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Information processing bottlenecks in macaque posterior parietal cortex: an attentional blink?

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When two brief stimuli are presented in rapid succession, our ability to attend and recognize the second stimulus is impaired if our attentional resources are devoted to processing the first. Such inability (termed the 'attentional blink' in human studies) arises around 200-500 ms following the onset of the first stimulus. We trained two monkeys on a delayed match-to-sample task where both the location and orientation of two successively presented grating patches had to be matched. When the delay between the two gratings was varied, monkey's behavioral performance (d') was affected in a way that was analogous to the attentional blink in humans. Furthermore, a subset of neurons in the monkey's lateral intraparietal area, known to be crucial in the control of attention, closely followed the variation in d', even on occasions when d' followed an atypical pattern. Our results provide the first behavioral demonstration of an attentional bottleneck in the macaque of a type similar to the human attentional blink as well as a possible single-neuron correlate of the phenomenon.

Keywords: Attention, Attentional Blink, Behavior, Lateral Intraparietal Area, Macaque

Introduction

When an observer is presented with a number of stimuli either simultaneously or in rapid succession, the brain's capacity for processing all the stimuli can be overloaded (for reviews, Treisman and Kanwisher 1998; Chun and Marois 2002; Dux and Marois 2009). This is often observed in terms of longer reaction times and poorer accuracy in visual search experiments, or reduced performance in a rapid serial visual presentation (RSVP) task (Potter and Levy 1969; Raymond et al. 1992; Wolfe 2003). The RSVP paradigm is often used to explore the "attentional blink" (AB), which is characterized by a reduced capacity to process the second of two target stimuli in the stream, following the correct identification of the first (Broadbent and Broadbent 1987; Raymond et al. 1992; Chun and Potter 1995; Luck and Vogel 1997; Vogel and Luck 2002). Such a limitation is typically observed when the second target (T2) is presented within a period of around 200-500 msec following the onset of the first target (T1). There is often no reduction in performance for very short intervals of less than 100 msec or so, which is known as "lag-1 sparing" (Potter et al. 1998), though such sparing is not always present in AB studies (Visser et al. 1999). Dominant explanations for the AB have been framed in terms of capacity limitations in the attentional "gating" of degraded sensory information into short-term memory, where the information can be consolidated into a more durable form and consciously reported (Reeves and Sperling, 1986; Chun and Potter, 1995; Shapiro et al. 1997; Jolicoeur and Dell'Acqua, 1998; Jolicoeur et al. 2001; Luck & Vogel, 2001; Hommel et al. 2006). Indeed, the AB, as measured in RSVP tasks, is probably the best-studied example of a broader class of phenomena reflecting information processing bottlenecks in attention and visual short term-memory (VSTM) processes (Marois and Ivanoff 2005; Awh et al. 2006; Dux and Marois 2009; Smith and Ratcliff 2009; Theeuwes et al. 2009), other examples being those apparent in change detection (Phillips 1974; Palmer 1988, 1990; Vogel et al. 2006; Woodman and Vogel 2005, 2008) and partial report (Sperling 1960; Duncan 1983; Gegenfurtner and Sperling 1993) studies.

Correlates of information bottlenecks such as the AB have been observed in human fMRI studies in the primary visual cortex (Stein et al. 2008; Williams et al. 2008; Hein et al. 2009) as well as frontal and parietal areas (Marois et al. 2000; Kranczoich

et al. 2005; Todd and Marois 2004). However, limitations in the temporal resolution of fMRI prevents the more precise localization of these effects. As an important first step in further elucidating the critical physiological bottlenecks and limiting factors in visual attention and VSTM, we have studied whether a behavioral process akin to the 'attentional blink' can be demonstrated in non-human primates and whether such a process might be reflected in activity at the level of the single neuron in the posterior parietal cortex.

