CME

# Hemispatial neglect

## Subtypes, neuroanatomy, and disability

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**Abstract—***Objective:* To assess the relative frequency of occurrence of motor, perceptual, peripersonal, and personal neglect subtypes, the association of neglect and other related deficits (e.g., deficient nonlateralized attention, anosognosia), and the neuroanatomic substrates of neglect in patients with right hemisphere stroke in rehabilitation settings. *Methods:* The authors assessed 166 rehabilitation inpatients and outpatients with right hemisphere stroke with measures of neglect and neglect subtypes, attention, motor and sensory function, functional disability, and family burden. Detailed lesion analyses were also performed. *Results:* Neglect was present in 48% of right hemisphere stroke patients. Patients with neglect had more motor impairment, sensory dysfunction, visual extinction, basic (nonlateralized) attention deficit, and anosognosia than did patients without neglect. Personal neglect occurred in 1% and peripersonal neglect in 27%, motor neglect in 17%, and perceptual neglect in 21%. Neglect severity predicted scores on the Functional Independence Measure and Family Burden Questionnaire more accurately than did number of lesioned regions. *Conclusions:* The neglect syndrome per se, rather than overall stroke severity, predicts poor outcome in right hemisphere stroke. Dissociations between tasks assessing neglect subtypes support the existence of these subtypes. Finally, neglect results from lesions at various loci within a distributed system mediating several aspects of attention and spatiomotor performance.

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Hemispatial neglect is defined as a failure to attend to the contralesional side of space. Its reported frequency varies widely from 13% to 81% of patients who have had right hemisphere stroke.[1] Patients with neglect are more impaired than patients without neglect on measures of impairment and disability, and have longer rehabilitation hospitalizations.[2] Neglect has been reported consequent to lesions to the right temporo-parietal-occipital (TPO) junction, parietal lobe, frontal lobe, thalamus, and basal ganglia,[3] but it has been proposed that lesions to the superior temporal lobe and associated subcortical structures are crucial to its occurrence.[4]

Neglect may differentially affect attention and perception versus intention and action.[3,5,6] Thus, some patients with neglect may exhibit directional hypokinesia for actions into and toward contralesional hemispace, whereas others may fail to respond to stimuli on the left of the eyes, head, or body, irrespective of the required motor response. Controversy exists as to whether the motor and perceptual subtypes may be associated with anterior versus posterior lesions.[5,7] Neglect may affect the contralesional body (personal neglect), contralesional near space within reaching distance (peripersonal neglect), or space beyond reaching distance (extrapersonal neglect).[8,9] Nonlateralized deficits in attention may be prominent,[10] and an important influence on its severity and persistence.[11] Neglect patients may be severely impaired in detecting targets in both hemispaces,[12] and may perform poorly on simple tone-counting tasks measuring nonlateralized attention.[13]

Somatosensory, visual field, and motor deficits are all more frequent after right than left hemisphere stroke, suggesting that primary sensory deficits may be augmented by neglect.[14] Anosognosia, or unawareness of deficit, is also more frequent after right than left hemisphere lesions, and may compound the disability deriving from the neglect itself.[15]

Given this diversity, an impediment to progress in neglect treatment has been difficulty defining the subject population. Recent large-scale studies of neglect[16] have described the frequency of occurrence of neglect, its clinical course, and its neuroanatomic correlates. To our knowledge, there have been no large studies assessing the frequency of neglect subtypes or deficits in nonlateralized attention. These factors may have implications for the level of patients' disability, as well as for development of treatment studies targeted to the pattern of impairment.

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the March 9 issue to find the title link for this article.

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***Table 1*** *Demographic information*

| | American acute, n = 62 | | Italian acute, n = 24 | | American chronic, n = 34 | | Italian chronic, n = 46 | |
|---|---|---|---|---|---|---|---|---|
| Characteristics | Mean (SD) | Range | Mean (SD) | Range | Mean (SD) | Range | Mean (SD) | Range |
| Age, y | 66.2 (12) | 37–89 | 70.5 (10.4) | 50–88 | 66.6 (11.9) | 43–89 | 63.6 (11.7) | 33–82 |
| Years of Education | 12.9 (2.9) | 5–20 | 4.9 (3.2) | 1–18 | 12.9 (3.9) | 5–20 | 7.5 (4) | 3–19 |
| Days post onset | 16.8 (6.8) | 5–37 | 26.2 (7.8) | 15–41 | 303.0 (169.5) | 94–700 | 376.3 (304.7) | 60–1272 |
| No. men/no. women | 29/33 | | 12/12 | | 20/14 | | 27/19 | |

Before designing such studies, it is important to assess the frequency with which the putative subtypes and co-occurring deficits can be detected in a rehabilitation population with right hemisphere stroke.

