Attention dependent suppression of metabolic activity at the early stages of the macaque visual system

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Abstract

We review the results of a double label 2-deoxyglucose study in the awake monkey demonstrating that attention can suppress activity at early levels in the primate visual system, but in regions surrounding the representation of the attended stimulus. These findings are in agreement with human imaging results and were modeled in a dynamic simulation, highlighting the role of the reticular thalamic nucleus in these suppressive effects.

I. Introduction

This chapter is devoted to the effects of spatial attention at very early levels of the visual system. A series of publications including both single cell studies in the monkey (e.g. Reynolds et al 2000, Treue and Maunsell 1999) and human imaging studies (e.g. Tootell et al 1998, Brefczynski and DeYoe 1999) have generated the view that attention effects in the visual system 1) are mainly positive effects enhancing visual responses, 2) occur relatively late in the hierarchy, at the level of V4 or beyond, and 3) have their source in parieto-frontal networks (Corbetta et al 1998, Wardak et al 2002). The study (Vanduffel et al 2000) reviewed in the present chapter provides evidence for suppressive attention-dependent modulation of activity at very early levels of the visual system: the dorsal Lateral Geniculate Nucleus (LGN) and striate cortex (or V1). This study also suggests that a subcortical structure, the reticular thalamic nucleus (RTN), might play a role in these attentional effects.

The Vanduffel study also stands out in the use of the relatively uncommon double label 2-deoxyglucose (2-DG) technique (Hubel and Livingstone 1982, Geeseman et al 1997), with which the metabolic activity evoked during two behavioral conditions can be compared at a very high spatial resolution (50 micron or better) throughout the brain. The double label 2-DG lacks the temporal resolution of optical recording, but is applicable to all parts of the monkey visual system. The technique has a better spatial resolution than monkey fMRI, but lacks the versatility of fMRI since only two conditions can be compared. That is the principal reason that we, and others, developed monkey fMRI (Logothetis et al 1999, Vanduffel et al 2001), which enables the investigator to sample, albeit indirectly, brain ‘activity’ over a large number of conditions in the same monkey.

In single cell studies or functional imaging, the dominant paradigm consists of looking for effects of attention in those neurons, or the population of neurons, processing the stimuli to which attention is directed. Here, we observed a modulation of metabolic activity in the neurons representing regions in visual space surrounding the attended stimulus. While the monkeys fixated nearly identical displays containing a central grating in the two attention conditions, the monkeys either used or did not use the grating to make their behavioral response (an eye movement to a left or right target). Tritiated 2-DG labeled neurons that were activated during the attention to the grating condition, while ^{14}C-labeled 2-DG marked neurons that were activated in the attention away from the grating condition (the respective order was randomized between animals). When the monkey used the grating to guide its behavior, i.e. was paying attention to the grating, we observed a ring of suppressed metabolic activity in the parts of LGN and V1 surrounding the retinotopic representation of the grating.

In the original publication the two behavioral conditions are referred to as featural and spatial attention conditions respectively. This choice of terminology introduced by the review process, proved unfortunate. Indeed, when the monkey uses the grating, he pays attention to this region of visual space because he has to process the grating orientation. Thus, both spatial and featural attention are likely to be engaged in this condition. In the other condition, only the position of the target matters and thus, only spatial attention (directed to other parts of the display, away from the grating) comes into play.

In the discussion of the experimental findings, we will introduce a simple dynamic network, showing that the known connections between geniculate relay cells, cortical layers 4 and 6 and reticular neurons can generate the suppressive ring when a stimulus is attended, exactly as observed in our experiments.