The posterior parietal cortex, and in particular the lateral intraparietal cortex (LIP), has a well-established role in directing attention toward behaviorally-relevant objects or locations in visual space (Colby and Goldberg 1999; Bisley and Goldberg 2003; Saalmann et al. 2007). In earlier work (Pigarev et al. 2001; Vidyasagar and Pigarev 2007; Saalmann et al. 2007), we trained monkeys in a delayed match-to-sample (DMS) task, where they had to attend to and remember the location and orientation of two successively presented grating patches. We reported that with delays of around 800 msec between the two stimuli, clear attentional effects could be observed in many LIP neurons (Saalmann et al. 2007). There was significant enhancement of responses to the second of the two stimuli presented at the locations that had captured attention. We trained the same two monkeys further in a variation of the task to study the effects of varying the delay between the two grating stimuli, ranging from 50 to 600 msec. Though the DMS task is different to the RSVP task used in classical studies of the AB it has a long history in neurophysiological studies of attention and VSTM (e.g. Fuster and Jervey 1981; Miller et al. 1993; Miller and Desimone 1994; McAdams and Maunsell 1999; Bisley and Pasternak 2000). By varying the delay between the sample and test stimuli, it is nevertheless procedurally similar and can be used to probe the temporal limits of attention and VSTM consolidation, of which the AB is perhaps the best-known example (Marois and Ivanoff 2005; Awh et al. 2006). We were able to demonstrate in both monkeys results consistent with an information overload causing a reduction in performance similar to that observed in some studies of the AB (e.g. Broadbent and Broadbent 1987; Joseph et al. 1997) and VSTM consolidation (e.g. Vogel et al. 2006; Woodman and Vogel 2005, 2008) in human subjects. In one of the monkeys, we also obtained electrophysiological recordings from LIP that showed neural activity in a subpopulation of cells that reflected the pattern of the behavioral performance of the monkey. Preliminary accounts of the data have been reported as

abstracts (R. T. M. et al., Soc. Neurosci. Abstr. 757.7/Z32, Chicago, IL. 2009; E. L. et al., Aust. Neurosci. Soc. Ann. Meeting Abstr. 099, Auckland, 2011).

Materials and Methods

Surgical procedures

All experiments and procedures were approved by the University of Melbourne Animal Experimentation Ethics Committee and conformed to the Australian Animal Welfare Act 1992 and the National Health and Medical Research Council Australian Code of Practice for the Care and Use of Animals for Scientific Purposes. Two male macaques (*Macaca nemestrina*) participated in this study. These animals were housed together, fed daily with water available *ad libitum*.

The techniques used for head fixation ('halo method') have been described elsewhere (Pigarev et al 2009). Briefly, a circular aluminum frame that enclosed the entire scalp was fixed to the skull using 6-8 stainless steel pegs. Access to brain areas for recordings was through small conical tubes that were placed in 2.5 mm diameter holes drilled in the skull. Platinum-Iridium microelectrodes (1-4 MΩ, Frederick Haer and Co, Bowdoin, ME) were inserted into the recording area using a hydraulic Microdrive (David Kopf Instruments, Tujunga, CA) that was mounted each day onto the head frame. All implantation procedures were performed under ketamine (10-15 mg/kg i.m. Parnell Laboratories, Australia) and xylazine (0.5-2 mg/kg i.m. Troy Pharmaceuticals, Australia) anesthesia. Positioning of the electrodes at the coordinates of the lateral intraparietal area (LIP) was performed with the guide of a structural magnetic resonance imaging scan obtained prior to the implantation. The localization of LIP was further confirmed by the functional properties of the neurons such as their characteristic peri-saccadic and visual responses (Colby et al. 1996). Finally, after a lethal dose of sodium pentobarbitone (Nembutal, Merial Australia), the animal was transcardially perfused with 4% paraformaldehyde and the brain sectioned and histologically examined. The burr-hole sites on the skull of the macaque were confirmed to be at the sites that matched the cortical sites established by the MRI.

Stimuli

Stimuli consisted of achromatic sine-wave gratings that subtended 8° x 8°, with a Michelson contrast of 0.3 and mean luminance of 15 cd/m^2. During cell recordings, the spatial frequency and orientation of the gratings were adjusted to meet the cell's preference. The grating orientation was usually along the cardinal axes (vertical or horizontal) for all purely behavioral experiments, but during the electrophysiological recordings, it was often necessary to adjust the stimulus orientation to match the preference of the cell (which was never greater than 25° from the cardinal orientations for our sample of cells). Spatial frequency was within the range 0.5-3 cycles/°.

Behavioral task

The monkeys performed a delayed-match-to-sample task similar to that used previously (Saalmann et al. 2007); see Fig. 1A. In each trial the monkey covertly attended to, and remembered, two gratings presented with a temporal separation and reported whether they had identical orientation and location. A tone announced to the monkey the arrival of a trial, after which he depressed the response lever, prompting the appearance of a black circular fixation point (FP; 0.5° diameter). After 250 ms of fixation, a grating (the sample, or first target, T1) was flashed for 100 ms somewhere in the display. Within a testing session, there were either two or three possible parafoveal locations at which the gratings could appear. Each location was an equal distance from the FP. During recording, one of these locations was adjusted so that it covered the receptive field of the cell.

