NeuroImage **17,** 769–779 (2002)
doi:10.1006/nimg.2002.1204

Unmasking Motion-Processing Activity in Human Brain Area V5/MT+ Mediated by Pathways That Bypass Primary Visual Cortex

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Received December 7, 2001

Most models of the human visual system argue that higher-order motion-processing cortical regions receive their inputs only via the primary visual cortex (striate cortex), rather than also via direct projections from the thalamus that bypass primary visual cortex. However, recent evidence in non-human primates, along with some evidence in humans with damaged primary visual cortex (e.g., "blindsight" for motion in the blind visual hemifield), have argued for the existence of a direct thalamic-to-extrastriate projection for motion processing. This evidence remains controversial. Here we tested the idea that direct thalamic input to extrastriate motion processing areas exists in humans but might be masked in scalp recordings by activity from early visual areas. To do this, we employed stimuli that induced strong refractory effects in primary visual cortex—thereby creating a brief "reversable lesion" in primary visual cortex—immediately before the presentation of a motion stimulus. Under these conditions, we then assessed whether motion areas of cortex were still able to process the motion stimuli by recording event-related potentials (ERPs) and event-related magnetic fields (ERFs/MEG). We found robust motion-related activity in extrastriate motion processing areas in the ERP and MEG signals even when primary visual cortex was heavily suppressed by our manipulation. This finding provides evidence for a direct thalamic functional pathway to extrastriate visual cortical motion processing areas in the human that bypasses primary visual cortex.

Key Words: **ERP; MEG; visual motion; V1; V5/MT+.**

INTRODUCTION

The perception of motion plays a critical role in daily life. A brain area on the lateral aspect of the human occipital lobe has been found to be highly specialized for visual motion perception (Zeki *et al.*, 1991). This cortical area, termed in different literatures V5/MT or MT+, is thought to be the human homologue of the well-studied monkey MT-MST region. In non-human primates, the MT-MST region has been shown to have anatomical connections not only from V1, V2, V3, and V4 (reviewed in Zilles and Clarke, 1998), but also directly from the lateral geniculate (Fries, 1981; Yukie and Iwai, 1981) and pulvinar (Standage and Benevento, 1983) nuclei in the thalamus, bypassing primary visual (striate) cortex, V1.

The existence and role of these direct thalamo-V5/MT+ connections in humans are at present unclear. Most neuroimaging studies have failed to provide evidence for activity related to these direct connections. A few studies of patients with lesions in V1, however, have provided some evidence for the existence of such direct connections in humans (Barbur *et al.*, 1993). One electrophysiological study in healthy subjects (Ffytche *et al.*, 1995), using a limited number (nine) of electroencephalography (EEG) and magnetencephalography (MEG) channels, reported evidence for very early parallel input into V5/MT+ (for fast motion) that bypasses V1. Although these EEG/MEG results in humans have not been replicated, studies of projections in primates (Gross, 1991; Rodman *et al.*, 1989, 1990) have demonstrated the existence of a pathway from the retina to V5/MT+ via the superior colliculus and pulvinar. Further, it has been suggested that this pathway might play an important role in blindsight, a phenomenon in which patients with V1 lesions can detect motion in their blind visual field, but often without awareness (Weiskrantz *et al.*, 1974).

The goal of the present study was to elicit activity in V5/MT+ resulting from direct subcortical-to-V5/MT+ pathways and to provide evidence for this activity using EEG and MEG. There are several experimental problems with pursuing this goal, however. The main difficulty is that when several activated areas are close spatially, with substantially overlapping timing, they are difficult to separate in the scalp-recorded activity.

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1053-8119/02 $35.00

Unfortunately, this is exactly the case for a motion stimulus. The early-latency field activity is usually dominated by activity generated in the primary visual cortex (V1) and other early sensory areas (e.g., V2, V3). Since area V5/MT+ is not very far spatially from these other visual areas, any early activity in V5/MT+ resulting from direct thalamic connections would likely overlap with this other early visual activity and be masked by it at the scalp. This may partly explain why most studies using electrophysiology have been unable to clearly demonstrate early V5/MT+ activity.

Given this complication, an effective approach might be to employ an experimental method or manipulation that would attenuate or otherwise minimize V1 activity, thereby possibly unmasking V5/MT+ activity. One possibility for this would be to use transcranial magnetic stimulation (TMS). TMS, which involves the triggering of strong magnetic and electrical transients right next to the skull, allows the functional inactivation of nearby cortical regions. Such an approach has been previously used in attempts to study the behavioral effects of inactivating V1 and V5/MT+ (Beckers and Zeki, 1995). One limitation of this method is the difficulty in determining the exact cortical site affected by the TMS (Kamitani and Shimojo, 1999). In addition, the cortical area stimulated by the TMS is not very focal, and thus not so specific. Moreover, the strong electrical and magnetic transients produced by this technique make it difficult to combine with simultaneous EEG or MEG recordings, which would allow a direct measure of the V5/MT+ activity (although see Ilmoniemi *et al.*, 1999; Virtanen *et al.*, 1999).

In the present study we chose a different approach for decreasing the V1 activity elicited by a motion stimulus—namely, by using stimulus sequences aimed at inducing sustained refractoriness in V1. Subjects were presented stimulus sequences in which a bright flash stimulus was presented just prior to a moving-dot motion stimulus or just prior to a brightness-increment stimulus. We hypothesized that in both cases the flash would induce substantial refractoriness in V1/V2, so that the activity elicited in these areas by the motion or brightness-increment stimulus that followed would be highly attenuated. If it turned out that the motion stimulus preceded by a flash elicited little measurable activity anywhere at the scalp, then this would support the hypothesis that V1 is indeed the only major input into V5/MT+. However, we hypothesized that the flash-preceded motion stimulus would still elicit substantial occipital scalp activity, which would be laterally distributed and derive from V5/MT+, whereas the flash-preceded brightness increment would produce little scalp activity anywhere over occipital cortex. The most parsimonious explanation would then be that strong refractoriness had been induced in V1/V2, and that the motion information for the motion stimulus in this case had been mainly transmitted to V5/MT+ through direct subcortical connections that bypassed V1. Such an experimental manipulation would then have unmasked direct-connection neural activity in V5/MT+ that is typically masked under normal circumstances by V1/V2 activity.