**Methods.** *Patients.* We studied 166 patients who had right hemisphere stroke. Patients were recruited from inpatient and outpatient stroke services of MossRehab, Bryn Mawr Rehab, and Magee Rehabilitation Hospitals in the greater Philadelphia area in the United States, as well as the National Institute for Research and Care in Aging Fraticini Glicini and San Camillo Hospitals in Italy. Patients were considered eligible for the study if they had sustained a hemorrhagic, embolic, or thrombotic right hemisphere stroke within the previous 3 years. See E-Methods at www.neurology.org for subject criteria and testing schedules. Of an original 623 charts (503 American, 120 Italian) of right hemisphere stroke patients screened, 268 (188 American, 80 Italian) met study criteria, 257 (177 American, 80 Italian) were approached for consent to participate, and 166 (96 American, 70 Italian) gave informed consent. There were 86 patients with acute lesions and 80 patients with chronic lesions (more than 3 months, less than 3 years post right hemisphere stroke). Table 1 provides demographic information for all subjects.

Italian and American patients did not differ in age (acute: $t = -1.6$, $p = 0.12$; chronic: $t = 1.4$, $p = 0.16$), but Italian patients had fewer years of education than American subjects (acute: $t = 11.2$, $p < 0.0001$; chronic: $t = 6.2$, $p < 0.0001$). Acute American patients had had strokes more recently than acute Italian patients ($t = -5.5$, $p < 0.0001$), likely reflecting differences in health care delivery, but stroke recency was equivalent in the American and Italian chronic groups ($t = -1.2$, $p = 0.21$). There proved to be no difference in the proportion of patients with operationally defined neglect in the Italian and American populations in either the acute ($\chi^2 = 2.5$, $p = 0.15$) or chronic group ($\chi^2 = 0.005$, $p > 0.99$). There also proved to be no difference between the American and Italian acute patients in clinical severity as measured by the Functional Independence Measure (FIM, 1996; FIM Physical Scale $t = -0.94$, $p = 0.35$; FIM Cognitive Scale $t = -0.82$, $p = 0.41$). There were insufficient FIM data from chronic patients to perform a similar comparison. The reported analyses combined American and Italian patients into a single group unless otherwise noted.

*Test battery.* Patients were assessed with a comprehensive battery of tests. They were seated in a quiet, dedicated testing room at a desk. The examiner sat beside them to the right. Examiners were trained to administer all tests in a standardized manner. Patients were instructed with simple directions, which were read to them aloud from a standard script. Order of test administration was randomized.

Clinical tests of neglect. Five tests comprised the clinical neglect battery: The Bells Test[17] and four subtests of the Behavioral Inattention Test (BIT)[18]: Letter Cancellation, Picture Scanning, Menu Reading, and Line Bisection. See E-Methods at www.neurology.org for test descriptions and scoring procedures.

Motor examination. Right and left grip strength was measured with a hand-held dynamometer. Three trials were performed with each hand at midline and the mean grip strength (kg) was recorded.

Active range of motion of the left shoulder, elbow, wrist, and fingers was measured using a standard 12-inch goniometer. Range of motion of the index finger was assessed with a 6-inch finger goniometer.

Sensory examination. Visual fields and visual extinction were assessed with presentation of four unilateral right, four unilateral left, and four bilateral visual stimuli (slight finger movement) in randomized order. Head and body were aligned.

Tactile sensation and tactile extinction were assessed with presentation of a light tactile left, right, or bilateral stimulus on the dorsum of the hands (n = 4 each).

See E-Methods at www.neurology.org for scoring information.

Sustained and divided attention. The Sustained Attention to Response Test (SART[13]) was used to assess sustained attention and response inhibition.

The Dual Task test was used to measure simple response time with and without a secondary task load.[19] See E-Methods at www.neurology.org for test descriptions and scoring information.

Motor and perceptual neglect. Because most common paper and pencil tests of neglect confound the need to perceive left sided stimuli with the requirement to respond (e.g., cancel them), we developed two tasks that would separate these factors. The Lateralized Target and Lateralized Response Tests[20] measured response latencies in two different stimulus/response conditions. See E-Methods at www.neurology.org for test description and scoring information.

Personal and peripersonal neglect. The determination of peripersonal neglect was based on performance below a cutoff score on any one of the five clinical paper-and-pencil tests listed above. The cutoff scores were as follows: Bells Test (L − R difference) = −4; Letter Cancellation (L − R difference) = −4; Menu Reading (L − R difference) = −3; Picture Scanning (L − R % difference) = −20%; Line Bisection (mean deviation, mm) = 13. See E-Methods: Determination of cut-off scores at www.neurology.org for more details.

