Allen's monkey (U76951), mangabey (U76928), guereza colobus (U76925), and from Hanuman (U76929), dusky (U76926), Francois' (U76927) and purple-faced (U76940) langurs. The new lysozyme sequences have been deposited into GenBank under the accession numbers listed above. Institutional abbreviations are as follows, with contact persons in parentheses: NE, New England Regional Primate Research Center (D. Lee-Parritz); Yerkes, Yerkes Regional Primate Research Center (H. McClure); SD, The Zoological Society of San Diego (O. Ryder); HZG, Houston Zoological Gardens (B. Lester and J. Flanagan); UCB, University of California at Berkeley (P. Dolhinow); SL, St. Louis Zoological Park (I. Porton); SFBR, Southwest Foundation for Biomedical Research (K. Rice); MMZ, Miami MetroZoo (W. Zeigler); BR, Greater Baton Rouge Zoo (C. Lehn); NY, New York Zoological Society (G. Amato). The previously published[5] non-human primate sequences were verified in the present study; as suggested[5], the baboon lysozyme sequence differs slightly from the published protein sequence used in earlier analyses[4,6]. Only in gorilla and orangutan did we find allelic differences in the coding region (G. Maston and C.-B.S., manuscript in preparation); the less-derived alleles are considered here. For each species, we sequenced the entire coding region; only the mature region is used in the present analyses. K_A and K_S values for all pairwise comparisons were calculated with the computer program *Li93* (ref. 10). Similar overall results were found using the method of Nei and Gojobori[29,30]; the results from the Li method[9,10] are presented because the primate lysozyme sequences best meet its assumptions. Statistical significances for the K_A and K_S values were calculated by *t*-tests[16,30]. For a matrix of K_A-to-K_S values, see Supplementary Information. Rate comparisons between the introns and synonymous sites were done using *MEGA*[30], and included the published human sequence.

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CORRESPONDENCE and requests for materials should be addressed to C.-B.S. (e-mail: c.stewart@albany.edu). Primer sequences of intron 3 of the lysozyme gene are available from C.-B.S., and the GenBank accession numbers for the new lysozyme sequences are listed in the Methods section.

Abnormal temporal dynamics of visual attention in spatial neglect patients

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When we identify a visual object such as a word or letter, our ability to detect a second object is impaired if it appears within 400 ms of the first[1–5]. This phenomenon has been termed the attentional blink or dwell time and is a measure of our ability to allocate attention over time (temporal attention). Patients with unilateral visual neglect are unaware of people or objects contralateral to their lesion[6,7]. They are considered to have a disorder of attending to a particular location in space (spatial attention)[6–11]. Here we examined the non-spatial temporal dynamics of attention in patients, using a protocol for assessing the attentional blink. Neglect patients with right parietal, frontal or basal ganglia strokes had an abnormally severe and protracted attentional blink. When they identified a letter, their awareness of a subsequent letter was significantly diminished for a length of time that was three times as long as for individuals without neglect. Our results demonstrate for the first time that visual neglect is a disorder of directing attention in time, as well as space.

Visual neglect is a common disorder following stroke. It is most severe after right hemisphere lesions, affecting over 70% of such patients[12]. These individuals are unaware of people or objects to their left and have a poor prognosis for recovery of independent function[12,13]. Despite the intense interest in neglect, the mechanisms underlying this disorder remain obscure[6,7]. One prominent theory considers left-sided neglect to be the result of a bias to attend to the right[8]. An alternative hypothesis is that neglect patients have a direction-specific impairment of disengaging attention from a stimulus on the right when they are required to shift attention to the left[9–11]. Both theories make the same fundamental assumption that neglect is an impairment of spatial attention. We investigated whether there is a non-spatial component of attention in neglect by measuring the temporal dynamics of attention at one location. The protocol we used allowed us to measure directly the time required to discriminate an object and release processing capacity for another, when no directional shift of attention is required.

Individuals without any neurological abnormality experience a significant 'loss' of attention for ~400 ms after engaging a target for purposes of identification[1–5]: this has been referred to as the attentional blink or dwell time. A standard procedure for determining this loss of temporal attention requires individuals to view a rapid serial visual presentation (RSVP) sequence of letters presented successively at the same location (see Fig. 1 and Methods for further details). In each RSVP sequence, all the letters are black except one, which is white. This is the first target (T1) the subject is asked to identify. In half the trials, T1 is followed at some point in the sequence by a black 'X'. This is the second target (T2). Individuals' ability to detect T2 correctly after successfully identifying T1 in this dual-target task is then plotted over time (interval between T1 and T2).