Since, generally speaking, MEG measurements have somewhat higher spatial resolution than EEG, we expected that it might not be as difficult to separate the MEG activity arising from relatively close sources, such as V1 and V5/MT+. Thus, in the MEG, possible early direct-connection V5/MT+ activity might be somewhat less masked by V1/V2 activity, even under normal conditions, although the V1-saturating unmasking approach might further unveil such V5/MT+ activity.

In addition to these electrophysiological experiments, we performed several related behavioral experiments. In particular, we examined the effects of these refractorizing flash stimuli on discrimination and detection thresholds of motion and brightness-increment stimuli. Our combination of EEG, high-density MEG, and behavioral experiments using V1-refractorizing sequences were aimed at gaining new insights into the existence, role, and timing of the direct thalamo-V5/MT+ activations in the visual system.

METHODS

Electrophysiological Experiments

Subjects

Ten healthy subjects (four male, six female, ages 21–27 years) with normal or corrected-to-normal vision participated as paid volunteers in the study. All gave informed consent, and the study was approved by the local ethics committee.

Stimuli and Experimental Design

Subjects were presented with five types of event trials, each composed of different sequential combinations of stimuli (Fig. 1). The stimuli were presented in a square (3° × 3°) in the lower visual field, 2° below fixation on a dark background (0.22 cd/m^2). One hundred stationary dots were continuously present in this location between the different trials. The five event trial types were as follows:

Trial Type I (flash only). This trial consisted of a 100-ms flash (35.05 cd/m^2) stimulus presented in the 3° × 3° square, transiently replacing the stationary dots.

Trial Type II (flash + motion). This trial consisted of the same 100-ms flash stimulus, followed by the stationary dots (2.35 cd/m^2) for 50 ms, and then by random movement of the dots (2.35 cd/m^2) lasting 200 ms. Thus, the dot-motion stimulus began at time = +150 ms relative to the beginning of the trial.

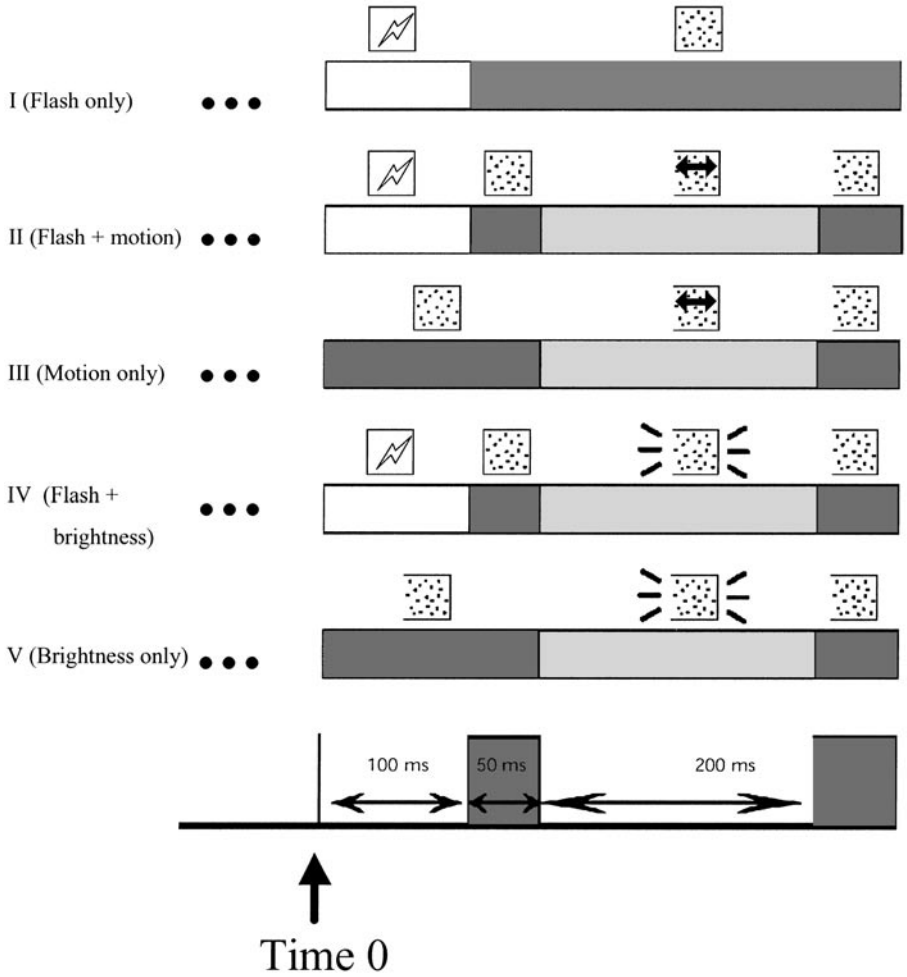


FIG. 1. The five different stimulus trial types. For each of the trial types, 350 ms are depicted. Stationary dots were always present on the screen between successive trials and between stimuli within the compound trial types. Trial Type I (flash only) started with a bright flash lasting for 100 ms, which was followed by stationary dots for 250 ms. Trial Type II (flash + motion) also started with a flash lasting 100 ms, followed by dots that were stationary for the first 50 ms and moving for the subsequent 200 ms. Trial Type III (motion only) consisted of dots that remained stationary for 150 ms and then were in motion for the subsequent 200 ms. Trial Type IV (flash + brightness increment) started with a bright flash lasting 100 ms, followed by the stationary dots for 50 ms, followed by the brightness increment of the dots increasing for the following 200 ms. Trial Type V (brightness increment only) consisted of stationary dots for 150 ms, which then brightened for the subsequent 200 ms. Note that the initial stimulus onset was at time point 0 in Trial Types I, II, and IV but at 150 ms in sequences III and V.

Trial Type III (motion only). The third trial type consisted of just the 200-ms-duration random dot movement that was in Trial Type II above, also beginning at time = +150 ms relative to the trial trigger.