Personal neglect was assessed by placing six cotton balls on a blindfolded participant's left side at shoulder, chest, elbow, forearm, wrist, and hip (for a similar test, see reference 21). Upon removal of the blindfold, the participant was instructed to locate and remove the cotton balls. The number of detected targets was tallied (0 to 6).

Anosognosia. At the end of each test session, a five-question Anosognosia Questionnaire (adapted from reference [22]) was administered that addressed sensorimotor impairment and general awareness of deficit. See E-Methods at www.neurology.org for test description and scoring information.

Clinical severity. The 18-item FIM[23] was administered to acute inpatients at admission and discharge by clinicians trained and certified according to procedures of the Uniform Data System. See E-Methods at www.neurology.org for test description and scoring information.

Caregiver ratings of burden. The families of all chronic patients were administered the Family Burden Questionnaire (FBQ; adapted from the Questionnaire on Resources and Stress[24]). This is a 10-point true/false questionnaire, which is designed to assess stress placed on the family of the stroke patient (e.g., "_____" is hard to live with; "_____" doesn't do as much as s/he should do).

Lesion analyses. Clinical neuroimaging scans were available for 156 of the 166 patients (94%). Scans for the majority (83%) of patients were CT; the remainder (17%) were T2/proton density MRI. Scans were interpreted by the project neurologists (H.B.C. and F.F.) who were naïve to patients' identities and clinical presentations. Patients with left hemisphere lesions larger than

***Table 2*** *Scores of acute and chronic neglect and non-neglect patients on tests of "clinical" neglect*

| Test | A+, Mean (SD) n = 42 | A−, Mean (SD) n = 44 | C+, Mean (SD) n = 38 | C−, Mean (SD) n = 42 |
|---|---|---|---|---|
| Bell Cancellation, L − R difference | −4.9 (4.6) | −0.1 (1.6) | −4.9 (4.3) | −0.3 (1.3) |
| Letter Cancellation, L − R difference | −2.7 (4.9) | 0.6 (1.5) | −4.3 (5.9) | 0.6 (1.5) |
| Menu Reading, L − R difference | −2.6 (3.9) | −0.1 (0.3) | −2.8 (4.2) | 0 (0) |
| Picture Identification, L − R percent difference | −29.7 (32.1) | 0.7 (4.5) | −24 (35.2) | 1.1 (4.9) |
| Line Bisection, deviation, mm | 9.7 (21) | 0.9 (6.4) | 18 (20.4) | −0.4 (5.4) |
| | N (% of gp) | N (% of gp) | N (% of gp) | N (% of gp) |
| Field Defects | 12 (30) | 0 (0)† | 15 (40) | 1 (2)† |
| Visual Extinction | 14 (34) | 4 (9)* | 9 (24) | 6 (14) NS |
| Tactile Sensory Loss | 16 (41) | 5 (11)* | 15 (40) | 1 (2)† |
| Tactile Extinction | 9 (23) | 7 (16) NS | 13 (34) | 12 (29) NS |

Significance of $\chi^2$: * $p < 0.01$; † $p < 0.001$; NS = not significant.

A+ = acute patients with neglect; A− = acute patients without neglect; C+ = chronic patients with neglect; C− = chronic patients without neglect.

small lacunes were to be excluded at this stage; however, there were none. Lesion location was coded using 37 regions adopted from template A18 or A20 (depending on slice angle) of Damasio and Damasio.[25] Eight subcortical regions in the internal capsule, thalamus, and basal ganglia not appearing on the template were also coded. For the purpose of some of the analyses to be reported (see below), these were subsequently collapsed into 10 regions of interest: 1. cingulate and orbital frontal; 2. prefrontal, periventricular, and deep white matter; 3. sensory-motor; 4. superior and middle temporal; 5. inferior temporal/mesial temporal; 6. inferior parietal; 7. superior parietal; 8. occipital; 9. basal ganglia (caudate, putamen, globus pallidus); 10. thalamus and internal capsule (including but not limited to anterior limb).

*Data analysis.* See E-Data analysis at www.neurology.org for information on data analysis.

**Results.** *Frequency of neglect in the study population.* Forty-two (49%) of the acute and 38 (47%) of the chronic patients exhibited neglect on at least one of the five clinical tests. For acute patients, determination of motor, perceptual, personal, and peripersonal neglect was based upon data from the last testing session. Hereafter, acute patients meeting the criteria for neglect will be identified as A+, acute patients without neglect as A-, chronic patients with neglect as C+, and chronic patients without neglect as C-.

Table 2 shows patients' scores on all five clinical tests of neglect (Bells Test, Letter Cancellation, Picture Scanning, Menu Reading, Line Bisection). All scores were correlated ($0.22 < r < 0.69$; all $p < 0.05$). Consequently, for each patient we calculated the percentile rank on each of the five clinical tests, and then averaged this rank. The resultant score (hereafter, average neglect percentile) was used in several of the analyses reported.