II. The Experimental Findings

The main data obtained in these experiments consist of differences in 2-DG concentration, reflecting differences in metabolic activity evoked during the two behavioral conditions. Figure 1 shows the concentration of radioactive 2-DG sampled over trajectories covering different parts and different layers of striate cortex in one of the four monkeys participating in the experiment. This figure illustrates the basic finding of the study: differences in 2-DG concentration were observed between the two attention conditions in certain layers and in certain parts of V1. Further analysis revealed that 1) these differences occurred mainly in the magnocellular input layer 4Cα and 2) they were restricted to an annular region surrounding the representation of the grating. The laminar specificity of the effect allowed us to disambiguate the signs of these differences. Since only two conditions were compared the reduced metabolic activity in the annular region surrounding the representation of the grating could have represented either a reduced activation in the attention to the grating condition or alternatively an increased inhibition in the same condition. We compared the ratio of activity in layer 4Cα and a control layer (layers 4B) for each condition at different parts of V1 (inside the ring, over the ring, outside the ring). This procedure enabled us to establish that in the attention-to-the-grating condition, metabolic activity in the ring was lower in layer 4Cα than in layer 4B, whereas the ratio of these activities was similar in all parts of V1 in the other condition (see Fig. 11 of Vanduffel et al 2000). Thus, our main finding was an attention-dependent suppression of metabolic activity surrounding the representation of the grating, rather than an enhancement of activity in the attention-away condition.

Figure 2 shows the distribution of the differential 2-DG uptake of the two conditions in layer 4Cα for the four different animals as a function of eccentricity, along with the radius of the grating

used in each animal. This figure indicates that the ring of suppression changed in diameter with that of the grating confirming that the suppression surrounded the stimulus representation. Note, however, that the strength of the suppression varies little with stimulus diameter.
Remarkably, similar observations were made in the LGN, at least in the magnocellular layers. Again, the suppression varied with the grating diameter (see Fig. 13 of Vanduffel et al 2000), but in the LGN, the depth of this suppression increased with the diameter. In addition, another subcortical change was observed in the visual thalamus: metabolic activity of the reticular thalamic nucleus increased in the attention-to-the-grating condition relative to the attention-away condition.

III Discussion and Computational Modeling

The results reviewed here clearly indicate that suppressive changes occur in those parts of V1 and LGN that surround the representation of an attended stimulus. This finding is remarkable because of the level in the system at which it occurs, its retinotopic location and its sign. Human fMRI studies have also reported suppressive effects in human V1 (e.g. Tootell et al 1998, Smith et al 2000) and even in human LGN (O'Connor al 2002). The effects occur in regions outside the representation of the attended stimulus (typically the fovea when attending a peripheral stimulus), rather than in the representation of the attended stimulus itself. The belief that attention modulates only the representation of the attended stimulus can be so entrenched that analysis is sometimes restricted to this part of cortex (e.g. Gandhi et al 1999). Only a single study (Smith et al 2000) has provided hints of a ring of suppression surrounding the representation of the attended stimulus. Human fMRI has also indicated (modestly) increased activation at the level of the stimulus representation, even in V1 (Tootell et al 1998, Brefczynski and DeYoe 1999, Gandhi

et al 1999, O'Connor et al 2002). Such effects were weak in our data and rarely reached significance. There are obvious differences between the two types of experiments: different species, differences between metabolic and hemodynamic measurements and different control conditions. To underscore the importance of the latter factor, it is worthwhile to consider the evidence of O'Connor et al 2002 for enhanced geniculate responses to attended stimuli. The authors compared two conditions: one in which the subjects attend a central stimulus (to count letters) and one in which the subjects attend a peripheral checkerboard stimulus (to detect its dimming). They compared responses to the checkerboard in the two conditions and reported that the activity evoked by the checkerboard was larger when the subjects attend to the checkerboard. Since only two conditions were compared, an alternative interpretation of their data would be that there is a smaller response to the checkerboard when the central stimulus is attended. The suppressive effects they described would then be an enhancement of this suppressive effect when the attention to the central stimulus is further loaded.