The performance of ten right-handed volunteers who had not suffered a stroke (mean age, 73 years) is shown in Fig. 2. When asked to identify T1 and also say whether T2 was present (dual-target task), their ability to detect T2 varied according to its temporal position in the RSVP sequence: if it occurred within 360 ms of T1, detection was significantly impaired. This is the standard attentional blink outcome[1–5]. These subjects were also tested on a control task in which they viewed similar RSVP

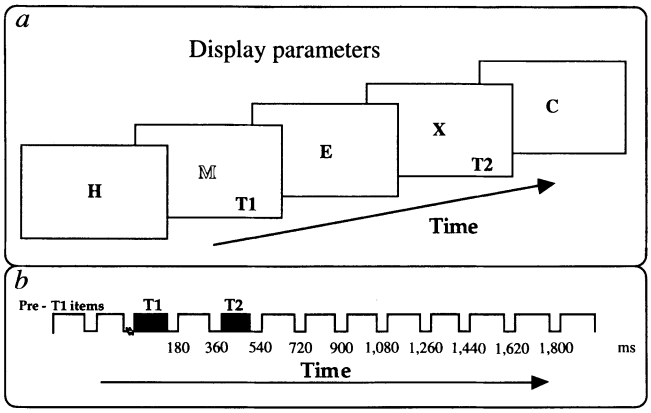

FIG. 1 *a*, Some of the stimuli in a RSVP stream. *b*, The temporal sequence of a typical RSVP trial. All sequences contained one white letter (T1), which in this case is 'M'. The number of letters presented before T1 varied randomly between 7 and 15. T2 was always a black 'X' that was present in only half the trials. In this example, it is shown as the second letter in the (10-letter) series that follows T1. In dual-target trials, subjects had to identify T1 and also say whether T2 was present. In single-target trials they had only to report the presence or absence of T2.

sequences but simply had to detect the presence of T2, ignoring T1. In this single-target task, they detected T2 correctly on >90% of trials, regardless of when it occurred in the sequence after T1 (Fig. 2). This shows that the attentional blink (observed in the dual-target task) is not due simply to a failure to maintain attention throughout the duration of the RSVP sequence.

When eight right-handed right-hemisphere stroke patients without neglect (mean age, 64 years; mean lesion volume, 23.5 cm^3) were tested (mean, 26 days after stroke), their attentional blink also lasted only 360 ms and was not significantly different in magnitude from that of the volunteers without stroke (Fig. 2). Neither was their performance different from normal volunteers on the single-target task during the interval associated with the attentional blink. Lesions defined by computed tomography were plotted using the templates of Damasio and Danasio[14]. Four of these patients had suffered infarction of

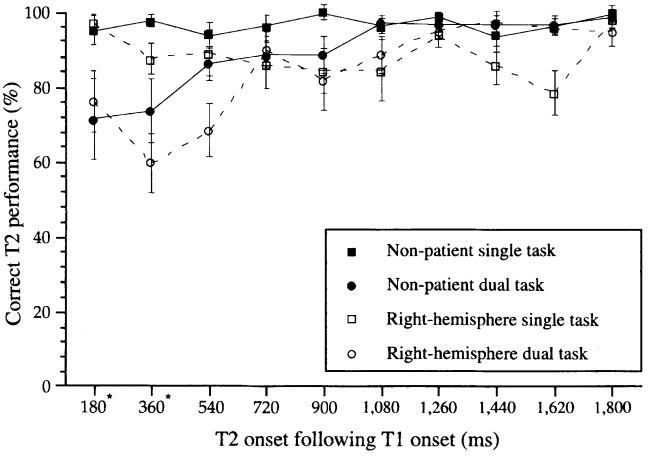

FIG. 2 Performance of normal individuals without stroke (filled symbols) and right-hemisphere stroke patients without neglect (open symbols). In both groups, T2 detection on the dual-target task (circles) was significantly different from that on the single-target (squares) task for T1–T2 intervals up to 360 ms (indicated by asterisked times on the abscissa; $P < 0.05$). Error bars represent standard errors of the mean. T1 was correctly identified on 86 and 81% of dual-target trials, respectively, by normal volunteers and those with stroke.