*Additional characteristics of the neglect syndrome.* Motor function. Range of motion (ROM) scores from all joints were highly correlated by Spearman correlation coefficient (rho > 0.85, $p < 0.0001$ for all analyses). Consequently, ROM scores were averaged, and a percentile score computed (average ROM percentile). There was a moderate correlation between the average neglect percentile and average ROM percentile scores ($r = 0.45$, $p < 0.0001$), indicating that patients with more severe neglect were likely to have more severe ROM impairment.

See E-Results: Motor function at www.neurology.org for further detail.

Sensory function. Table 2 presents results of visual and tactile sensory testing. To summarize, visual and tactile sensory loss is more likely to occur in patients with neglect than in those without neglect. Visual extinction is also associated with neglect, but only in the acute population. Tactile extinction is not strongly associated with neglect. The association of visual extinction and neglect is consistent with previous findings.[26]

Anosognosia. Mean scores on the anosognosia test differed by Mann Whitney tests for the A+ and A- groups (A+ mean = 2.0, SD 2.0; A- mean = 0.3, SD 0.8, U = −4.0, $p < 0.0001$) as well as for the C+ and C- groups (C+ mean = 1.6, SD 1.7; C- mean = 0.1, SD 0.4, U = −4.5, $p < 0.0001$). Patients with neglect had less awareness of deficit than did patients without neglect. One limitation of these

***Table 3*** *Frequency of neglect subtypes*

| Tests | Acute | Chronic |
|---|---|---|
| Completed motor and perceptual tests | 71 | 76 |
| Both motor and perceptual neglect | 2 (3) | 8 (11) |
| Motor neglect only | 12 (17) | 8 (11) |
| Perceptual neglect only | 15 (21) | 10 (13) |
| Neither motor nor perceptual neglect | 42 (59) | 50 (65) |
| Completed personal and peripersonal tests | 84 | 80 |
| Both personal and peripersonal neglect | 15 (18) | 11 (14) |
| Personal neglect only | 1 (1) | 1 (1) |
| Peripersonal neglect only | 23 (27) | 24 (30) |
| Neither personal nor peripersonal neglect | 45 (53) | 44 (55) |

Values are n (%).

***Table 4*** *Patterns of performance on the measures of neglect subtypes, ranked by numbers of subjects*

| Peripersonal | Personal | Perceptual | Motor | Acute | Chronic | Total |
|---|---|---|---|---|---|---|
| + | − | + | − | 10 | 12 | 22 |
| + | − | − | − | 9 | 10 | 19 |
| + | − | − | + | 12 | 6 | 18 |
| + | + | + | − | 6 | 4 | 10 |
| − | − | − | + | 6 | 4 | 10 |
| + | + | + | + | 1 | 7 | 8 |
| + | + | − | − | 5 | 3 | 8 |
| + | − | + | + | 0 | 8 | 8 |
| − | − | + | − | 6 | 2 | 8 |
| + | + | − | + | 1 | 2 | 3 |
| − | + | − | − | 1 | 1 | 2 |
| − | − | + | + | 1 | 1 | 2 |

− = no neglect, ≥ 20th percentile; + = neglect, <20th percentile.

data, however, is that there is less opportunity for underestimation of actual disability in patients with less disability.[27]

*Subtypes of neglect.* Table 3 shows the data from subjects who completed testing for both perceptual and motor neglect (lateralized target, lateralized response), as well as from a partially overlapping group of subjects who completed testing for personal and peripersonal neglect (clinical neglect tests, fluff test). These data indicate that combinations of subtype deficits appear in the population, with the exception of isolated personal neglect, which is relatively uncommon, at least as assessed by the single measure employed here (see Discussion for additional comment). We also assessed the number of patients exhibiting a neglect subtype (<20th percentile on relevant task) whose score was above average (>50th percentile) on the contrasting relevant task. See E-Methods: Subtypes at www.neurology.org for details. Even with this more conservative estimate, there were still patients who could be characterized as exhibiting a pure neglect subtype.

In addition, we looked at the numbers of subtypes tasks on which patients were impaired, and thus the degree to which patients could be characterized as exhibiting a complex combination of deficits. As shown in table 4, a pattern of impairment on multiple tasks was quite common.

*Relationship of lateralized and nonlateralized attention deficits.* Table E-5 (available at www.neurology.org) shows patients' scores on the Dual Task tests and on the SART, along with normative data from 20 healthy adult participants we recently reported[28] (mean age 62 years, SD 11; mean education 13.4 years, SD 2.7; 8 men and 12 women).

