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LETTERS

Guarding the gateway to cortex with attention in visual thalamus

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The massive visual input from the eye to the brain requires selective processing of some visual information at the expense of other information, a process referred to as visual attention. Increases in the responses of visual neurons with attention have been extensively studied along the visual processing streams in monkey cerebral cortex, from primary visual areas to parietal and frontal cortex[1–4]. Here we show, by recording neurons in attending macaque monkeys (*Macaca mulatta*), that attention modulates visual signals before they even reach cortex by increasing responses of both magnocellular and parvocellular neurons in the first relay between retina and cortex, the lateral geniculate nucleus (LGN). At the same time, attention decreases neuronal responses in the adjacent thalamic reticular nucleus (TRN). Crick[5] argued for such modulation of the LGN by observing that it is inhibited by the TRN, and suggested that "if the thalamus is the gateway to the cortex, the reticular complex might be described as the guardian of the gateway", a reciprocal relationship we now show to be more than just hypothesis. The reciprocal modulation in LGN and TRN appears only during the initial visual response, but the modulation of LGN reappears later in the response, suggesting separate early and late sources of attentional modulation in LGN.

We recorded responses of LGN and TRN neurons in three awake behaving macaque monkeys. Monkeys were directed by a central cue at the point of fixation to attend to one of two peripheral visual stimuli on randomly interleaved trials (Fig. 1a inset). One of these stimuli was in the receptive field (RF) of the recorded neuron. Figure 1a shows the responses of an example magnocellular LGN neuron (LGNm) to a light bar within the RF when attention was directed out of the RF (dashed curve, ATTout) or into the RF (solid curve, ATTin). Responses shown are from correct trials. The ATTin response falls above the ATTout response, indicating an increase in neuronal response with attention. The mean response to the same stimulus increased 12% with attention. Figure 1b shows the responses of a parvocellular LGN neuron (LGNp) that also increased (21%) when attention was directed into the RF.

If a similar increase in attention were to occur in TRN, however, Crick's hypothesized interaction between TRN and LGN encounters a problem: TRN inhibits LGN. The visual sector of TRN receives excitatory inputs from LGN, but projects modulatory inhibitory input back to LGN[6–13]. Therefore, TRN responses should instead decrease with attention, reducing the inhibitory influence of the TRN on LGN, thereby causing the increase in the responses of LGN neurons that we observe. We did in fact find a decrease in the TRN visual response with attention (Fig. 1c). When attention was directed into the RF of this TRN neuron, the mean response to the same visual stimulus was 13% less than when attention was directed out of the RF.

We have summarized the effect of attention on mean visual responses of 57 on-centre LGN neurons (19 LGNm and 38 LGNp) in Fig. 2a, and of 29 TRN neurons in Fig. 2b. In each plot, the ordinate is the baseline ATTout response and the abscissa is the attentional modulation, ATTmod. ATTmod can be expressed either as the contrast measure (ATTin − ATTout)/(ATTin + ATTout), or the ratio of modulation (ATTin/ATTout). We have included both, with the

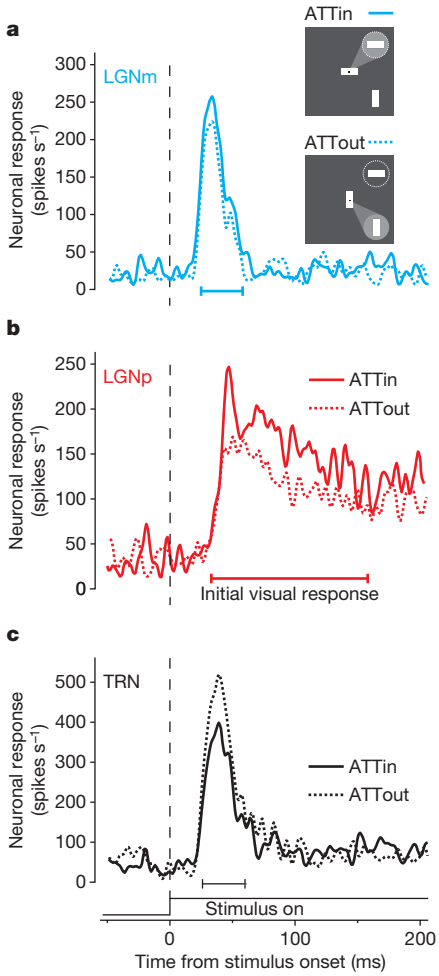

Figure 1 | Sample responses to shifts of attention in LGN and TRN. Solid traces are spike density plots of the neuron's ATTin response (as illustrated by the 'spotlight' of attention in the inset cartoon directed to the circle representing the RF). Dashed traces are ATTout responses. Responses are aligned to stimulus onset (the dashed vertical line), and have been smoothed with a Gaussian window of 2 ms s.d. **a**, Responses of sample magnocellular LGN neuron (LGNm). **b**, Responses of sample parvocellular LGN neuron (LGNp). **c**, Responses of sample TRN neuron.

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bottom axes representing the ratio of modulation, and the top axes indicating the contrast measure of ATTmod. Figure 2a shows the bulk of points to the right of the vertical unity line, indicating that the predominant effect of attention in LGN neurons was to increase mean responses to the visual stimulus. Distributions of ATTmod appear above the scatter plot, with small arrows indicating sample medians. In LGN, attention increased the median response 11 ± 2.6% in the magnocellular layers ($P = 0.011$), and 9 ± 1.1% in the parvocellular layers ($P = 0.0007$). All indications of variability are ±1 standard error of the median, and all P values were determined using the Wilcoxon signed rank test for zero median, unless otherwise specified.

