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Visual Extinction: The effect of temporal and spatial bias

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Abstract

Unlike patients with neglect, neurological patients with extinction can detect a single event presented at any location. However when shown two brief near-simultaneous stimuli they only report the ipsilesional item. The question of what inter-stimulus delay leads to maximal extinction has clear clinical and theoretical implications. Di Pellegrino and colleagues (1997) report that extinction is maximal when the two stimuli are presented simultaneously, with less extinction when either item has a slight temporal lead. This finding supports traditional clinical diagnosis (which only presents simultaneous events), and is in accord with theories of extinction that entail individuation of objects (e.g., “token” accounts). In contrast, Cate and Behrmann (2002) report that extinction is maximal when the ipsilesional item is presented slightly prior to the contralesional item. This finding appears to support disengage models of attention. Our aim was to reveal whether the difference between these studies reflects different patients, or different methods. Specifically, we note that the stimuli used by Cate and Behrmann were biased both temporally (more ipsilesional first trials) and spatially (more items presented in ipsilesional field). We examined the performance of nine individuals with extinction, and found that maximal extinction was not influenced by temporal biases, but extinction was modulated by the spatial location of stimuli. This finding reconciles previous studies and offers new insight into this syndrome.

Keywords

parietal lobe; prior entry; visual attention

Introduction

Visual extinction is relatively common in patients shortly after sustaining unilateral brain damage (Becker and Karnath, 2007). A patient with visual extinction will correctly detect a single stimulus presented in either hemifield, but will report only the ipsilesional stimulus when two stimuli are presented bilaterally. The classic clinical test for extinction is the ‘double simultaneous stimulation’ (DSS) paradigm, where both targets are presented simultaneously (e.g. the clinician wiggles both fingers at the same time). An implicit assumption of this diagnostic test is the notion that extinction is most severe when both stimuli are presented precisely simultaneously. The conditions that create the greatest visual extinction are of great theoretical importance to the study of extinction, and normal attention functioning alike, because they adjudicate between competing theories concerning the nature of perception.

The first study to directly investigate whether extinction is maximal with simultaneous stimulation was a single case study by di Pellegrino, Basso and Frassinetti (1997). In this study, pairs of visual stimuli were presented such that the stimulus in either field could have a temporal lead. They found that extinction was maximal when stimuli were presented at exact simultaneity. Unfortunately the di Pellegrino et al. (1997) study did not also ask their patient for temporal order judgments. In a study published in the same year, Rorden et al. (1997) presented patients with visual stimuli in both hemifields and asked to make a temporal order judgment, i.e., to say which stimulus was presented first. Patients consistently reported the ipsilesional item as appearing first unless the contralesional item had a substantial lead (200 ms or more). This suggests that stimuli in the contralesional field are subjectively delayed to the patient. Thus simultaneity to an extinction patient occurs when the contralesional item leads by a considerable period, not when the stimuli are objectively simultaneous. Following on the studies of di Pellegrino et al. (1997) and Rorden et al. (1997), a recent study by Baylis et al. (2002) provided evidence for the importance of objective simultaneity. In one part of this study, patients made temporal order judgments to determine whether the patients experienced subjective slowing on the contralesional side. In accordance with Rorden et al. (1997), patients required the contralesional item to have a significant lead in order to be judged as occurring first. Nonetheless, all patients demonstrated maximal extinction when stimuli were presented at objective simultaneity.

In sharp contrast, Cate and Behrmann (2002) found maximal extinction when the ipsilesional item leads the contralesional item. In this study, extinction patients were tested for within-hemifield and between-hemifield visual extinction at various temporal asynchronies. While results were not always consistent, certain conclusions can be drawn. A clear pattern was seen for patient LD, where extinction could only be tested within the ipsilesional field, who exhibited maximal visual extinction when the ipsilesional stimulus had a lead of about 300–00 ms prior to the contralesional item. The pattern of performance was less clear for patient RB, where testing occurred in both hemifields. In Experiment 4, the target pairs were randomly presented at different locations (with some trials showing both targets in the contralesional hemifield, other trials showing one target in each hemifield and other trials presenting both items in the ipsilesional hemifield). Experiment 5 used the same stimulus locations, but the stimuli were presented in a blocked fashion, so that all stimuli in a single session appeared at the same locations. In both Experiments 4 and 5 patient RB showed more extinction when the pairs were presented in the left hemifield. However, Experiment 4 found no effect of the relative timing between the left and right stimuli, with Experiment 5 finding a statistically significant effect that appears to show slightly better performance when the contralesional item appears slightly before the ipsilesional item.

It is very important to determine the temporal conditions under which visual extinction is maximal, since the temporal dependence of extinction will constrain the range of possible theories of extinction. Further, understanding the temporal properties of extinction is crucial for sensitive diagnosis – if some patients experience maximal extinction when there is a temporal delay between stimuli, the traditional method of testing may fail to detect many patients. Here we discuss theories that predict three different patterns of maximal extinction.

Several theories predict maximal extinction should occur when stimuli are objectively simultaneous. The notion that visual extinction may represent a tokenization failure (Baylis et al., 2001) crucially requires that all information is present at the same time. This model suggests that extinction is similar to ‘repetition blindness’ seen in neurologically healthy individuals (Kanwisher, 1987). This phenomena is observed when individuals are asked to recount a rapidly presented stream of items, whereby they tend to only report one instance of two identical events that occurred in close succession (e.g. after seeing the words ‘dog’, ‘cat’, ‘pig’, ‘cat’, ‘bat’ the individual tends to only report one occurrence of the repeated item ‘cat’). A common

explanation for this effect is that visually presented stimuli generate episodic markers referred to as ‘tokens’ that identify the particular instance of when and where a particular class of object (the type) occurred. In other words, types refer to our generic concepts and semantic network attached to an object, while tokens denote when and where a specific type occurred. According to this account, repetition blindness occurs because token information is capacity-limited, especially for a token that is the same as one recently produced. In other words, when two instances of the same type are seen in rapid succession, the brain often forms only a single token. Similarly, the binding failure account (Baylis et al., 2001; Shisler et al., 2004) states that information in the contralesional field is analyzed by both the dorsal and ventral visual pathways such that both identity and location are processed. Although differing in many ways, both these accounts of extinction would predict that any asynchrony, with a lead of either the contralesional or the ipsilesional item should decrease the deficit, and that maximal extinction would occur at objective simultaneity.

In contrast, disengage models of extinction predict maximal extinction when the ipsilesional item is presented slightly prior to the contralesional item. Posner et al. (1984) showed that patients with parietal lobe damage were slow to detect contralesional stimuli when they followed ipsilesional attentional cues. A similar slowing was not seen when contralesional stimuli followed contralesional cues. It was suggested that parietal damage leads to an inability to disengage attention from ipsilesionally-cued locations. This model could explain the extinction effect in terms of an ipsilesional capture of attention – a single contralesional item can attract attention, but the presence of an ipsilesional item captures attention and prevents contralesional processing. Such a view might potentially explain extinction as a failure of attention disengagement, and would predict greater extinction when an item in the ipsilesional field precedes a contralesional item. With an ipsilesional lead, attention would be drawn to the ipsilesional side by that onset, and the disengage deficit would hamper detection of the subsequent ipsilesional item. On the other hand, when the contralesional item is presented before the ipsilesional item, there is no competing ipsilesional item to disengage from. Therefore, the disengage model predicts little or no extinction when the contralesional item is presented before the ipsilesional item.

