Facilitation as well as inhibition of the blink reflex by a visual prepulse requires intact striate cortex

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Abstract

Objective: The role of visual cortex in modulation of the human eye blink reflex was assessed.
Methods: Participants were 13 patients with unilateral striate cortex damage. Nonreflexogenic gratings were presented in their intact or blind hemifield prior to white noise or air puff blink-eliciting stimuli.
Results: Inhibition of reflex amplitude was observed at asynchronies ranging from about 120 to 600 ms for visible but not invisible prepulses. Facilitation by intact-hemifield gratings was observed for (1) the latency of the acoustic blink reflex, (2) the amplitude of the disynaptic cutaneous blink reflex, R1, and (3) the latency of voluntary hand-grip reactions to the reflexogenic stimuli. These facilitatory effects were absent on trials with blind-hemifield prepulses.
Conclusions: An intact V1 is required for prepulse facilitation as well as inhibition.
Significance: These results extend a popular model of sensorimotor gating deficits in schizophrenia.

Keywords: Prepulse inhibition; Startle-blink reflex; Sensorimotor gating; Visual cortex; Blindsight; Choice reaction time

1. Introduction

Since its discovery by Dodge in 1931, prepulse inhibition (PPI) has emerged as an important paradigm in behavioral neuroscience. Neuroanatomical research has identified much of the circuitry that underlies PPI of whole-body acoustic startle in rats (reviewed in Fendt et al., 2001; Koch, 1999; Swerdlow et al., 2001). This work confirms earlier findings that, in the case of simple acoustic transients, PPI requires only subcortical structures (Davis and Gendelman, 1977). However, the inhibition of rat whole-body startle by gaps or brief increments in an otherwise continuous noise does require an intact neocortex (Bowen et al., 2003).

The anatomical substrate for inhibition by visual prestimuli may be even more dependent on cortical structures. The most systematic previous study was that of Ison et al. (1991). By functionally deactivating visual cortex of rats with potassium chloride, these investigators were able to eliminate visual PPI of the acoustic whole-body startle response. In the absence of PPI, robust amplitude facilitation was evident at lead times ranging from 70 to at least 500 ms. These results suggest that visual PPI requires processing at neocortical levels, whereas prepulse facilitation (PPF) is subcortically mediated.

To extend these findings to humans, patients with a condition known as homonymous hemianopsia have been examined in two case studies (Burke and Hackley, 1997; Hilgard and Wendt, 1933). Homonymous hemianopsia is
a lateralized blindness caused by damage to the visual cortex of one hemisphere or its postchiasmatic input. This damage results in an absence of conscious awareness of stimuli presented to either eye from within the half of the visual field contralateral to the lesion. However, even if no sparing is detected by standard neuro-ophthalmological testing, blindness is typically less than complete. Brainstem visual pathways, such as those that mediate the photic blink reflex (Hackley and Johnson, 1996) and some extrastriate cortical pathways may be spared. As is well known, these spared pathways permit some hemianopic patients to perform at better than chance levels in forced choice tasks that concern the properties of unseen stimuli, a phenomenon known as “blindsight” (e.g., Weiskrantz, 1997).

The two case studies of hemianopic patients produced results that were congruent with Ison and colleagues’ rat study (1991) for PPI, but that differed somewhat with regard to PPF. Working at Dodge’s lab, Hilgard and Wendt (1933) studied the effects of visual prestimulation on the acoustically elicited blink reflex in a patient with complete surgical resection of the left occipital cortex. They used two stimulus onset asynchronies (SOAs), one that was optimal for PPF (45 ms) and the other, for PPI (120 ms). Reflex amplitude was assessed using sophisticated optical recording methods, but latency was not measured. Relatively weak prestimuli (11 or 52 lux) were used during the first and third day of testing. In these sessions, the prestimuli caused inhibition at 120 ms and facilitation at the 45 ms asynchrony when presented in the good hemifield, but neither form of modulation was observed for blind-hemifield prestimuli. During the second session a very intense (>11,000 lux) prepulse was presented at 45 ms, the asynchrony favoring PPF. In this session, facilitation was triggered by the prepulse regardless of which side it was presented to. However, the authors suggested that the blind-hemifield prestimulus may have produced scattered light that stimulated the functioning hemiretinae, because it could be consciously observed by the patient.