In contrast to LGN, values of attentional modulation in TRN (Fig. 2b) tend to lie to the left of the unity line, showing a median decrease in neuronal response with attention of 4 ± 0.6% ($P = 0.004$). Over our sample of neurons, the reciprocal effect of attention holds; LGN responses increase with attention whereas TRN responses decrease.

If attention modulates neuronal responses, we would not necessarily expect such modulation during trials on which the monkeys made incorrect behavioural responses. For TRN neurons with more than five error trials, responses on those trials increased by 1.5 ± 1.5% ($n = 18$, $P = 0.62$). Similarly, for LGNm and LGNp neurons, respectively, responses changed by 2.3 ± 3.6% ($n = 11$, $P = 0.58$) and 1.3 ± 2.6% ($n = 22$, $P = 0.71$). The lack of significant response modulation on incorrect trials provides further evidence that the factor enabling the monkeys to perform the task correctly was the same one modulating neuronal responses, namely, visual attention.

We found no significant modulation of the background activity preceding the initial visual response or in the latency or duration of the initial visual response in either LGN or TRN. To observe any residual effect of attention beyond the initial visual response, we examined mean neuronal responses from 100 ms before stimuli appeared to 500 ms after they appeared (the shortest presentation time common to all trials). For each neuron, we normalized the response to the neuron's maximum firing rate. Figure 3a shows the mean normalized response for each area with solid curves for the ATTin condition and dashed curves for the ATTout condition. We calculated ATTmod for the six 100-ms time epochs in this timescale. Figure 3b shows ATTmod (as ATTin/ATTout) over time. Median changes for each area are connected across epochs with solid lines, and error bars denote ±1 standard error of the median. Significant changes within an epoch are denoted by coloured asterisks.

All areas demonstrate a significant response modulation in the initial 100 ms epoch after the stimuli appear. However, this modulation disappears in the next 100 ms epoch, but LGNm and LGNp show a second, later period of modulation that becomes significant in both divisions as time progresses. Also, both LGNm and LGNp showed significant attentional modulation just before the monkey needed to make a decision about the stimulus. Note that, in contrast to LGN, TRN had no second period of attentional modulation.

Because only the initial visual response in TRN is modulated by attention, measuring over the whole 500 ms period would have yielded a much smaller modulation in TRN (−1.8%) that would not have been significant ($P = 0.31$). However, owing to the second phase of modulation in LGN, we still would have measured attentional modulation of 13% in LGNm ($P = 0.014$) and 8.1% in LGNp ($P < 0.0001$), but the influence of TRN on the initial visual response would have gone undetected.

We see that careful consideration of responses over time is critical to detect the attentional effects in TRN, but analysis of the interactions between LGN and TRN requires an even more precise examination of

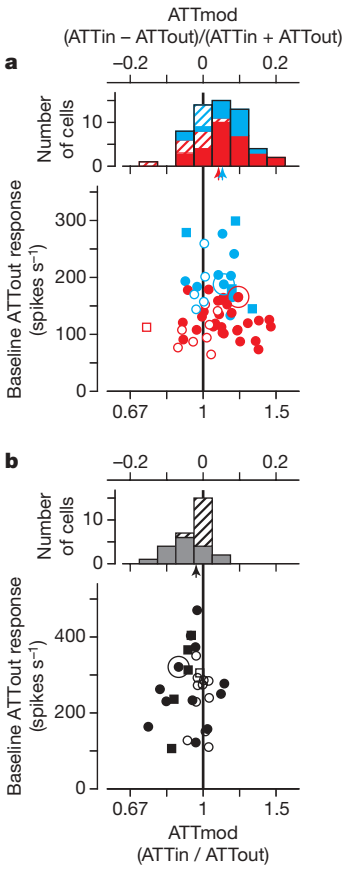

Figure 2 | Effect of attention on LGN and TRN. a, Scatter plot showing mean baseline ATTout response versus attentional modulation (ATTmod) for 19 LGNm neurons (blue) and 38 LGNp neurons (red). Solid symbols are significant response changes (Wilcoxon rank-sum test, $P < 0.01$). Squares denote experiments in which performance did not guarantee attention (see Methods). Distributions of ATTmod appear above the scatter plots. Hatched areas of each bar denote changes that did not reach significance. Arrows show median ATTmod for LGNm (blue) and LGNp (red). **b**, Similar scatter plot and histogram for TRN. In all plots, the larger circles indicate the Fig. 1 example neurons.

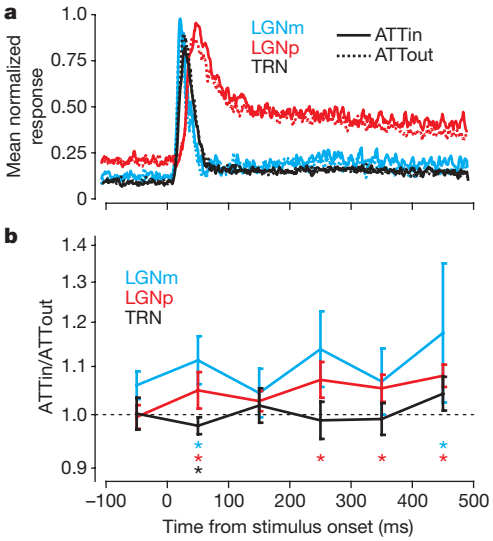

Figure 3 | Time courses of visual and attentional influences. a, Mean normalized ATTin (solid curves) and ATTout (dashed curves) responses for each area. Each curve is the mean normalized spike density plot over all neurons in an area. Mean responses have been smoothed with a Gaussian kernel of 2.8 ms s.d. **b**, Median effect of attention on each area in 100 ms epochs. Each trace shows ATTmod over time. Error bars are ±1 standard error of the median. Significant changes in each epoch are denoted by coloured asterisks coded to each area below the curves.

response timing. To compare visual response latencies, Fig. 4a shows the mean normalized initial responses for neurons in each area aligned on stimulus onset. To determine the significance of visual latency differences, we performed a bootstrap analysis (see Supplementary Notes) yielding estimates of the median visual latency in each area, and the significance of differences between areas using the Wilcoxon rank-sum test for equal medians. Although TRN responses (median latency 22 ± 0.92 ms) begin well before those in LGNp ($P < 0.0001$, median latency 37 ± 1.43 ms), LGNm neurons (median latency 21 ± 1.25 ms) tend to respond before TRN neurons ($P < 0.0001$).