Previous investigators have suggested that deficits in basic attention and sensorimotor response speed are a prominent component of the neglect syndrome.[29] We assessed that hypothesis in an analysis that can be viewed online (see E-Results: Attention and sensorimotor response speed at www.neurology.org). The data support previous findings suggesting that neglect is associated with deficits in sensorimotor response speed[10] and nonexecutive aspects

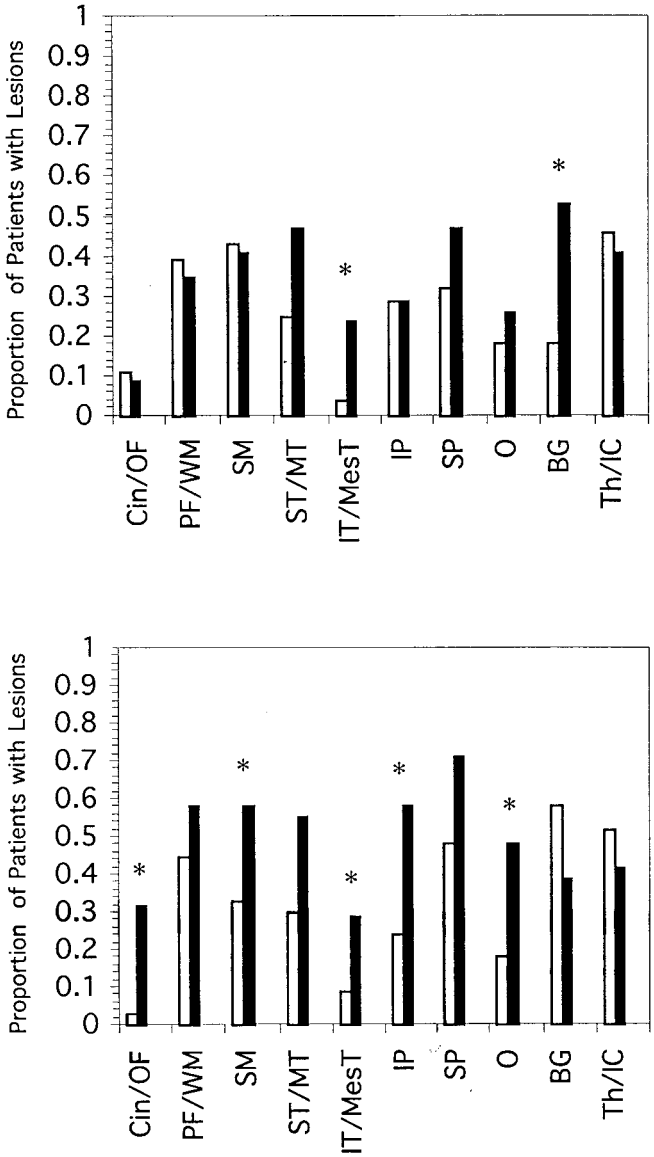


*Figure 1. Proportion of acute (top) and chronic (bottom) patients with neglect (black bars) and without neglect (white bars) having lesions in defined neuroanatomic regions of interest. Asterisks mark significant differences. Cin/OF = cingulate, orbito-frontal; PF/WM = prefrontal, periventricular white matter; SM = sensory-motor; ST/MT = superior temporal, middle temporal; IT/MesT = inferior temporal/mesial temporal; IP = inferior parietal; SP = superior parietal; O = occipital; BG = basal ganglia; Th/IC = thalamus, internal capsule.*

of attention (i.e., what has been called "posterior attention"[30]). These capacities have been linked to the attention system of the right hemisphere, and in particular the right parietal lobe.[31] On the other hand, neglect is not associated with executive capacities involved in performing under dual task load and in inhibiting responses to infrequent targets. These functions are frequently attributed to frontal lobe structures.[30]

*Clinical implications of the neglect syndrome.* A discussion of FIM and caregiver burden data may be viewed online (see E-Results: Clinical implications of the neglect syndrome at www.neurology.org). These data indicate that

