

## DETERMINANTS AND MECHANISMS OF ATTENTIONAL MODULATION OF NEURAL PROCESSING

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### TABLE OF CONTENTS

1. Abstract
2. Overview
3. Attention Paradigms and their Ecological Validity
  - 3.1. Visuospatial (non-foveal) Attention
  - 3.2. Nonspatial Visual Attention
4. Effects of Attention on Brain Activity Measurements
  - 4.1. Visuo-spatial attention
  - 4.2. Nonspatial Attention
5. An anatomical hierarchy of attention effects?
6. A temporal hierarchy of attention effects?
7. Brain Mechanisms of Attentional Modulation
  - 7.1. Neuronal circuits
  - 7.2. Physiology
8. Linkage Between Neural Effects and the Cognitive Impact of Attention
  - 8.1. Neuronal and perceptual amplification
  - 8.2. Dynamic change in cellular connectivity
9. Conclusions
  - 9.1. Toward an Adequate Model of Attention
    - 9.1.1. Operational Dynamics
    - 9.1.2. Perceptual and Neural Mechanisms
10. Acknowledgements
11. References

### 1. ABSTRACT

This review contrasts the most-studied variety of attention, visuospatial attention, with several types of nonspatial visual attention. We: 1) discuss the manner in which spatial and nonspatial varieties of attention are experimentally defined, and the ecological validity of the paradigms in which they are studied, 2) review and compare differing effects of spatial and nonspatial attention on neural processing, 3) discuss the manner in which attention operates within the framework of an anatomical visual hierarchy, as well as 4) how attention relates to the temporal dynamics of visual processing, 5) describe cellular circuits and physiological processes that appear to be involved in attention effects, 6) discuss the relationship of attentional physiology to the perceptual and cognitive effects of attention, and 7) consider the strengths and limitations of several current models of selective attention. Throughout, we attempt to integrate the findings of monkey and human studies whenever possible.

We have three main conclusions. First, two models, the *Neural Specificity Model* of Harter and colleagues and the *Feature Similarity Gain Model* of Treue and colleagues best incorporate findings in relation to both spatial and nonspatial varieties of attention. Significantly, these models explicitly note that the specific neuronal

components used in attentional modulation of processing are flexible and determined by task demands. Second, current evidence also provides strong bases for deriving testable hypotheses about the specific brain mechanisms utilized by attention. Cellular processes, brain circuits and neurotransmitter components can and should be incorporated into our models of attention. Finally, it is increasingly evident that we can and should analyze temporal patterns of attentional modulation, both within and across brain areas. These patterns provide critical information on the dynamics of attention.

### 2. OVERVIEW

Sensory processing begins when a stimulus initiates a volley of activity in a population of peripheral sensory receptors. This volley of activity courses centrally along parallel neural pathways extending through subcortical relays and an array of hierarchically-organized cortical regions. The initial sampling of a stimulus by different receptors provides a complex of input signals. The patterns of feedforward and feedback connections between neurons which bridge each ascending step in a pathway produce convergence and/or divergence of these signals during their transit through the synaptic stages of the

ascending systems. The result is progressive transformation or “processing” of the original sensory input. Studies in the visual (1), auditory (2) and somatosensory systems (3) of macaque monkeys have outlined many basic selectivities of sensory receptor populations, as well as subsequent signal transformations, that provide passive mechanisms for sensory processing.

Selective attention has a crucial role in information processing, which becomes immediately obvious when we consider the size of the sensory input set in a complex natural setting. There are, for example, more than 1,000,000 output lines (axons) in each optic nerve, and more than 30,000 axons in each auditory nerve. Thus, a moderately salient stimulus that impinges on these two senses is likely to send several million signals per second into the brain, creating an enormous processing bottleneck. Selective attention helps to solve this problem, by modulating sensory-evoked neuronal responses so that processing of task relevant stimuli is enhanced, and that of irrelevant stimuli is diminished (4, 5, 6). This controlled, active processing is essential to normal perception and cognition because it enables processing to adapt to the immediate goals of the observer. Dysfunctions of controlled processing contribute to pathophysiology in conditions ranging from learning disability and attention deficit disorder to Schizophrenia.

This review will contrast the most-studied variety of attention, visuospatial attention (7), with two types of nonspatial visual attention. We will: 1) discuss the manner in which spatial and nonspatial varieties of attention are experimentally defined, and the ecological validity of the paradigms in which they are studied, 2) review and compare differing effects of spatial and nonspatial attention on neural processing, 3) discuss the manner in which attention operates within the framework of an anatomical visual hierarchy, as well as 4) how attention relates to the temporal dynamics of visual processing, 5) describe cellular circuits and physiological processes that appear to be involved in attention effects, 6) discuss the relationship of attentional physiology to the perceptual and cognitive effects of attention, and 7) consider the strengths and limitations of several current models of selective attention. Throughout, we will integrate the findings of monkey and human studies whenever possible.

### 3. ATTENTION PARADIGMS AND THEIR ECOLOGICAL VALIDITY

Human event-related potential (ERP) studies have examined several varieties of visual selective attention, including visual spatial attention (8, 9, 10), visual feature attention (8, 11, 12) and intermodality attention (13, 14, 15, 16, 17). Studies in nonhuman primates have used a number of behavioral paradigms to study “state-dependent” and attention-related discriminative processing in primate visual cortex (18, 19, 20, 21, 22). With a few exceptions, however (23, 24, 25, 26, 27), the specific study of selective attention in monkeys has focused on the effects of spatial attention (28, 29, 30, 31, 32, 33, 34, 35, 36, 37).