To track the timing of attentional modulation in each area, we represented the effect of attention in Fig. 4b as the difference between the mean ATTin and ATTout curves from Fig. 4a. The latency of attentional modulation was obtained from a similar bootstrap analysis. Whereas the visual response appears first in LGNm, Fig. 4b shows that attentional modulation occurs first in TRN (22 ± 0.37 ms), 4 ms before LGNm (26 ± 0.31 ms, $P < 0.0001$). The attentional effect shows up significantly later in LGNp (37 ± 0.31 ms) than either TRN or LGNm ($P < 0.0001$ for both). Therefore, even though LGNm visual responses precede those of TRN (consistent with LGNm driving the visual response in TRN), attention affects TRN responses first, consistent with attentional modulation in LGN coming from TRN.

In summary, we find that attention modulates thalamic visual responses in two phases: an initial modulation that attenuates TRN responses and enhances LGN responses, followed by a slowly building later enhancement limited to LGN. Until now, demonstration of attentional modulation of LGN neurons has been limited to preliminary experiments on monkey[14] and fMRI studies in humans[15]. For the TRN, in addition to the recent growth in anatomical and cellular studies of monkey visual TRN[6,8,9,13], we recently found attentional modulation of neuronal activity in visual TRN during a visual/auditory attention task[16]. The differences between the visual/auditory attention task and the current task, along with a comparison of their results, are given in the Supplementary Discussion.

The initial LGN modulation might provide a substantial fraction of the modulation seen subsequently in cortical area V1 (refs 17–23). Although it is difficult to compare across studies, the approximately 10% increase in responses we find in LGN is similar to the 6.9% median increase across V1 neurons[17], and the 8.9% median increase in V1 simple cells[18]. The presence of the initial modulation in both TRN and LGN, their reciprocal increase and decrease, and the timing of their visual and attentional responses are consistent with TRN serving as the source of the initial LGN modulation, as proposed by Crick.

The later attentional effects in LGN, and effects others have reported in higher cortical visual areas, might be more closely related to goal-directed attention, which frequently also develops later in the visual response particularly in higher cortical areas[2,4,24]. This later modulation in LGN might in fact reflect feedback from cortex onto the LGN[25,26] via the established connections from V1 layer 6 (refs 25, 27), whereas the initial modulation in LGN by way of TRN may have its origins in subcortical structures, possibly including the superior colliculus[28–30]. Although obviously separate in time course, the two phases of modulation may represent two distinct attentional influences, and may be early indicators for identifying and distinguishing feed-forward and feedback visual attentional mechanisms.

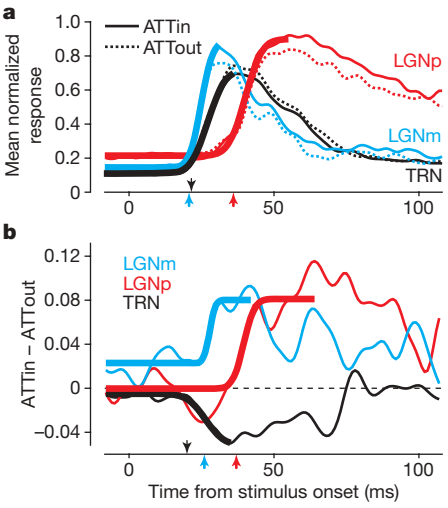

Figure 4 | Latencies of visual and attentional influences. a, First 100 ms of the visual responses from Fig. 3a. Thick lines are sample descriptive fits to ATTin responses from the bootstrap analysis. Arrows indicate median visual latencies. **b**, Latency of attentional effect in each area. Each trace shows the difference between the mean ATTin and ATTout responses. Thick lines show sample descriptive fits used to extract latency estimates in the bootstrap analysis. Arrows indicate the median latencies for the effect of attention.

METHODS SUMMARY

Two monkeys performed a task in which a central cue directed them to attend to one of two peripheral stimuli (a horizontal and a vertical bar of light; Fig. 1a inset). On each trial, while the monkey fixated on a central spot, a cue appeared at the fixation point matching one of the two upcoming stimuli. On any trial, the cue had an equal chance of matching either the vertical or horizontal stimulus. After 250 ms, the two peripheral stimuli appeared, one in the RF of the neuron, and the other some distance from the RF. After a period of 500–1,000 ms, each peripheral stimulus independently had a 50% chance of transiently dimming about 40% in luminance. The monkey indicated if the stimulus matching the cue dimmed by making a saccade to it. If the matching stimulus did not dim, the correct response was to remain fixating. The correct response depended only on the stimulus matching the central cue. We compared neuronal responses when the cue matched the stimulus in the RF (ATTin) with responses when the cue matched the remote stimulus (ATTout). For each neuron studied, we always presented the same stimulus in the RF, and only the cue changed randomly between trials. This ensured that neurons responded to the same stimulus regardless of which stimulus matched the central cue. Eye movements were monitored to make certain the monkey remained fixating during trials. The possible contribution of changes in the monkeys' eye position on the attentional modulation is considered in Supplementary Discussion. Because the stimulus in the RF always remained the same, this also allowed the monkey to shift attention as soon as the cue came on, as the location of each stimulus was consistent from trial to trial.

