Intermodal Selective Attention in Monkeys. II: Physiological Mechanisms of Modulation

Of all areas studied in the accompanying study, attention effects were most consistent and well resolved in V4. In this study, to define some of the anatomical circuits and neural processes underlying the influence of attention, we examined the laminar distribution and physiology of attention effects in V4 and in two lower areas, V1 and V2. Laminar event-related potential (ERP), current source density (CSD) and multiunit activity (MUA) profiles allowed identification of processes occurring in the local ensembles, as well as their sequence and laminar distribution. These methods also permitted us to analyze the brain processes reflected in attention-sensitive components of the surface ERP. As outlined in the previous study, the first robust modulation by attention occurred in V4 during the 100–300 ms poststimulus interval. This is the time frame of the net refractoriness which follows the net local excitatory response to luminance increment. Over this interval, attention reduced CSD amplitudes and increased action potential firing rates, findings consistent with disinhibition as a mechanism for attention in V4. Similar effects were observed during the 100–300 ms time frame in V2. In V4, attention had no effect on the initial excitatory response at the depth of lamina 4, but it did produce large modulations in supragranular and deep laminae, origins of both feedforward and feedback projections. Attentional modulation in V2 was later than in V4 and concentrated in extragranular laminae, with no modulation of the initial layer 4 response. Attentional modulation in V1 was smaller and still later than that in V2 and was focused in the supragranular laminae. In this paradigm, attention did not modulate either the response in lateral geniculate nucleus (LGN) or the initial excitation in lamina 4C of V1. The timing of effects across areas and the laminar distribution of effects within areas indicate that attention effects are mediated by feedback projections. Moreover, our findings suggest that attention may increase the perceptual salience of stimuli by reducing stimulus-evoked refractoriness and/or inhibition in cortical ensembles. Finally, attentional modulation of transmembrane current flow in V4 produced a sustained negative deflection in the laminar ERP profile, that was manifested in the ERP over the occipital surface. This posits a mechanism for the ‘selection negativity’, a scalp ERP effect noted under similar experimental conditions in human subjects.

Introduction

Numerous varieties of selective attention have been identified (Parasuraman, 1984) but only a subset of these have been studied in detail at the physiological level. Earlier studies using noninvasive measurement techniques in human subjects have suggested that several of the varieties of selective attention contribute to perception by modulating sensory processing within multiple cortical areas (Harter et al., 1982; Moran and Hillyard, 1988; Corbetta et al., 1991) [this area has also be reviewed recently (Tootell et al., 1998; Martinez et al., 1999)]. For one of these varieties — visual spatial selective attention — effects on multiple cortical areas have been amply confirmed by direct intracortical recordings in monkeys (Moran and Desimone, 1985; Maunsell, 1995; Connor et al., 1996; Treue and Maunsell, 1996; Luck et al., 1997; Roelfsema et al., 1997; Vidyasagar, 1998; Ito and Gilbert, 1999; McAdams, 1999; Reynolds et al., 1999; Treue and Trujillo, 1999). Another variety — intermodal attention — has been implicated by human studies in the modulation of sensory processing at multiple cortical locations, as well as in subcortical structures (Hackley et al., 1990; Alho et al., 1992; Woods et al., 1992; Eimer, 1993). The companion study (Mehta et al., 2000) confirmed that the effects of intermodal selective attention are also distributed across multiple cortical areas in monkeys. Two generalities emerged regarding the areal distribu- tion of intermodal selective attention effects. First, attentional modulation was larger in the ventral than in the dorsal stream. Second, attention effects on processing were larger in the higher areas of the ventral stream than in the input pathways. We observed no attentional modu- lation in lateral geniculate nucleus (LGN), small modulations in V1 and successively larger modulations in V2 and V4.

Such an ascending gradient of attentional influence over processing is consistent with earlier findings both in human (Heinze et al., 1994; Tootell et al., 1998; Martinez et al., 1999) and monkey (Treue and Maunsell, 1996; Luck et al., 1997; Mehta et al., 2000) studies and is consistent with the general propositions of a processing hierarchy (Maunsell, 1995). In the present study we explored further the mechanisms of attentional modulation in the portion of the visual system within which intermodal attention effects were largest and most consistent, i.e., in area V4 and in its input pathways.

A significant part of our effort to relate selective attention to the hierarchical model of cortical processing lies in defining the anatomical circuits that project attention’s influence onto the different cortices. It is widely assumed that attentional modulation reflects the action of a ‘top-down’ mechanism using corticocortical feedback projections (Harter and Aine, 1984; Olhausen et al., 1993; Desimone and Duncan, 1995). Temporal patterns of ‘state-dependent’/attentional modulation observed to date (Haenny and Schiller, 1988; Maunsell, 1995; Luck et al., 1997) provide some support for this view, in that effects tend to be largest during the late phase of a response. The timing of intermodal attention effects as revealed by the companion study bears similarly on this issue. 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 decreased over the successive hierarchical stages represented by V1, V2 and V4. Both of these results align best with the projection of attentional influences onto sensory processing areas through cortical feedback circuits. A promising approach to this issue that is largely untapped is examination of the laminar distribu- tion of attention effects. This can help to dissociate feedforward
from feedback modulation, because the laminar patterns of origin and termination for descending and ascending projections are distinctive in many structures (Rockland and Pandya, 1979; Felleman and Van Essen, 1991). The first goal of this study was to define the laminar pattern of attention effects in V1, V2 and V4.