The sample (T1) was followed by a blank delay before the second stimulus (the test, or second target, T2) appeared, also for 100 ms duration. The delay between T1 and T2 was one of five different lengths: 50, 150, 300, 450 and 600 ms. Other ranges of delay were initially tested, but this series was chosen because it covered the "blink sensitive" period suggested in AB studies (Raymond et al. 1992), and also avoided making the task prohibitively difficult for the monkeys. The delays varied randomly (with equal probability) from trial to trial within a block. There were 4 different stimulus conditions. On "matched" trials, T2 shared the same location and orientation as T1. On "non-match" trials, T2 could differ according to orientation (non-match orientation), location (non-match location), or both (double non-match). When the T1

and T2 orientations differed, they were always orthogonal. The monkey continued fixation for a further 700 ms after the offset of T2 before the FP underwent a uniform decrease in luminance. In matched trials, this change in luminance cued the monkey to respond by releasing the lever (within 100-650 ms). On non-match trials, the monkey needed to withhold the lever release and respond later (also within 100-700 ms), when the FP disappeared, which occurred 700 ms after the luminance change. Correct responses were rewarded with a drop of fruit juice, and distinctive auditory tones were provided as feedback for correct and incorrect trials, as well as those trials that were terminated because of a break in fixation. Figure 1A describes the different stages in a typical trial from the task. As a further behavioral strategy to encourage the monkey to maintain fixation during each trial, 10% of trials were "catch" trials that involved the disappearance of the FP before, or after T1 (but before T2). On these trials the monkey was required to immediately release the lever in order to obtain reward. The remaining test trials were presented pseudorandomly with the restriction that match and non-match trials each occurred with a probability of 0.5.

Behavioral data analysis

We assessed monkeys' performance on the DMS task in terms of the proportion correct responses for each trial type (match, non-match orientation, non-match location and double non-match), $P(C)$. We also calculated *d*', a measure of perceptual sensitivity from signal detection theory (SDT; Green and Swets. 1966). It was gauged with respect to the hit and false alarm rates, where the hit rate was the proportion of correctly-answered matched trials, $P(C)$, and the false alarm rate was the overall proportion of incorrectly-answered non-match trials (across all non-matched conditions), or 1-$P(C)$. The hit rate, $P(S|s)$, is the probability of answering "signal", S, on a signal-plus-noise (matched) trial, s. Conversely, the false alarm rate, $P(S|n)$, is the probability of a "signal" response on a noise (i.e. non-matched) trial, n. Sensitivity (*d'*) was calculated according to the formula:

$$d' = z(S \mid s) - z(S \mid n), \qquad (1)$$

using the standard normal deviates (z-scores) of the probabilities just described at each delay (Green & Swets, 1966).

P(*C*) and *d'* from each monkey were analyzed using the method of within-subject linear contrasts (Smith 2000). These contrasts are similar to the contrasts used in analysis of variance, however, they allow for specific hypotheses about the main effects and interactions of the delay and stimulus matching condition to be tested in the behavior at the individual subject (i.e. monkey) level. The contrasts were formed using weighted sums of the *P*(*C*) and *d*' values from each condition, where each weight is a set of contrast coefficients that test a particular hypothesis. Details are given in the online supplementary material.

Electrophysiological recordings

Single unit electrophysiological recordings were carried out from area LIP of one monkey (Monkey 1). Neuronal activities that were recorded were amplified using an AM systems amplifier and filtered from 1 to 4000 Hz. These signals were then digitized at 10 kHz using a Power 1401 A/D converter (Cambridge Electronic Design, UK). From the recorded signals, after further filtering (300- 4000 Hz), spike templates were built and single unit spikes were categorized using Spike2 (Cambridge Electronic Design, UK).

In addition to the spike categorization described above, the raw neural signals were exported from Spike2 into the MATLAB computing environment (Version 7.8; The MathWorks, Natick, MA) for offline analysis using the sigTOOL open-source software package (Lidierith 2009). Each block of 100 trials consisted of approximately 10 minutes of recorded signals. Spike sorting was conducted on separate blocks, using the Wave_clus automatic clustering software (Quian Quiroga et al. 2004), as implemented through sigTOOL (Lidierith 2009).