Full Methods and any associated references are available in the online version of the paper at www.nature.com/nature.

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1. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* **18,** 193–222 (1995).
2. Maunsell, J. H. & Cook, E. P. The role of attention in visual processing. *Phil. Trans. R. Soc. Lond. B* **357,** 1063–1072 (2002).
3. McAdams, C. J. & Maunsell, J. H. Effects of attention on the reliability of individual neurons in monkey visual cortex. *Neuron* **23,** 765–773 (1999).
4. Reynolds, J. H. & Chelazzi, L. Attentional modulation of visual processing. *Annu. Rev. Neurosci.* **27,** 611–647 (2004).
5. Crick, F. Function of the thalamic reticular complex: The searchlight hypothesis. *Proc. Natl Acad. Sci. USA* **81,** 4586–4590 (1984).
6. Conley, M. & Diamond, I. T. Organization of the visual sector of the thalamic reticular nucleus in *Galago*. *Eur. J. Neurosci.* **2,** 211–226 (1990).
7. Crabtree, J. W. & Killackey, H. P. The topographic organization and axis of projection within the visual sector of the rabbit's thalamic reticular nucleus. *Eur. J. Neurosci.* **1,** 94–109 (1989).
8. Fitzgibbon, T., Szmajda, B. A. & Martin, P. R. First order connections of the visual sector of the thalamic reticular nucleus in marmoset monkeys (*Callithrix jacchus*). *Vis. Neurosci.* **24,** 857–874 (2007).
9. Harting, J. K., Van Lieshout, D. P. & Feig, S. Connectional studies of the primate lateral geniculate nucleus: Distribution of axons arising from the thalamic reticular nucleus of *Galago crassicaudatus*. *J. Comp. Neurol.* **310,** 411–427 (1991).
10. Jones, E. G. Some aspects of the organization of the thalamic reticular complex. *J. Comp. Neurol.* **162,** 285–308 (1975).
11. Kim, U., Sanchez-Vives, M. V. & McCormick, D. A. Functional dynamics of GABAergic inhibition in the thalamus. *Science* **278,** 130–134 (1997).
12. Montero, V. M., Guillery, R. W. & Woolsey, C. N. Retinotopic organization within the thalamic reticular nucleus demonstrated by a double label autoradiographic technique. *Brain Res.* **138,** 407–421 (1977).

13. Uhlrich, D. J., Manning, K. A. & Feig, S. L. Laminar and cellular targets of individual thalamic reticular nucleus axons in the lateral geniculate nucleus in the prosimian primate *Galago*. *J. Comp. Neurol.* **458,** 128–143 (2003).
14. Casagrande, V. A., Sary, G., Royal, D. & Ruiz, O. On the impact of attention and motor planning on the lateral geniculate nucleus. *Prog. Brain Res.* **149,** 11–29 (2005).
15. O'Connor, D. H., Fukui, M. M., Pinsk, M. A. & Kastner, S. Attention modulates responses in the human lateral geniculate nucleus. *Nature Neurosci.* **5,** 1203–1209 (2002).
16. McAlonan, K., Cavanaugh, J. & Wurtz, R. H. Attentional modulation of thalamic reticular neurons. *J. Neurosci.* **26,** 4444–4450 (2006).
17. McAdams, C. J. & Maunsell, J. H. Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J. Neurosci.* **19,** 431–441 (1999).
18. McAdams, C. J. & Reid, R. C. Attention modulates the responses of simple cells in monkey primary visual cortex. *J. Neurosci.* **25,** 11023–11033 (2005).
19. Motter, B. C. Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli. *J. Neurophysiol.* **70,** 909–919 (1993).
20. Roelfsema, P. R., Lamme, V. A. & Spekreijse, H. Object-based attention in the primary visual cortex of the macaque monkey. *Nature* **395,** 376–381 (1998).
21. Ito, M. & Gilbert, C. D. Attention modulates contextual influences in the primary visual cortex of alert monkeys. *Neuron* **22,** 593–604 (1999).
22. Posner, M. I. & Gilbert, C. D. Attention and primary visual cortex. *Proc. Natl Acad. Sci. USA* **96,** 2585–2587 (1999).
23. Roberts, M., Delicato, L. S., Herrero, J., Gieselmann, M. A. & Thiele, A. Attention alters spatial integration in macaque V1 in an eccentricity-dependent manner. *Nature Neurosci.* **10,** 1483–1491 (2007).
24. Treue, S. Neural correlates of attention in primate visual cortex. *Trends Neurosci.* **24,** 295–300 (2001).
25. Briggs, F. & Usrey, W. M. A fast, reciprocal pathway between the lateral geniculate nucleus and visual cortex in the macaque monkey. *J. Neurosci.* **27,** 5431–5436 (2007).
26. Sillito, A. M., Cudeiro, J. & Jones, H. E. Always returning: feedback and sensory processing in visual cortex and thalamus. *Trends Neurosci.* **29,** 307–316 (2006).
27. Lund, J. S., Lund, R. D., Hendrickson, A. E., Bunt, A. H. & Fuchs, A. F. The origin of efferent pathways from the primary visual cortex, area 17, of the macaque monkey as shown by retrograde transport of horseradish peroxidase. *J. Comp. Neurol.* **164,** 287–303 (1975).
28. Jones, E. G. in *The Thalamus* 1270–1271 (Cambridge Univ. Press, 2007).
29. Kolmac, C. I. & Mitrofanis, J. Patterns of brainstem projection to the thalamic reticular nucleus. *J. Comp. Neurol.* **396,** 531–543 (1998).
30. Wilson, J. R., Hendrickson, A. E., Sherk, H. & Tigges, J. Sources of subcortical afferents to the macaque's dorsal lateral geniculate nucleus. *Anat. Rec.* **242,** 566–574 (1995).