Regardless of the exact circuits that project and coordinate attention’s influences, it is of interest to identify the local physiological 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 regard to spatial selective attention, there is evidence for suppression of unattended input (Moran and Desimone, 1985; Luck et al., 1997) as well as enhancement of a neuron’s response to stimulation of attended locations within its receptive field (Maunsell, 1995; Treue and Maunsell, 1996). However, there are several physiological mechanisms (e.g. disinhibition versus enhancement of excitation) that could accomplish these effects, and thus the second goal of this experiment was to elucidate the physiological processes underlying intermodal attention effects in V1, V2 and V4, particularly in the latter two, where effects are moderate to large.

Human selective attention paradigms that entail feature discrimination of stimuli presented at fixation tend to produce an attention-related negative deflection in the posterior scalp ERP (Harter et al., 1982; Hillyard and Munte, 1984; Hillyard, 1985; Alho et al., 1992; Woods et al., 1992). This ‘selection negativity’ (Harter and Aine, 1984) is very similar to the effect we noted in the occipital surface ERP in monkeys. A third goal of the present study is to elucidate the physiological processes contributing the selection negativity and to define their laminar distribution.

Materials and Methods

For each of five experiments in LGN, 41 experiments in V1, 24 experiments in V2 and 25 experiments in V4, a linear array multi-electrode was positioned to span the laminar expanse of each area (e.g. Fig. 1a), and laminar current source density (CSD) profiles elicited by the visual stimuli were sampled while subjects performed the discriminations. The same signals were also high pass filtered (500 Hz; roll-off 24 dB/octave), then full-wave rectified, in order to extract multiunit activity (MUA). Previous studies have established procedures for combined application of CSD and action potential profile analysis in striate and extrastriate cortices of awake monkeys (Givre et al., 1994; Schroeder et al., 1995, 1998).

The angle and position of electrode penetrations were guided by each subject’s MRI (Schroeder et al., 1995; Schroeder et al., 1998). Continuous electroencephalographic (EEG) and MUA signals were recorded from all electrode contacts, digitized at 2 kHz and stored with records of vertical and horizontal eye position, stimulus events, and lever responses.

Attention effects were assessed by comparing responses to discriminated visual stimuli (attend-visual condition) with responses to the same stimuli when looked at, but ignored, during performance of equally difficult auditory discriminations (ignore-visual condition). Definition of laminar activity patterns associated with attentional modulation of
sensory processing and underlying attention-induced deflections in the surface ERP is facilitated by the use of linear array multielectrodes, because these permit simultaneous sampling of responses across the laminae of a cortical structure. Laminar CSD analysis indexes transmembrane current flow (Nicholson and Freeman, 1975). This is the first-order response to synchronous synaptic input, and it generates postsynaptic potentials, and thus initiates action potentials. CSD analysis, in combination with analysis of local action potential profiles (indexed by MUA), provides a sensitive means of identifying net excitatory and inhibitory processes, and does so at a level of analysis appropriate for examining processes occurring in ensembles of neurons, distributed across the depth of a region of interest (Schroeder et al., 1998). The fact that the transmembrane current flow patterns, indexed by CSD analysis, are also the prime generators of surface ERPs (Schroeder et al., 1995), also makes the CSD measure ideal for the purposes of the present study.

Quantification
We applied several strategies for data quantification. Condensed representations of the CSD profile were derived with three variations: (i) a simple Average Rectified current flow waveform (AVREC) obtained by full-wave rectifying each waveform of one CSD profile and averaging across the profile; (ii) the sum AVREC (sAVREC) obtained by summing attend and ignore AVRECs; and (iii) the difference AVREC (dAVREC) obtained by subtracting ignore CSD from attend CSD profiles prior to rectification, and then deriving an average of the rectified difference CSD profile. The sAVREC reflects total transmembrane current flow summed across attend and ignore conditions, while the dAVREC reflects the net attend-ignore difference in transmembrane current flow.

Results
Based on both surface ERP data and intracortical recordings, the companion paper defined mid-latency (100–300 ms) and long-latency (300–500 ms) windows during which intermodal selective attention modulates stimulus responses across a number of visual areas (Mehta et al., 2000). Here, we examine further the mechanism(s) operating during these activity phases in areas V4, V2 and V1, as well as the contributions of these areas to surface ERPs.

Attentional Modulation in V4
CSD and MUA profiles from one V4 recording (Fig. 1a) illustrate a typical laminar activation sequence elicited by the stimulation used here. In V4, the onset of layer 4 activation is usually preceded by a low-amplitude modulatory input, evident as a series of short-latency current sources and sinks, distributed throughout the laminae, with little or no correlated change in MUA (Givre et al., 1994; Schroeder et al., 1998). The initial excitatory response is observed at the depth of lamina 4 (open arrow — current sink and MUA beginning at ~50 ms latency). This is followed by activity in the extragranular laminae. Figure 1a also illustrates four reliable findings concerning attentional modulation of mid latency (100–300 ms) activity in V4 and the consistency of these findings across the V4 sample is illustrated in Figures 2–5.