In addition to classes of theories that predict maximal extinction with an ipsilesional lead, or at objective simultaneity, it is also reasonable to suggest that maximal extinction may occur at subjective simultaneity. Selective attention can be seen as a race between competing stimuli, with extinction reflecting a slowing or other handicapping of stimuli in the contralesional field. If this slowing occurs at a stage prior to selection it might follow that greatest extinction would occur with a contralesional lead, resulting in stimuli reaching the selection stage (as well as subjective awareness) at the same time. For example, Bundesen’s (1998) Theory of Visual Attention argues that the salience of a stimuli influences the speed of initial encoding processes, such that brighter items will enter high level visual short term memory more rapidly than a dimmer item.

It should be noted that the different models of maximal extinction are not mutually exclusive, and it is theoretically possible that different patients may show different patterns of extinction. For example, damage to early visual processing may lead to maximal extinction at subjective simultaneity (due to handicapping, as described above), while higher level injury might lead to the performance patterns described by the tokenization or disengage accounts. If this is the case, identifying the pattern of extinction may have clear clinical relevance, potentially revealing which patients are most likely to recover normal perception.

The pattern of visual extinction observed by Cate and Behrmann (2002) is distinctly different from di Pellegrino et al (1997) and by Baylis et al. (2002). One possible explanation for these

differences is that there are different forms of extinction. Alternatively, differences in paradigm might explain the different findings.

In their discussion, Cate and Behrmann acknowledge that their results diverge from previous work. They suggest that the findings of di Pellegrino et al. (1997) may be biased by the fact that every trial presented two stimuli, without any single-stimulus catch trials, while their own work included single stimulus trials. They argue that this feature of the di Pellegrino design could lead to biased performance. However, they concede that this explanation does not reconcile their findings with those of Baylis et al. (2002), and they suggest that unspecified 'different details of the system of stimuli presentation clearly influences the results of experiments.' Therefore, our aim is to discover whether this difference reveals that there are different forms of extinction, or whether the differences can be explained by differences in experimental design. This work has clear clinical implications (e.g. should extinction be diagnosed only using simultaneous events) as well as implications regarding mechanism underlying extinction.

However, we note that other design differences may explain the apparently contradictory findings of previous work. Specifically, we note that the study by Cate and Behrmann presented stimuli that were always temporally biased, and in the experiments with clear results their stimuli were spatially biased. On the other hand, di Pellegrino et al. (1997) and Baylis et al. (2002) did not include these biases.

In both di Pellegrino et al. (1997) and Baylis et al. (2002), equal numbers of stimuli are presented with a left lead and a right lead, and thus it can be said that there is no external temporal bias in the overall stimulus set. In contrast, Cate and Behrmann (2002) presented more stimuli with an ipsilesional lead than stimuli with a contralesional lead. One possibility is that the introduction of overall ipsilesional temporal bias into the stimulus set leads to a recalibration of interhemispheric timing such that the temporal mid-point of the stimulus range would become the point of maximal extinction. In other words, the patient may anticipate that the ipsilesional item will come first, and therefore preferentially attend to that location (or exhibit a response bias on trials of uncertainty). Of course in the temporally unbiased stimulus sets of di Pellegrino et al. (1997) and Baylis et al. (2002), the mid-point of the temporal range was at objective simultaneity; hence such a view explains these results equally well.

Another design difference between Cate and Behrmann (2002) and other studies is the inclusion of a spatial bias. In the case of Cate and Behrmann's patient LD, all stimuli had to be presented in the ipsilesional hemifield, whereas in di Pellegrino et al (1997) and Baylis et al. (2003) stimulus pairs always straddled the midline. It is conceivable that participants adopt a strategy of attending to one side of a display if the stimuli are predominantly presented on this side.

The present study was therefore designed to attempt rapprochement between these two apparently conflicting results concerning the temporal parameters of visual extinction with clear divergence in theoretical implications between these two results. The results of Cate and Behrmann (2002) support attentional-disengagement views of visual extinction, since maximal extinction is seen with an ipsilesional lead that can lead to orienting to the ipsilesional field. On the other hand, the finding of maximal visual extinction at simultaneity favors object-individuation or token accounts of extinction (Baylis et al., 1993; Baylis et al., 2001). The three experiments in the present study examine the effects of temporal and spatial bias on the temporal relation that leads to maximal visual extinction.

Experiment 1

This experiment was carried out to examine the effect of a substantial temporal bias introduced into the set of bilateral stimuli. For every trial in which a contralesional lead was present, there

were five in which an ipsilesional lead was seen. If the introduction of this temporal bias led to a recalibration of interhemispheric interactions, we would expect that the point of maximal visual extinction would shift from simultaneity towards some degree of ipsilesional lead.

Methods

Participants

A total of nine patients from HealthSouth Rehabilitation Hospital were recruited for this study, across the three experiments reported here. The lesion localization, sex, age and brief clinical details are given here for all participants. Where available, reconstructed lesions were created using the free MRIcro software package (Rorden and Brett, 2001) and are shown in Figure 1. Participants P2, P5, and P6 took part in Experiment 1. In agreement with Karnath et al. (2003), the individuals we tested who had extinction following cortical injury tended to have damage that included the temporoparietal junction

P1 was a 64 year-old man admitted with initial confusion and inconsistent signs of visual neglect, weakness in the left upper body; and paresis of the left lower limb. Confusion and paresis had resolved at the time of testing; but there was reduced grip strength on the left hand and weakness of the left leg. P1 showed consistent extinction to clinical confrontation at the time of testing. An MRI at the time of admission showed a large lesion in the right parietal lobe.

P2 was a 72 year-old man who presented with mild weakness of the left arm, slight facial drooping, and swallowing difficulties. Initial cognitive testing showed a low level of confusion, severe extinction, and mild left neglect. However, at the time of this experiment, the neglect was not detectable, and cognitive function was apparently normal. MRI showed damage to the inferior parietal lobe and temporo-parietal junction.

P3 was a 58 year-old woman who presented with mild left hemiparesis and mild left-sided extinction; she was well oriented with otherwise intact cognitive function. MRI scan showed a small pontine infarct according to the radiologists report, but no scan was available for reconstruction.

P4 was a 62 year-old man who presented with left hemiparesis and left visual extinction to clinical confrontation. Initial CT and subsequent MRI showed an acute cerebral bleed in the basal ganglia with intraventricular extension. Damage was largely confined to part of the right thalamus and posterior limb of the right internal capsule. There was also a mild degree of diffuse cerebral atrophy.

P5 was a 66 year-old woman who showed initial confusion, severe visual and tactile extinction to clinical confrontation, as well as reduced left hand strength. Confusion and mild paresis had largely resolved at the time of testing, but visual extinction remained.

P6 was a 74 year-old woman who initially showed severe neglect, confusion, dysarthria and impaired memory. However, all these symptoms had largely resolved at the time of testing, while auditory and visual extinction remained.