Peristimulus time histograms (PSTHs) of 20 ms binwidth were computed for each trial type with no smoothing. The neuronal response to the first grating (R1) was defined as the response lasting 140 ms starting at 40 ms from the onset of T1 (i.e. 40 to 180 ms) for all delays except the shortest delay (50 ms) where the response window width was 100 ms (i.e. 40 – 140 ms after stimulus onset). The neuronal response for the second grating (R2) was also defined as a response within a 140 ms window that

began 40 ms after the onset of T2. Background activity was recorded from a 140 ms window beginning 200 ms before the onset of T1. With longer delays (typically, 800 ms), LIP neurons show significant attentional enhancement in their responses when the first and second stimuli match (Saalmann et al. 2007). In order to quantify the attentional effect on the responses to the two gratings, T1 and T2, we calculated a response ratio of the average neuronal response between the two stimuli (R2/R1). A value of greater than 1 represents attentional enhancement and a value less than 1 indicates attentional suppression of responses, while a value equal to 1 indicates no change in response.

Results

Behavior

The two monkeys performed the DMS task as shown in Fig. 1A. As described earlier under Materials and Methods, in each trial the monkey covertly attended to, and remembered, two gratings presented with a temporal separation and reported whether they had identical orientation and location. Fig. 1B shows the performance of the two monkeys in the DMS task. The two upper panels give the proportion of correct responses, $P(C)$, for each stimulus condition as a function of the length of the delay. There was a tendency for performance to improve with increasing delay, consistent with the classic AB effect. Though this is particularly apparent in Monkey 1, the trend was significant in both monkeys in all the conditions, except for the non-matched orientation condition for Monkey 2 (see Table S1, in the online supplementary material). See Materials and Methods and Supplementary material for details of the linear contrast tests (Smith 2000) used to analyze the behavioral effects.

The lower panels of Figure 1B give the perceptual sensitivity (*d'*) for each monkey in the DMS task as a function of delay (Equation 1, Materials and Methods). For both monkeys, sensitivity (*d'*) increases as a function of delay in the task. This trend was significant in both monkeys, Monkey 1: $\chi^2(2) = 535.27$, $p < 0.001$; Monkey 2: $\chi^2(2) = 47.24$, $p < 0.001$ (results of linear contrast tests; see materials and methods and the supplementary material for the contrast weights used). This trend is qualitatively similar to performance in both AB and change detection studies, where two or more

stimuli presented in rapid succession must be remembered and reported (e.g. Broadbent and Broadbent 1987; Vogel et al. 2006). While both the $P(C)$ and the d' data are similar to AB in this task, it should be noted that there was no evidence of any lag-1 sparing, where the classical deficit in the report of T2 is absent when T2 appears 100 ms or less following the onset of T1 (i.e. at lag-one; Raymond et al. 1992; Potter et al. 1998). We however were more interested in performance within the "blink sensitive" period between lag-one and recovery of performance, so at our shortest delay of 50 ms, T2 onset was in fact 150 ms after T1 onset (i.e. 100 ms for T1 duration plus a 50 ms blank delay), so it is probable that our stimuli were outside the range where lag-one sparing is possible. Furthermore, lag-one sparing is by no means universal in the human AB. In their detailed review, Visser et al. (1999) found that lag-one sparing occurs in only about half of AB studies, and indeed never occurs if there is a change in the spatial location of T1 and T2, as was the case in many of the trials in our DMS task. Both factors might explain the lack of lag-one sparing effects observed in our dataset.

Electrophysiology

In one of the monkeys (Monkey 1), we also recorded extracellular potentials from 86 isolated units in the lateral intraparietal area (LIP), whilst the monkey performed the DMS task. Twenty-two of these units responded reliably to visual stimulation (response to the first grating being significantly greater than the neuronal spike rate at background levels for each trial). Seventeen of these LIP neurons showed a clear orientation preference in the raw recordings and the orientation of the stimuli in the task was adjusted to match this preference (non-matching orientation stimuli were thus orthogonal to the preferred orientation). The analyses that follow focused upon the activity recorded during match trials at the preferred orientation. For those neurons that did not show a clear orientation preference (n=5), the responses were pooled for both orientations for further analysis.