First, attentional modulation of short latency (<100 ms) activity, including the initial excitatory response in lamina 4 (open arrow) was small and irregular, while modulation of mid latency (Figs 1–5) and longer latency (Figs 3, 4) phases of the response was robust (shaded regions indicate significant modulation — see Materials and Methods). Second, during the mid-latency interval, CSD amplitude was significantly reduced by attention, and this was associated with attention-induced
relief of the MUA suppression that typically follows the net local excitatory response to an ascending sensory input (filled arrows in Figs 1, 3, 4). Third, significant modulation was distributed throughout the laminae of V4 (Figs 1, 3, 5). Fourth, effects of attention on transmembrane current flow patterns over the 100–300 ms interval in V4 generate local field potential effects that are consistent in sign and time course with a sustained attention-induced negative deflection in the surface ERP (see Figs 1a and 5 – top).

Overlay of the sAVREC and dAVREC waveforms from the CSD profiles in Figure 1a is shown in Figure 1b. These AVREC variants reflect total transmembrane current flow and net attend-ignore difference in current flow respectively (see Materials and Methods). A quantitative version of the same sAVREC/dAVREC comparison based on cross-subject, grand mean waveforms from V4 is shown in the companion paper (Fig. 9). As suggested above, significant attentional modulation in V4 occurs in the period after 100 ms. We quantified the net effect by computing a modulation index (MI), the ratio of the time-integrated dAVREC to the time-integrated sAVREC. The MI for the site shown in Figure 1 equals 0.29. The average MI computed for all V4 sites was 0.16 ± 0.02, which corresponds to an average 38% modulation of the lower-amplitude response.

The direction of the effect over the 100–300 ms interval is addressed by overlay of attend (Fig. 1c, thick lines) and ignore (thin lines) AVRECs. Additional examples of the same comparison are given in Figure 3 (bottom) and a grand mean (across-subject) version of this comparison is shown in Figure 4. The same comparison for the long latency (>300 ms) period in Figures 3 and 4 shows that attention effects in this interval reflected a net increase in transmembrane current flow, and were thus opposite in direction to those in the mid latency interval. Direction of the modulation was quantified using a direction index (DI), the ratio of the difference between the time-integrated attended and ignored AVRECs to the time-integrated sAVREC. The average DI computed for all V4 sites over the mid latency interval was −0.09 ± 0.03. Over the long latency interval average DI was 0.11 ± 0.06. The preponderance of negative DIs (21/25 sites) indicates that attention reduced net transmembrane current flow amplitude across V4 during the 100–300 ms interval, and the preponderance of positive DIs in the long latency interval indicated net attention-induced increase in transmembrane current flow amplitude during the 300–500 ms interval.

Physiology

The processes reflected in attention effects over the 100–300 ms interval are characterized by the CSD–MUA comparison (Figs 1a and 3 – between the dotted drop lines). In the ignore condition, the lamina 4 current sink (net inward transmembrane current flow; open arrow) is associated with increased MUA. This reflects feedforward cortico-cortical activation from lower areas of the visual hierarchy (Givre et al., 1994), which exhibits modest to no attention effect. During the 100–300 ms interval for the ignore visual condition, there is a marked depression of MUA. Depression of MUA below the prestimulus baseline indicates that coincident CSD components index net local hyperpolarization (Givre et al., 1994; Schroeder et al., 1991, 1998). Thus, after the net excitatory response to the ascending input, there is a period of net reduction in excitability or refractoriness in the local ensemble. Significant attention-induced reduction of CSD amplitudes between 100 and 300 ms is associated with relief of MUA depression, indicating that the main effect of attention is to reduce the net postexcitatory refractoriness of the local neuronal ensemble. As indicated above, attentional modulation of CSD and MUA is similar across laminae. Consistency of attention’s effect on V4 physiology is illustrated by additional examples of lamina 4 MUA modulation in different subjects (Fig. 2) and a grand mean for these measurements (Fig. 4). dAVRECs from the individual observations (Fig. 2) and a grand mean dAVREC (Fig. 4) confirm significant CSD modulation over the same interval as the relief of MUA suppression. Based on the same set of comparisons for the 300–500 ms interval, the physiology of attentional modulation in this period is less clear. Comparison of the post-300 ms CSD and MUA profiles (Fig. 3) shows that the only correlate of attentional increase in transmembrane current flow is a slight increase in MUA in the attend relative to the ignore condition. This CSD/MUA configuration is suggestive of attentional increase in local neuronal excitability; however, although the CSD amplitude increase is significant, the MUA effect in Figure 3 is small and is not maintained throughout the late epoch in the grand mean data for lamina 4 (Fig. 4).