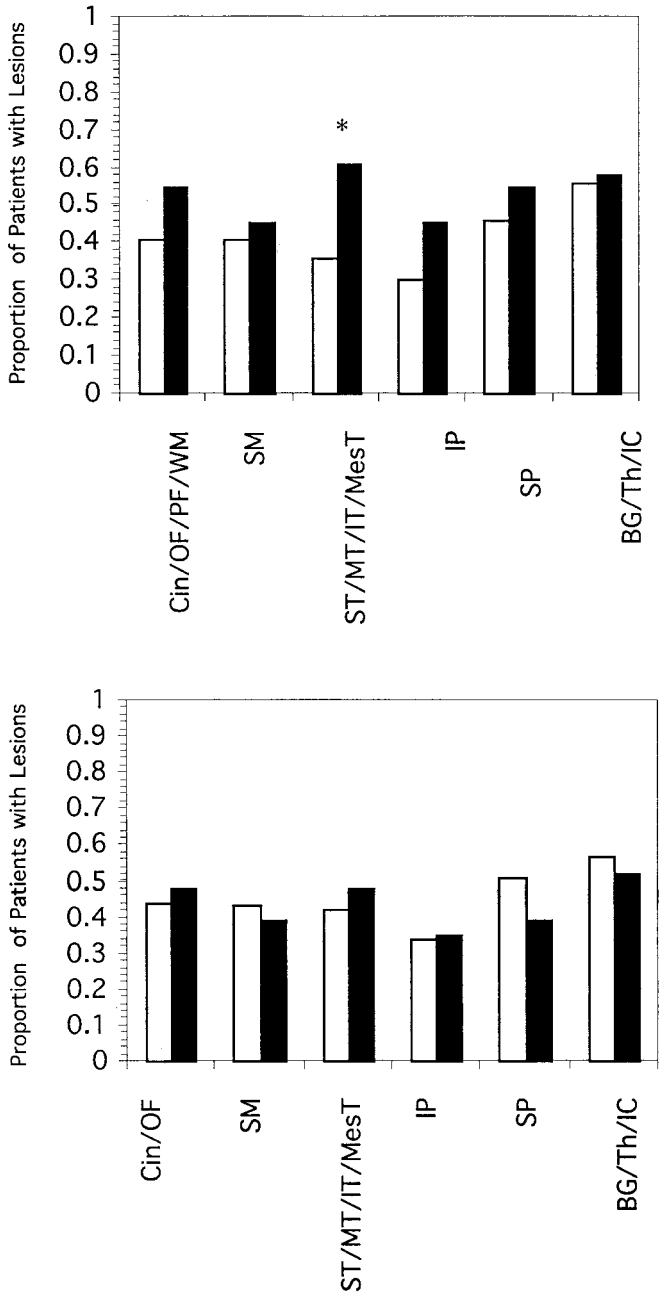


*Figure 2. Top graph shows proportion of patients having lesions in defined neuroanatomic regions of interest (ROI) with perceptual neglect (black bars), as compared to motor neglect, both perceptual and motor neglect, and neither perceptual nor motor neglect (white bars). Bottom graph shows proportion of patients having lesions in defined ROI with motor neglect (black bars), as compared to perceptual neglect, both motor and perceptual neglect, and neither perceptual nor motor neglect (white bars). The asterisk marks the sole significant difference. Cin/OF/PF/WM = cingulate, orbitofrontal, prefrontal, periventricular white matter; SM = sensory-motor; ST/MT/IT/MesT = superior temporal, middle temporal, inferior temporal, mesial temporal; IP = inferior parietal; SP = superior parietal; BG/Th/IC = basal ganglia, thalamus, internal capsule.*

average neglect percentile makes an independent contribution to the prediction of family burden above and beyond that predicted by FIM.

*Lesion localization analyses.* Patients for lesion localization analyses were 126 patients who had CT/MRI evidence of at least one lesioned area. As described in Methods, 10 neuroanatomic regions were included in the analyses and coded by two raters. Data on interrater reliability are reported in E-Results: Reliability study at www.neurology.org.

*Lesion patterns: Patients with and without neglect.* The first analysis examined whether neglect and non-neglect patients exhibited differences in lesion location(s). Categorical modeling using the CATMOD procedure[32] was used to assess whether neuroanatomic region(s) of involvement predicted the presence or absence of neglect, and whether region(s) of involvement predicted neglect subtype. The proportion of patients in each group with a lesion in each area of interest can be seen in figures 1 and 2.

See E-Results: Categorical modeling at www.neurology.org for a description of statistical analyses.

CATMOD was used to establish a distribution of variance for a $2 \times 2 \times 10$ contingency table, for neglect (non-neglect versus neglect) $\times$ chronicity (acute versus chronic) $\times$ lesion area (lesion present or absent in each of 10 areas). Three main effects and all possible interactions were specified. With an alpha level of 0.05, main effects of neglect ($\chi^2$ [1, n = 126] = 13.23, $p < 0.001$), chronicity ($\chi^2$ [1, n = 126] = 7.52, $p < 0.01$), and area ($\chi^2$ [9, n = 126] = 120.08, $p < 0.001$) were all significant, as was a three-way interaction between neglect, chronicity, and area ($\chi^2$ [9, n = 126] = 25.02, $p < 0.01$). No other interactions were significant. The main effect of area reflects the fact that lesions did not occur equally in all neuroanatomic regions. The main effect of neglect indicates that the probability of lesioned areas was 1.8 times higher in neglect than in non-neglect patients. Post hoc testing revealed that 13 of the 37 A+ patients (45%) had four or more lesioned areas, compared to 7 of the 42 A- patients (17%). Similarly, 22 of the 35 C+ patients (63%) versus 13 of 43 (30%) C- patients had four or more lesioned areas. Both comparisons are significant ($\chi^2 > 9.1$, $p < 0.01$). The main effect of chronicity indicates that the probability of lesioned area(s) was 1.6 times higher in chronic than acute patients. The three-way interaction indicates that significantly different lesion patterns are associated with neglect in acute as compared to chronic patients (figure E-1, available at www.neurology.org).