Trial Type IV (flash + brightness increment). Trial Type IV consisted of the 100-ms flash stimulus, followed by stationary dots for 50 ms, followed by a 200-msec-duration brightness increment of the dots (6.38 cd/m^2) beginning at time = +150 ms.

Trial Type V (brightness increment only). The fifth trial consisted of just the 200-msec-duration brightness increment of the dots (6.38 cd/m^2) (again, beginning at time = +150 ms).

The way these trial types were to be used to address our hypotheses was as follows:

Analysis of I, III, or V: Flash Alone, Motion Alone, Brightness Increment Alone

PREDICTION. All three will elicit robust medial occipital activity (V1/V2). Motion will **ALSO** elicit robust lateral occip. activity (V5/MT+).

Analysis of II minus I: Flash + Motion minus Flash Only

PURPOSE. Subtracts out overlapping fields elicited by preceding flash. To reveal response to motion stimulus when preceded by bright flash, i.e., when V1 and V2 are highly refractory.

PREDICTION. Little activity will be observed from medial occip. (V1/V2). But robust lateral occip. activity (V5MT+) will still be elicited.

Analysis of IV minus I: Flash + Brightness Increment minus Flash Only

PURPOSE. Subtracts out overlapping fields elicited by preceding flash. To reveal response to brightness increment when preceded by flash, i.e., when V1 and V2 are highly refractory.

PREDICTION. Little activity will be observed from medial occip. (V1/V2). Assuming other higher visual areas depend on V1/V2 throughput, little activity will be observed anywhere over occip. cortex.

To control fixation and minimize eye movements, subjects were given the task of fixating on a central cross and pressing a button as quickly as possible upon detecting a transient change of the fixation cross into a square. Subjects were also instructed to ignore the stimuli in the lower visual field. Prior to the EEG/MEG recording, subjects were trained to fixate during the task until no eye movements were observed in the electroculogram (EOG). During EEG/MEG recording eye movements were monitored using EOG as well as a video system. The overall performance of the subjects in the fixation task during recording was 99.2% hits and 0.8% misses.

Four 5-min experimental blocks were run, each containing 100 trials of each of the five trial types presented in randomized order. The interstimulus interval between the trials randomly varied between 1 and 1.2 s. The fixation targets (cross changing to square) occurred randomly 5–8 times per run. In the trials with motion, the dots moved in random directions (incoherent motion) at a speed of 4°/s.

Data Acquisition and Analysis

MEG and EEG were recorded simultaneously on a BTI Magnes 2500 WH (Biomagnetic Technologies, Inc.) whole-head system with 148 magnetometer (MEG) channels and 32 EEG channels (NeuroScan, Inc.) using a DC-50-Hz bandpass and a 254-Hz sampling rate. The MEG recording also employed an online noise reduction system that removes a weighted sum of environmentally induced magnetic noise (first-order spatial gradients of the field) recorded by eight remote reference sensors. Artifact rejection was performed offline by removing epochs with peak-to-peak amplitudes exceeding 3.0×10^{-12} T in the MEG or 500 μV in the EEG.

Subjects' individual head shapes and the sensor frame coordinate system were brought into reference by spatially digitizing (Polhemus 3Space Fastrak) individual landmarks (nasion, left and right preauricular points). The landmarks also served to match and coregister anatomical MR scans recorded to constrain realistic source reconstruction. The 32 electrode locations were also spatially digitized in order to determine their geometric relation to the landmarks. To adjust for sensor-location variability across subjects, prior to the computation of the grand-average responses, individual sensor-frame coordinate systems were adjusted to the sensor-frame coordinate system of one of the subjects using the ASA program (AMT Software). In this approach, a hypothetical minimum-norm distribution of the measured field on a spherical shell is computed, from which a forward solution is computed for the sensor locations in this canonical subject. These field values could then be used in the grand-average computation. The MR scan of this subject was also used to display the source analysis.

Separate time-locked averages for the EEG and MEG were computed for the five trial types. In addition, the following response subtractions were computed:

(II) minus (I) = (flash + motion) minus (flash only) (FM-F)

(IV) minus (I) = (flash + brightness increment) minus (flash only) (FB-F)

Effects were subjected to repeated-measures analysis of variance (ANOVA) in the relevant latency windows using WinSPSS V7.5. EEG and MEG source analyses were performed using Curry V3.0 multimodal neuroimaging software (NeuroScan, Inc.) in the time range of the various peaks or effects. Dipole analyses were performed using regional dipoles in a realistic head model computed using the boundary element model (BEM) approach. The source analyses were performed on each individual subject's data using a BEM computed from that individual's MRI and on the grand-average fields using the BEM from the subject whose brain dimensions were closest to the mean.

For the dipole source modeling, a criterion was set that a model would have to explain at least 90% of the variance of the observed field in order to be acceptable. To obtain these models, the following procedure was used. First, the field was modeled using a single, unconstrained, equivalent current dipole (ECD). For several of the modeled components—in particular, for the C1's and N1's for both the flash-only and brightness increment-only stimuli—this resulted in a midline dipole near striate cortex explaining more than 90% of the variance. For the N1's elicited by stimuli containing motion, however, such single-dipole solutions did not explain 90% of the variance, and thus a second unconstrained dipole needed to be added. Typically, the iterative best-fitting procedure resulted in these two dipoles settling into symmetric locations in lateral occipital cortex.

Although these two-dipole models for the trial types containing motion stimuli were generally stable in location and orientation, they typically still explained only around 80% of the variance. Since these models did not reach the 90% criterion, a third dipole was added, but with the other two dipoles constrained to the location and orientation from the two-dipole model.

This third dipole typically settled into a stable location in the midline near striate cortex, and this three-dipole model would explain over 90% of the variance. Last, the location and orientation constraints of the lateral occipital ECDs were released to ensure that these fits were stable.

Behavioral Experiments

Subjects

Five healthy subjects (three male, two female, ages 23–27 years) with normal or corrected-to-normal vision participated as paid volunteers in the behavioral experiments.