Laminar Distribution

Anatomically, it has been shown that inputs to V4 include both ‘ascending feedforward’ inputs to lamina 4 from V1 and V2 and ‘descending feedback’ inputs to superficial and deep laminae from higher-level areas of the temporal stream (Rockland and Pandya, 1979; Felleman and Van Essen, 1991). Thus the laminar pattern of attention effects in a cortical region provides clues to the anatomical mechanism which projects attentional modulation onto sensory responses. As illustrated in Figures 1–5, the excitatory response onset at the depth of lamina 4 is unmodulated (open arrow Figs 1 and 3), indicating that the initial feedforward input is unaffected by attention. On the other hand, mid latency and long latency activity throughout the laminae, is significantly modulated by attention. The consistency
of these observations is illustrated by data from additional V4 sites (Figs 3, 5). Thus, based on laminar distribution, as well as timing, attention effects in V4 most likely reflect the influence of descending or feedback cortical projections. The main alternative possibility is that feedforward input from V1 and V2 is, in itself, differentially sensitive to attention over time, so that the early phase of the output of V1 is not modulated by attention, but the later phase of the output is. This possibility is rendered unlikely by results in V2 and V1 (see below).

**ERP Contributions**

The main attention effect noted in the monkey surface ERP is a negative deflection occurring reliably between 100 and 300 ms poststimulus, in the attend relative to the ignore condition (see Fig. 1a, top). As pointed out above, this appears to correspond to the selection negativity in the human ERP. A selection negativity is evident in surface ERPs recorded simultaneously with each of the laminar activity profiles shown in Figure 5 (top), as well as in the grand mean surface ERP (preceding paper, Fig. 10, bottom). In the laminar ERP profile (Fig. 5, left column), attention-induced negative deflection of the ERP is prominent in the time between 125 and 275 ms, where it appears to stem from a reduction of a large positive ERP component (asterisk) in attend relative to ignore visual conditions. CSD analysis of these profiles (next column) reveals several current sources that appear to contribute to the positive ERP component in the ignore visual condition. These current sources, like the positive ERP component are reduced by attention. Figure 5 also illustrates the point that only a portion of the attention effect visible in the intracortical ERP distribution is manifest in the surface ERP. Moving toward the pial surface across the depth marked by the asterisk (Fig. 5, left), there is a clear amplitude drop in the positivity, associated with a current sink/source configuration. That is, in the ignore condition, the negative deflection of the net field potential...
stemming from the superficial current sink partially masks the large positivity generated by the underlying current sources. This appears to reduce the size of the selection negativity at more superficial sites. The qualitative similarity of the attend and ignore CSD profiles suggests that the sink/source configuration is a part of the laminar activation profile that is largely determined by local anatomy. The size of the sink/source is reduced by attention, resulting in a late, relative negativity in superficial laminar recording sites. This effect appears to volume conduct to the brain surface and to manifest as a late negative deflection in the ERP. That is, relative negativity in the attend versus ignore ERPs (e.g. Fig. 6, top) is coincident with attentional modulation of CSD components; this point is elaborated below. It is important to note that, despite the wide variation in the size of attention effects across recording sites in V2 (Mehta et al., 2000), modulation form and amplitude were reliable across trials within a recording site. Reliability of the above observations across the sites with significant attention effects is addressed by Figures 7–9. Magnitude of effects was quantified as in V4, using the MI (Fig. 6b) (Mehta et al., 2000). The direction of effects is addressed by overlay of attend and ignore (Fig. 6c, think versus thin traces) and quantified using the average DI. Average DI over the 100–300 ms interval was –0.04 ± 0.02, and over the 300–500 ms period, the corresponding value was 0.06 ± 0.05. On average, therefore, and as in V4, transmembrane current flow was decreased (19/24 cases) by attention in the mid latency period and increased by attention in the long latency period (15/24).

**Physiology**

The laminar activity profile in the ignore visual condition outlines a characteristic activation sequence in V2. The MUA increase at the depth of lamina 4 (Fig. 6, open arrow) is collocated with a current sink. The increase of MUA in the presence of a current sink is consistent with a feedforward excitatory input response (Schroeder et al., 1991; Givre et al., 1994). Given the laminar specificity of this afferent input to V2 (Rockland and Pandya, 1979; Lund, 1988), this CSD/MUA configuration appears to reflect the main input from area V1, and it is followed by activation of the extragranular laminae. Little attentional modulation of this excitatory response was...
detected in either CSD or MUA. It is important to note that none of the MUA tracings shown in Figures 6–9, nor those from V4 (Figs 1, 2, 4), were baseline-corrected, and thus would reveal attention-related changes in baseline neuronal firing if it were present in net neuronal firing. Following this largely unmodulated excitatory input, there was typically a depression of the MUA between 100 and 300 ms, poststimulus, in both granular and extragranular laminae (Fig. 6, filled arrows). This depression was most pronounced in the response to ignored visual stimuli. In the response to attended stimuli, this MUA depression was reduced or transformed into a later excitatory burst. Additional examples of this comparison based on lamina 4 MUA recordings from each of the subjects are shown in Figure 7, and the grand mean of all lamina 4 MUA recordings is shown in Figure 9 (middle). The modulation of coincident CSD components entailed a reduction in CSD amplitude or even change in direction of transmembrane current flow (Figs 6, 8 — left, filled arrows). This attention effect was characteristic of most recording sites in V2, as shown by comparison of the grand mean AVRECs for the visual attend and ignore conditions (Fig. 9). Thus, when visual stimuli were ignored, the response they elicited during the 100–300 ms period was limited by a period of net refractoriness that appeared to be coupled to the excitatory response. On the other hand, when attended, the same visual stimuli tended to elicit a more sustained excitatory response during the mid latency period. Although attention produced a significant increase in transmembrane current flow between 300 and 500ms (above), there were no consistently related