Post hoc analyses indicated that in acute patients, lesions in the basal ganglia ($\chi^2 = 8.1$, $p = 0.004$) and in the inferior/mesial temporal region ($\chi^2 = 4.9$, $p = 0.03$) were more likely to be associated with neglect than not, and there was a slight trend in the same direction for the superior temporal/middle temporal gyri ($p = 0.11$). In the chronic patients, lesions in the cingulate/orbitofrontal region ($\chi^2 = 9.6$, $p = 0.001$), inferior/mesial temporal lobe ($\chi^2 = 4.1$, $p = 0.05$), superior/middle temporal lobe ($\chi^2 = 4.1$, $p = 0.05$), inferior parietal lobe (IPL) ($\chi^2 = 7.6$, $p = 0.01$), and occipital lobe ($\chi^2 = 6.6$, $p = 0.02$) were more likely to be associated with neglect than not. In the chronic group, there were also trends for lesions in sensory-motor cortex ($\chi^2 = 3.9$, $p = 0.07$) and superior parietal lobe ($\chi^2 = 3.4$, $p = 0.08$) to be more likely associated with neglect than not. These data suggest that several regions, includ-

ing the inferior/mesial temporal, middle/superior temporal, inferior parietal, basal ganglia, and occipital lobes, are all more likely to be involved in neglect than non-neglect patients.

*Lesion patterns: Neglect subtypes.* The second CATMOD analysis examined whether patients with motor neglect, perceptual neglect, both motor and perceptual neglect, or neither exhibited different lesion patterns (see E-Results: Lesion patterns of subtypes at www.neurology.org). As shown in figure 2, patients with perceptual neglect were more likely to have lesions in the temporal lobe than were patients in the other groups.

*Role of temporal lobe involvement.* These data are potentially consistent with recent claims that 1) neglect is critically dependent upon lesions to the superior temporal gyrus (STG) and associated subcortical structures,[4] and 2) previous assertions of the importance of parietal structures have been confounded by the presence of patients with visual field defects. See E-Results: Temporal lobe involvement at www.neurology.org for details. There are three predictions deriving from these claims. Prediction 1 is that there should be an absence of patients with STG lesions without neglect. Prediction 2 is that there should be an absence of patients who have neglect without STG lesions. If previous claims that neglect is linked to IPL and TPO damage are an artifact of the inclusion in those studies of patients with field cuts, then prediction 3 is that there should be an absence of patients with lesions in IPL and TPO who have neglect without field cuts. For the analyses addressing these questions, lesions were coded according to 37 regions of the Damasio and Damasio[25] template, plus eight additional subcortical regions in the basal ganglia, thalamus, and white matter.

The first analysis, relevant to prediction 1, indicated that there were patients with STG lesions without neglect: of 50 patients with STG lesions, 16 (32%) did not exhibit neglect. Six of these 16 were acute and 10 were chronic. None had visual field deficits. The second analysis, relevant to prediction 2, indicated that there were neglect patients without STG lesions: of 65 patients with neglect, 37 (57%) had no involvement of the STG. Twenty of the 37 were acute and 17 were chronic. Twenty-three of the 37 (62%) had no visual field deficits. Seventeen of the 37 had no basal ganglia or thalamic involvement. In this subsample of 17 patients, the parietal lobe was involved in 13, frontal lobe in 2, and occipital in 2.

In the analysis relevant to prediction 3, we determined that there were patients with IPL/TPO lesions and no field cuts who nevertheless exhibited neglect: of 44 patients with IPL/TPO lesions (P1, P2, T9, O4), 33 did not have field cuts. Of these 33 patients, 17 (51%) had neglect. Five of the 17 were acute and 12 were chronic. Thirteen of the 17 had no basal ganglia or thalamic involvement.

*Effect of number of lesioned areas on disability, decreased attention, and family burden.* If number of lesioned regions is viewed as a proxy for lesion size, patients with neglect in our study have larger lesions than those without the disorder. One obvious question is whether many of the findings reported here suggesting greater disability (e.g., lower FIM scores), more cognitive dysfunction (e.g., longer response times to visual stimuli), and increased burden on families in neglect patients can be reduced to an effect of number of lesions (or overall severity of neurologic dysfunction).