P7 was a 70 year-old man who presented with left paresis to upper and lower body, which subsequently resolved in the lower body, but left hand strength remained significantly reduced. P7 showed left-sided neglect as well as visual extinction to clinical confrontation. Initial difficulty swallowing had also resolved at the time of testing.

P8 was a 68 year-old man who presented with dense hemiparesis and severe visual extinction to clinical confrontation. Some personal and extrapersonal neglect that was largely resolved at

the time of testing, although line cancellation showed some remaining omissions on the left side. At the time of testing, there was no direction of gaze to the right, and line bisection and clock drawing tasks were both normal. No visual field defects were present at the time of testing. MRI showed a small hemorrhage in the right basal ganglia.

P9 was a 73 year-old man who presented with severe hemiparesis of upper and lower body as well as visual neglect as assessed by deviation of line-bisection, cancellation errors as well as initial deviation of gaze. At the time of testing, there was no deviation of gaze, no evidence of neglect by clock drawing, but a very small number of line cancellation omissions; lower limb paresis was largely resolved, with some improvement of function in the upper body. MRI showed a large right hemisphere lesion primarily confined to the cortex of the parietal and posterior temporal lobe.

Apparatus and Stimuli

Tasks were run on a Fujitsu laptop connected to a 17-inch LCD monitor. Participants were seated approximately 60 cm from the monitor. The stimuli consisted of the uppercase letters 'E' and 'O' presented in either red or green at approximately 15 degrees to the left or right of a central fixation point that was present at all times. The screen background was black. The stimuli were 3.0 cm in height and 1.8 cm in width, a size at which all patients were able to read with ease. During data collection, the stimulus duration was maintained at the value titrated for each observer, as described below.

Design

There were two variants of the task: a color task and a shape task. In the color task, patients were asked to verbally report the color at each location, while for the shape task they had to report the letter at each location. In each case, patients were asked to make a forced choice between the two alternatives and "nothing". Specifically, after each trial they were requested to point both to the left and to the right (in any order) and report what they saw at that location. There were 42 trials with four types of displays, presented in a pseudo-random order. The four types of displays are as follows:

- Catch trials: No stimulus was presented
- Single left target: A single red or green 'E' or 'O' letter was presented on the left only.
- Single right target: A single red or green 'E' or 'O' letter was presented on the right.
- DSS: A colored letter was presented on each side of the display. Within each condition of timing the two colors were equally likely, and equally likely to be the same as to be different.

Each participant was presented with a screening block of 42 trials. They received 6 trials each of the catch, single left, single right conditions, and 24 bilateral stimuli. This titration block estimates appropriate stimulus durations for each participant, according to the algorithm described in Baylis et al. (1993). In most cases, as stimulus duration is increased, performance will improve until few errors are seen. In contrast, when stimulus duration is progressively decreased, contralesional errors will increase until omissions are seen in both single and DSS trials. By automatically selecting an intermediate duration we ensured that extinction was neither at a floor or ceiling of performance. The stimulus durations found were 600 ms (P2), 480 ms (P5) and 300 ms (P6). Having determined this stimulus duration, we carried out all further testing with this timing.

After the initial screening, experimental testing with different degrees of temporal asynchrony proceeded as follows. Within each block of 42 trials, there were 2 catch trials, and 6 trials each of single ipsilesional and contralesional stimuli. The remaining 28 trials presented items

bilaterally, with four trials at each of seven stimulus onset asynchronies (SOAs). These seven SOAs comprised four examples with the contralesional stimulus presented prior to the ipsilesional (at 0.25 x stimulus duration), twenty examples with the ipsilesional presented first (four at 0.25 x, 0.5 x, 1.0 x, 1.5 x, or 2.5 x stimulus duration), and four trials of simultaneous presentation. Thus there was a large preponderance (5 to 1) of trials with the ipsilesional stimulus presented prior to the contralesional, versus those with a contralesional lead.

Procedure

The task was explained to the patient by the experimenter, and it was emphasized that only the task-relevant dimension of the stimuli should be considered and reported (i.e., only report color or only report identity). The patient was instructed to point to each side in turn and report the stimulus or lack of a stimulus on that side. If a patient failed to mention one side he was asked about it, and he was reminded of his instructions. The experimenter initiated each trial by pressing the spacebar on the keyboard. The patient reported the stimuli either while they were present or immediately afterwards. The experimenter then entered each answer into the computer at the end of each trial. Throughout data collection, the experimenter sat on the opposite side of the computer monitor, at a location where they could monitor gaze direction. Before initiating each trial, the experimenter ensured that the direction of gaze remained at the center of the screen (with verbal reminders if the gaze deviated toward one side or if eye movements were made during the previous trial). All patients showed excellent compliance with these instructions and maintained fixation over more than 98% of all trials in every case.

Results

All patients were able to understand both tasks (color and shape), and performed both with approximately equal error rates. P2 completed 3 blocks of the color task and 4 blocks of the letter task; for P6, the corresponding totals are 3 and 3 blocks while P5 completed 5 blocks of the color task and 9 blocks of the letter task. As the pattern of errors was not different in the two tasks, error rate data were pooled across the two tasks. All patients showed a very small number of ipsilesional errors of omission, with an overall rate of 0.9% (P2), 1.0% (P6), and 1.7% (P5), and are not further discussed. Contralesional errors were almost always errors of omission, although a very small number of contralesional errors of identification were made. These very few (0.6%) identification errors generally followed the same pattern as the errors of omission and are also not further discussed. Accuracy for single stimuli occurring on the left were 92.9% (P2), 67.9% (P5) and 86.1% (P6). The vast majority of all errors made by these patients were contralesional omission errors, and occurred primarily when stimuli were presented in both fields at or about the same time. The effects of varying the asynchrony of the two stimuli are shown in Figure 2A. A Chi-squared analysis revealed that stimulus asynchrony significantly influenced performance (P2 $X^2(6) = 26.259$, $p < 0.0002$, P6 $X^2(6) = 57.069$, $p < 0.00001$, P5 $X^2(6) = 52.887$, $p < 0.00001$).

These results show very clearly that the greatest extinction was seen when the two stimuli are presented simultaneously. Even the smallest asynchrony in this study (one quarter of the total stimulus duration) led to a reduction in extinction compared to that seen for simultaneous stimuli. There is absolutely no evidence of a shift in the point of maximal extinction towards trials with an ipsilesional lead. Indeed, a very slight trend in the opposite direction is seen for P6 and P5. The performance for all three patients replicate the results seen in the single case study reported by di Pellegrino et al (1997) and those seen in the study by Baylis et al (2002). Thus, it appears that a preponderance of ipsilesional-lead trials is not sufficient to shift the point of maximal extinction away from objective simultaneity.

Experiment 2

In order to fully understand whether a temporal bias can influence maximal extinction, we conducted an experiment where the preponderance of trials had a large contralesional lead. This experiment was analogous to Experiment 1, with the interchange of ipsilesional lead and contralesional lead. Thus, for every trial in which an ipsilesional lead was present, there were five in which a contralesional lead was seen. If a temporal bias can shift the point of maximal visual extinction, we would expect a move of this point towards some degree of contralesional lead.