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**Figure 8.** Laminar profiles obtained from concurrent dual electrode recordings in V1 and V2 show differential modulation by attention across visual areas. Laminar profiles of ERP and CSD are shown for V2 (left) and V1 (right), with responses to attended (thick lines) versus ignored (thin lines) visual stimuli overlaid. In both cases, laminar profiles are depicted with the pial side up, so that in the case for V2, the deepest channel of the recording array is positioned at the most superficial Laminae. The VEP shows modulation at both sites, since it indexes both local and distantly generated phenomena. (I = 50 µV). However, the locally generated CSD shows little modulation in V1, while at the same time, the CSD in V2 shows marked modulation. (I = 1 mV/mm²). The sAVREC/dAVREC waveforms collapse laminar information to depict the modulation across time (T = 250 µV/mm²). When integrated over time, MIs for this V1 and V2 site are 0.0164 and 0.294 respectively.

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**Figure 9.** Grand mean AVRECs for V2. (Top) AVRECs for the attend (thick lines) and ignore (thin lines) conditions are normalized with respect to average transmembrane current flow and averaged across all V4 penetrations in both subjects. The attend–ignore overlay shows that, from 100 to 300 ms poststimulus, attention reduces the amplitude of transmembrane current flow evoked by visual stimuli. (Middle) Equivalently normalized and averaged layer 4 MUA shows initial (<100 ms) elevation of action potential firing rate, followed by suppression below baseline firing rate over the 100–300 ms interval that is marked for ignored stimuli. The dAVREC outlines the normalized and averaged significant difference in current flow to occur over the same 100–300 ms interval as the relief of MUA suppression. Scale bar = 0.125 × average transmembrane current flow.
changes in the MUA profile, and thus the physiology of the late modulation is currently unknown.

Laminar Distribution
In Figure 6 and in the additional case displayed in Figure 8 (left), response onset at the depth of lamina 4 was unmodulated (open arrows), indicating that the feedforward input is unaffected by attention. On the other hand, later activity, distributed throughout the laminae, was strongly modulated by attention. Thus, based on laminar distribution, as well as timing, attention effects in V2 most probably reflect the influence of descending or feedback cortical projections. As for V4, the main alternative possibility is that feedforward input, in this case from V1, is differentially sensitive to attention over time, so that the early phase of the output of V1 is not modulated by attention, but the later phase of the output is. This possibility is not supported by findings in V1. On the right side of Figure 8 is displayed a V1 laminar activity profile recorded simultaneously with the V2 profile (left). Three additional examples of V1 profiles are given in Figure 10. The main finding in V1 relevant to the attention sensitivity of the initial response epoch in V2 is that statistically significant attentional modulation is extremely small and late (>250 ms latency). In this case, there is a striking lack of early modulation (<250 ms) in the supragranular laminae, which are the source of the major ascending inputs to V2 (Rockland and Pandya, 1979). This conflicts with the idea (above) that late attentional modulation in V2 is ‘fed-forward’ from V1.

Contributions to Surface ERPs
Above the CSD profiles in Figure 6 are the simultaneously recorded surface ERPs. These show the typical attention-induced negative deflection between 100 and 300 ms poststimulus. Inspection of the laminar activity profiles concurrently sampled from V1 and V2 (Fig. 8) suggests differential contribution of these regions to the selection negativity in the surface ERP. While attend–ignore differences are evident in the intracortical ERP profile in both regions, as shown by the CSD analysis, only those observed in V2 receive large contributions from local transmembrane current flow. There are several complexities in considering a V2 generator of surface ERPs. First, gross V2 anatomy is convoluted, such that only a small strip of V2 near the V1/V2 border has its pial surface pointing toward the brain surface, while in the remainder of V2, the orientation of the cortex is radial to or even away from the brain surface. Second, local field potential patterns in V2 are clearly contaminated by intrusions from nearby regions. In sites along the underside of the striate operculum, which are thus oriented away from the occipital surface, the first ERP component is a positivity peaking...
at 65 ms (see dotted lines, Fig. 8), which receives little contribution from transmembrane current flow in V2, but falls off linearly in the direction of the pial surface and is largely unmodulated by attention. This is a volume-conducted manifestation of a component that arises primarily from initial thalamocortical activation in the overlying regions of V1 (Schoeder et al., 1990, 1991, 1997, 1998; Givre et al., 1994, 1995). Third, ERP components that are generated in V2 portions not immediately on the brain surface suffer passive decay, interference and cancellation in volume conduction through other cortical regions toward the brain surface. An ERP positivity peaking at ∼225 ms, for example (see dashed lines Fig. 8, right), is mainly generated by current sources in V2. These are associated with net postexcitatory hyperpolarization of neurons in V2 (see Figs. 6, 7, 9), and are modulated by attention. The main positive ERP component (P225) is severely attenuated as it is volume conducted through the laminae of V1 toward the occipital surface (Fig. 8, right). That is, the positivity evident in the deep laminae of V2 (those nearest the white matter aspect of V1) falls off rapidly over the several millimeters comprising the laminar depth of V1, and surface ERP recordings show little evidence of this component (e.g. Figs 1, 5, 6 and Fig. 10 in the companion paper). The degree to which attentional modulation in V2 during either the 100–300 or the post-300 ms time frames manifest in the surface ERP distribution is unclear. The selection negativity between 100 and 300 ms is not apparent even in concurrent recordings from the nearby deep tissues of V1; these show the opposite (positive) attend/ignore deflection of the ERP waveform. Thus, while attention clearly modulates transmembrane current flow patterns in V2, the effects of this modulation are not clearly apparent in the surface ERP in the monkey. Similarly, while there is an average attention-related increase in transmembrane current flow over the 300–500 ms period in V2, this effect is inconsistent across recording sites and is, therefore, difficult to relate to late attention-induced positive deflection in the surface ERP.