Supplementary Information is linked to the online version of the paper at www.nature.com/nature.

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METHODS

Physiological methods. One recording chamber allowed access to both TRN and LGN. It was implanted stereotaxically 10 mm anterior from the interaural line and 13 mm lateral from the midline on three male rhesus macaque monkeys (monkey B, O and G—monkey G provided only TRN data). The surgical procedures, recording of single neurons and eye positions, and control of the monkeys' behaviour have been described previously[16]. All procedures were approved by the Institute Animal Care and Use Committee and complied with Public Health Service Policy on the humane care and use of laboratory animals.

We initially localized LGN using an MRI image after the recording cylinder was implanted. LGN recordings were verified by the nature of the visual response and the signature alternation of the ocularity of these responses as the electrode progressed through layers. TRN was located by its position in relation to LGN. The short latency of the visual response (about 22 ms) and its brief duration (~60 ms) identified the neurons as being from TRN as determined previously with histological verification[16], rather than from the parvocellular layers in dorsal LGN.

For most units, RF centre and extent were quantitatively determined. While the monkey fixated on a central spot 0.4° in diameter, a spot of light (0.8° to 1.0°) appeared sequentially in a series of locations centred on the estimated RF centre, arranged in a 5 × 5 grid. Horizontal and vertical separation between grid points was equal to the diameter of the spot. Each trial lasted as long as 800 ms and the spot appeared in each randomly chosen location for either 200 ms (LGN) or 100 ms (TRN). Responses to the spot at each location were analysed online and the centre of the RF was adjusted accordingly. We subsequently determined RF diameter in a similar manner, this time by presenting a sequence of spots with varying diameters centred on the RF. Spots were 0.5° to 6° in diameter, and appeared in random sequence during each 800 ms trial, each spot remaining for 200 ms (LGN) or 100 ms (TRN). The quantitatively determined RF centre and diameter were then used to place the stimuli for the attention task. Visual stimuli in all tasks were back projected onto a tangent screen 58 cm in front of the monkey by a liquid crystal display projector.

Attention task details. During a trial, the monkey was required to maintain fixation within 1.0° or 1.5° of the central fixation point (Supplementary Fig. 1). If the monkey broke fixation early, the trial was aborted and excluded from analysis. The central cue was 1.5° × 0.6° or 2.0° × 0.8°, whichever was closest to the size of the peripheral stimuli. The peripheral stimuli were 1.5° to 2.0° long and 0.6° to 0.8° wide, depending on the eccentricity and size of the RF. One of the stimuli was placed in the RF of the LGN or TRN neuron. The other stimulus was placed some distance away, typically about 20°, but at the same eccentricity from the fixation point as the stimulus in the RF. Each peripheral bar of light independently had a 50% chance of dimming for 600 ms. Therefore on 25% of trials both stimuli dimmed (simultaneously), on 25% of trials neither stimulus dimmed, on 25% of trials only the horizontal stimulus dimmed, and on 25% of trials only the vertical stimulus dimmed.

We used a criterion of 75% correct responses to indicate that the monkey was attending to the cued target, although performance was typically better. To flag possible response strategies, we first divided the trials into eight trial types according to which stimulus was cued (horizontal or vertical) and which stimuli dimmed (horizontal only, vertical only, both, or neither). If the monkey followed some response strategy rather than attending as directed by the cue, performance on one or more of these trial types would necessarily suffer. We flagged possible response strategies by requiring the monkey get each of these eight trial types correct at least 50% of the time. So when we refer to the monkey performing the attention task to criteria, the monkey is getting at least 75% of the trials correct overall and is getting at least 50% of each type of trial correct.

Analysis of results. We measured the activity of neurons as the mean neuronal response within several different epochs. We measured mean background activity in the 100 ms period before onset of the visual stimuli. Visual response latency was determined by fitting a normal cumulative density function (CDF) to the spike density plot obtained over at least 20 but usually more than 50 trials and smoothed with a 2.8 ms s.d. Gaussian kernel (Supplementary Fig. 2a). The onset of the visual response was taken as the time at which the fit curve reached 10% of the neuron's peak response. The latency of this response was the time between onset of the visual stimulus (determined by a photo cell attached to the screen) and this response onset time. The end of the initial response was taken as the point at which a Weibull probability density function (PDF) fit to the falling phase of the response declined 75% from the neuron's peak response to the asymptote of the fit curve. The duration of the initial visual response was then the time between the visual response onset and the end of the initial visual response. Both the gaussian CDF and the Weibull PDF were fitted by minimizing the sum-squared error between the fit curve and the spike density plots. The mean response is the average response rate during this epoch.

Comparisons with other studies. The percentage response modulation we report for other studies was calculated from available firing rates with baseline activity included. From the neuronal response rates with and without attention, we were able to extract a comparable percentage change from the ratio of modulation by calculating $100 \times [(\mathrm{ATTin}/\mathrm{ATTout}) - 1]$.

SUPPLEMENTARY DISCUSSION

Analysis of variation in eye position on attention modulation

A critical feature of attention experiments is that the visual stimulus remains the same, and only the subject's use of the stimulus changes. Within a given experiment, we always placed the same stimulus in the RF. However, small changes in fixation from trial to trial slightly change the position of the stimulus in the RF, and may possibly result in differences in neuronal response. This is particularly important for LGN and TRN RFs because of their small size. For eccentricities ≤ 20°, RF diameters of TRN neurons in our experiments (n = 12) were on average 0.83°, while LGNm (n = 15) were 0.73°, and LGNp RFs (n = 23) were 0.62°. The RFs in the two structures were therefore about the same size and should be similarly affected by any small eye position changes.