#### 3.1. Visuospatial (non-foveal) Attention

The classic “Posner” paradigm for studying visuospatial attention (see 38) entails fixation of gaze at a

central spot, and direction of attention to a location removed from the fixation point. Attention effects are found in the comparison of responses to stimuli in the attended location with the responses to the same stimuli, when they were viewed the same way in the same location, but were ignored (i.e. when attention was being directed to a different location). Assuming that sensory variables are controlled for, and that task difficulty is balanced across conditions to control for the effects of arousal, the attend-ignore difference should correspond to the modulation of neural processing due to selectively attending particular locations in space. Considering human and monkey studies together, this is by far the most extensively used selective attention paradigm. However, the ecological validity of the sustained (trial blocked) version of this paradigm as a model for object analysis is arguable, since the overwhelming tendency for primates is to look directly at objects which we are inclined to attend to. There are, of course, exceptions to this. For example, one may be highly motivated to scrutinize the features of another individual, but direct gaze is precluded by shyness, fear or social convention. Generally, however, the tendency to analyze objects with direct gaze is so strong that for both monkeys and humans, we can infer the target of a subject’s attention from their direction of gaze. A trial-by-trial cueing version of this paradigm may be a better model for the attentional components of visual search (39, 40) than it is for selective attention in object analysis. The ecological validity of the Posner paradigm appears much stronger when it is used as a model for attention to peripheral optic flow, induced by the subject’s own movement. Driving a car down a narrow street, or running through a crowd, for example, are both situations in which gaze is held in the direction of movement, but where attention may be focused on the flow of objects streaming by in the near peripheral fields. The study of Treue and Maunsell (36) is a case in point, as it used a variation of the Posner Paradigm to examine the effects of attention on directionally selective responses in cortical areas MT and MST.

#### 3.2. Nonspatial Visual Attention

In visual **feature** attention paradigms, the subject must discriminate a specific feature, such as the shape, texture or color of the visual stimulus, while ignoring all other dimensions of the stimulus. Attention effects for a specific feature are extracted by comparing stimulus evoked responses obtained when the feature in question is attentionally relevant with responses to the same stimulus, viewed the same way, in a condition when that feature is ignored (i.e., another feature of the same stimulus is relevant). The relevant feature is either contained within a stimulus at the point of fixation, or it has the potential to occur at an arbitrary point in the visual field but, *location itself is task-irrelevant*. Assuming appropriate control for sensory and arousal variables, the attend-ignore difference should correspond to a feature attention effect. There have been numerous studies of feature selective attention in human subjects (e.g., (8, 12, 41)), but only two thus far in monkeys (25, 27), and a third which addressed the related issue of “**object** attention” (26). The case in which stimuli are presented at the point of fixation has strong ecological validity as a model for visual attention in object analysis, since, as indicated above, attended objects are

usually fixated directly. Attention to features of stimuli presented away from fixation, again, appears to best apply as a model for visual search.

In an **intermodal** attention paradigm, the subject is required to alternate attention between sensory modalities, in each case discriminating stimuli in one modality (e.g., visual), while ignoring those in the other (e.g., auditory). This may be done in either a blocked (sustained) or trial-by-trial cueing paradigm, and attention effects are extracted by attend-ignore subtraction as described above. Control for arousal effects is no more difficult than it is for the other paradigms. However, control for sensory stimulation in the visual condition requires additional measures (e.g., see (24)), since there is no built-in performance measure to control for eye position and focus, when the subject is attending to the non-visual modality. Nonetheless, several laboratories have successfully implemented intermodal attention paradigms in humans (13, 42, 15, 14, 43, 17, 16, 44, 45, 46) and our laboratory has used this paradigm in monkey studies (23, 24). The intermodal paradigm, particularly in its trial-by-trial cueing form, has strong ecological validity as a model for studying dynamic aspects of attention in multisensory stimulation conditions. One good example would be the salience of combined visual-auditory stimulation in speech perception (e.g. (47)). Furthermore, as in feature attention paradigms, the case in which the visual stimulus is presented at the point of fixation has strong ecological validity in the study of attentional contributions to object identification.

## 4. EFFECTS OF ATTENTION ON BRAIN ACTIVITY MEASUREMENTS

Neurophysiological investigation of the brain mechanisms of attention has used event related potential (ERP) studies in animals (48, 49) and humans (50, 51, 52, 53, 54, 55), and later, single unit recordings in monkeys (18, 32, 56, 33, 21, 57). The study of attention in monkeys has grown rapidly since the mid 1990's and effects have been demonstrated throughout the structures of the primary visual pathways (28, 58, 29, 30, 5, 59, 23, 24, 34, 26, 27, 36, 37), including most recently, the lateral geniculate nucleus (LGN) (60). There has been a parallel expansion in ERP studies and in those incorporating magneto-encephalographic, metabolic and hemodynamic measures, as well as corresponding evidence of attentional modulation throughout the visual processing hierarchy (61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77).

### 4.1. Visuo-spatial attention

The specific effects of sustained visuospatial attention on the visual ERP include enhancement of early P1 and N1 components (8, 78). Initial findings on the specific effects of spatial selective attention on unit firing in monkeys (32), however, diverged significantly from those of the preceding human studies. Effects on unit firing were found only with attention shifts over small regions of visual space, within the confines of unit receptive fields (32), while shifts of attention across visual hemifields, effective in modulating P1 and N1 amplitudes in human studies (8, 79, 78), had no effects on single neurons in V4 (32). Later single unit studies in monkeys conflicted on this

issue. Several studies emphasized the earlier finding that effects of spatial attention operate on and within the scale of single cell receptive fields (30, 34), while others indicated that attention to locations near a cortical unit's receptive field could systematically modulate the response to stimuli presented at a range of locations within the receptive field (28, 58, 31, 33). The latter findings suggest that at a given level of the visual hierarchy, attention can operate on a scale much larger than that of a single unit receptive field. This view is strongly supported by the widespread, recent demonstrations of attentional modulation in V1, in both monkeys (29, 59, 23, 24, 33, 26, 37) and humans (62, 71, 73, 74, 75, 77), because in no case, did the stimuli fit into the confines of a V1 neuron's receptive field.