The difference between hemodynamic measurements (fMRI) and metabolic measurements should not be underestimated. One reason why suppressive effects are less frequently reported in the fMRI studies, is that they could arise from purely vascular changes. This so-called plumbing hypothesis states that an increase in blood flow in an active brain region reduces blood flow in other less active parts of the brain. Such a hemodynamic effect cannot account for the suppressive effects reported here, supporting the view of those who claim that negative 'BOLD' reflects reduced neuronal activity. The metabolic measurements of the present study also clarify another point of contention in the interpretation of fMRI data, i.e. the contribution of inhibitory neurons to the fMRI signal. Our results suggest that inhibitory neurons contribute to the metabolic brain activity (and hence hemodynamic responses) as well as excitatory neurons. Indeed, structures such as the RTN which include only inhibitory neurons projecting massively to

a target structure (here the LGN) show changes in differential metabolic activity opposite in sign to those of the target structure. Activity in the LGN decreased with attention to the grating while activity in the RTN increased. Similar overall reversals in the sign of differential metabolic activity were observed in the basal ganglia (Vanduffel unpublished PhD thesis) where two inhibitory projections are known to occur in sequence: the sign of the differential 2-DG uptake changed twice when going from the ventral putamen over the ventral pallidum to the medio-dorsal thalamic nucleus.

The results reviewed here also point to the involvement of the reticular thalamic nucleus in the generation of attentional modulation at the early levels of the visual system, in agreement with earlier suggestions (Crick 1984, Montero 1999). In order to provide further support for this view we modeled the experimental results using four building blocks: the relay cells of the LGN, the RTN, and layers 4Cα and 6 of V1. The neurons in these structures simply have a sigmoidal transfer function, and no assumptions about the types of synapses were included. The model (figure 3) bears some resemblance to earlier attempts of Bazhenov et al 1998 and Montero 1999, but differs from these by including more anatomical data (albeit from lower animals such as cats and rats) and in the dynamic nature of the model. The connections assumed between the four elements are indicated in figure 3. Noteworthy are the direct inhibition of relay cells by the reticular axons, in agreement with Wang et al 2001, as well as the larger spread of the projections to and from the RTN compared to those to and from the relay cells, in agreement with the anatomical results of Bourassa and Deschenes 1995 and of Yen et al 1985. For simplicity other inputs to the RTN have been omitted. The attention signal is assumed to be applied to layer 6, in agreement with a large body of anatomical results indicating that feedback connections end outside layer 4. One other distinguishing feature of the model is the nature of the attention gating

signal, which can be uniform rather than spatially restricted. The main mechanism of the attentional modulation is the diffusion of stimulus driven relay cell activity to RTN, which in turn injects inhibition into regions of the LGN surrounding the stimulus representation. Critical to the model is the large spread of the RTN connections. The fixed-point states, obtained after 10 iterations, reproduce the experimental findings nicely (figure 3). The diameter of the suppressive ring increases with stimulus diameter and the depth of suppression depends on stimulus size much more in LGN than in V1. One apparent discrepancy is the absence in the 2-DG study of an attentional modulation in layer 6. This is in all likelihood due to the low level of spontaneous activity in layer 6. In regions surrounding the grating representation, no stimulus was present and therefore, a modulation could be observed only in regions in which spontaneous activity is high enough, such as the LGN and layer 4C of V1. Thus, this model, which is supported by our experimental data, opens new avenues in our thinking about the nature and source of the signals that cause the attentional modulation in the primate visual system.

Acknowledgements. WV is a fellow of the FWO. This work was supported by FWO and GOA 2000/11.