Method

All aspects of the method were the same as those for Experiment 1 except as noted. Three participants took part in this experiment: P1, P2, and P7. (see Figure 1).

Design

As before stimuli were presented at seven different temporal asynchronies, analogous to those seen in Experiment 1, but with the asynchrony bias reversed. Thus for the critical 28 bilateral trials out of each block, there were again four trials at each of seven stimulus onset asynchronies (SOAs). These seven SOAs now comprised four examples each with the ipsilesional stimulus presented prior to the contralesional (at 0.25 x stimulus duration), twenty examples with the contralesional presented first (four each at 0.25 x, 0.5 x, 1.0 x, 1.5 x, or 2.5 x stimulus duration), and four trials with simultaneous presentation.

Results

All patients were able to understand both tasks (color and shape) and performed both with approximately equal error rates. Stimulus durations were titrated to 400 ms (P1), 600 ms (P2), and 400 ms (P7). As before, data were pooled across the two tasks, as no differences were seen. P1 completed a total of 11 blocks of the tasks, P2 complete 16 blocks, and P7 completed 3 blocks. All patients showed a very small number of ipsilesional errors of omission with an overall rate of 0.9% (P1), 0.9% (P2), and 1.2% (P7), and are not further discussed. Accuracy for single stimuli occurring on the left were 95.5% (P1), 99% (P2) and 89% (P3). Contralesional errors were almost all errors of omission, although a very small number of contralesional errors of identification were made. These very few (1.5%) identification errors followed the same pattern as the errors of omission, and also are not further discussed. The vast majority of all errors made by these patients were contralesional omission errors, and occurred primarily when stimuli were presented in both fields at or about the same time. The effects of varying the asynchrony of the two stimuli are shown in Figure 2B. A Chi-squared analysis revealed that stimulus asynchrony significantly influenced performance (P1 $X^2(6) = 32.932$, $p < 0.00001$; P2 $X^2(6) = 48.133$, $p < 0.00001$; P7 $X^2(6) = 38.403$, $p < 0.00001$).

These results show again that the greatest extinction was seen when the two stimuli were presented simultaneously. Even the smallest asynchrony in this study (one quarter of the total stimulus duration) led to a reduction in extinction compared to that seen for simultaneous stimuli. There is no evidence of a shift in the point of maximal extinction towards trials with a contralesional lead. These results, along with Experiment 1, provide clear evidence that temporal bias – i.e., a preponderance of trials with either a contralesional lead or with an ipsilesional lead – does not alter the point of maximal extinction. Regardless of the proportion of trials with different timing, maximal extinction was seen with stimuli presented at objective simultaneity, as previously reported by di Pellegrino et al. (1997) and Baylis et al. (2002).

Experiment 3

Experiments 1 and 2 examined the effect of temporal bias of stimuli (that is a preponderance of ipsilesional-lead trials or of contralesional-lead trials) on extinction. It was found that neither asynchrony bias was enough to affect the tendency of extinction to be maximal when stimuli are presented at objective simultaneity. These results support prior work by our group (Baylis et al, 2002) and by di Pellegrino et al. (1997), but stand in contrast to the results of Cate and Behrmann (2002). However, one further difference in procedure between the former and latter studies is the fact that where Cate and Behrmann found unambiguous evidence of maximal extinction with asynchronous items they presented stimuli in the ipsilesional hemifield. This was done because patient LD tested by Cate and Behrmann had severe hemineglect and severe cancellation deficit in the contralesional field. It is possible that this manipulation inadvertently led to a shift in the point of maximal extinction. To determine whether this spatial bias could affect the temporal dependence of extinction, this third experiment was carried out.

As a result, in our third experiment, the stimuli were all spatially but not temporally biased. This goal was to isolate the effect of spatial bias on extinction (in contrast to most of the experiments reported by Cate and Behrmann, which combined temporal and spatial biasing). Specifically, both the items were presented in the ipsilesional hemifield.

Note that despite the fact that both stimuli are presented in the ipsilesional hemifield, patients with extinction will tend to show extinction of the more contralesional item (Cate and Behrmann, 2002). That is, within-hemifield extinction will be seen (at least for discrimination tasks, extinction within the ipsilesional hemifield is not seen with detection tasks, e.g. Di Pellegrino and De Renzi, 1995; Smania et al., 1996). We then investigated the temporal dependency of extinction in this spatially biased format in order to test whether spatial bias may lead to a shift in the temporal point of maximal visual extinction. The first patient tested (P9) was tested in counterbalanced order of spatially biased and spatially unbiased stimulus blocks of trials. The subsequent patients were only tested with a spatial bias.

Methods

All aspects of the method were the same as those for experiments 1 and 2 except as described. The potential target stimuli were the letters A, S, T and X drawn with a 40 point Arial typeface, with the base screen resolution set to 640×350 pixels. Stimuli were presented as white text on a black background. A white fixation cross was presented at the center of the screen. On trials where two stimuli were presented, each stimulus had a unique identity. The task was always to report the identity of the letter(s) presented. Each block consisted of 90 trials, with ten twin target trials at each SOA (with target asynchronies of -600, -400, -200, 0, 200, 400 and 600 ms) as well as ten left unilateral and ten right unilateral trials. During the spatially unbiased blocks (P9 only), the targets could appear 9.9° to the left or right of fixation, while the spatially biased blocks presented targets 4° and 11.8° to the right of fixation. Participants P3, P4, P8, and P9 took part in this study. P9 was tested in three sessions (completing 2, 3 and 3 blocks across four days). Stimulus duration was titrated prior to testing as previously described. In addition, stimulus duration was adjusted between blocks based on performance in the previous block, with the aim of avoiding floor or ceiling effects. Therefore, the stimulus duration (measured in terms of 60Hz frames) for P3 was 4,3,3; for P4 this was 4,4,3; P8 this was 5,7 and finally for P9 this was 4,4,3,4,4,3,2,4 frames for each of the blocks. As before, gaze direction and saccades were carefully monitored to avoid a strategic deviation of eye position or saccades during trials.

Results

All patients were able to understand the task of reporting the identity of the letters. P3 and P4 each completed 3 blocks (thirty stimuli for each SOA); P8 completed two blocks (twenty stimuli at each SOA). Patient P9 completed a total of eight blocks (not including a practice block that employed an exceptionally long target durations and a narrower span of SOAs), with four blocks of with a spatial bias (1st, 4th, 5th and 8th forty trials per SOA) as well as four blocks without a spatial bias (2nd, 3rd, 6th and 7th; forty trials per SOA). All patients showed a very small number of ipsilesional errors, with an overall rate of 1.7% (P3); 6.7% (P4), 10.6% (P8) and 5.2% (P9) and are not further discussed. Contralesional errors were almost all errors of omission. The vast majority of all errors made by these patients were the contralesional omission errors, which occurred primarily when stimuli were presented in both fields at or about the same time. The effects of varying the asynchrony of the two stimuli are shown in Figure 3. The upper panel (Figure 3A) shows the performance of P9 on spatially biased versus spatially unbiased blocks, while the lower panel (Figure 3B) shows the performance of the P3, P4 and P8 with the spatially biased trials. P3 $X^2(6) = 33.299$, $p < 0.00001$; P4 $X^2(6) = 17.032$, $p < 0.00917$; P8 $X^2(6) = 34.978$, $p < 0.00001$; P9 during biased blocks $X^2(6) = 54.067$, $p < 0.00001$; P9 during unbiased blocks $X^2(6) = 50.588$, $p < 0.00001$.