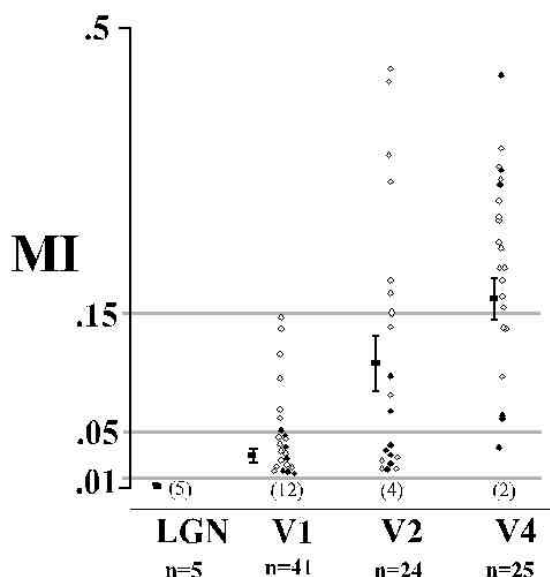
### 4.2. Non-spatial attention

Attention to stimulus features as opposed to locations, produces a sustained negative deflection in the posterior scalp ERP that begins well after the onset of the initial ERP components (80, 8, 12, 41). The same is true of intermodal attention, when a stimulus feature discrimination is required (13, 14). This "selection negativity" (11) has been noted in the occipital surface ERP in monkeys (23), and is believed to arise from an attentional reduction of refractory and inhibitory processes that follow stimulus-evoked excitatory responses in extrastriate cortex (24). It merits emphasis that in these particular studies, while attention does have a profound effect on the later portion of the neuronal response, the initial portion of the response is not modulated by attention. In the few experiments to date that have examined feature and object attention in monkeys, the timing of attentional modulation is consistent, in that it lags the initial sensory response (26, 27). These findings contrast with the observation by some of the earlier studies that attention can produce modulation at response onset (29, 30, 33), and can even modulate the baseline firing-rate of neurons in the absence of sensory stimulation (30). The temporal pattern of attentional modulation has important implications for our understanding of the neural mechanisms of attention and will be considered in greater detail in the following sections.

## 5. AN ANATOMICAL HIERARCHY OF ATTENTION EFFECTS?

The fact that neurons at successive levels of the visual system have increasingly larger and more complex receptive fields and are increasingly influenced by nonretinal input (1) has prompted the suggestion that potential for attentional modulation may increase over successive postretinal stages (11, 31, 81). The subset of earlier studies that held methods constant while investigating different cortical areas and were thus capable of directly analyzing this issue, have suggested an overall trend toward larger effects at higher levels of both the ventral stream (32, 33) and the dorsal stream (36). Recent studies entailing concurrent recordings of current source density profiles across cortical areas (Figure 1), confirm this trend (23, 24).

That is, as can be seen in figure 1, comparison of attentional "modulation indices" yielded by paired penetration sampling of LGN, V1, V2 and V4 reveal that



**Figure 1.** Magnitude of attentional modulation of transmembrane current flow, expressed as “modulation indices,” (MIs) and quantified across penetrations in 2 monkeys. Indices were computed by: 1) sampling laminar CSD profiles at each recording site during attend and ignore conditions, 2) determining statistically significant differences between attend and ignore CSD profiles at each site, 3) integrating the area under the significant difference curve over time in each lamina and averaging across laminae, 4) dividing by the total response for the same data (the absolute value of CSD for attend and ignore conditions averaged together, and then integrated over time and averaged across laminae). MIs were computed for all recording sites and are shown with respect to visual areas labeled on the x axis, with lower visual areas on the left and higher visual areas at the right. Total number of observations are shown at the very bottom. Closed (subject V) and open (subject R) circles denote observations from each of two subjects, and bars represent mean and standard error for each area. Numbers in parentheses between 0 and .01 represent the number of sites for which MIs were less than .01.

within the paradigm used in this study, there is a clear ascending gradient of modulation, with no effect in LGN, small effects in V1, and increasingly larger effects in V2 and V4. However, the often large attention effects in V1, and the variations across different paradigms in the size of attention effects both in monkeys (29, 59, 23, 24, 33, 26, 37) and humans (62, 71, 73, 74, 75, 77) precludes a simplistic conclusion. Thus, while the degree of attentional influence may indeed increase over successive hierarchical stages, current findings also support the view that the level of the system at which attention operates is governed by the precise nature of the stimuli and task demands (11, 81).

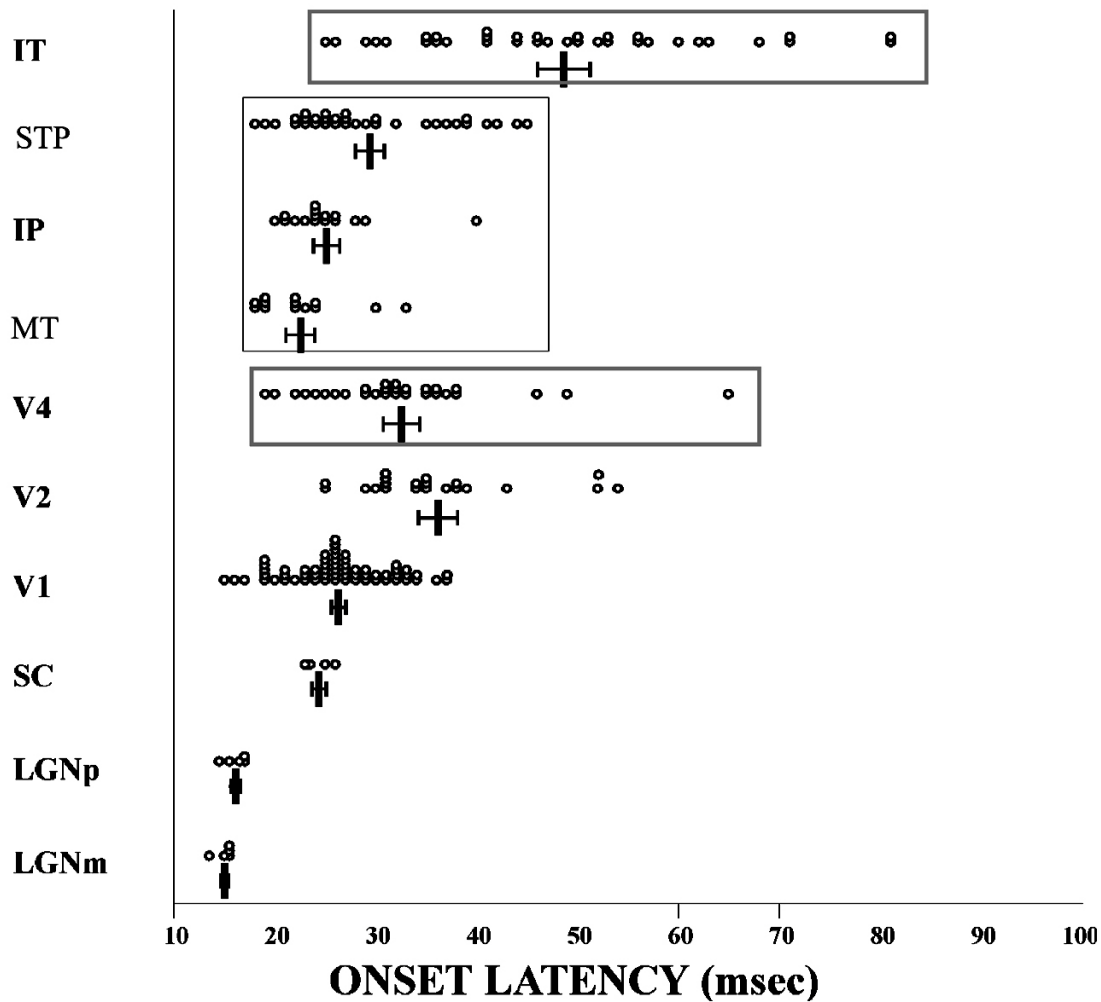
## 6. A TEMPORAL HIERARCHY OF ATTENTION EFFECTS?