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Figures

Figure 1

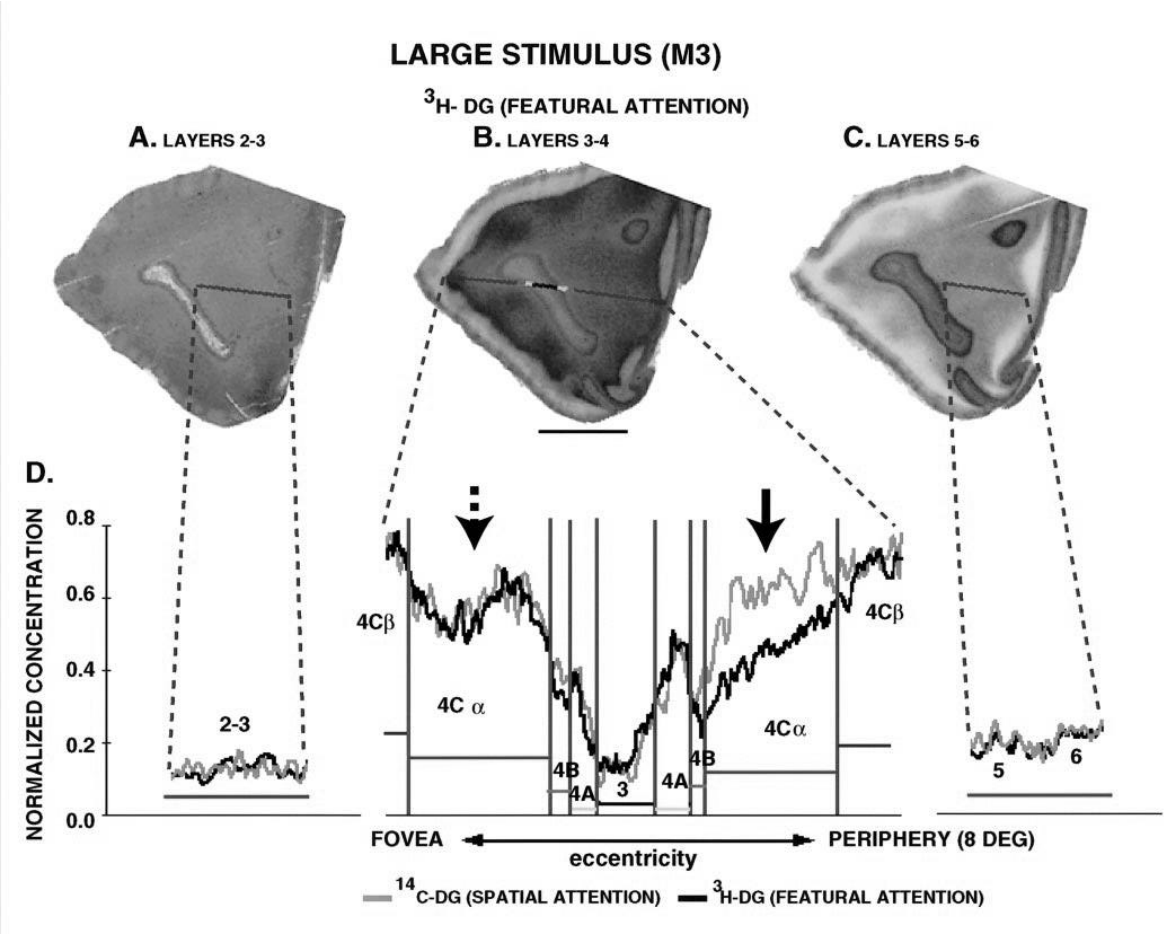

Figure 2

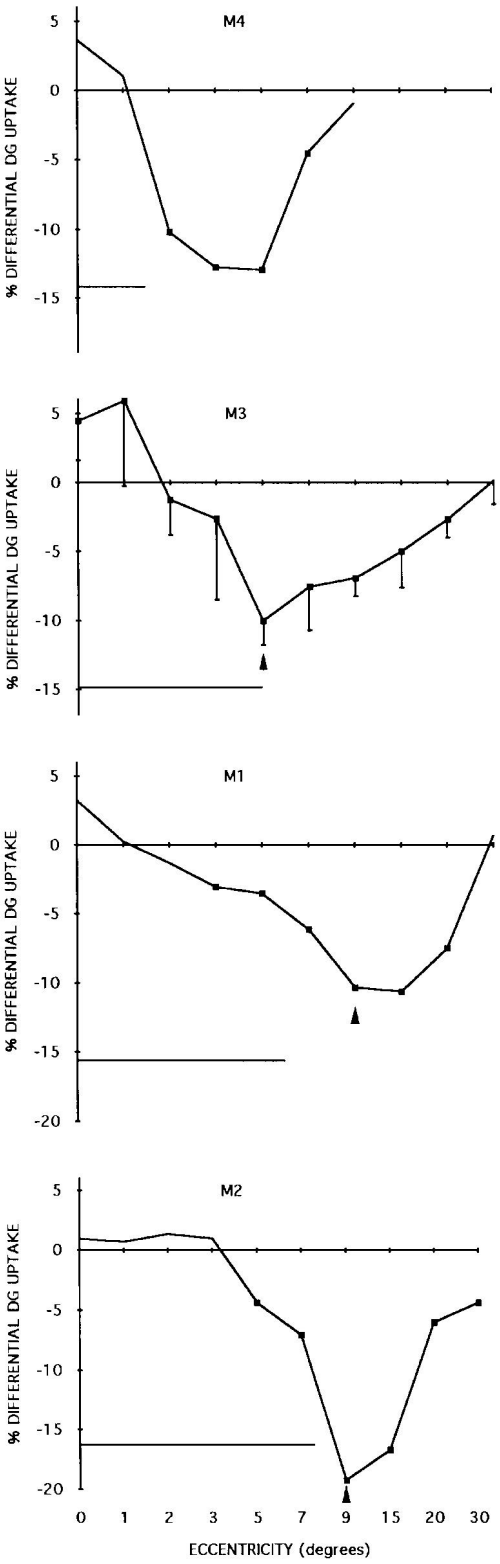
M4
M3
M1
M2
% DIFFERENTIAL DG UPTAKE
5
0
-5
-10
-15
-20
0 1 2 3 5 7 9 15 20 30