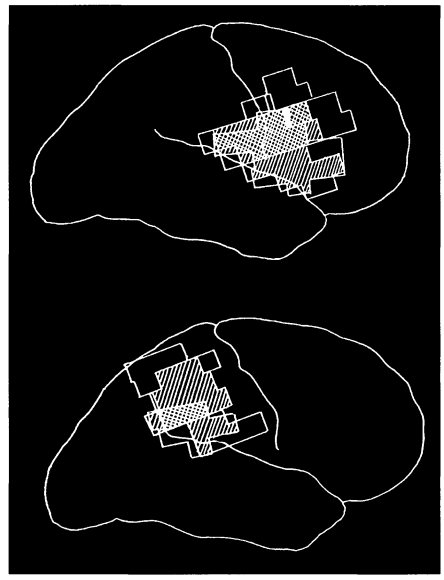

FIG. 3 Extent of cortical lesions in seven patients with left-sided visual neglect. Single hatching represents the region of overlap of 2 lesions; cross-hatching shows the overlap of 3 lesions; solid white is the zone of overlap of 4 lesions. The two-lesion foci are located in the inferior parietal lobe and in the inferior frontal lobe. One patient suffered a haemorrhage of the basal ganglia without cortical involvement (lesion not shown).

cortical and subcortical regions: two of the superior parietal lobe, one of the temporal lobe, and one of the medial frontal lobe. The other four had suffered subcortical strokes, but none had only a pure lacunar syndrome.

The performance of eight right-handed patients (mean age, 64 years) with left-sided visual neglect following right hemisphere stroke (mean lesion volume, 37 cm^3, not significantly different from patients without neglect; $t = 1.6$, $P > 0.05$) was then assessed (mean, 34 days after stroke, not significantly different from patients without neglect; $t = 0.6$, $P > 0.05$). Three subjects had suffered parietal stroke, with the region of greatest lesion overlap being confined to the inferior parietal lobe, the cortical area most commonly associated with neglect[15,16] (Fig. 3). Four patients had frontal infarcts, with the region of greatest lesion overlap in the inferior frontal lobe (Fig. 3). This region (part of the homologue of Broca's area in the left hemisphere) has been found to be the critical lateral frontal area associated with neglect[17,18]. One subject had suffered a haemorrhage of the basal ganglia.

All patients had visual neglect clinically and on the Mesulam shape-cancellation task[19]. The neglect patients found a mean of only 24 targets (range, 6–36) out of 60, all on the right side of the sheet. By comparison, the patients without neglect had found a mean of 57 out of 60 targets (range, 54–60), without any spatial bias in their omissions.

When patients with neglect were required to identify T1 and detect T2 (dual-target task), they were severely impaired in their ability to detect T2. Performance was worst (42% correct) when T2 appeared 180 ms after T1 and improved progressively as the interval between T1 and T2 increased, until it returned to baseline (single-target task) performance by 1,440 ms (Fig. 4). The attentional blink in visual neglect is thus of significantly greater magnitude and significantly more protracted than in normal subjects or stroke patients without neglect. Performance did not differ significantly between patients with parietal, frontal or basal ganglia lesions. In the single-target task, neglect patients detected T2 correctly on 80–95% of trials, regardless of when it was presented in the RSVP sequence. This did not differ significantly from the performance of patients without neglect. Overall, there was a significant correlation between Mesulam cancellation score and magnitude of attentional blink (integral or area between

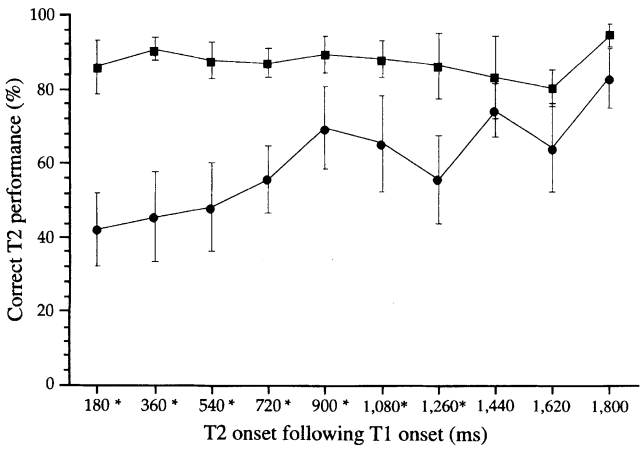

FIG. 4 Performance of patients with visual neglect. Detection of T2 on the dual-target task (circles) was significantly different from that on the single-target task (squares) for T1–T2 intervals less than 1,440 ms (indicated by asterisks on the abscissa; $P < 0.05$). Furthermore, the magnitude of visual unawareness during this attentional blink was much greater than in stroke patients without neglect or in normal individuals. T1 was correctly identified on 72% of dual-target trials.

dual- and single-task performance curves; $r = -0.71$, $n = 16$, $P < 0.05$).