Because attention operates on retinal input signals during their transit through the synaptic stages of

the visual pathways, one might expect that the timing of attention effects across levels of the system should parallel that of the input signal (see above). As indicated above, studies in monkeys conflict over whether or not attentional modulation begins at response onset (29, 30, 33), or lags the initial visual evoked response (23, 24, 35, 27, 37). However, as illustrated in Figure 2, the lag of visual response latency across many stages of the hierarchy is extremely small, or even nonexistent (82, 83, 84). This fact is most evident in the timing of responses in dorsal stream areas (enclosed by a dark box in Figure 2).

Moreover, findings from the one set of experiments that directly compared the timing of attentional modulation across levels of the hierarchy (Figure 3), actually revealed an inverse relationship between visual and attention modulation latencies (23, 24). Shown here are grand mean responses compiled by sampling laminar current source density (CSD) profiles during paired penetrations of LGN, V1, V2, V4 and inferotemporal (IT) cortex in 2 monkeys. In each case, the grand mean of the response (combined across attend and ignore conditions -black shading) is contrasted with the proportion of response modulation due to attention (grey shading)

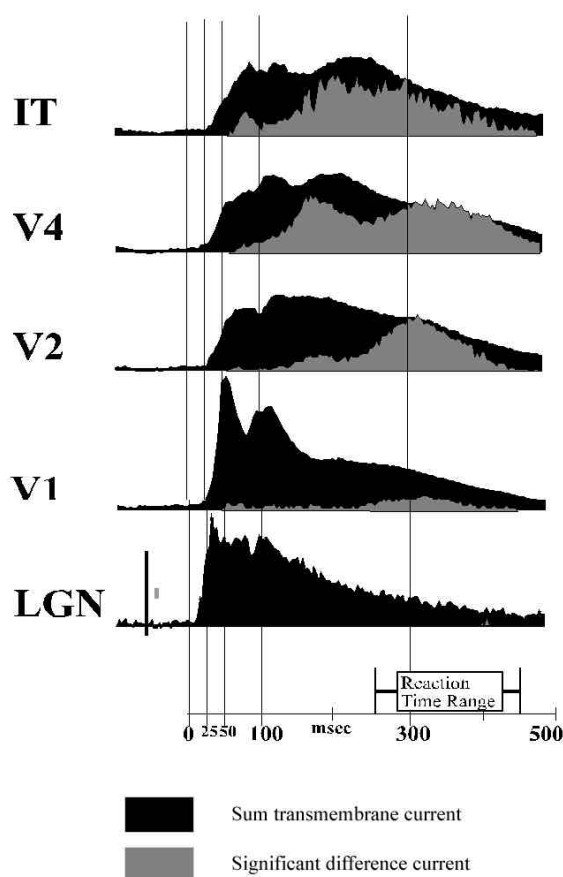
Examination of Figure 3 along with Figure 2 shows that, while onset latencies generally increase along the stages of the visual anatomic hierarchy, attention effects begin first at the higher levels of the hierarchy and then progress back down the system. While the latency pattern of attention effects across visual areas is helpful in determining the circuits utilized by attention (see following section), an equally important question for hierarchical processing models is: In any one location, does attentional modulation build over post-stimulus time? An affirmative answer to this question would indicate that: 1) attention both operates on, and contributes to, the accumulation of information in cell assemblies over post-stimulus time and 2) there is a significant, albeit presently invisible, temporal dimension to the anatomical hierarchy. The simple answer is that although not explicitly analyzed in most cases, this attentional build-up over time is clear in the data from numerous studies, in both monkeys (23, 24, 26, 27) and humans (see 85; 86). Examination of Figure 3 shows build-up of attentional modulation over time in V1, V2, V4 and IT, throughout the epoch leading up to and beyond the initiation of the behavioral response. Significantly, attentional build-up over time can also be seen in data from studies which report modulation at response onset (30, 33). This finding has the important implication that attentional modulation is not solely a tonic, pre-set “bias” of neuronal excitability, but also includes components that are dynamic and “activity driven.” As explained in the next section, attentional modulation can manifest as visual activity-driven feedback, in the absence of any obvious sign of tonic bias of ongoing (pre-stimulus) activity. For paradigms in which this occurs, it seems most useful to discuss the temporal dynamics of attentional modulation in the context of processing models based on numerous temporal components or “waves” of activity (82, 84). In V4 for example, irrespective of attention, there is evidence for



**Figure 2.** Scatter plots of onset latencies, organized by visual area, including the mean and standard error of the distribution for each for each area. Values represent onset latency, as determined with statistically based scoring. Each entry indicates one onset latency, scored for one electrode penetration. To facilitate inspection, a dark box encloses the areas of the dorsal visual pathway, and grey boxes enclose ventral pathway areas. Adapted from (2).

at least two early activity components - an initial modulatory input at ~ 35 ms latency that bypasses supragranular V1, as well as V2, followed by an excitatory feedforward input at ~ 50 ms latency, relayed through supragranular V1 (87, 84). While the initial component is subtle, requiring extensive averaging for resolution, and is unevenly distributed across sites, the latter is robust and reliable. In the intermodal discrimination paradigm, attentional modulation adds a third component that begins at ~100 ms latency and builds until at least 300 ms (23). The second (excitatory feedforward) and third (attention-sensitive) components are evident in the quantified transmembrane current flow patterns illustrated in Figure 4. These reflect a condensation of data from 25 multielectrode penetrations of Area V4 in two monkeys (23, 24). Regarding the present discussion, the main point evident in Figure 4 is that visual processing in V4 appears to consist of an initial attention-independent component (~50 ms duration), followed by an attention-sensitive

component (>300 ms duration). Separable temporal processing components in a location, such as V4, are completely predictable given that inputs from a common source (the eye) travel over several heterogeneous (lateral, feedforward and feedback) pathways and converge on a common location. Nonetheless distinguishing the input routes and origins of different activity components will be important in understanding the mechanisms of temporal processing within any one location (88). The main virtue of the concept of a temporal hierarchy is that it emphasizes sustained interactive processing across multiple levels of the hierarchy and it predicts that in a structure at any level of the system, its highest order representation of a stimulus evolves in the late phase of processing post-stimulus time (88, 89). Thus, the point in post-stimulus time that a neural signal is sampled is as important as the level of the system at which it is sampled, in determining the level of information represented in the signal.