It can clearly be seen that for all patients tested in the spatially biased task (P3, P4, P8, P9) the point of maximal extinction has been shifted from the point of objective simultaneity. In all cases a significant shift was seen in the direction of an ipsilesional lead, similar to the results reported by Cate and Behrmann. Indeed, the point of maximal extinction now occurred when the ipsilesional stimulus preceded the contralesional by 200 ms or more. The contrast is particularly striking for P9, who was tested with both alternating blocks of spatially biased and spatially unbiased trials. On the blocks where the stimuli straddled fixation (unbiased), P9 exhibited worst performance at objective simultaneity. In contrast, during blocks where the stimuli were presented only in the ipsilesional field, extinction was maximal when the peripheral (and ipsilesional) item occurred earlier than the more foveal item.

General Discussion

In this study, we attempted to explain an apparent contradiction between the results reported by di Pellegrino et al. (1997), as well as Baylis et al. (2002) with those reported by Cate and Behrmann (2002). The former studies reported maximal extinction when stimuli were presented at the same instant, with a decline in extinction when either item had a lead. In contrast, the latter study suggested patients exhibited maximal extinction when the ipsilesional item appeared slightly before the contralesional item. Our aim was to isolate the design differences between these studies to determine whether the different observations reflect different patient populations or different experimental designs. One major difference between these previous studies is that Cate and Behrmann included a temporal bias – with the majority of trials having an ipsilesional lead. Our first two studies suggest that this manipulation does not influence the SOA of maximal extinction- with patients tending to show maximal extinction near simultaneity regardless of the temporal bias. A second feature of most of the experiments reported by Cate and Behrmann is the presence of a spatial bias – with the cleanest findings observed when both stimuli were displayed within the ipsilesional field. Our final experiment replicated the pattern observed by Cate and Behrmann, suggesting that the spatial location of stimuli influences the SOA that elicits maximal extinction.

The first two experiments offer clear evidence that temporal expectancy has no detectable influence on the point of maximal extinction. In theory, this manipulation could have explained the discrepancy in previous studies. However, our experiments suggest that the expectation of temporal order has little influence on the extinction deficit.

In contrast, the final experiment does appear to reconcile previous studies: when stimuli were presented exclusively in the ipsilesional visual field, patients showed maximal extinction when the ipsilesional item appeared slightly before the contralesional item (dashed lines, Figure 3), replicating the finding of Cate and Behrmann's patient LD. On the other hand, when the two stimuli straddled fixation we observed that simultaneous presentation elicited maximal extinction (solid line, Figure 3A), replicating the findings of di Pellegrino et al. (1997) and Baylis et al. (2002).

This finding has direct clinical relevance. While clinicians classically only test for extinction by presenting simultaneous stimuli, we suggest that this method may not be particularly sensitive when testing patients who have hemianopia. In these cases, the perceptual field cut requires that both targets are presented in the ipsilesional hemifield. Our evidence suggests that in this situation extinction may be most dramatic when the peripheral item is presented slightly earlier than the foveal item.

We suggest that the most parsimonious explanation for this effect is a low-level (bottom-up) physiological bias. However, we concede that our findings could in theory also reflect top-down expectancy effects or difference gaze strategies. Therefore, we review each of these possibilities in detail.

Low level (bottom-up) visual factors may explain why extinction is maximal at objective simultaneity for bilateral stimuli but maximal with an ipsilesional lead when both stimuli are presented within the ipsilesional hemifield. Specifically, when both stimuli are presented in the ipsilesional hemifield, the "contralesional" stimulus is, of course, much closer to the fovea than the "ipsilesional" item. The architecture of the retina and visual system preferentially benefits centrally located stimuli. For example, healthy adults will report a foveal stimuli as appearing to occur prior to an objectively simultaneous peripheral item (Rutschmann 1966; Corwin and Boynton, 1968). According to this account, central items are processed more rapidly than peripheral items, as they excite a larger receptive field leading (which in turn allows these items to rapidly reach a threshold that spurs additional processing and eventually awareness). In our paradigm, bilateral stimuli receive equal low level processing, and therefore these events enter higher level processing with similar latency and amplitude. This unbiased low level information presumably leads to maximal binding deficits when both stimuli are objectively simultaneous (e.g. it is difficult to disambiguate the two tokens when they have similar low level timing and weighting). On the other hand, these physiological factors benefit the more foveal item during within-hemifield presentation. When two items are presented in one hemifield, the more foveal item builds a representation more quickly than the more peripheral item. Therefore, when the two objects with different eccentricities are objectively simultaneous, they do not simultaneously compete for binding (as the more central item is effectively 'earlier' when competing for higher level processing). On the other hand, maximal extinction will be observed when the peripheral item occurs slightly earlier than the central item, such that the processing of both items reaches higher-level processing with similar timing and activation strength. This explanation for the influence of bottom-up biases on extinction is essentially a 'race' model of perception, for example within Bundesen's (1998) theory of visual attention one would assert that visual eccentricity influences the sensory effectiveness of object, with foveal items completing the encoding processes earlier.

Alternatively, the influence of spatial bias could in principle also be accommodated by suggesting that extinction occurs at simultaneity when a participant expects items to occur in either hemispace, while in situations where a participant expects items to occur on the ipsilesional side their perception is biased such that maximal extinction occurs when the more ipsilesional item appears slightly earlier than the relatively contralesional item. This top-down account suggests that the influence of spatial bias may reflect strategic responses to the stimuli

rather than bottom-up perceptual influences. However, we note that the mechanism for this top-down control is not clear. One possible explanation would be the previously described disengage model. According to this model, on trials where attention is captured by an ipsilesional stimuli it is difficult to disengage to detect the contralesional stimulus, and therefore maximal extinction is observed when the ipsilesional item has a small temporal lead (as attention gets captured by this item). Indeed, this is precisely the model proposed by Cate and Behrmann (2002) to describe their data. However, this model would need to be modified to account for our observations. Specifically, one could posit that the disengagement penalty is modified based on the anticipated location of items: when an individual expects items to occur on the ipsilesional side there is a large disengagement cost (leading to maximal extinction when the ipsilesional item has a lead over the relatively contralesion item), but that this disengagement penalty is minimized when there is no spatial expectancy.