Stimuli and Experimental Design

Effects of the bright flash on motion discrimination. In these behavioral experiments, two stimulus trial types, namely Trial Types II (flash plus motion) and III (motion only) described above, were presented in the lower visual field. The dot movement was not random but rather was directed to the left or to the right with 10 different percentages of coherence (10–55% in 5% steps). Subjects were asked to maintain fixation on the central fixation cross and to discriminate the direction of the movement. Each subject was presented with 40 stimuli of each percentage of coherence (total of 400 stimuli). Half of these motion stimuli were preceded by a bright flash and half were presented without the flash. The timing of the sequences was the same as that used in the electrophysiological measurements (Fig. 1). One second after the presentation of a trial the central fixation cross changed into a square, at which point the subjects were to press one of two buttons to indicate whether the movement direction had been leftward or rightward. Following the button-press response the fixation changed again into a cross and after 500 ms the next sequence of stimuli was presented.

Effects of the bright flash on motion detection. In this experiment a similar design was used to investigate the effect of the preceding bright flash on the detection of motion. Subjects were presented with motion stimuli at different percentages of coherence (10, 15, 20, 25, and 30%) as well as with catch trials (no motion in 5% of the trials). Twenty trials of each of the five coherence percentages were presented with and without a bright flash preceding (total of 200 trials). One second after the presentation of a stimulus trial, the central fixation cross changed into a square, at which point the subjects were to press one of two buttons to indicate whether there was a movement or not.

Effects of the bright flash on brightness-increment detection. A similar design was used to investigate the effect of the preceding bright flash on the detection of brightness-increment stimuli. Trial Types IV (flash plus brightness increment) and V (brightness increment only) as well as catch trials (no brightness increment) with and without a flash preceding were used in these measurements. Forty trials of each stimulus sequence were used for a total of 160 trials. When the fixation cross changed into a square subjects were instructed to press one of two buttons to indicate whether a brightness increment occurred or not.

RESULTS

Electrophysiological Experiments

Responses to Flash Alone, Motion Alone, and Brightness Increment Alone (Trial Types I, III, and V) (Figs. 2 and 3)

The earliest observable EEG/MEG activity elicited by the flash-only stimulus (Trial Type 1) was the occipital C1/C1m component onsetting at ~50 ms poststimulus and peaking at ~90 ms. This component is generally believed to arise from primary visual (striate) cortex. This was followed by the N1/N1m onsetting at ~120 ms and peaking at ~175 ms. EEG activity in the time range of the C1 component (50–120 ms) was indeed well modeled using a single medial dipole located near striate cortex that explained 94% of the variance of the measured potentials. MEG activity in the C1/C1m time range had a low signal-to-noise ratio (SNR) that did not allow for accurate source analysis. In the time range of the N1/N1m component (120–200 ms), the EEG and MEG activity could each be well modeled by a single dipole in the same region as the C1-component dipole, explaining 92% of the N1/N1m variance in each case.

In Trial Type III (motion only), the motion stimulus started at 150 ms after the trigger signal (i.e., after time 0; see Fig. 1). This stimulus elicited EEG/MEG activity starting at ~200 ms (i.e., 50 ms poststimulus), with the C1/C1m component peaking at ~230 ms (i.e., 80 ms poststimulus). This was followed by the N1/N1m component with an onset at ~270 ms (120 ms poststimulus) and a peak at ~310 ms (160 ms poststimulus) (Figs. 2B and 3B). In the C1 latency, EEG activity could be well modeled with a single medial dipole near striate that explained 91% of the measured potentials. The low SNR of the MEG in this time range, again, did not allow source analysis. The robust activity in the N1/N1m latency, however, could be well modeled for both the MEG and the EEG, although the complexity of the fields resulted in a three-dipole solution being required. One dipole was located medially in the striate region, whereas the other two were located in the left and right lateral occipital–temporal cortex. These models each explained 92% of the variance.

In Trial Type V (brightness-increment only), the brightness-increment change occurred at 150 ms after time 0. This stimulus elicited activity starting at ~200 ms (50 ms poststimulus) with the C1/C1m component,

which peaked at 230 ms (80 ms poststimulus) (Figs. 2B and 3B). This was followed at 270 ms (120 ms poststimulus) by the N1/N1m component, peaking at ~310 ms (160 ms poststimulus). The C1-latency activity was again well modeled with a single medial dipole located in the striate region that explained 94% of the variance. In the N1/N1m latency, the activity looked very similar to that of the C1/C1m, and the EEG and MEG could each also be well modeled with a single medial dipole explaining 92% of the variance.

In the evoked responses for the flash-only and brightness-increment-only stimuli used here, the early components in the EEG (i.e., C1, N1), which were well-modeled as arising from single ECDs near striate cortex, were predominantly radial in orientation. This mostly radial orientation was also observed for the C1 dipole for the motion stimulus, as well as for the medial dipole of its N1. This orientation seen in the EEG presumably explains why the corresponding early components of these stimuli were fairly small in the MEG, which is mainly sensitive to tangential dipoles or to the tangential components of oblique dipoles.

Combination-Event Trial Types (Trial Types II and IV) (Figs. 2 and 3)

Contrasts of the EEG and MEG activity elicited by Trial Type II (flash followed by motion, or FM) and Trial Type I (flash only, or F) gave rise to a robust effect in the time range 280–420 ms (Figs. 2C and 3C). Repeated-measures ANOVA over occipital electrodes/sensors in this time range with the factor of trial type (FM vs F) showed this effect to be highly significant [EEG: $F(1,9) = 20.05$, $P = 0.002$; MEG: $F(1,9) = 9.76$, $P = 0.012$]. The difference waves for this effect are presented in Figs. 2D and 3D. These MEG and EEG difference-wave distributions could each separately be well modeled with three dipoles, one located in the striate region and two located laterally near the lateral occipito-temporal junctions. Such a model explained 92% of the variance of the MEG and 90% of the variance of the EEG.