**Figure 3.** Magnitude of attention effects, in relation to the magnitude of the sensory response, quantified from 5 electrode penetrations in LGN, 41 in V1, 24 in V2, 25 in V4 and 17 in Inferotemporal cortex (IT) in two monkeys. For each penetration, laminar current source density (CSD) profiles were sampled in visual attend and ignore conditions. Statistically significant differences between attend and ignore CSD profiles were determined and quantified by taking the absolute value of the significant difference current across each point in the laminar CSD profile, averaging these together), and then averaging across penetrations for both subjects. The resulting grand mean difference current (the dAVREC) represent that quantified effect of attention on visual processing. For each visual area, the attention effect is plotted against total response, that is, the attend plus ignore CSD profiles, condensed in the same way for the same data set (sAVREC). This is procedure similar to that used to compute the MI (Figure 1), except that responses were not integrated over time. The reaction time range to target stimuli is shown at the bottom right (250-450ms). Adapted from (24).

**7. BRAIN MECHANISMS OF ATTENTIONAL MODULATION** While it is likely that there are generally utilized neural mechanisms for attentional control of processing, it merits reemphasis that many details of mechanism are likely to be paradigm-specific.

### 7.1. Neuronal circuits

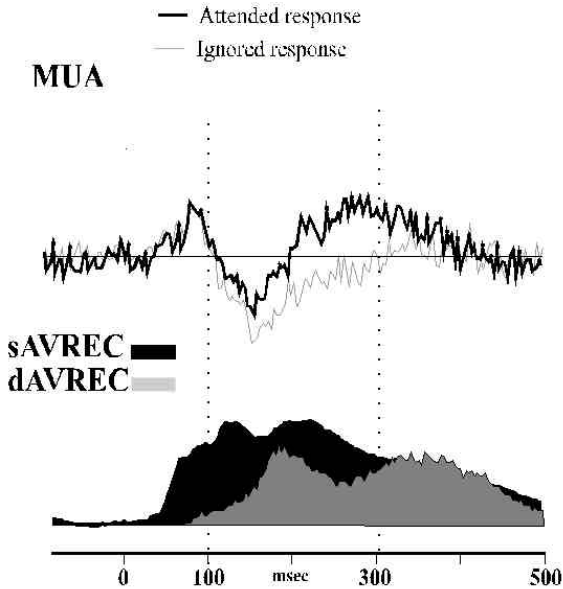
There is a prevailing view that attention is a “top-down” process that uses cortical feedback projections (4, 11, 31, 90, 81). Temporal patterns of “state-dependent”/attentional modulation observed to date (62, 20, 30, 71, 5, 23, 24, 91, 26, 16) provide some support for this view, in that, effects tend to be largest during the late phase of a response; this, at the least, allows time for ascending inputs to trigger feedback modulation.

Additional support for a feedback mechanism arises from a curious discrepancy between hemodynamic and ERP studies in humans. The former have revealed numerous examples of spatial attention effects in V1 (62, 71, 73, 74, 75, 77), despite the fact that ERP studies have consistently found no attentional modulation of the earliest visually evoked component, the so-called “C1”, which is believed to be largely generated in area V1 [e.g. (63, 86, 92, 71)]. Given the low temporal resolution of fMRI techniques, an obvious possibility is that the V1 effects indexed by the fMRI measures occur late in processing, as a result of cortical feedback. This explanation has received direct support from a recent combined fMRI/ERP study (71), which showed: that while spatial attention did not modulate the C1 component, it did modulate both the fMRI signal in V1 and later ERP components localized to V1, consistent with the idea that V1 modulation was a result of cortical feedback.

The timing and laminar distribution of intermodal attention effects, as revealed by concurrent multielectrode recordings across cortical areas [see Figure 3; (23, 24)], also bears on this issue in several ways. First, within each area, significant attentional modulation began relatively late in processing, 50-100 ms after the onset of the local response to the sensory stimulus, and the amplitude of modulation increased over time. Second, the onset latency of attentional modulation was reduced over the successive processing stages represented by V1, V2 and V4. Both of these findings indicate the projection of attentional influences onto sensory processing areas through cortical feedback circuits. Additional support for this interpretation is given by the laminar distribution of attention effects, as illustrated in Figure 5 (23, 24). The main relevant findings are that attentional modulation was distributed across the cortical laminae within each area, and that modulation of extragranular laminae (the layers receiving feedback projections) began as early as, or earlier than that in Lamina 4 (the afferent input layer). This finding strongly supports a feedback model of attentional modulation, in that, the laminar (spatial) profile of modulation onset fits with the pattern of feedback (extragranular onset), rather than feedforward (granular onset) cortico-cortical connectivity (93, 94). Area V1 (Figure 5) provides the clearest example of this.

In V1, the largest effects lagged the local response onset by over 150 ms, their distribution was weighted toward the supragranular laminae and, most importantly, the pattern of modulation clearly excluded the





**Figure 4.** Magnitude of attention effects, in relation to the magnitude of the sensory response, quantified from 25 electrode penetrations of Area V4 in two monkeys. At the top are multiunit action potential histograms (MUA), sampled from Lamina 4 in each of the 25 penetrations, and averaged separately for the attend and ignore conditions within the same selective attention paradigm. Below are the quantified transmembrane current flow patterns for the same penetrations. For each penetration, laminar current source density (CSD) profiles were sampled in visual attend and ignore conditions. Statistically significant differences between attend and ignore CSD profiles were determined and quantified by taking the absolute value of the significant difference current across each point in the laminar CSD profile, averaging these together, and then averaging across penetrations for both subjects. The resulting grand mean difference current is plotted against total response, that is, the attend plus ignore CSD profiles, condensed in the same way for the same data set. Adapted from (23).

initial Lamina 4c response, consistent with the lack of attentional modulation in LGN (23, 24) in this paradigm.