ECCENTRICITY (degrees)

Figure 3

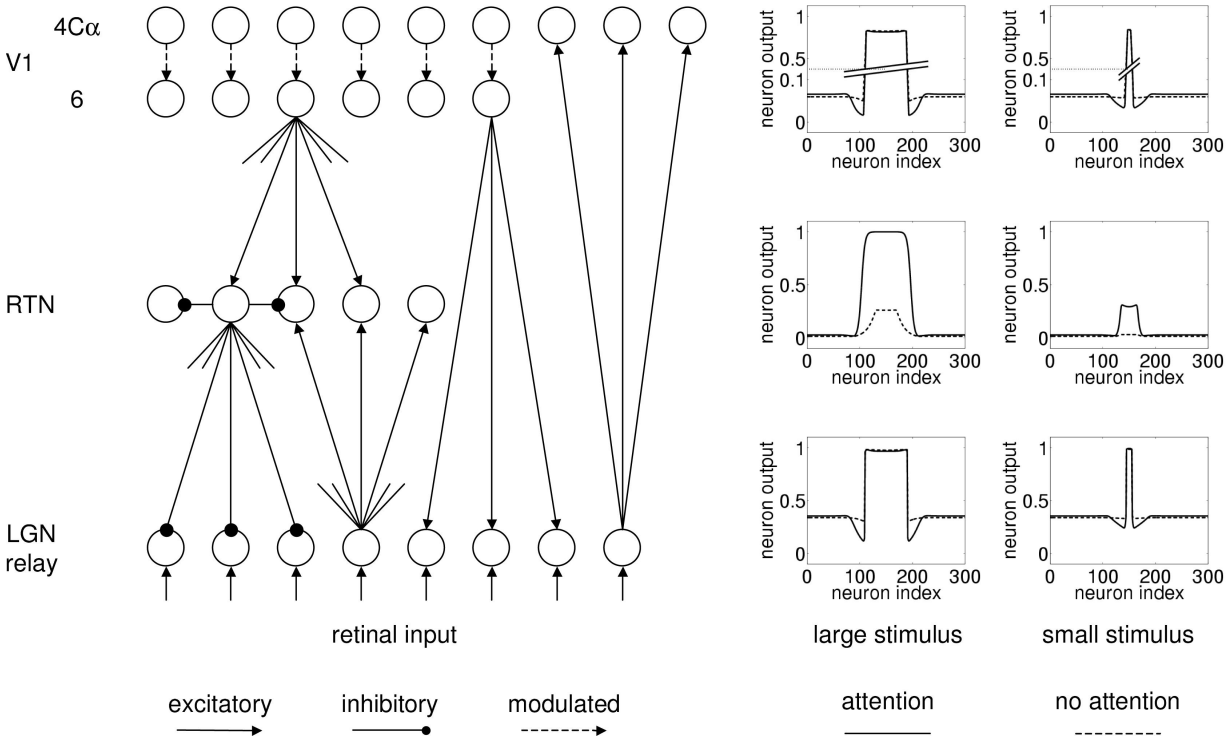
4Cα
V1
6
RTN
LGN
relay
retinal input
excitatory
inhibitory
modulated
neuron output
neuron index
large stimulus
small stimulus
attention
no attention