For both the MEG and the EEG data, the locations of the dipoles for this motion-related difference activity corresponded almost exactly to the location of the dipoles explaining the activity elicited by the motion-only condition (Trial Type III); however, the relative strengths of the dipoles appeared to be quite different, with the medial dipole amplitude now being highly attenuated relative to the lateral ones. To evaluate more closely these dipole strength differences, we conducted the following additional analysis. We took the three-dipole solution from the motion-alone condition (Trial Type III) and applied this solution to the field of the motion-related difference waves (flash-plus-motion minus flash-alone), constraining the dipoles such that they were not allowed to change their locations. The resultant solution still explained ~90% of the difference field. To assess for changes in the contributions of these sources to the fields in the motion-only condition vs the motion-related difference activity in the flash-then-motion condition, we compared the strengths (dipole moments) of the three dipoles in the two cases. For the motion-related difference activity, there was some decrease of the dipole strength in all three dipoles relative to the motion-only response, but the proportions of these attenuations differed substantially for the different dipoles. More specifically, for the MEG the strength of the medial (striate) dipole decreased by 74% (69.8 to 18.2 μAmm) whereas the left V5/MT+ dipole strength decreased only 22% (−16.0 to −12.5 μAmm) and the right V5/MT+ dipole only 24% (−11.6 to −8.8 μAmm). For the EEG, the corresponding decrease in the medial dipole strength was 70%, with decreases of 21 and 18% for the left and right V5/MT+ dipoles, respectively.

In contrast to the motion-related stimuli, analyses of the EEG and MEG activity elicited by Trial Type IV (flash-plus-brightness increment) vs Trial Type I (flash alone) did not reveal any significant activity (Figs. 2C and 2D, 3C and 3D). In the key N1/N1m range (280–420 ms), repeated-measures ANOVA of the EEG activity over occipital electrodes with the factor condition (flash-plus-brightness increment vs flash alone, FB-F) did not yield any significant differences ($F(1,9) = 1.46$; $P > 0.05$). In the MEG data, although there was a suggestion of a small effect in this time range (Fig. 3B), repeated-measures ANOVA of flash-only vs flash-plus-brightness-increment did not reveal any significant differences here either ($F(1,9) = 1.54$; $P > 0.05$).

Behavioral Experiments

Effects of the Bright Flash on Motion Discrimination

For each subject the coherence threshold was set at the percentage of coherence at which the subject performed over 70% in the discrimination task see (Newsome and Pare, 1988). Figure 4 shows the calculated mean percentages for each of the 10 coherence steps for stimulus sequences with and without a preceding bright flash. In the absence of the preceding bright flash subjects reached this criterion of 70% correct responses at a coherence of 25%. When the bright flash preceded the motion stimuli the subjects reached the 70% criterion at 35% coherence. Repeated-measures ANOVA across subjects with the factor flash showed this difference to be highly significant ($F(1,4) = 96$; $P < 0.001$).

Effects of the Bright Flash on Motion Detection

In this experiment we investigated the effect of the bright flash on the detection of motion using dot-motion coherences ranging from 10 to 30% in 5% steps.

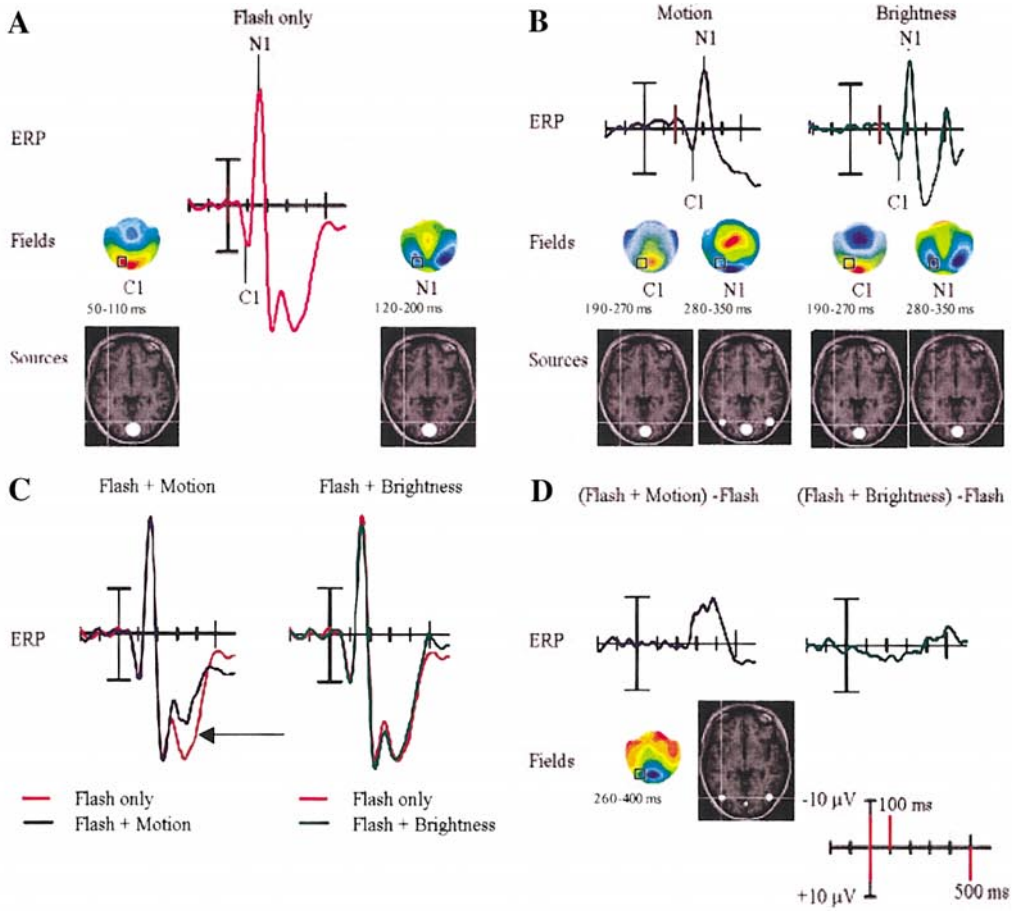
Subjects always performed above 90% in this task regardless of the presentation of a preceding flash. Repeated-measures ANOVA across subjects with the factors flash/no-flash and coherence percentage did not reveal any significant main effects for the factors flash ($F(1,4) = 0.877$; $P > 0.05$) or coherence ($F(1,4) = 0.487$; $P > 0.05$), nor for the interaction ($F(1,4) = 0.134$; $P > 0.05$).