**Attentional Modulation in V1**

The accompanying paper shows that, under our experimental conditions, attentional modulation was much weaker in V1 than in V2 (Mehta et al., 2000). Of 40 V1 penetrations, 40% were in sites displaying no significant attentional modulation, 38% revealed weak modulation and 18% revealed moderate levels of attentional modulation. One profile from each category is shown in Figure 10; these profiles display MIs of 0.0, 0.07 and 0.12. Note that across the cases shown, automatic stimulus-evoked activity was comparable, so that the amplitude of the attention effect does not appear to be directly related to the quality of the response. As shown previously (Schoeder et al., 1990, 1991, 1997, 1998; Givre et al., 1994, 1995), the laminar activation sequence elicited by visual inputs in V1 consists of initial depolarization (current sinks associated with MUA bursts) in thalamic input sublaminae 4cα and 4cβ (open arrows), followed by activation of the extragranular laminae. The small attention effect displayed in Figure 8 (filled arrows, right) represents one of the earliest attention effects we have recorded in V1, but even in this case, the onset of attention effects lags the onset of the neuronal response initiated by the afferent volley. Effects shown in Figure 10 have the more typical (late) timing.

**Physiology**

In contrast to the initial epochs of attentional modulation in V2 and V4, attention tends to produce an increase in CSD amplitude in V1. This is most clearly evident for the larger effects in Figure 10 (middle and right). However, there is no detectable MUA correlate to the attentional modulation of the CSD profile. This is typical of our V1 recordings. Therefore, while attention does appear to modulate excitability during the late response phase in the extragranular laminae of V1, the physiological processes underlying the effects are unclear.

**Timing and Laminar Distribution**

The examples shown in Figure 10 and the grand mean AVRECs and dAVRECs for V1 (Fig. 11) show that modulation of low and moderate amplitude is detectable during the late phase of the response, between 200 and 400 ms poststimulus. The laminar CSD profiles (Figs 8, 10) show that significant attentional modulation occurs mainly in the extragranular laminae. Although the initial response in lamina 4c is robust, it displays no detectable attentional modulation. These were consistent observations across the data set, with average MIs computed at granular lamina (0.036) being significantly (P < 0.01; t-test) smaller than average MIs computed at extragranular laminae (0.065), for sites displaying modulation (MI > 0.01). Long latency and extragranular distribution is particularly clear for larger V1 effects (Fig. 10, center and right).

**Lack of Attentional Modulation in LGN**

Five electrode penetrations were made into the right hemisphere of the LGN of one subject. Reconstruction of the electrode tracts revealed that electrodes were positioned in the posterior region, near the dorsal pole of the LGN and usually straddled both M and P laminae. This region of the LGN includes the foveal and immediate parafoveal representation of the lower contralateral quadrant (Maple, 1975; Connolly, 1984). Positioning of the electrode was guided by the pattern of voltage gradients and MUA patterns that have previously been shown to delineate the M and P laminae, and by alternating monococular stimulation (Schoeder et al., 1989, 1990, 1992). In two cases, an extremely small late modulation was noted. However, the average MI across the LGN was 0.001 ± 0.0008, and the MI computed within the LGN was always <0.01.

**Discussion**

The companion paper reveals that intermodal selective attention modulates visual processing in multiple cortical areas, with a distinct distribution across areas (Mehta et al., 2000). Average modulation amplitude was found to be larger in the ventral than in the dorsal visual processing stream. Within the ventral stream, attention effects had the most consistent distribution in V4, and there was an ascending gradient of attentional modulation in the pathways to V4. In terms of temporal pattern of modulation, the companion paper noted that attention effects lag the onset of the visually evoked response in each area, and grow larger over poststimulus time. The degree to which attentional modulation affects the onset of stimulus-evoked responses varies across reports. Motter (Motter, 1993), for example found neither an attentional modulation of prestimulus baseline firing, nor an attention effect at response onset in the V4 population at large, while Luck et al. (Luck et al., 1997) reported both types of effects in V4 neurons. Build-up of modulation over time, however, is a more robust phenomenon, which while not explicitly analyzed by most experiments, can be observed in data from numerous other laboratories, as well as ours (Motter, 1993; Luck et al., 1997; Mehta et al., 2000). The build up occurs during the decay of the visually evoked response, so that during the late
phase of response, attentional modulation comes to dominate the activity pattern. The present study explored in greater detail the largest and most consistent attention effects identified in the accompanying paper. That is, we examined the laminar distribution and physiology of attentional modulation in area V4 and in the lower visual pathways leading up to V4.

