stroke Type		
ischemic	75 (70%)	94 (67)
hemorrhagic	28 (26%)	115 (80)
ischemic and hemorrhagic	2 (2%)	105 (96)
Hemispheric lesion site		
left hemisphere	42 (40%)	87 (60)
right hemisphere	54 (51%)	102 (69)
bilateral	7 (7%)	129 (86)
Intra-hemispheric lesion site		
frontal	34 (32%)	117 (85)
temporal	20 (19%)	106 (70)
parietal	36 (34%	111(81)
occipital	2 (2%)	36 (23)

Table 1. Incidence of specific clinical characteristics and associated mean length of stay across the entire sample (n=106). LOS = length of stay; s.d. = standard deviation.

Clinical Characteristics	No. missing
	cases
Upper/lower spastic limb	1
Flaccidity	9
Hemianopia	15
Intra-hemispheric lesion site	22

Table 2. Clinical characteristics for which data were missing from those cases statistically analysed (n=91).

Clinical Characteristics	Left Neglect		
	Present	Absent	
Spasticity*	27/31 (87%)	34/60 (57%)	
Flaccidity	4/31 (13%)	8/51 (16%)	
Hemianopia*	8/22 (37%)	5/54 (9%)	
Age*			
<60years	13/31 (42%)	33/60 (55%)	
>60 years	18/31 (58%)	27/60 (45%)	
Depression*	14/31 (45%)	15/60 (25%)	
Right hemisphere lesion site			
Frontal*	15/21 (71%)	17/48 (35%)	
Temporal*	8/21 (38%)	7/48 (15%)	
Parietal*	15/21 (71%)	18/48 (38%)	
Occipital	0/21 (0%)	2/48 (4%)	

Table 3a. Frequency of clinical characteristics in patients with and without left neglect. Asterisk (*) denotes a statistically significant association (Pearson Chi-square) with the presence/absence of left neglect.

Clinical Characteristics	Left and Right Neglect Combined		
	Present	Absent	
Spasticity*	39/46 (85%)	34/60 (57%)	
Flaccidity	5/46 (11%)	8/51 (16%)	
Hemianopia*	12/33 (36%)	5/54 (9%)	
Age*			
<60years	16/46 (35%)	33/60(55%)	
>60 years	30/46 (65%)	27/60 (45%)	
Depression	19/46 (41%)	15/60 (25%)	
Intra-hemispheric lesion site	, ,	, ,	
Frontal	17/32 (53%)	17/48 (35%)	
Temporal*	13/32 (40%)	7/48 (15%)	
Parietal	18/32 (56%)	18/48 (38%)	
Occipital	0/0 (0%)	2/48 (4%)	

Table 3b. Frequency of clinical characteristics in patients as function of the presence/absence of hemi-spatial neglect (irrespective of whether the neglect was left- or right-sided). Asterisk (*) denotes a statistically significant association (Pearson Chi-square) with the presence/absence of neglect.

Clinical Characteristics	β	t	Sig.	95% lower/upper confidence interval
Neglect	0.514	3.1	0.002	.187 / .841
Age	0.574	3.8	0.001	.274 / .874
Spasticity	0.098	0.6	0.56	234 / .431

R squared = .21

Table 4. Final regression model for predicting Length of Stay