Effects of the Bright Flash on Brightness-Increment Detection

In pilot experiments the subjects were not able to perform at a 70% level on any luminance manipulation of the brightness-increment stimulus when it was preceded by the bright flash. Therefore it was not possible to calculate a luminance threshold and we used the maximum luminance for the brightness-increment detection task (the luminance of each single dot was equal to the luminance of each pixel of the bright flash). In the absence of the preceding bright flash the subjects performed at 75% correct responses (Fig. 5). When the bright flash preceded the brightness increment, the subjects' performance dropped dramatically to 24.8%. Repeated-measures ANOVA across subjects with the factor flash vs no-flash showed this difference to be highly significant ($F(1,4) = 103.95$; $P < 0.001$).

FIG. 2. (A) ERP waveforms elicited by the flash stimulus (Trial Type I) at an electrode over the left parietal–occipital lobe (site P01), grand-averaged over the 10 subjects. This stimulus elicited a C1 component with an onset at ~50 ms poststimulus and an N1 component with an onset at ~120 ms. The corresponding ERP topographic distributions on the scalp for the C1 (left) and N1 (right) are also shown, with the location of the electrode site for the ERP traces indicated (small square). Also shown are the estimated source locations from the dipole source analyses. Both components were well modeled with a medial dipole located near striate (primary visual) cortex. (B) Grand-average ERPs elicited by motion only (Trial Type III) (left side of figure) and by brightness increment only (Trial Type V) (right side of figure), along with the corresponding potential distributions and the source analysis results. Note that the time of stimulus occurrence here was at 150 ms (see also Fig. 1). Both stimuli elicited a C1 and an N1 component. The fields and the sources were highly similar for both stimulus types with regard to the C1 component but different for the N1. The C1 components for these two stimulus types were both well modeled using one medial–occipital dipole located near primary visual (striate) cortex (V1). In addition, the N1 to the brightness increment could also be modeled with a single medial–occipital dipole. In contrast, modeling of the motion-only N1 component required three dipoles, a medial–occipital one in the striate region and two lateral occipital ones in the left and right V5/MT+ regions. The diameter of the dots depicting the dipole locations in the figure are set to be proportional to the magnitude of the estimated dipole strength. (C) Left: Overlay of the ERPs elicited by flash followed by motion (Trial Type II, blue trace) and by flash only (Trial Type I, red trace). This comparison shows a robust difference in the time range 280–420 ms (arrow), or 130–270 ms after the motion. Right: Overlay of the ERP's elicited by flash followed by brightness increment (Trial Type IV, in green) and by flash only (Trial Type I, in red). No effect could be observed for this comparison, suggesting there was heavy attenuation of the response to the brightness increment when it was preceded by the flash. (D) Difference waveforms for the ERPs presented in (C). For the difference waveform for the flash-preceded motion stimulus—namely, the flash followed by motion response minus the flash-only response—the electrical potential distributions for the C1 and N1 latency range are presented below the ERP, and the results of the dipole source analyses below that. Note that the N1 of this difference distribution (i.e., the N1 of the flash-preceded motion stimulus after subtracting out the overlapping flash response waves) could be modeled with three dipoles in the same locations as for the motion-only stimulus (B); however, the relative strength of the medial dipole was greatly attenuated (see text). (As in (B) the diameter of the dots depicting the dipole locations are proportional to the magnitude of the estimated dipole strength.) The difference waveform for (flash followed by brightness increment) minus (flash only) did not yield any significant effect over visual cortex and thus could not be modeled.