**Circuits Projecting and Coordinating Attentional Modulation:**
In attention-sensitive sites in V1, V2 and V4, effects were distributed across the laminar depth of the structure. Based on our earlier studies in striate and extrastriate cortices (Schroeder et al., 1990, 1991, 1997, 1998; Givre et al., 1994, 1995; Schroeder, Steinschneider et al., 1995), we were able to resolve a reliable laminar activation sequence in each area and to distinguish initial responses to ascending inputs from neural responses reflecting later intracortical processing. One clear finding is that the initial response at the depth of the granular laminae, that which best reflects the ascending input from lower areas, was largely unmodulated by attention. On the other hand, attention consistently modulated later neural responses in V2 and V4, particularly in the extragranular laminae. The smaller effects in V1 also conformed to this pattern.

The facts that modulation was distributed across the laminae within each area, and that extragranular modulation began as early as, or earlier than, that in lamina 4, strongly support a feedforward model of attentional modulation. That is, the spatio-temporal profile of modulation fits with the pattern of feedback, rather than feedforward corticocortical connectivity (Rockland and Pandya, 1979; Felleman and Van Essen, 1991). This is particularly clear for V1, the area whose laminar activation profile is best documented by physiological studies (Mitzdorf and Singer, 1979; Kraut et al., 1985; Schroeder et al., 1990, 1991, 1995, 1997, 1998; Maunsell and Gibson, 1992; Lamme et al., 1993; Givre et al., 1994, 1995). In V1 sites displaying attentional modulation (60% of the sample), the largest effects had extremely long latencies (>200 ms) and either a bilaminar or superficial laminar distribution (Felleman and Van Essen, 1991).

In both cases, the pattern of modulation clearly excluded the initial lamina 4c response, consistent with the lack of attentional modulation in LGN. This agrees with an earlier conclusion by Clark and Hillyard (Clark, 1996) based on human ERP recordings. The fact that the latency of attentional modulation increases progressively over successively lower stages of the hierarchy (i.e. from V4 to V2 to V1), also supports a feedback model. Because feedback projections originate, as well as terminate in the extragranular laminae, attention effects in V4 are in a position to contribute to modulation in V2 and the same for V2 relative to V1.

**Physiology of Attentional Modulation**
The laminar profile of current sources and sinks, along with the associated MUA, outlines a characteristic activation sequence elicited by an irrelevant stimulus. In V1 and V2, this consists of excitatory responses, initially in and near the position of lamina 4, and later in the upper and lower laminae. The same sequence is observed in V4, with the exception that a brief period (~15 ms) of activity depression often precedes initial excitation at the depth of lamina 4 (Givre et al., 1994; Schroeder et al., 1998). In all areas, initial excitatory responses are followed by a period of net local hyperpolarization, which appears to limit the excitatory response. The size of the postresponse hyperpolarization and its obligatory linkage to the excitatory response driven by irrelevant stimuli is consistent with the view that perceptual suppression of irrelevant stimuli is a ‘passive’ consequence of cortical physiology. From this perspective, the net response in cortical ensembles is essentially conservative, due to processes such as afterhyperpolarization and synaptically mediated inhibition. Thus, the net amplitude of the response to any stimulus, and presumably its perceptual salience, would be limited by postresponse refractory/inhibitory processes. Although derived from intermodal selective attention, the basic observation is consistent with the hypothesis that spatial selective attention modulates by reducing the mutual inhibition between competing stimuli in the receptive field (Desimone, 1995).

Attention’s main effect in V2 and V4 is to reduce or eliminate the net hyperpolarization that follows net local excitation, increasing both the amplitude and duration of the excitatory response. This is clearly consistent with the phenomenology of attention, in that the resulting enhancement of visually evoked responses should contribute to the selective enhancement in the perceptual salience of relevant stimuli. There are at least two broad possibilities regarding the local mechanisms through which this is accomplished. First, attention-induced activity in feedback projections could produce direct enhancement of excitatory responses to visual stimuli, within each processing stage. Alternatively, attention-induced feedback could, through a series of interneurons, produce disinhibition. We favor the first, direct excitation, as a principal cellular mechanism for the effects we observe at the ensemble level. First, it is consistent with the widely recognized fact that most corticocortical connections, including descending ones, are excitatory. Second, based on studies of rat visual cortex, ~90% of feedback afferents target parvalbumin-negative (non-GABAergic) neurons (Gonchar, 1999). Third, while in feedforward connections, excitation is balanced or dominated by inhibition; in feedback connections, the reverse is true (Shao, 1995). According to Shao and Burkhalter (Shao, 1999), when forward and feedback inputs are simultaneously active, feedback inputs can provide polysynaptic excitation that can offset slow IPSs evoked by forward inputs. Such feedback excitation may or may not be equivalent to locally induced disinhibition (Schroeder et al., 1997), but in any case, it provides a mechanism for amplifying afferent signals in lower areas (Shao, 1999).

The physiology of attention effects in V1 is difficult to define because the effects are small to moderate in amplitude, they occur within a subset of V1 sites, and the CSD modulation is not associated with a detectable modulation of action potential rates. The fact that attentional modulation was never detected in thalamocortical input activity in lamina 4c (n = 40), or in the LGN (n = 5) helps to control for the possibility that V1 effects result from a failure to equate retinal stimulation across attend and ignore conditions in our paradigm. The CSD effects in V1 appear to reflect a ‘top-down’ modulation of neuronal excitability, but at present its physiological significance remains obscure.