First, we assessed whether there was a relationship between number of lesioned areas and FIM scores. For these analyses we used 45 coded regions (37 from the templates of Damasio and Damasio,[25] and 8 additional subcortical regions). Number of lesioned areas was weakly negatively correlated with discharge FIM total score ($r = -0.3$, $p = 0.03$), and there was a trend in the same direction for admission FIM total ($r = -0.2$, $p = 0.08$). We next performed several regression analyses to assess whether neglect scores predicted patients' functional disability and family burden when number of lesioned areas was factored in (see E-Results: Regression analyses at www.neurology.org). Number of lesioned areas made no statistically reliable contribution to the prediction of performance. In contrast, neglect scores were strong independent predictors of both dependent variables.

**Discussion.** Data from 166 patients with right hemisphere stroke corroborate previous findings of the prevalence and impact of neglect in post-acute populations. In addition, the results indicate that neglect has an impact upon basic attention, functional disability, and family burden that is significantly greater than that predicted by number of lesioned areas. This suggests that it is the neglect syndrome per se, rather than overall stroke severity, that predicts poor outcome in right hemisphere stroke. Given the strength of the association between neglect and disability, future studies of neglect treatment efficacy may benefit from including measures of disability and family burden as indices of treatment success.

The current data also support previous claims that neglect is a complex constellation of symptoms. We observed numerous patterns of association and dissociation of personal, peripersonal, motor, and perceptual neglect. Pure motor, perceptual, and peripersonal neglect were not infrequently observed. On the other hand, isolated personal neglect appeared rarely. The observed dissociations support the proposal that there are identifiable neglect subtypes. This has potential implications for investigators undertaking treatment studies, as the success of a particular treatment may be linked to patients' subtype profile. The first step in exploration of such relationships is the inclusion of subtype data in future studies of treatment efficacy.

Based on the fact that task effects have proven to be strong determinants of the performance of neglect patients,[33] one caveat is that different results may have been obtained had we used other, or additional measures of the subtypes. The distinction between motor and perceptual neglect, for example, has been assessed with pulleys, mirrors, landmark tasks, and video monitors[5,6,34-36] and these measures tend to disagree in their characterization of patients.[37] Another limitation, as noted above, is that our measure of motor neglect confounded intentional neglect and directional hypokinesia. An additional concern is the adequacy of the number of tasks employed, as well as the sensitivity of these tasks. For example, we

used only a single measure of personal neglect—the fluff test. Also, the version of the fluff test we adopted, which permits patients to find targets on the body with eyes open, may not have been sufficiently sensitive to detect personal neglect. It remains possible that some or all neglect subtypes occur more frequently than reported here. Another concern is sampling bias. The study criteria involved exclusion of patients with attentional or cognitive deficits so severe as to preclude participation, were biased by those who were willing to participate (with willingness itself possibly affected by presence or absence of neglect, and anosognosia), and were unevenly biased by greater relative participation of Italian than American patients. This may limit the generalizability of our determination of neglect prevalence. We also did not perform studies of test reliability (intrarater, inter-rater, or inter-center), and although test administration was standardized, it is nevertheless possible that differences in testing procedures may have affected results. Finally, as noted, there was no statistical adjustment for multiple test comparisons performed. For all of these reasons, caution should be used in interpreting the study results.

The lesion data are not consistent with the claim that lesions of the superior temporal lobe are critical in producing neglect. Nor are they consistent with the suggestion that previous reports of the importance of IPL and TPO lesions were confounded by inclusion of patients with field cuts. On the other hand, patients with the perceptual subtype of neglect were twice as likely to have damage to temporal lobe structures as were patients with motor neglect, perceptual and motor neglect, or neither. Given that previous investigators did not perform subtype analyses, a possible reason for the disparity is that the previous sample contained a relatively large number of pure perceptual neglect patients.

There are several differences in the methods used previously and the present study. The previous investigators required evidence of neglect on at least two clinical tests, whereas we required evidence on only one test; thus we may have included patients who were relatively mild. Even with this more inclusive criterion, however, we still found patients who had STG lesions without neglect. Additionally, the previous study used a method of lesion overlap, rather than an examination of individual patients for the presence or absence of involvement in the critical regions. Thus, their determination of the most likely locus of involvement in patients with neglect and without field cuts might be correct, while still not speaking to the critical substrates of the disorder.

There are several possible interpretations of the present data. One interpretation is that we may have simply failed to detect one or more key regions damaged in all neglect patients based on the limited sensitivity of the (predominantly CT-derived) data, or because the regions are affected indirectly, by diaschisis, and thus cannot be visualized on CT or MRI scans.[38] Alternatively, the data are consistent with the possibility that neglect may result from lesions to any one of several regions within a distributed network mediating basic (nonlateralized) and spatial aspects of attention.


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