FIG. 3. (A) MEG waveform elicited by the flash stimulus (Trial Type I) at a left lateral–occipital sensor site. Also presented is the corresponding magnetic field distribution between 120–200 ms (with the sensor site indicated with a small square), along with the dipole source analysis results. This field was well modeled with a medial–occipital dipole located in the striate region. (B) MEG waveform elicited by motion only (Trial Type III) (left side of figure) and by brightness increment only (Trial Type V) (right side of figure), along with corresponding magnetic field distributions and the source analysis results. Note that the stimulus onset is at 150 ms (see also Fig. 1). Both trial types elicited a C1m and an N1m component. Source analysis was only performed for the N1m component due to the low signal-to-noise ratio for the C1m. The fields and the sources were different for the N1m components for the two stimulus types. Like with the EEG, the N1m component elicited by the brightness increment could be well modeled with a single medial–occipital dipole in the striate region. In contrast, the N1m component elicited by the motion-only stimulus required three dipoles for a good model, one in the striate region and two lateral ones in the left and right V5/MT+ regions, also consistent with the EEG results. As in Fig. 2, the diameter of the dots depicting the dipole locations is proportional to the magnitude of the estimated dipole strength. (C) Left: Overlay of the MEG waveforms elicited by flash followed by motion (Trial Type II, blue color) and flash only (Trial Type I, red color). This comparison gave rise to a significant effect in the time range 280–420 ms (arrow), or 130–270 ms after the motion. Right: Comparison between the MEG waveforms elicited by flash followed by a brightness increment (Trial Type IV, in green) and by flash only (Trial Type I, in red). No significant activity difference was observed for this comparison. (D) Difference waveforms for the MEG traces in (C). On the left are the difference waveform of (flash followed by motion) minus (flash only) and on the right is the corresponding difference waveform for (flash followed by brightness increment) minus (flash only). The magnetic field distributions as well as the source analysis results are presented below the waveforms. Note that the field of the first of these difference waves [(flash followed by motion) minus (flash only)] was similar to the field elicited by the motion-only stimulus (see (B) left) and could be well modeled with three dipoles in the same locations; however, as with the EEG (Figs. 2B and 2D), the relative strength of the medial dipole was greatly attenuated. (As in the other panels of Figs. 2 and 3, the diameter of the dots depicting the dipole locations are set to be proportional to the magnitude of the estimated dipole strength.) In contrast to the flash-preceded motion response, the difference fields for [(flash followed by brightness increment) minus (flash only)] did not yield any significant activity. A plot of the difference field distribution in the corresponding time range suggested some residual activity that appeared to possibly be a very weak version of the field elicited by flash only (Trial Type I) or by brightness increment only (Trial Type V) in the corresponding time range, but this activity did not reach significance.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Flash only
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C1
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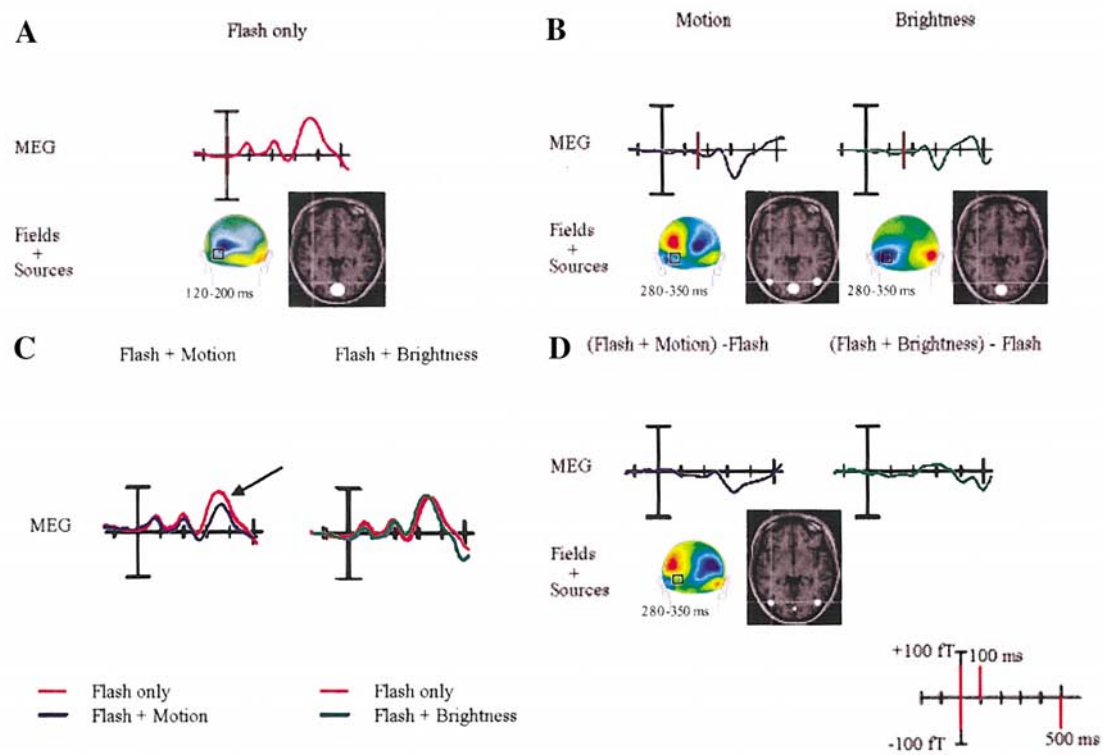
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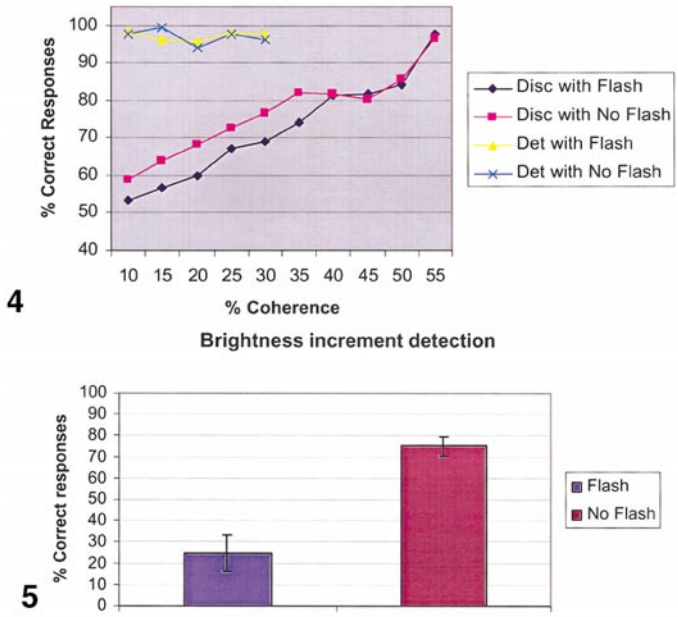

FIG. 4. Results of the motion direction discrimination and motion detection tasks. The percentage of correct responses is plotted for the different percentages of dot-motion coherence. Main section of panel: Performance on the direction-discrimination task are shown, with trials in which the motion stimulus was preceded by a flash (Disc with Flash) shown in the pink trace, and trials without a flash preceding (Disc with No Flash) in the blue trace. Note that when the motion stimulus was presented without a preceding flash, subjects did not attain 70% performance at a motion coherence of 25%, whereas when the motion was preceded by a flash, subjects did not attain 70% performance until the coherence reached 35%. Upper left: The percentage of correct responses in the motion detection task are presented in light blue for the trials without a flash preceding (Det with No Flash) and yellow for trials with a flash preceding (Det with Flash). Note that the preceding flash did not affect the detection of motion.

FIG. 5. Results of the brightness-increment detection task. Shown are the percentage of correct responses (± standard error bars) for trials in which the brightness increment was preceded by a flash vs those without the preceding flash. Note the severe impairment when the brightness increment was preceded by a flash.

DISCUSSION

Flash, motion, and brightness-increment stimuli all elicited scalp EEG/MEG activity starting at 50 ms poststimulus. The similar onsets of these stimulus types suggests that if there is V5/MT+ activity elicited by motion via direct thalamo-V5/MT+ pathways, this is likely masked by activity in striate or other early visual cortical areas. This results in difficulty in isolating V5/MT+ activity *in vivo* using scalp electrophysiological recordings.