## 7.2. Physiology

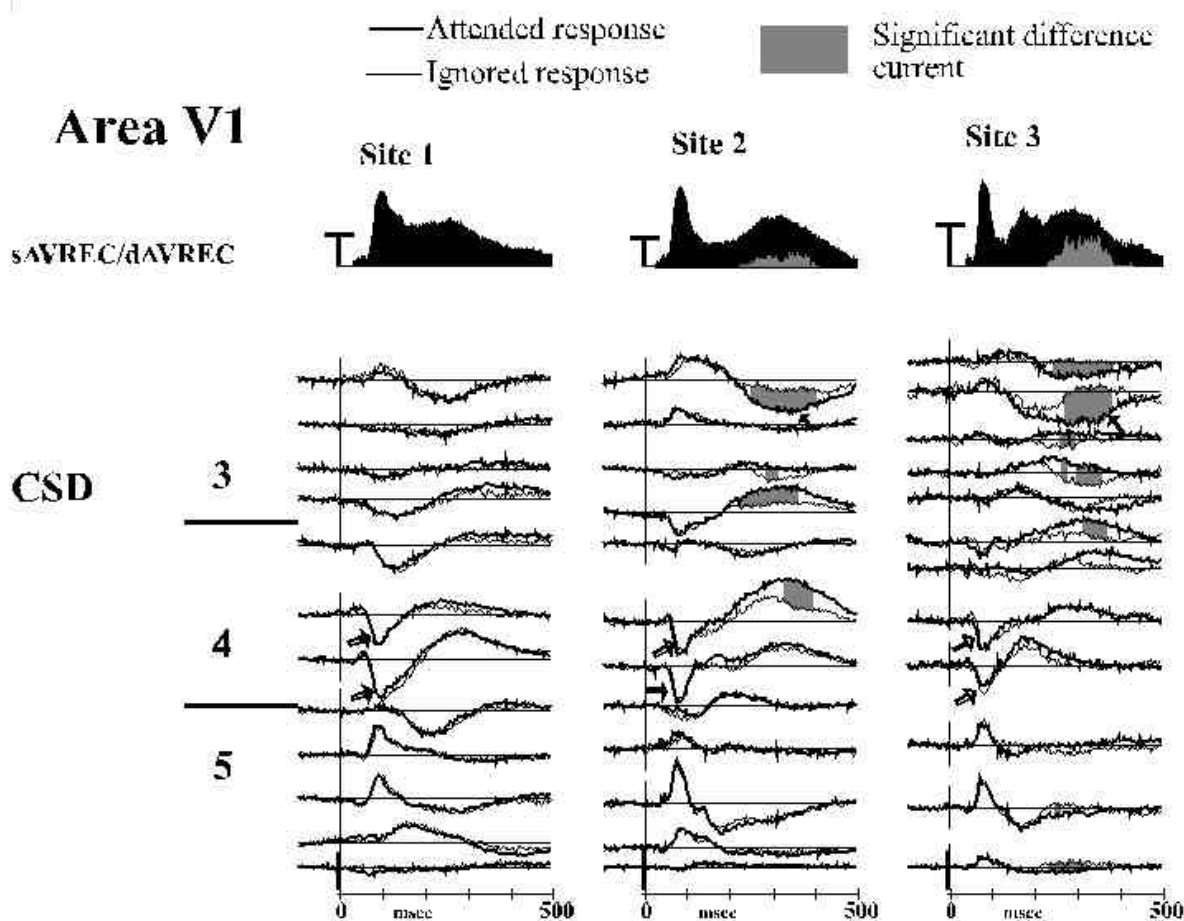
Regardless of the exact circuits that project and coordinate attention's influences, it is of interest to identify the local physiologic processes utilized by attention to modulate neuronal responses. Perceptual attributes of attention predict both enhancement of neuronal responses to relevant stimuli and inhibition of responses to irrelevant stimuli. In spatial selective attention, for example there is evidence for suppression (30, 32) as well as enhancement of a neuron's response to stimulation of attended locations within its receptive field (31, 36). However, with regard to the enhancement effects alone, there are several physiologic mechanisms (e.g., disinhibition vs. enhancement of excitation) that could be involved. We have put considerable effort into characterizing neuronal processes involved in modulation of sensory processing by

intermodal attention (23, 24). In this paradigm, there is an initial "feedforward" excitatory response in Lamina 4 that is not modulated by attention ("1" in Figure 6), followed by a period of marked hyperpolarization ("2" in Figure 6) that limits the excitatory response. The main effect of attention ("3" in Figure 6) on the physiology of V2 and V4 is seen during the period of hyperpolarization (~100-300 ms post-stimulus), and appears to offset the hyperpolarization. Our thinking is that the postresponse hyperpolarization constitutes a mechanism that renders the neocortex generally conservative in its response to any unattended stimulus, so that such stimuli do not effectively activate the higher areas of the system. As shown in Figure 6A, attention's main effect is to increase both the amplitude and duration of the excitatory response, thus overcoming the net post-response hyperpolarization. An hypothetical circuit for this effect is illustrated in Figure 6B.

Regarding the exact cellular mechanism of the attention effect, although it is tempting to conclude that attention "rules by disinhibition," a more parsimonious view is that attention operates through direct enhancement of excitatory responses to visual stimuli, within each processing stage (our first feedback alternative – left). This is consistent with the facts that most corticocortical connections, including the descending ones implicated in attentional control, are excitatory, and that ~90% of feedback afferents target parvalbumin-negative (excitatory, rather than inhibitory) neurons (95). Significantly, while in feedforward connections, excitation is balanced or dominated by inhibition, in feedback connections, the reverse is true (96). It is important to note that when feedforward and feedback inputs are simultaneously active, feedback inputs can provide polysynaptic excitation that can offset slow IPSPs evoked by forward inputs (97). The effects of such feedback excitation may be equivalent to locally-induced disinhibition (98), but regardless, it provides a mechanism for amplifying afferent signals in lower areas (97).