For neurons in each area, we analyzed the position of the eyes during fixation to determine whether there were any systematic differences in eye position between ATTin and ATTout trials that might account for the response differences we observed. For each neuron, we calculated the mean point of fixation for both ATTin and ATTout trials during the first 100 ms of stimulus presentation (when attentional changes were observed in both LGN and TRN). We calculated a difference vector showing the difference in fixation between ATTin and ATTout trials. We then rotated the vector representing the difference in fixation around the center of the screen (the actual fixation point), so that the neuron's RF was directly to the right. This enabled us to see any systematic variations in fixation relative to the RF. Supplementary Figure 3 shows each of the resulting fixation differences (the endpoints of the mean difference vectors for each neuron ± 1 SE of the mean). Differences in fixation while recording from TRN neurons are shown in black, while blue and red are for LGNm and LGNp, respectively. The mean horizontal and vertical fixation differences between ATTin and ATTout trials relative to the

neuronal RF are shown as arrows on the axes. The magnitude of the mean difference for all neurons was only 0.04° (TRN: 0.07°, LGNp: 0.05°, LGNm: 0.01°).

There was neither substantial nor significant correlation between the magnitude of the attentional effect on neuronal responses and the difference in fixation. TRN ($r = -0.11$, $p = .954$), LGNm ($r = .14$, $p = .577$), and LGNp ($r = 0.23$, $p = 0.158$) all had very weak correlations. In retrospect, it would have been puzzling to find that the effects we observed were due to differences in fixation position. Recall that the modulation of neuronal responses was different in TRN and LGN: LGN increased with attention whereas TRN decreased. Since all the neurons we recorded responded similarly to the stimuli, with fast rigorous on-responses, the pattern of fixation differences would have to be different for days on which we recorded from TRN and for those on which we recorded from LGN. That is, the monkeys would have had to consistently change their fixation patterns for experiments in TRN and experiments in LGN to cause systematic differences in modulation. Since the monkeys had no way of knowing from which area we were recording on any given day, it is implausible on principle that fixation differences caused the modulation we observed.

Comparison of TRN attentional modulation in visual/visual and visual/auditory tasks

Our first account of attentional modulation in TRN[31] used a task very different from the task in the current report. Our previous task did not shift attention between two visual stimuli, but between a visual stimulus (a spot) and an auditory stimulus (a tone). When shifting attention into the RF of a visual TRN neuron from an auditory stimulus, the initial visual responses in TRN did not decrease, but rather increased. The two different attention experiments were done in the same two monkeys so that in making comparisons we can exclude any differences between animals. Supplementary Figure 4a shows the

results for both experiments using the same ATTmod measure. Closed symbols show neuronal changes in the within-modality experiments, when attention shifted from a localized visual stimulus outside the RF of the TRN neuron to a stimulus in the RF. Open symbols show modulation in the across-modality experiments, when attention was shifted from an unlocalized auditory stimulus to the visual stimulus in the RF. The ordinate is the baseline TRN response when attention was directed away from the visual TRN RF, and the abscissa is ATTmod due to directing attention toward the visual stimulus in the RF. Both the previous experiment and the current experiment include the condition when attention is shifted to a visual stimulus in the RF, but note that the stimulus in the RF was a spot when shifting attention between modalities, and a bar when shifting attention within the visual modality. Although the difference in stimuli (and the relative invasion of any RF surround) makes it difficult to directly compare the absolute magnitudes of the responses, we can still compare the effects attention had on these responses.

The most obvious difference between the two experiments is the direction of the attentional effect. Shifting attention within modality from one visual stimulus to another yields a decrease in initial TRN visual activity as shown by the solid symbols falling largely to the left of the vertical unity line. Shifting attention to a visual stimulus across modalities (from an auditory to a visual stimulus) yields an increase in TRN activity as shown by the open symbols in Supplementary Figure 4a falling largely to the right of the unity line. The mean change in response from attention for the shift within modalities for these two monkeys was -4.8%, whereas across modalities it was +6.3%.

Note also the difference in the magnitudes of the responses. Baseline responses in the absence of attention were on average higher within the visual modality (closed symbols, mean = 294 spikes/s), than across modalities (open symbols, mean = 179 spikes/s). When attention was directed to the stimulus in the RF in each experiment, the mean ATTvis response (across modalities) was 189 spikes/s, and the mean ATTin response (within

modality) was 278 spikes/s, a difference possibly attributable to the different stimuli used in the two experiments, as mentioned above.

While the observations in these two attention experiments appear at odds with each other, the combination of the directions of the attentional effects and the magnitudes of the visual responses might provide some insight into understanding the differences. The key is considering the nature of the attention experiments: global attention shifting between visual and auditory modalities in our previous experiments and local shifts between two visual stimuli in our current visual attention experiments. When shifting attention across modalities, attending to the auditory stimulus inhibits the visual modality so firing rates are lower in visual TRN during ATTaud trials as shown schematically in the left half of Supplementary Figure 4b. Attention shifting from the auditory to the visual modality (ATTvis) increases the visual response in TRN by presumably releasing visual TRN from the inhibitory influence of the auditory sector, as there is clear evidence of interactions between different sectors of TRN[32-34]. Provided auditory TRN acts on visual TRN more uniformly, rather than in a spatially selective manner, the modulation of visual TRN in the across-modalities task can be viewed as visual TRN being activated and deactivated by global inhibition from auditory TRN.