In principle, it is possible that different gaze strategies might influence performance on these tasks. Specifically, the spatial location of targets in Experiment 3 might have encouraged patients to deviate their gaze away from the center of the display (e.g. toward the right side of space (where the targets were likely)). In contrast, the targets straddled the central fixation point in the first two experiments, offering a strong incentive to maintain gaze at the center of the display. Furthermore, it is known that patient's with right parietal injury have spatially biased patterns of eye movements (Pierrot-Deseilligny et al., 1991), beyond what can be described due to perceptual biases (Ro et al., 2001). Potentially, there are different patterns of eye movement biases when both items are presented in ipsilesional space (such that an initial eye movement from fixation to either target would be ipsilateral) relative to the situation where the targets straddle fixation (where the contralesional stimuli requires a contralesional saccade from fixation). However, gaze was carefully monitored during the experiment, with trials only initiated when fixation was achieved, and verbal feedback to discourage saccades during the trials (with excellent compliance). Therefore, we think that overt eye movements are unlikely to explain our observations. Never-the-less, we concede that eye movement planning may be different between our experiments, and this might explain different patterns of performance, as suggested by Rizzolatti et al.'s (1987) "premotor" model of attention suggests that spatial attention is controlled by the same circuitry as motor planning.

Clearly, the bottom-up and top-down views are not mutually exclusive. Nevertheless, we note that the bottom-up physiological explanation is simpler, and therefore desirable. In our Experiment 3, trials always appeared in the same hemifield throughout a block (for P9) or throughout the experiment (P3, P4, P8). One way to disentangle whether spatial expectancy influences performance would be to collect data where the spatial location was varied from trial to trial, so that the participant would not be able to predict whether targets would appear in the contralesional or ipsilesional hemifield. This manipulation was actually done with patient RB described by Cate and Behrmann. Specifically, their Experiment 4 included trials with interleaved trials of within and between hemifield stimuli, while in their Experiment 5, the trials were blocked so that throughout a block all stimuli occurred at the same spatial locations. We note that their Experiment 4 showed no significant effect of SOA, while an effect was observed in their Experiment 5. Therefore, it does seem like spatial expectancy could explain these differences.

Our data suggests that previous discrepancies are unlikely to reflect different forms of extinction. According to this account, some patients always show exhibit maximal extinction when the ipsilesional item occurs before the contralesional item (e.g. Cate and Behrmann, 2002), while other patients always exhibit maximal extinction near objective simultaneity (di Pellegrino et al 1997; Baylis et al., 2002). Our findings make this explanation unlikely – in each experiment the different patients showed similar patterns of performance. In addition, P9 showed one pattern of performance when the targets were both ipsilesional (mimicking Cate

and Behrmann), yet exhibited a different pattern when the targets straddled fixation (cf di Pellegrino et al 1997; Baylis et al., 2002), as illustrated in Figure 3A.

While each experiment revealed a point of maximal extinction, it is important to note that each individual's performance tends to show gradual changes with respect to the timing between the two targets. For example, in the first two experiments, all participants showed maximal extinction when the two items were near simultaneity, with gradually better performance as the two items became more asynchronous. This gradual temporal function is similar to previous studies with extinction patients (di Pellegrino et al 1997; Baylis et al., 2002; Cate and Behrmann, 2002), and is clearly distinct from an all-or-none function (e.g. where extinction is clearly seen only when items are precisely simultaneous and absent when either item has a temporal lead). This suggests that there is a long period where the two stimuli compete with each other. This finding is consistent with previous studies that have shown that patients with extinction (di Pellegrino et al., 1998) and neglect (Husain et al., 1997; Hillstrom et al., 2004) exhibit pathologically long attentional blinks (also referred to as the 'attentional dwell time', where individuals tend to miss targets that appear rapidly after a salient event).

Our current investigation focused on neurological extinction, with the aims of helping clinicians best diagnose this syndrome and attempting to reconcile previous findings with patients. Our preferred explanation suggests that spatial bias can influence the point of maximal extinction. If correct, this low-level physiological mechanism is not specific to pathological extinction, and similar effects could be induced in healthy adults. Specifically, Gorea and Sagi (2002) argue that healthy adults exhibit extinction-like performance when they are shown trials that combine high-contrast and low-contrast targets. While extinction is classically thought to represent an attentional deficit rather than a low-level sensory impairment (based on the fact that patients with extinction can accurately detect unilateral items in their contralesional hemifield), Gorea and Sagi's provocative account suggests that low level sensory bias is sufficient to induce extinction-like behavior. This account would be strengthened if healthy individuals show the same patterns of performance that we report here, conducting a detection task similar to the temporal order judgment tasks previously reported (Rutschmann 1966; Corwin and Boynton, 1968). Specifically, if 'natural extinction' is a direct analogue of pathological extinction, one would expect that temporal biases do not influence the effect, but that spatial biasing can modulate normal performance.

As noted in the introduction, the temporal dynamics of extinction are important not only for sensitive clinical diagnosis, but also for discriminating between different theoretical accounts of perception. Cate and Behrmann's finding that extinction is maximal when the ipsilesional item leads was interpreted as support for an attentional disengage model. On the other hand, previous work that reports maximal extinction when two items are simultaneous appears to support token-based accounts of perception. We believe that the current findings are most consistent with the latter.

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References

- Baylis GC, Driver J, Rafal R. Visual extinction and stimulus repetition. *Journal of Cognitive Neuroscience* 1993;5:453–66.
- Baylis GC, Gore CL, Rodriguez PD, Shisler RJ. Visual extinction: the importance of binding dorsal and ventral visual pathways. *Visual Cognition* 2001;8:359– 379.