## 8. LINKAGE BETWEEN NEURAL EFFECTS AND THE COGNITIVE IMPACT OF ATTENTION:

Two observations make compelling predictions that merit discussion in the context of our current understanding of the cognitive effects of attention. These are: 1) attention-mediated enhancement of later phases of neuronal responses (above) and 2) attention-mediated increase in prestimulus baseline activity rates (99, 30). While "late enhancement" and "baseline increase" tend to associate with different experimental paradigms, they both appear to represent feedback-mediated increase in neuronal excitability. This increase corresponds to some degree of net depolarization in local neurons, which in turn, is predicted to increase the probability of engagement of N-methyl-D-aspartate (NMDA) receptors. At resting membrane voltages, NMDA receptors are blocked in a voltage-dependent fashion by physiological concentrations of  $Mg^{2+}$ . As a consequence, current flow through NMDA channels occurs only if presynaptic glutamate release coincides with postsynaptic neuronal depolarization (100). *In vitro* studies have shown that this situation can be



**Figure 5.** Laminar CSD and sAVREC/dAVREC comparisons are shown from three recording sites in V1. The attentional modulation ranges from none (site 1) to moderate (sites 2 and 3), though comparable neuronal responses are elicited by the visual stimuli. The initial Lamina 4 response (open arrows) is unmodulated, and later modulation, when it occurs, is distributed primarily in extragranular Laminae. (\*= 1 mV/mm<sup>2</sup>. T = 250  $\mu$ V/mm<sup>2</sup>). Adapted from (23).

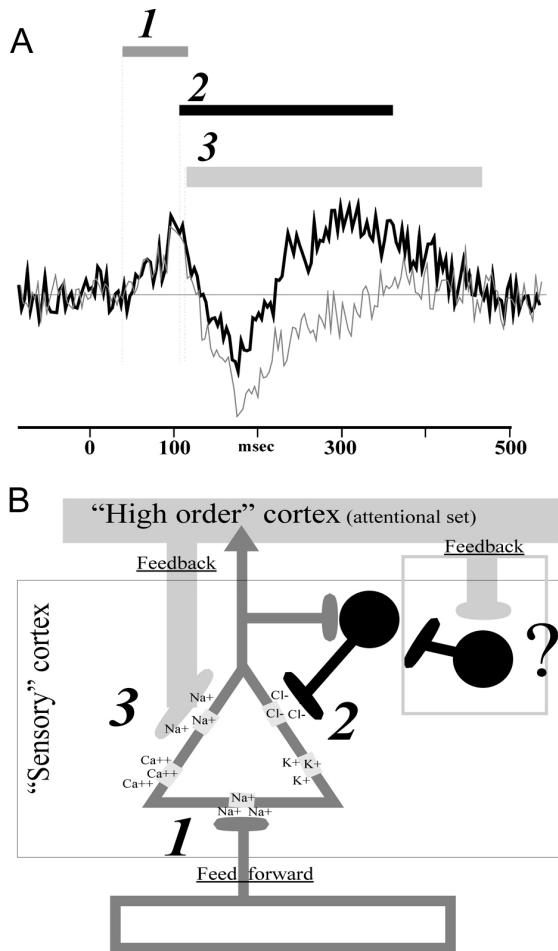
produced by a variety of manipulations, that have in common the increase in postsynaptic excitability [e.g., (101)]. The reason that NMDA receptor activation is important is that it produces two effects relevant to the cognitive phenomenology of attention. The first is a nonlinear increase or amplification of local excitability, related to NMDA receptor gated influx of  $\text{Ca}^{++}$  ions (symbolized by the breaching of ions at the outside of the  $\text{Ca}^{++}$  ionopore in Figure 6 – left). Due to feedforward and feedback connections, this nonlinear excitation transmits itself in a lawful and interesting way (98). The second effect is a potentially enduring change in connectivity.

### 8.1. Neuronal and perceptual amplification

NMDA-mediated increase in excitability is clearly consistent with the phenomenology of attention. Because NMDA-mediated response enhancement appears biased toward the supragranular laminae (98), NMDA enhancement of visually-evoked responses should contribute to the selective enhancement in the perceptual

salience of relevant stimuli. While there is as yet, no direct evidence for this proposition, studies in auditory cortex are supportive of it (102). In keeping with a proposition by Daw et al, (103), we have suggested that the NMDA-mediated excitatory response represents a neural amplifier, which due to its focus in the upper laminae, preferentially influences the ascending feedforward projection circuits (98). Whether or not the attentional increase in excitatory response is NMDA mediated, the association of large, post-response hyperpolarization with the response to irrelevant stimuli in the ignore condition has an interesting implication for the relationship of perception with cortical physiology. That is, “ignorance” of irrelevant stimuli on a perceptual level is an automatic consequence of cortical circuitry and physiology. The net response in cortical ensembles is made essentially conservative, by processes such as after-hyperpolarization and synaptic inhibition. These processes limit net amplitude of the response to any stimulus, and thus its perceptual salience, and for most stimuli, attentional modulation may





**Figure 6.** **A:** Grand mean multiunit response histograms for the attend visual (thick trace) and ignore visual (thin trace) conditions in Area V4, Lamina 4. The same histograms are shown with the associated condensed CSD measures in Figure 3. These illustrate 3 components (1) initial excitatory response unmodulated by attention, (2) post-response hyperpolarization in the ignore condition and (3) attention-mediated offset of refractoriness, and consequent increase of the net excitatory response. **B:** A model circuit to account for the parameters and physiology of intermodal attention effects as observed by Mehta et al (23, 24). The model circuit incorporates a feedforward circuit (dark grey), with excitatory input from a lower sensory level and output to a higher cortical level. Intrinsic inhibitory (presumptive GABAergic) elements are depicted by filled clack symbols. Feedback from higher order cortex is symbolized by broad projections in light grey. The physiology of ascending excitatory (glutamatergic) input (1) is depicted by Na<sup>+</sup> ions breaching an ion channel from the outside. The physiology of postresponse hyperpolarization (2) is depicted by Cl<sup>-</sup> ions breaching an ionopore from the outside near an interneuron synapse (recurrent inhibition) and by K<sup>+</sup> ions breaching a channel from the inside of the cell membrane (after-hypolarization). The physiology of feedback excitation (3) is depicted by Na<sup>+</sup> ions breaching an ion channel adjacent to the synapse made by the feedback projection (left – light grey). An alternate feedback scheme, disinhibition, is depicted to the right. For several reasons, the disinhibition alternative is considered unlikely (see text). The physiology of feedback-induced non-linear excitation is depicted by ions at the outside of a Ca<sup>++</sup> (presumably NMDA-gated) channel.

be necessary to produce a robust response and to allow the input to penetrate effectively to the higher levels of the system.