Figure 2 shows the mean response of an example LIP neuron to the preferred orientation as the monkey performed the DMS task. Figure 2a shows PSTHs of the neuronal responses to the stimuli with increasing delay between the two gratings. The response, R2, to the second grating, T2, shows considerable variation across the

different delays with the response (R1) to the first grating (T1) being relatively constant. The longest delay (600 ms) in our example shows an attentional enhancement (R2/R1 > 1.0). The responses at the shorter delays show a reduction in the response to T2 (R2/R1 < 1.0). The relationship between the different delays and the *d*' for this particular recording session and the normalized difference in the neuronal response between the two gratings for this example cell (R2/R1) are plotted in Figure 2B. To make comparison across the different recording sessions and stimulus delays more meaningful, we have normalized the *d'* and the response ratios (R2/R1) to the mean *d'* and response ratios across all delays within each recording session. Both these variables significantly increase with increasing delays for this particular recording session. The data from the example recording session shown in Figure 2B also shows a particularly close agreement between behavioral *d'* and neural R2/R1. This result is indicative of other observations from a subgroup of LIP neurons that were recorded during separate recording sessions on different days.

The population data for the responses of the twenty-two recorded visual units for all the different delays are shown in Figure 3. The ratio between the normalized responses to the two stimuli (R2/R1) is significantly correlated with the normalized behavioral *d'* estimates (Pearson's correlation coefficient, $R = 0.32$, $p < 0.002$, $n = 95$). Within this population, there was a subgroup of neurons (n=12), each of which showed a close to significant correlation (Spearman correlation coefficient $p < 0.1$) between the sensitivity measure *d'* as measured for that particular recording session, and the R2/R1 neuronal response ratio across the different stimulus delays.). Not surprisingly, the major contribution at the population level to the trend observed in R2/R1 neuronal responses and the *d'* were from this subgroup ($R = 0.85$, $p < 0.0001$, $n = 53$; shaded circles in figure 3). The remaining cells that responded to the stimuli did not show a significant correlation between *d'* and R2/R1 (triangles in Figure 3).

In order to further illustrate the close relationship between the responses of these neurons and the behavior of the animal, two example LIP units recorded on two separate occasions, are shown in Figure 4. On one occasion (Day 1, left panel in A), both *d'* and the response ratio (R2/R1) increased nearly monotonically with longer delays (top left subplot in 4A). This was the typical relationship seen for most of the cells in this subgroup. On another occasion (Day 2), the *d'* showed an atypical decline

at delays of 300 and 600 ms respectively (top right subplot in 4A). Despite this rather unexpected pattern observed in the *d'*, the response ratio (R2/R1) for the two gratings of the recorded unit in LIP also followed a similar pattern, namely, similar dips at 300 and 600 ms (bottom right subplot in 4A).

We further analyzed whether, within the above subpopulation of 12 LIP cells, there was a systematic relationship between the pattern of neuronal responses for the various delays as measured by the response ratios (R2/R1) of the LIP cell and the pattern of *d'* obtained during the corresponding recording session. For this, we first ranked the *d'* pertaining to all different delays from the lowest to the highest sensitivity for each session's performance (shown as red numbers in 4A). The relationship between such ranked sensitivity and the response ratio (R2/R1) for this subpopulation of cells is shown in figure 4B, and was significant (Kruskal- Wallis *H* test, $H = 16.45$ $p < 0.005$, $n = 53$).

The activity of a subset of the cells recorded here therefore appeared to show a relationship with the task performance of the monkey that depended on the delay between T1 and T2, in particular, a tendency toward lower R2/R1 response ratios at shorter delays. If the dips in the response ratios (R2/R1) for particular delays reflect a processing bottleneck like the attentional blink, one might expect the responses to the optimal orientation to become smaller at the shorter delays, to the extent that they become indistinguishable from the responses to a non-optimally oriented stimulus. The first two bars in Figure 4C show the average responses (R2) to the second stimulus when it is of optimum orientation (dark red bar) and non-optimum orientation (dark blue bar) for delays that showed the maximum sensitivity (*d'*) for the recording session. The second two bars show the average responses to optimum and non-optimum orientations (hatched red and blue bars respectively) for minimum *d'* for a particular recording session. There was a significant difference in the responses to preferred orientation and the orthogonal orientation for maximum *d*' (Wilcoxon signed-rank test, $p = 0.012$). There was no significant difference between the responses to the stimuli with the neuron's preferred orientation and the non-optimum orientation for those delays when *d*' was minimum (Wilcoxon signed-rank test, $p = 0.78$).