Burke and Hackley (1997) replicated the results of Hilgard and Wendt using photically rather than acoustically evoked blinks. This patient had right-sided hemianopsia resulting from an infarct in his left occipital lobe. Consistent with previous results (Hackley and Johnson, 1996), the photic blink reflex was the same whether evoked from within the blind or intact hemifield. Prepulse-reflexogenic stimulus onset asynchrony was fixed at 120 ms, to maximize inhibition. The results confirmed Hilgard and Wendt’s (1933) and Ison and colleagues’ (1991) finding that visual PPI is dependent on an intact neocortex. Although a 120-ms lead time is not optimal for PPF, an apparent facilitation of blink latency was obtained for both intact- and blind-hemifield prestimuli.

The present study was intended to replicate and extend these earlier findings. A wider range of SOAs was employed, the blink reflex was elicited by both cutaneous and acoustic stimuli, and a group of patients was studied so that the reliability and generality of findings could be assessed with inferential statistics. Also, voluntary as well as reflexive responses to the reflexogenic stimuli were recorded. Studies of normal individuals in which voluntary and reflexive responses to intense stimuli were simultaneously recorded have found that both types of motor responses are speeded by prestimulation at long (e.g., Zeigler et al., 2001) and very short (Low et al., 1996) lead times.

Based on the human and animal data reviewed above, the following predictions were made: In the absence of functioning striate cortex, PPI of reflex amplitude will not be obtained, PPF of reflex amplitude and latency will still be observed (perhaps at a broader range of lead times than normal, due to the absence of PPI), and facilitation of voluntary reaction time might be evident (i.e., a blindsight variant of the normal warning effect).

2. Methods

2.1. Participants

There were 13 participants with unilateral visual field defects, 6 with right hemifield defects and 7 with left (Table 1). Five of the patients were male, eight were female, all were right handed, and the mean age was 59.2 years (range: 18–78). These participants were recruited through the Neuro-Ophthalmology Service of the Mason Eye Institute at the University of Missouri-Columbia. All subjects granted their informed consent and were reimbursed for participation in this 3- to 4-h long experiment.

2.2. Apparatus and stimuli

Participants were seated in a reclining chair in a well lit room during the experiment. All visible surfaces had been painted black or covered with black felt to minimize light scatter. Prestimuli were produced by two 14-cm (about 5°) wide incandescent lamps placed in symmetrical locations on the left and right of a continuously illuminated, 5-mm wide, light-emitting diode (LED) that served as the fixation point. To further reduce light scatter, the lamps were located at the back of felt-covered, cube-shaped boxes that measured 35 cm on each side.

Each prepulse had a duration of 130 ms, comprising a rise-time of 50 ms and a decay time of 80 ms. Note that this duration is longer than that of our shortest lead times, therefore the offset transient would not contribute to reflex modulation effects in these conditions. Lamps were covered with translucent glass that was painted with stripes in order to achieve a one-cycle-per-degree pattern of light and dark bars. This spatial frequency had been shown to be optimal for PPI in humans (Ulrich, 1983). The translucent glass was covered with a 2-log unit neutral density filter in order to reduce the intensity of the lamps. This was necessary because the unreduced prestimuli were shown to elicit photic blink reflexes in several normally sighted pilot subjects. After the reduction in intensity, the light bars of
the prestimulus lamp had a brightness of 453 cd/m² and the dark bars were 1.3 cd/m². For each patient, one lamp was positioned within a perimetrically defined dense region of the scotoma. The other was placed in the mirror-image location of the good hemifield. For example, if the patient had an upper left quadrantanopia, then the lamps were placed above fixation at an elevation and symmetrical azimuths that centered the left lamp in the region of poorest vision.