## 8.2. Dynamic change in cellular connectivity

NMDA receptor involvement in attention-mediated excitation would also be expected to produce potentiation of the specific neuronal connections that are active during the sensory discrimination (104). This suggests an intriguing functional significance for attentional increases in pre-stimulus baseline activity rates (99, 30). If, as is likely, the active neurons are essentially chains, extending through many levels of the visual pathways, NMDA-based potentiation could serve to link relevant neurons at different levels of the system together. One might also suppose that the connections of the “linked” neurons with their neighbors that are not in the relevant chain would be depressed. It is noteworthy that this selective aggregation process predicts neuronal effects associated with attention, such as, “shrinkage of inferotemporal neuron receptive fields around attended stimuli.” In the very short term (i.e., during an experimental session), potentiation and depression would increase the efficiency of processing and lead to improved discriminative performance with practice (105). In the longer term, these processes could provide a causal link between attention and memory (106).

## 9. CONCLUSIONS

### 9.1. Toward an Adequate Model of Attention

From the foregoing discussion, it is clear that selective attention is a flexible process that can operate on a variety of different neural substrates, depending on task demands. Because of failure to acknowledge this basic fact, conceptual definitions and models of attention are often paradigm-specific. Overcoming this limitation is the fundamental step in developing a general theory of attention. The perspective of this review is that an adequate neuroscience-based model of attention must: a) address the operational dynamics of attention, at the least, by being capable of incorporating findings from different experimental paradigms; b) account for the perceptual aspects of attention in terms of specific brain mechanisms, including neuronal circuits, cellular processes and even neurotransmitter systems; c) address the “spatiotemporal dynamics” of attention, that is, it must specify how the neural activity patterns in different brain areas proceed and interact over time.

#### 9.1.1. Operational Dynamics

The “*Biased Competition*” model (4) can account for spatial selective attention at the level of inferotemporal cortex, where receptive fields are quite large. However, its tenet that competition between attended and ignored stimuli occurs within the confines of single neuron receptive fields is often violated by empirical findings. “P1” attention effects, for example, appear in the human ERP when attention is switched across entire hemifields to positions up to 40 degrees apart (8, 67, 71, 76), but the P1 component is generated mainly by extrastriate regions whose receptive fields are generally too small to contain both the attended and ignored stimulus positions. Biased competition confined to single cell receptive fields is supported by some of the attention

## Mechanisms of attentional modulation

effects observed in monkey V2 and V4 (30, 32), but others show that attending to locations outside of a cell's receptive field can affect its firing rate (28, 31, 59). Similarly spatial attention effects in V1 (29, 59, 37) are problematic, as they do not occur on the spatial scale of single V1 cell receptive fields. The biased competition model also predicts increase in baseline firing rates at attended locations, as well as attentional modulation at response onset. As discussed above, these effects are not observed consistently across paradigms. Finally, because of its exclusive reference to spatial location, the biased competition model does not account well for the effects of feature attention (27), object attention (26), or intermodal attention (13, 16, 44, 45, 23, 24, 14). In each case, the primary dimension along which attention is directed is nonspatial. Harter (11), proposed a "*Neural Specificity Model*" which holds that attentional modulation involves both the attentional set (target features, location, etc.) and neurons' sensory selectivities along all target dimensions. This is much like the "*Feature Similarity Gain*" model proposed recently by Treue (27). As broadly stated, either one can incorporate findings in relation to both spatial and nonspatial varieties of attention. More importantly, these models explicitly note that the specific neuronal components used in attentional modulation of processing are flexible and determined by task demands. These are crucial steps toward an adequate model of attention.

### 9.1.2. Perceptual and Neural Mechanisms

Most models of attention acknowledge the correlation between the neural and behavioral/perceptual effects of selectively attending, however, explicit investigation along these lines has been limited. The growing evidence that there are "common circuits" which are observed to participate across a variety of attention tasks in humans (107, 108), is important in this regard, in that it allows one to make predictions that can be addressed by correlating the effects of lesions with cognitive/behavioral deficits in humans and by experimental lesion/inactivation studies in monkeys. A key element in the circuit diagram, is cortical feedback. Whether attentional modulation is due to a tonic bias (30), or to a combination of attentional set and stimulus input (23), the explicit inclusion and investigation of feedback circuitry as a component of the model is critical. Recent studies in both humans (71) and monkeys (23, 24) test the predictions of a feedback model of attention. Similarly, there is an accumulation of evidence pointing to specific physiological processes underlying attentional modulation of sensory processing (23). These processes need to be clearly identified and linked to the populations in which they occur. This will place attention mechanisms directly in the context of current feedforward (and feedback) circuit models of information processing. As discussed above, current evidence also provides strong bases for deriving testable hypotheses about the involvement of NMDA and other neurotransmitter systems. Cellular processes, brain circuits and neurotransmitter components all need to be incorporated into our models of attention.

### 9.1.3. Spatiotemporal Dynamics

The most neglected element of attention effects,

and of sensory processing in general, concerns the interaction between neuronal populations, distributed across neural regions, over time. As reviewed above, attentional modulation in any neuron or group of neurons has a fundamental temporal dynamic. This statement is true no matter how effects are analyzed, and is independent of whether attentional modulation is seen to begin at sensory response onset (29, 30), or to lag response onset (23, 24, 35, 27, 37). The fact that modulation of neural activity over time occurs in different neuronal populations distributed across cortical regions (30, 23, 24, 36) underscores the fact that the temporal dynamic has a spatial dimension. Although concurrent neural recordings across areas suggest that higher cortical regions utilize phasic, "data-driven," feedback to control processing in lower cortical areas (23, 24), this theme has not yet been explored in detail. It is increasingly evident that we can and should analyze temporal patterns of attentional modulation, both within and across brain areas. These patterns provide critical information on the *dynamics*, the very "flesh on the bones" of attention.

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