Local spatial modulation, however, is related to the competition within different regions of the visual TRN. Consequently the results from our current experiments can be viewed as the interactions within visual TRN in its active state, when attention is on visual stimuli (Supplementary Figure 4b, right side). Now when attention is directed within the visual modality, TRN responses are reduced at the location of attention and this reduction selectively enhances LGN responses by reducing inhibition at the attended location. Directing visual attention out of the RF of a TRN neuron increases its response, inhibiting LGN at the unattended location. The part of the puzzle that is missing is the behavior of LGN when attention shifts between auditory and visual stimuli

(Supplementary Figure 4b, left side). Shifting attention from a visual stimulus to an auditory one results in a decrease in TRN activity, which, according to the local TNR/LGN circuit, should result in an increase in the initial visual response in LGN when attention shifts to an auditory stimulus. Although we did not record from LGN neurons in our previous experiment, and so have no data from LGN for this condition, recall that the current experiment shows that there are other attentional influences acting on LGN, as the later stages of the visual response are modulated in the absence of any TRN modulation: additional influences that could possibly create the desired effect in LGN when attention is shifted to an auditory stimulus. So although the previous and current experiments appear to have conflicting results, consideration of the difference between global and local spatial selectivity provides a possible resolution to this perceived conflict.

SUPPLEMENTARY NOTES

Bootstrap analysis

To obtain latency estimates and to compute their significance, we used a bootstrap analysis. For the latency of the visual response in areas LGNm, LGNp. and TRN, we calculated the mean spike density plot for the ATTin condition. If the data set for an area, and therefore the mean spike density plot, consisted of N neurons, we created a subset of N neurons chosen from the original set with replacement. That is, if the original set consisted only of neurons A, B, and C, possible subsets might be (A, A, B), (A, C, C), (A, B, C), (B, B, C), etc. For each of 1000 iterations a new subset was chosen and the mean ATTin spike density plot was calculated from this subset. We fit a normal cumulative density function (CDF) to each of these 1000 spike density plots, and estimated the latency from the curve fit to the spike density plot in the same way we did for individual neurons (when the fit curve reached 10% of the spike density plot peak). In this manner we acquired a distribution of 1000 latency estimates for each area. From these distributions of estimates we were able to obtain the median latency (used as the characteristic latency for an area) and we were also able to determine the significance of the latency differences between areas using the Wilcoxon rank-sum test for equal medians.

For the latency of the attentional modulation for each area, a bootstrap analysis identical to the one above was performed, but rather than fitting the normal CDF to the ATTin curve, we fit it to the difference between the ATTin and ATTout curves.

References for Supplementary Information

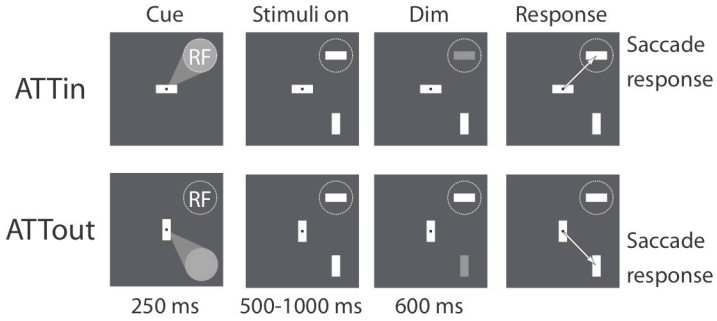
31. McAlonan, K., Cavanaugh, J. & Wurtz, R. H. Attentional modulation of thalamic reticular neurons. J Neurosci 26, 4444-50 (2006).

32. Crabtree, J. W., Collingridge, G. L. & Isaac, J. T. A new intrathalamic pathway linking modality-related nuclei in the dorsal thalamus. Nat Neurosci 1, 389-94 (1998).

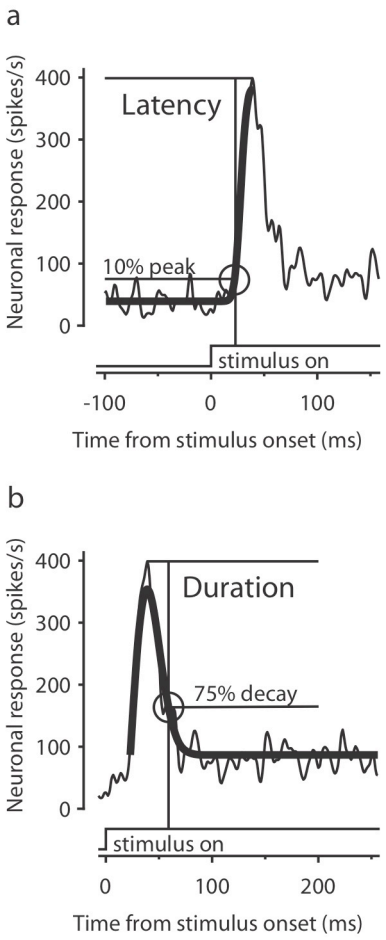
33. Crabtree, J. W. & Isaac, J. T. New intrathalamic pathways allowing modality-related and cross-modality switching in the dorsal thalamus. J Neurosci 22, 8754-61 (2002).

34. Kimura, A., Imbe, H., Donishi, T. & Tamai, Y. Axonal projections of single auditory neurons in the thalamic reticular nucleus: implications for tonotopy-related gating function and cross-modal modulation. Eur J Neurosci 26, 3524-35 (2007).