- Baylis G, Simon S, Baylis L, Rorden C. Visual extinction with double simultaneous stimulation: what is simultaneous? *Neuropsychologia* 2002;40:1027–034. [PubMed: 11900754]
- Becker E, Karnath H. Incidence of Visual Extinction After Left Versus Right Hemisphere Stroke. *Stroke* 2007;38:3172–174. [PubMed: 17962601]
- Bender, MB. Disorders in perception. Springfield: Thomas; 1952.
- Berti A, et al. Levels of processing for stimuli in an “extinguished” visual field. *Neuropsychologia* 1992;30:403–15. [PubMed: 1620321]
- Bundesen C. Visual selective attention: Outlines of a choice model, a race model and a computational theory. *Visual Cognition* 1998;5:287–09.
- Cate A, Behrmann M. Spatial and temporal influences of extinction. *Neuropsychologia* 2002;40:2206–225. [PubMed: 12417452]
- Corwin TR, Boynton RM. Transitivity of visual judgments of simultaneity. *Journal of Experimental Psychology* 1968;78:560–68. [PubMed: 5705866]
- di Pellegrino G, Basso G, Frassinetti F. Spatial extinction on double asynchronous stimulation. *Neuropsychologia* 1997;35:1215–223. [PubMed: 9364492]
- di Pellegrino G, Basso G, Frassinetti F. Visual extinction as a spatio-temporal disorder of selective attention. *NeuroReport* 1998;9:835–39. [PubMed: 9579675]
- di Pellegrino G, De Renzi E. An experimental investigation on the nature of extinction. *Neuropsychologia* 1995;33:153–70. [PubMed: 7746361]
- Gorea A, Sagi D. Natural extinction: A criterion shift phenomenon. *Visual Cognition* 2002;9:913–36.
- Hillstrom AP, Husain M, Shapiro KL, Rorden C. Spatiotemporal dynamics of attention in visual neglect: a case study. *Cortex* 2004;40:433–40. [PubMed: 15259324]
- Husain M, Shapiro K, Martin J, Kennard C. Abnormal temporal dynamics of visual attention in spatial neglect patients. *Nature* 1997;385:154–56. [PubMed: 8990117]
- Kanwisher NG. Repetition blindness: Type recognition without token individuation. *Cognition* 1987;27:117–43. [PubMed: 3691023]
- Karnath H-O. Deficits of attention in acute and recovered visual hemi-neglect. *Neuropsychologia* 1988;26:27–3. [PubMed: 3362343]
- Karnath H, Himmelbach M, Küker W. The cortical substrate of visual extinction. *NeuroReport* 2003;14:437–43. [PubMed: 12634499]
- Pierrot-Deseilligny C, Rivaud S, Gaymard B, Agid Y. Cortical control of reflexive visually-guided saccades. *Brain* 1991;114:1473–1485. [PubMed: 2065261]
- Posner MI, Walker JA, Friedrich FJ, Rafal R. Effects of parietal injury on covert orienting of visual attention. *Journal of Neuroscience* 1984;4:1863–874. [PubMed: 6737043]
- Rizzolatti G, Riggio L, Dascola I, Umiltà C. Reorienting attention across the horizontal and vertical meridians—evidence in favor of a premotor theory of attention. *Neuropsychologia* 1987;25:31–40. [PubMed: 3574648]
- Ro T, Rorden C, Driver J, Rafal R. Ipsilesional biases in saccades but not perception after lesions of the human inferior parietal lobule. *J Cogn Neurosci* 2001;13:920–29. [PubMed: 11595095]
- Robertson IH, Mattingley JB, Rorden C, Driver J. Phasic alerting of neglect patients overcomes their spatial deficit in visual awareness. *Nature* 1998;395:169–72. [PubMed: 9744274]
- Rorden C, Brett M. Stereotaxic display of brain lesions. *Behav Neurol* 2000;12:191–00. [PubMed: 11568431]
- Rorden C, Mattingley JB, Karnath H-O, Driver J. Visual extinction and prior entry: Impaired perception of temporal order with intact motion perception after unilateral parietal damage. *Neuropsychologia* 1997;35:421–33. [PubMed: 9106271]
- Rutschmann R. Perception of temporal order and relative visual latency. *Science* 1966;152:1099–101. [PubMed: 5931462]
- Shisler RJ, Baylis GC. Auditory Extinction: The Effect Of Stimulus Similarity And Task Requirements. *Neuropsychologia* 2004;42:836–46. [PubMed: 15037062]
- Smania N, Martini MC, Prior M, Marzi CA. Input and response determinants of visual extinction: a case study. *Cortex* 1996;32:567–591. [PubMed: 8954240]

- Sternberg, S.; Knoll, RL. The perception of temporal order: Further issues and a general model, in Attention and Performance IV. Kornblum, S., editor. Academic Press; New York: 1973. p. 629-85.
- Vallar G, Rusconi ML, Bignamini L, Geminiani G, Perani D. Anatomical correlates of visual and tactile extinction in humans: A clinical CT scan study. *Journal of Neurology, Neurosurgery and Psychiatry* 1994;57:464–70.
- Volpe BT, Ledoux JE, Gazzaniga MS. Information processing in an “extinguished “ visual field. *Nature* 1979;282:722–24. [PubMed: 514351]
- Vuilleumier P, Rafal R. “Both” means more than “two”: localizing and counting in patients with visuospatial neglect. *Nature Neuroscience* 1999;2:783–84.
- Vuilleumier PO, Rafal RD. A systematic study of visual extinction - Between- and within-field deficits of attention in hemispatial neglect. *Brain* 2000;123:1263–279. [PubMed: 10825363]
- Weinstein EA. Hemineglect and Extinction. *Neuropsychological Rehabilitation* 1994;4:221–24.

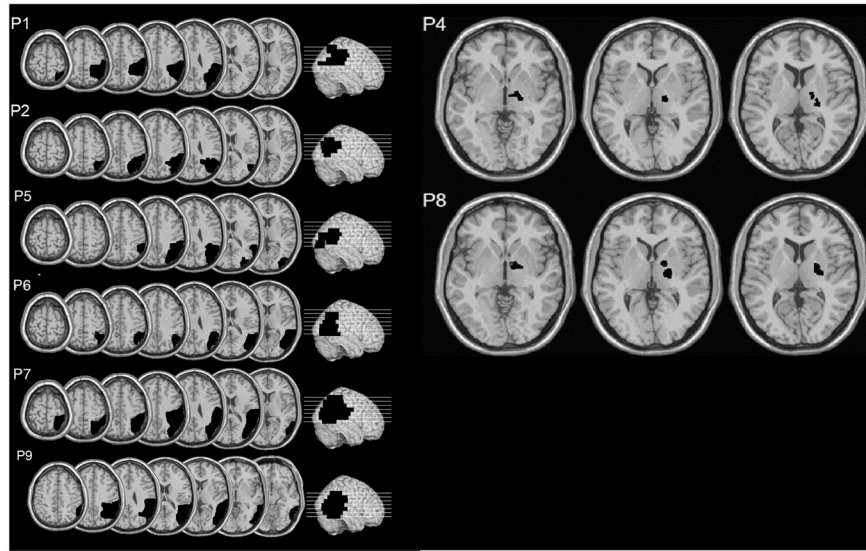


Figure 1. The extent of the lesions in these patients as reconstructed on the International Consortium of Brain Mapping single subject template image. No scan was available for P3.