What causes the temporal impairment in neglect? Studies of the attentional blink in normal individuals have raised the possibility of at least two types of underlying mechanism[1–5]. First, the visual system may take time correctly to conjoin or bind features of the target (that is, white colour with the shape of the letter to which it belongs) before features belonging to the subsequent item can be processed (compare with refs 20 and 21). Alternatively, there may be competition between critical stream items for selection after features belonging to each item have been conjoined correctly (compare with ref. 22). So far, the evidence in normal individuals suggests that the latter is a more likely explanation[3,5]. By contrast, evidence for an impairment of feature binding in an individual with bilateral parietal lesions has been presented[23]. Furthermore, positron emission tomography has demonstrated increased activity in parietal cortex when conjunctions between features are required[24]. There is little evidence to suggest a role for the frontal lobe in feature binding, but abnormal temporal dynamics of attention have been reported in subjects following frontal lobe surgery[25].

Whatever the exact mechanism responsible for the abnormal attentional blink, the results presented here require a reformulation of prevailing spatial accounts of visual neglect. Previous studies have demonstrated impairments of spatial attention in this condition[9–11,26]. We have shown that once attention is committed to the analysis of a visual object, there is an impairment in the ability to direct it to another, even if both stimuli are presented at the same location. We suggest neglect has two components. First, there is a spatial bias to direct attention towards stimuli processed by the undamaged cerebral hemisphere, and second, there is a deficit in temporal processing, regardless of where attention is directed. Our finding may also help to explain a non-spatial disorder of visual attention associated with bilateral lesions of the posterior parietal lobe—simultagnosia in Bálint's syndrome[27,28]. Individuals with this condition are able to attend to only one of two overlapping objects presented simultaneously at the same location, even though they have no apparent deficit when attending to either of these objects presented alone[29]. In this case, we suggest that there is no spatial bias because both hemispheres are damaged. Nevertheless, a fundamental disorder of visual processing remains: patients experience profound difficulty engaging a second stimulus after engaging a first. We suggest that this is a severe form of the temporal component of neglect. □

Methods

All subjects viewed from a distance of 35 cm a rapid serial visual presentation (RSVP) stream of letters presented at the centre of a computer monitor. Each letter was presented for 131 ms, with an interstimulus interval of 49 ms, yielding a presentation rate of 5.6 letters per second (Fig. 1). Letters subtended ~1.4° of visual angle in height and 0.7° in width. All letters were black except the first target letter (T1), which was white. The background was a uniform grey field, present throughout the sequence. Subjects initiated a trial when ready by depressing a computer mouse button. Each trial began with a 360-ms presentation of a small white fixation dot. The number of letters presented before T1 varied randomly between 7 and 15. T1 appeared on all trials and was always followed by a sequence of ten letters (Fig. 1). T1 could be any letter in the alphabet except 'X'. The second target (T2) was a black 'X'. It appeared on a randomly chosen half of the trials, and was presented randomly as one of the ten letters that followed T1. An 'X' was never presented before T1 and never appeared twice within a single RSVP stream.

Subjects were instructed in separate trial blocks to report the presence or absence of T2 alone (single-target trials), or to identify T1 and then also report on whether T2 was present (dual-target trials). T2 was presented eight times at each of the 10 possible serial positions after T1, yielding a total of 80 T2-present trials and 80 T2-absent trials for each condition (single or dual target). Subjects received 20 practice trials in each condition before data collection. The order of conditions was counterbalanced across subjects, and stroke patients performed either the single- or dual-target task on two different days. The interval between the two tests was less than a week in all cases. In each condition, subjects performed eight blocks, each consisting of 20 trials (10 with T2 present and 10 with T2 absent). Within a block, T2 was randomly presented once at each of the ten serial positions following T1. Short rest breaks were taken between each block.

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