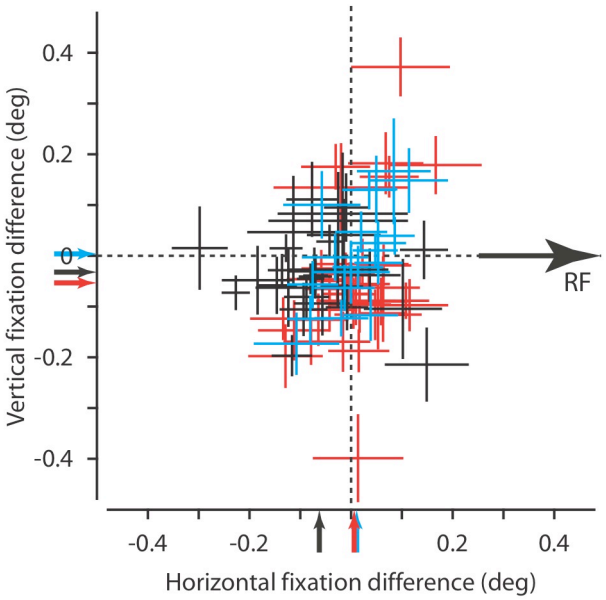
SUPPLEMENTARY FIGURES AND LEGENDS



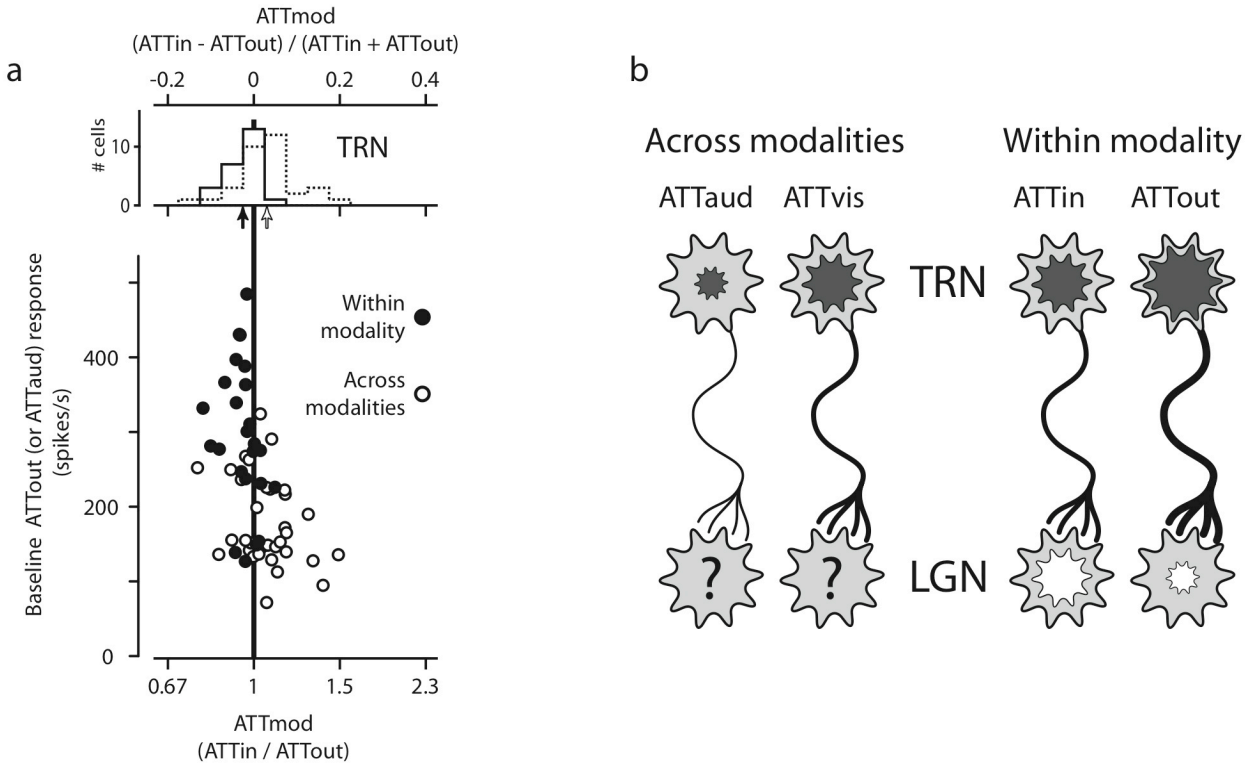
Supplementary Figure 1. Visual Spatial Attention task used for both LGN and TRN neurons. See Methods for further details.



Supplementary Figure 2. Determination of visual response latency and duration. **a**, The visual response latency is taken as the time at which the fit curve climbed to 10% of the peak neuronal response (circle), and the latency extracted from this fit is shown by the vertical line through the circle. **b**, The end of the visual response duration was taken as the time the fit curve decays to the point 75% of the way from the peak response to the end of the fit curve (circle). The vertical line denotes the end of the visual response. See Methods for details.



Supplementary Figure 3. Differences in eye position during the initial visual response. For each neuron we have plotted the difference in eye position between ATTin and ATTout trials during fixation as the intersection of each pair of lines. The lengths of the lines represent ±1 SE of the horizontal and vertical differences during the first 100ms of stimulus presentation. Positions have been rotated around the center to place the neuronal RF to the right, as indicated by the large black arrow.



Supplementary Figure 4. Modulation of TRN from attentional shifts within and across sensory modalities. **a**, Baseline response versus attentional modulation (ATTmod) for attentional shifts within and across sensory modalities. Solid symbols are a subset of those in Figure 3c. Baseline response for data across modalities is the ATTaud response. Distributions of ATTmod appear above the scatterplot for within modality (solid lines) and across modalities (dashed line). Distribution medians are denoted by the solid arrow (within modality) and open arrow (across modalities) below the distributions. **b**, Schematic representation of relative activity in LGN and TRN from shifting attention within and across modalities.