Discussion

Two macaque monkeys performed a delayed match-to-sample task where the delay between the targets, T1 and T2, was varied in a manner similar to studies of the attentional blink. The behavioral results were qualitatively quite similar to the human attentional blink (e.g. Broadbent and Broadbent 1987; Joseph et al. 1997), as well as other studies examining the consolidation of sensory inputs into VSTM (e.g. Reeves and Sperling 1986; Vogel et al. 2006), in that performance was impaired at shorter interstimulus intervals. Even though the paradigm we have used is procedurally different from the RSVP paradigm typically used in studies of the AB in humans, we believe it is nevertheless probing the same (or very closely related) mechanisms. In fact, the time course seen in our paradigm closely follows that of the AB found in human subjects (with the exception of the "lag-one sparing" effect, which, as noted above, is not a universal feature of the AB; Visser et al. 1999). One important way in which our paradigm differs from the classical RSVP paradigm is that there were no distractors between the two stimuli (T1 and T2) that were attended to. This was necessary both to avoid making the task too difficult for the monkeys to be trained upon and also to avoid confounding the visual response to the targets with the response to any masks/distractors. Still, our DMS task resembles the "skeletal" task commonly used in AB studies, where T1 and T2 are presented alone and often without masks. Earlier work has shown that such skeletal forms of the task are still sufficient to produce an AB effect (e.g. McLaughlin et al. 2001; Hein et al. 2009). Furthermore, a pattern of behavioral performance as a function of delay similar to that reported for the monkeys was found when we repeated the study using the same parameters in a human subject (linear contrast test for main effect of delay, $\chi^2(2) = 6.22$, $p < 0.05$).

Even without distractors, the monkeys' performance was similar in its temporal characteristics to the human AB. This suggests that the AB, or similar limitations in VSTM consolidation processes, can arise in non-human primates by virtue of the processing demands imposed by T1 without the additional load caused by the distractors of the classical RSVP paradigm. Note also that the stimulus presentation was 100 ms in our study, around 5 times longer than that typically used in human studies (e.g. Raymond et al. 1992). Despite such differences, our paradigm

demonstrates an animal model of the AB that can be used for further in-depth studies of the neurophysiological properties of capacity limitations in attention and visual short-term memory, which have been the subject of much speculation (Marois and Ivanoff 2005; Awh et al. 2006; Dux and Marois. 2009).

While neuronal responses that are modulated by attention have been demonstrated in many cortical (Moran and Desimone 1985; Motter 1993; Vidyasagar 1998; Colby and Goldberg 1999; Treue and Maunsell 1999; Bisley and Golderg 2003; McAdams and Reid. 2005; Saalmann et al. 2007) and even subcortical sites (McAlonan et al. 2008), a causal relationship between the neuronal responses seen in a particular brain region and the attentional state is not easily established, as with many other behavioral and cognitive situations. Much work, both in the human and the macaque, has implicated the posterior parietal cortex in the control of attention (Critchley 1953, Colby and Goldberg 1999; Bisley and Golderg 2003; Saalmann et al. 2007; Corbetta et al. 2008; Bisley et al. 2011), but these have largely shown changes in neuronal response that matched the (often assumed) presence or absence of attention to the visual stimulus. Here, we also show that the relationship between the behavioral response as a function of the interstimulus delay is also seen in the ratio of the second stimulus response to that of the first. As the delay increases to 600 ms, the response to T2 steadily increases to match the response to T1. This suggests that the process that causes the response enhancement of LIP neurons at longer delays (Saalmann et al. 2007) is handicapped at shorter delays and may well underlie the typical decrement in performance in the AB. Another behavioral task where the activity of LIP neurons seems to be related to performance is in visual search. As set size increases in a conjunction search task, reaction times increase and accuracy falls, while cells in LIP also show a reduction in their response to the optimum target as the number of distractors increases (Balan et al. 2008).