We sought to address this question by including conditions in which we induced sustained refractoriness in V1/V2 with the presentation of a bright flash stimulus prior to the motion or brightness-increment stimuli. More specifically, the flash was expected to elicit substantial processing in the V1 and V2 regions, thereby reducing the V1/V2 response to the subsequent stimulus while not influencing activity derived from any direct thalamo-V5/MT+ pathways that bypassed V1.

As expected, the source of the early components (C1, N1) of the flash-elicited activity was found to be in the vicinity of V1/V2. Similar sources were also found for the early EEG components that were elicited by the brightness-increment stimulus alone and the motion stimulus alone. However, the subtraction of the Trial Type IV activity (flash + brightness increment) minus the Type I activity (flash only) left essentially no significant occipital activity. The processing of the brightness-increment stimulus in V1/V2 thus appeared to be heavily suppressed in the field potentials by the processing of the previously presented flash stimulus. In contrast, the subtraction of the activities elicited by Trial Type II (flash + motion) and by Trial Type I (flash only) still yielded a robust effect in both the MEG and the EEG in the time range 280–420 ms. Thus, first of all, this provides evidence that the flash-induced refractoriness occurred later than at retinal level because otherwise motion processing would have been suppressed in the same way as for the brightness increment. Moreover—and central to the evidence for direct thalamic–V5/MT+ connections—this effect was in the same time range and generated by the same lateral occipital (i.e., MT+) sources as the effect for motion alone. The difference activity [(flash + motion) − (flash only)] clearly shows this lateral–occipital N1 activity for motion whereas the medial C1 component was heavily suppressed, presumably due to refractoriness at the level of V1/V2. By attenuating the V1/V2 activity that is usually elicited by motion, clear activity in bilateral V5/MT+ was then unmasked. Although this was seen in both the EEG and the MEG data, since the earlier V1/V2 activity (for all trial types) was substantially smaller in the MEG than in the EEG, the V5/MT+ MEG activity for the motion stimulus appeared to be less masked in the first place.

Regardless, since most of the activity in areas V1 and V2 had been heavily suppressed in the field potentials, one would expect a major proportional decrease in activity in area V5/MT+ if V1 and V2 were its only source of input. Our data, however, indicated only a minor decrease (~20%) of activity in V5/MT+ for the flash-preceded motion stimulus, despite a major decrease of the activity in the medial (striate) area. This provides evidence for considerable independence of V5/MT+ activity from activity saturation in V1/V2, in turn providing evidence that it receives input other than from V1, presumably over direct subcortical connections via pulvinar. This decrease in V5/MT+ activity is consistent with the finding of Girard *et al.* (1992), who found that 50–60% of MT+ neurons still fire after V1 inactivation, their firing being much weaker. Additional support for this theory is provided by several animal studies using single-cell recordings also demonstrating

that MT+ neurons still fire after V1 inactivation (Rodman *et al.*, 1989; Gross, 1991).

An alternative explanation for our electrophysiological results could be that not all V1/V2 neurons were affected by the presentation of the bright flash, and that those specifically tuned for motion were left relatively unimpaired. In this case these unaffected neurons would have provided their regular input to V5/MT+, and perhaps this constitutes most of the input into V5/MT+ anyway. The decrease of 20% in the V5/MT+ regions would then simply have resulted from the lack of input from the V1/V2 neurons affected by the bright flash. Following this line of thinking one would expect that the quality of the motion information mediated through the V1 pathway would be fairly good. However, Girard *et al.* (1992) have shown that due to strong reductions in the response of MT neurons too close to the preferred and nonpreferred directions, the quality of motion perception mediated through direct subcortical pathways is relatively poor, especially for discrimination of motion direction.

We investigated whether the quality of motion perception is affected by the presentation of a preceding strong flash by measuring motion coherence thresholds. We found that the coherence threshold for discriminating motion direction was significantly higher for motion stimuli preceded by the bright flash. This finding provides evidence that the quality of the motion information was indeed reduced by the preceding flash. On the other hand, the detection of motion stimuli was not influenced at all by the occurrence of the preceding flash—even at the lowest level of dot-movement coherence. Moreover, and in sharp contrast, the detection of brightness increments was severely disrupted by the preceding flash (see Fig 4). This pattern of results is interestingly similar to the findings in patients with V1 lesions. More specifically, a hallmark of such patients is that in their blind visual field they have mostly intact motion detection, but very poor motion-direction discrimination, as well as extremely poor (or nonexistent) pattern flash perception (e.g., of brightness increment) (Benson *et al.*, 1998; Zeki and Ffytche, 1998). Thus the behavioral effects of the V1-refractorizing stimuli in the present experiment would appear to parallel those found in V1-lesion patients and to argue against the hypothesis that motion information was mediated through V1 when the motion stimulus was preceded by the bright flash.

Another important question concerns the timing of the V5/MT+ activity elicited over this direct pathway. Some single-cell animal data have suggested that this subcortical pathway can be very fast (e.g., 30–50 ms; see Ffytche *et al.*, 1995). One EEG/MEG study in humans has reported evidence of very early activity in V5/MT+ starting at ~30 ms poststimulus (Ffytche *et al.*, 1995), although no other EEG or MEG studies have thus far found similar results. In our study, neither the EEG nor the MEG activity started earlier than 50 ms poststimulus, which was the onset latency of the C1 component. Moreover, the sources of this earliest activity were localized to the striate cortex. In contrast, the unmasked V5/MT+ activity started at ~120 ms poststimulus, a time range which corresponds to the N1/N1m component elicited by motion. If there is earlier and faster input into V5/MT+, we did not detect it in either the EEG or the MEG.

In conclusion, our experimental manipulation of saturating V1 prior to a motion stimulus appeared to unmask activity in the motion-sensitive area V5/MT+ that is best explained as having been mediated by a direct thalamic pathway to V5/MT+ that bypasses V1. The onset timing of the EEG and MEG activity from V5/MT+ does not support the idea that this pathway is faster than the classic sequential input via the LGN and V1.

ACKNOWLEDGMENTS

We thank two anonymous reviewers for valuable comments on earlier versions of the manuscript. The study was supported by Grants DFG He1531/3-5 and BMBF 01ZZ9510TPC5 accorded to H.-J.H. and NIMH R01 Grant MH60415 to M.G.W.

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