Figure legends

Figure 1:

Plots of normalized [^{14}C]DG and [^{3}H]DG concentrations as a function of eccentricity in different layers of flattened area V1. (*A*-*C*) The ^{3}H signals (related to the featural-attention task, i.e. the attention-to-the-grating condition) from single V1 sections through layers 2-3, 3-4 and 5-6 respectively. No orientation columns or visually driven enhanced activity can be observed. In the three sections, the fovea is represented towards the left, with more peripheral visual field representations towards the right. The upper visual field is represented in the lower portion of the section. (*D*) Plots of normalized [^{3}H]DG and [^{14}C]DG concentrations as measured along the lines indicated in (*A*-*C*) (along the representation of the horizontal meridian from foveal to more peripheral visual field representations). Note the suppressed [^{3}H]DG concentration in more peripheral (solid black arrow in *D*), but not foveal (dotted black arrow in *D*) visual field representations of layer 4Cα.

Figure 2:

Normalized differential DG uptake (using the spatial attention task as baseline) in layer 4Cα of V1 as a function of eccentricity is plotted for all four subjects. Percentage differential DG uptake = [(the normalized DG concentration related to the featural attention task) - (the normalized DG uptake related to the spatial attention task)] / (the normalized DG uptake related to the spatial attention task) × 100. The measurements along the horizontal and vertical meridians are averaged and thus, each data point represents the average of 90 isotope concentration measurements. The

standard deviations are shown for monkey M3. Squares indicate the eccentricities for which the difference in isotope concentration reached a *P*-value of < 0.05; two-tailed *t*-test. The radius of the gratings which were presented in each experiment is indicated by the lines at the bottom of each panel. Note that the shift of lower featural-attention DG uptake from parafoveal to larger eccentricities is correlated with the size of the stimulus.

Figure 3:

Model for attentional modulation in the thalamocortical network. Left panel shows synaptic connections between LGN relay neurons, RTN and V1 layers 4Cα and 6 neurons. For each layer, a chain of 300 model neurons with sigmoidal output functions is used. Connectivity to and from RTN is broader (indicated by larger numbers of connections). All connections are excitatory except those coming from RTN; the dashed lines indicate the uniform attentional input in layer 6. Right panel shows the resulting neural output as a function of the neuron's position in the layer in the case of attention (solid lines) and no attention (dashed lines), and for two stimulus sizes (left and right columns). Upper row corresponds to layer 4Cα, middle row to RTN, and bottom row to LGN relay neurons. The thalamocortical model forms a recurrent network with fixed-point iteration dynamics. The plots in the right panel represent the fixed-point states, which are reached after 10 iterations.