Beyond a correlation between “psychometric” and “neurometric” functions as reported here, there are at least two ways of establishing a closer link between neurophysiology and behavior. One is the use of microstimulation that has been used in linking the activity of neurons in MT/V5 with motion perception (Salzman et al. 1990). The approach that we adopted here was to more closely examine the day-to-day departures from the general trend of the data and studying whether such

variations are also matched in measurements of the putative neural substrate. For close to half of our sample of LIP cells, this was indeed the case. Sensitivity (*d'*) was found to vary between separate recording sessions and on some occasions it departed from the typical monotonic relationship with delay in the DMS task. However, on about half of the occasions when LIP cells were concurrently recorded, the neural response metric (the response ratio, R2/R1) also followed a similar pattern of variation as the sensitivity (*d'*). Since there is no change in stimulus attributes between the different delays, there is some unknown, possibly top-down, factor that causes the monkey to perform less efficiently at longer delays than shorter ones on some occasions. It is remarkable that activity in some LIP cells in our sample also showed the same variation, suggesting a possible role for LIP in the AB, as measured in our task. Our results are consistent with the finding that patients with parietal neglect also show a severe and prolonged AB (Husain et al. 1997), as well as human fMRI studies showing a role for the intraparietal sulcus in both VSTM consolidation (Todd et al. 2011) and the AB (Marois et al. 2000; Kranczioch et al. 2005). The departures from a monotonic relationship between d' and delay as well as the day-today variations in this relationship that we have observed in our data have also been reported in normal human subjects (Klein et al., 2011).

There is a possibility the results reported here (both behavioral and neuronal) are associated with post-excitatory suppression or adaptation effects. Purely sensory adaptation processes known from earlier visual areas can be engaged by very brief presentations (Dragoi et al. 2002; Schummers et al. 2005) and provide an alternative interpretation perhaps neglected in the broader AB literature. Namely, it is possible that T1 desensitizes (adapts) those neurons responding vigorously to it, and therefore deforms their response to T2, an influence that might be more pronounced at the shorter delays. Such an interpretation can be ruled out here for a few reasons, however. Firstly, the response deficit within the blink-sensitive period was present across all conditions in both monkeys, even in the non-matched location and double non-match conditions were T1 and T2 were presented at different locations. Adaptation effects should presumably only occur in those conditions where the stimuli share the same retinotopic location. Additionally, for both monkeys, the effect was most pronounced in the non-matched orientation condition, where the location was shared but the orientations of the targets were orthogonal. Adaptation would not

necessarily produce the observed AB-like impairment under these circumstances – in fact there is evidence that orthogonal adaptation actually improves orientation discrimination (Clifford et al. 2001). Secondly, using a similar DMS task and stimulus set as in the present experiment (albeit with a single delay of 900 ms), Vidyasagar and Pigarev (2007) found no evidence for a consistent adaptation effect in the responses of V1 cells. Instead, they showed that the response to T1 and T2 was modulated by spatial attention independently. Importantly, these modulations disappeared during an otherwise identical passive fixation task where the monkeys were not required to attend to the stimuli. If the modulations in the response to T1 and T2 were due to adaptation, they would be expected to be in the same direction every time, and should still be present in the passive viewing condition. While it is important to consider adaptation effects in studies of the AB/VSTM consolidation, it is unlikely they can account for the results observed here.

Since the effect we report in LIP cells was observed in only a subset of cells and these results are from one animal only, one cannot make strong conclusions and it is pertinent to ask the question whether area LIP does indeed subserve the function we have attributed to it in this study. There are two responses to the latter criticism. Area LIP, like many other brain areas, may comprise a heterogeneous group of cells that code stimulus and response attributes not redundantly, but sparsely. Thus, the attentional bottleneck we have observed in about half the cells in our sample may be typical only for those cells that are in the direct pathway that leads to the behavioral outcome. Furthermore, even if all the cells in a focal region of LIP were to directly influence the behavioral action, that the animal still performs at a greater than chance level even at short delays may be the result of an appreciable (though reduced) neuronal response to the second stimulus, as well as the resultant integrated activity of all the cells in a focal region of LIP.

In our particular delayed match-to-sample paradigm, the attentional enhancement of responses observed in previous studies (Saalmann et al. 2007) typically becomes evident only at longer delays. In the study by Saalmann et al (2007) conducted using the same two macaques as those used here, the task delay used in most cases was 800 ms. For the present study, we had deliberately used a range of delays to observe whether an attentional overload similar to the AB would be apparent. It had been