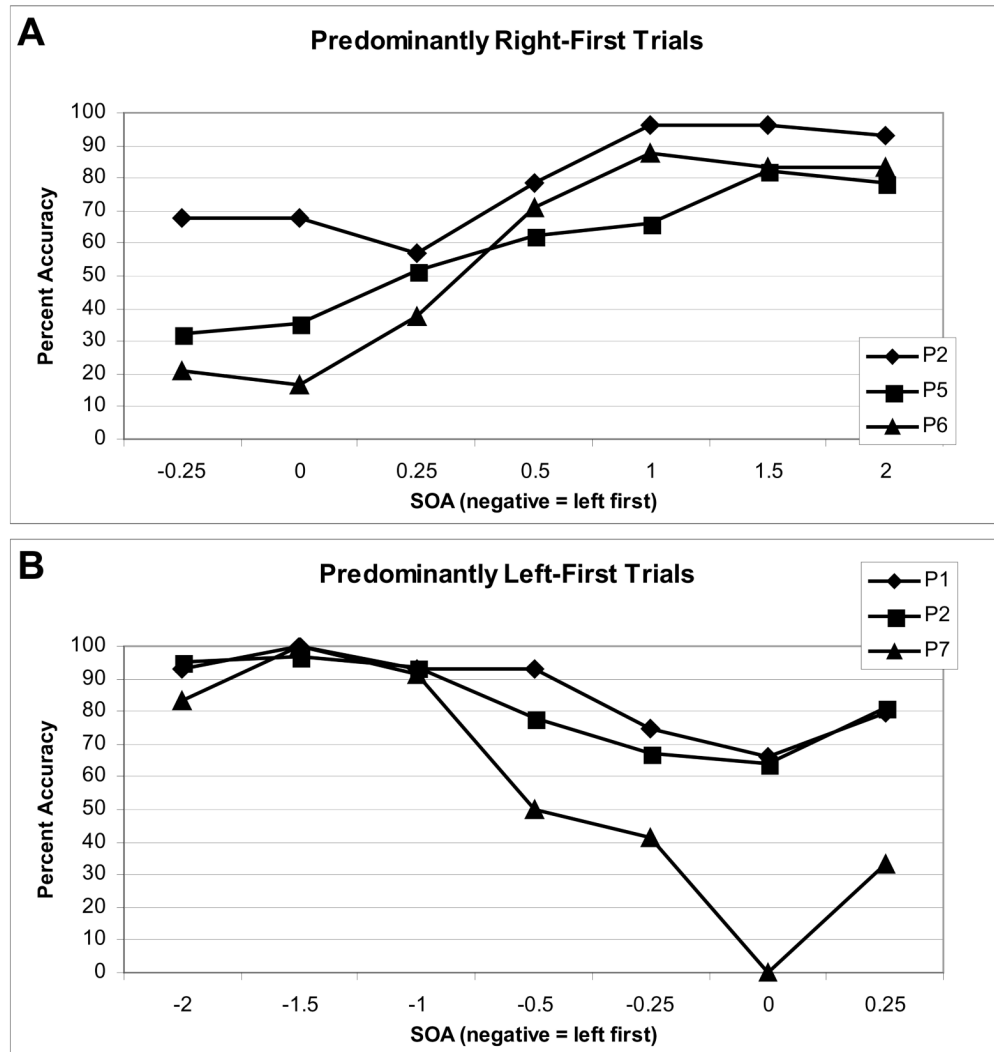


Figure 2. Temporal bias does not influence point of maximal extinction. (A) Experiment 1: the proportion of correctly reported contralesional stimuli under conditions of double presentation with different temporal asynchronies. Each line illustrates the performance of an individual participant. In this experiment, double stimulation trials straddle the fixation, but with a high proportion of presentations with a ipsilesional lead. The stimulus onset asynchronies (SOA) are expressed from the left stimulus having an onset a prior to the right (a negative value), to the right stimulus having an onset prior to the left (a positive value). The SOAs are expressed in units of stimulus durations, which was titrated between participants (P2 = 600ms, P5 = 480ms, P6 = 300ms). Note that maximal extinction is observed near objective simultaneity (SOA = 0). (B) Results from experiment 1: the proportion of correctly reported contralesional stimuli under conditions of double presentation with different temporal asynchronies. This experiment is similar to Experiment 1, except that there was a preponderance of stimulus pairs with a contralesional lead. The target durations were 400ms of P1, 600ms for P2 and 400ms for P7. Note that again maximal extinction is observed near maximal simultaneity.

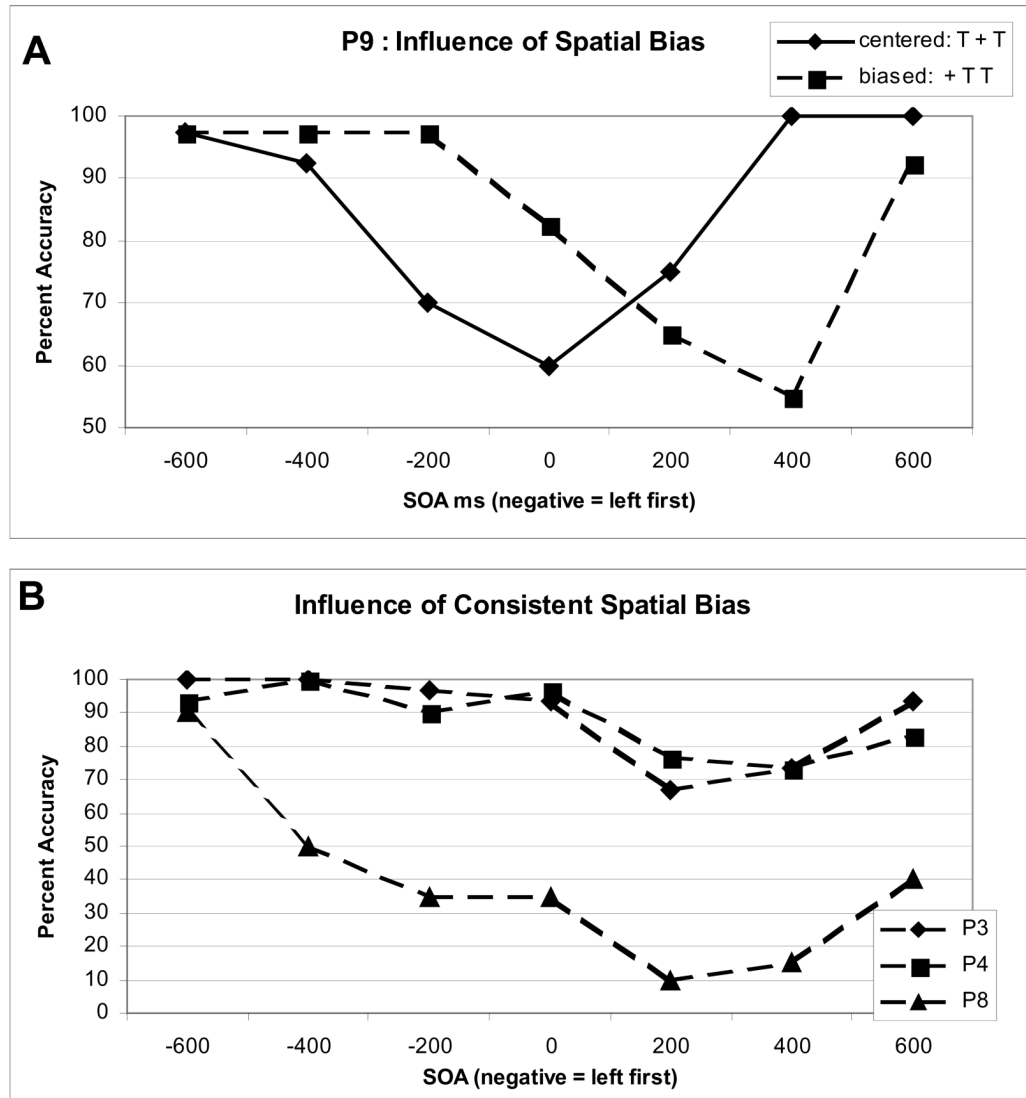


Figure 3.

Spatial bias influences extinction. The vertical axis shows the participant's accuracy, while the horizontal axis shows the temporal asynchrony between the relatively left and right targets (e.g. -400 suggests that the leftmost target appears 400 ms prior to the rightward target). (A) The solid line shows P9's performance on spatially unbiased blocks, where targets straddled fixation. The dotted line shows this individual's performance on spatially biased blocks where both targets appeared in the ipsilesional hemifield. Note that the point of maximal extinction shifts when items are presented in the ipsilesional hemifield. (B) Performance of participants P3, P4 and P8 on spatially biased trials. Note that all individuals perform worst at positive SOAs (e.g. when the more peripheral and ipsilesional right item occurs before the more foveal and relatively contralesional item).