**Attentional Modulation of ERPs**
The main attention effect noted in the monkey surface ERP is a negative deflection occurring reliably between 100 and 300 ms poststimulus. Physically as well as paradigmatically this corresponds closely to the selection negativity noted in human ERP studies of selective attention. This deflection is evident in surface ERPs recorded simultaneously with each of the V4 laminar activity profiles shown in Figures 1 and 5 (top), as well as in the grand mean surface ERP (Fig. 10) (Mehta et al., 2000).
In the V4 laminar ERP profile, relative negativity of attend versus ignore ERPs is most prominent in the middle latency (100–300 ms) phase of the response, where it appears to stem from a reduction or loss of a large positive ERP component. CSD analysis revealed of the laminar ERP profile several current sources that contribute to the positive ERP component, i.e. they are associated with rapid changes in the spatial voltage gradient of the component. These current sources, like the ERP positivity, are reduced by attention.

It merits emphasis that although the net effect of attention on V2 physiology appears to be much like its effect on V4 physiology, the contributions of attention effects in a 'V2 to the selection negativity in the simian surface ERP are much less clear. The uncertainty stems partly from the fact the sign of the ERP deflection depends on whether the volume conducting component(s) arise from the superficial or deep surface of the cortex. Because the gross anatomy of macaque V2 is extremely convoluted, a complex mixing of surface negative and surface positive deflections is predicted, and the net result of these effects is very difficult to ascertain. Defining V2’s contribution to the surface selection negativity is further complicated by the fact that contributions from deeper portions of V2 are predicted to suffer masking and cancellation from potentials generated in overlying visual regions.

A similar set of anatomical considerations must be undertaken to fully exploit these results for understanding the neural origins of the human selection negativity. Human V2, for example, based on its gross anatomy, is a more likely contributor to the occipital surface ERP than monkey V2. Our results do, however, strongly implicate cortical area V4 over other, particularly parietal, areas. This conclusion is predicted by the earlier finding that the main dipolar source of the human selection negativity for attention to color localizes to the vicinity of human V4 (Anllo-Vento, 1998). Moreover, our findings indicate that the underlying process is feedback-mediated reduction of postresponse refractoriness and/or inhibition.

**Implications for the Neurophysiology of Perception and Cognition**

Attention effects appear to occur in all V2 and V4 laminae, thus influencing both ascending and descending (feedback) brain circuits (Rockland and Pandya, 1979; Fellemann and Van Essen, 1991). Reduction of postresponse refractoriness in granular and supragranular laminae is likely to produce a larger output signal to higher-order visual areas, contributing to enhanced perceptual salience for attended stimuli. As pointed out above, these findings at the ensemble level in primates converge with findings at the cellular level in rodents, in pointing to a mechanism by which feedback signals can amplify inputs in lower visual areas (Schröder et al., 1997). When driven by attention, the same ‘cellular amplifier’ in the infragranular layers, similarly, should increase the magnitude of feedback signals to lower visual areas. Extension of the present analysis to other areas of the visual hierarchy will help to determine the extent to which the net prolongation and amplification of neuronal firing we observe in V2 and V4 is a general phenomenon. It will also define more completely the circuits underlying attentional modulation of retinal inflow.

At a more speculative level, attentional amplification is intriguing because it is widely recognized that learning is enhanced by attention, and a presumptive cellular mechanism of learning, NMDA-receptor-mediated long-term potentiation (LTP), requires membrane depolarization (Tsumoto, 1990). The physiological mechanism likely to account for the present findings (see above) is identical to or equivalent to disinhibition. An immediate consequence of disinhibition in primate neocortex is engagement of nonlinear, NMDA-mediated excitatory responses (Schröder et al., 1997). In addition to the fact that engagement of NMDA receptors would increase the degree of attention-induced amplification, it should also increase the probability of producing LTP. Thus, attention’s impact on excitability may also represent the physiological linkage of attention with learning and memory.

Regardless of the physiological mechanism by which it is achieved, extending the duration of the stimulus-evoked excitatory response provides a means of overcoming the essential conservatism of cortical processing in order to enhance the integration and throughput of activity related to behaviorally relevant stimuli. Whether or not attentional modulation at response onset (Luck et al., 1997) is an obligatory feature of spatial selective attention, the present results predict that whenever attention is directed to a stimulus feature at the point of fixation, attentional modulation will tend to operate later in processing time. This differential is observed in comparing the latencies of spatial versus feature selective attention effects in human ERPs (Harter and Aine, 1984). The factors that may promote attentional modulation in early processing time include the extent to which there is a superimposed spatial selection, presence of multiple competing stimuli, and bias in task requirements favoring speed over accuracy. The factors that may provoke attentional modulation at early processing stages, such as LGN, include the above, but also depend critically on the stimuli. In agreement with recent views (Desimone and Duncan, 1995; Maunsell, 1995), we suggest that a challenge of future studies will be to devise task and stimulus parameters that can reveal the full power of attention.

**Notes**

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