noted in the earlier study (Saalmann et al. 2007) that a gradual build up of delay activity was present in LIP neurons in the 200-300 ms just prior to the appearance of the second stimulus, T2. In the present study with different delay periods of up to 600 ms, such 'ramping' up of the response was not observed and the attentional enhancement apparent at 800 ms in our earlier study was not observed either (see our Fig. 2A). In fact, at shorter delays, there was a reduction in the response to T2. Such significant delay activity in LIP, which purportedly focuses attention for top-down facilitation of incoming sensory signals, may be essential not only for the enhancement of the neuronal responses reported in earlier stages of the visual pathway (Vidyasagar 1998; Treue and Maunsell 1999; McAdams and Reid 2005; Saalmann et al. 2007), but also for the behaviorally-observed full recovery of sensitivity seen in classical AB experiments for delays greater than 500 ms (Broadbent and Broadbent 1987; Raymond et al. 1992; Chun and Potter 1995).

Performance at delays shorter than 500 ms does not fall to zero in either human subjects or the macaques in our study, even though there is no appreciable increase in delay activity in the LIP neurons. Such performance at shorter delays, though poorer, may be due to activity at an alternative site such as the prefrontal cortex (Buschman and Miller, 2007) which finally leads to increased spike activity in LIP after about 500 ms. Alternatively, it could be due to a phase, not rate, code in LIP spike activity, such as that observed in the delay period activity of LIP neurons recorded from the same two monkeys that has been the subject of a recent preliminary report (Huckins et al. 2012). The phase code that can presumably lead to synchrony and neuronal facilitation in MT/V5 (Saalmann et al. 2007) does facilitate the responses sufficiently to yield some measurable improvement in performance, albeit less than when there is also a significant increase in the spontaneous spike rate. It is possible that the mechanisms responsible for such a phase code may be subject to variations on a day-to-day basis and sometimes produce the occasional, non-monotonic relationships in behavioral performance with the delay period as described here.

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Notes

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Figure legends:

Figure 1. Behavioral task and performance. **a**. Schematic diagram of the delayed match-to-sample (DMS) task. T1 and T2 stimuli were separated by variable delays. Monkeys released the lever when the fixation point (FP) dimmed for match trials, or when the FP disappeared for all categories of non-match trial. **b**. Behavioral results. Data for each monkey are shown separately. All plots give measures of performance as a function of the delay between T1 and T2. Upper panels give the proportion of correct responses for each stimulus condition (error bars: ± 1 binomial standard error). Lower panels show perceptual sensitivity (± 1 SD, given as the square root of asymptotic variance estimates (see Equation S2, Electronic Supplementary Material).

Figure 2. LIP neuronal responses at different interstimulus delays. a. Peristimulus time histograms (PSTHs) showing the neuronal responses (R1 and R2) of an example LIP neuron in the behavioural task (described in methods, figure 1), with the various delay periods between the two grating stimuli shown above each PSTH. The two stimuli (T1 and T2) are presented during the time indicated between the vertical dotted lines. The period during which the response was calculated (R1 and R2) is indicated by the grey rectangles on the abscissa. **b**. Normalized sensitivity (*d*', red curve) and normalized response ratios (R2/R1, blue curve) plotted against the different delays between the two grating stimuli for the same LIP neuron as in **a**.

Figure 3. Population data comparing neurometric and psychometric functions. The figure shows the relationship between the normalized sensitivity (*d*') and the normalized response ratios (R2/R1) for all 22 units and the different delays used while recording from these units (95 data points). The shaded circles represent 12 units that showed a significant relationship between *d*' and R2/R1, pooling results across all the delays for the recording session (53 data points). The open triangles represent the rest of the recorded units (42 data points). Pearson correlation coefficient and significance are shown in the inset for all cells and the two subgroups.

Figure 4. Co-variation of neurometric with typical and atypical psychometric functions. a Two examples of results that were obtained on two separate recording sessions on different days (note: typically only one unit could be isolated and

recorded while the monkey performed the task within a single recording session). The top panels of 4A represent the sensitivity (*d*') computed for the two separate sessions. The bottom panels of 4A show the response ratios (R2/R1) of the neuron recorded during those separate sessions. As evident from 4A, although there is considerable variation in the trend with the different delays, the responses of the cells recorded also show a similar variation. In order to normalize this variability, the *d*' values were ranked according to their magnitude on a particular recording session. **b** The relationship between the ranked *d*' and R2/R1 pooled across all the delays. **c**. Comparison of average response to second stimulus (R2) for preferred and non-preferred orientations when *d*' was maximum and when *d*' was minimum in each recording session, pooled for the 8 cells that showed significant orientation selectivity.