The cutaneous blink-eliciting stimulus consisted of a 50-ms, 10-psi burst of compressed air presented to the lower mid-forehead (i.e., the glabella). The duration and onset of the stimulus was determined by a computer-controlled solenoid valve. The air was vented through plastic tubing held in place by a headband. The air puff produced an acoustic artifact that measured about 80 dB and had a rise-time of less than 5 ms. The acoustic reflexogenic stimulus was an unramped (rise time <2 ms), 50-ms, 100-dB (SPL-A), white noise burst presented binaurally over a pair of Sony (Model MDR-25) headphones. An artificial-ear coupler was not available for these headphones; hence, calibration of the acoustic stimuli was only approximate.

Voluntary responses were made by squeezing one of two 2.5 cm-wide dowel rods that protruded from a board placed across the patient’s lap. These isometric grips were placed one in front of the other in line with the fixation point to avoid stimulus-response compatibility effects. A personal computer controlled presentation of the experimental stimuli and data acquisition.

2.3. Procedure

Before arriving at the psychophysiology laboratory for testing, each participant had his or her visual field defects mapped by means of computerized Humphrey perimetry (Carl Zeiss Ophthalmic Systems, Inc.; Dublin, CA) at the Mason Eye Institute. Performance on this routine clinical test was the primary criterion for subject selection. In these

<table>
<thead>
<tr>
<th>Case/Sex/Age (lesion-test interval)</th>
<th>Neurological status</th>
<th>Visual field defect</th>
</tr>
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<tbody>
<tr>
<td>PD/M/72 (5 years 6 months)</td>
<td>Left occipital lobe cerebro-vascular accident</td>
<td>Right hemifield defect with some sparing along vertical meridian of inferior right quadrant</td>
</tr>
<tr>
<td>FM/F/64 (9 months)</td>
<td>Resection of metastatic tumor in cuneous region of occipital lobe</td>
<td>Left hemifield defect with some sparing along vertical meridian of superior left quadrant</td>
</tr>
<tr>
<td>GG/M/54 (6 years 2 months)</td>
<td>Right occipital lobe arteriovenous malformation, surgically embolized, then resected; Postoperative occipital hematoma, surgically evacuated; hypometria of saccades directed towards the scotoma; disturbance of movement perception</td>
<td>Left hemifield defect with sparing of macula and vertical meridian along upper left quadrant</td>
</tr>
<tr>
<td>CS/F/69 (16 months)</td>
<td>Right occipital lobe cerebro-vascular accident</td>
<td>Shallow inferior left visual field quadrantanopsia</td>
</tr>
<tr>
<td>JL/M/74 (15 months)</td>
<td>Left inferior occipital lobe infarct with intermittent palinopsia (visual perseveration)</td>
<td>Superior right visual field quadrantanopsia, defect extends slightly into lateral aspect of right inferior visual field</td>
</tr>
<tr>
<td>JE/F/78 (4 years 6 months)</td>
<td>Left parieto-occipital lesion</td>
<td>Right hemifield defect with significant sparing along vertical meridian of right inferior quadrant, defect extends into superior left quadrant which shows a mild loss</td>
</tr>
<tr>
<td>TG/F/76 (2 years 7 months)</td>
<td>Right occipital lobe cerebro-vascular accident with previous right parietal lobe lacunar infarct</td>
<td>Left hemifield defect with macular sparing and slight impairment of superior and inferior most portions of right hemifield</td>
</tr>
<tr>
<td>VA/M/56 (6 years 9 months)</td>
<td>Motor vehicle accident at age 6 requiring 3 craniotomies. Struck in occiput of head which resulted in right parieto-occipital lesion and visual disturbance</td>
<td>Inferior left visual field quadrantanopsia with slight sparing in inferior portion along vertical meridian, defect extends slightly into lateral portion of superior visual field</td>
</tr>
<tr>
<td>DB/M/55 (13 months)</td>
<td>Left hemispheric stroke secondary to left vertebral artery occlusion</td>
<td>Right hemifield defect with inferior paracentral sparing superior to the horizontal meridian</td>
</tr>
<tr>
<td>SB/F/58 (9 months)</td>
<td>Paralyzed on right-side following intracranial aneurysm with Terson’s syndrome</td>
<td>Right hemifield defect</td>
</tr>
<tr>
<td>JH/F/57 (10 years)</td>
<td>Left carotid artery occlusive disease with a basilar tip artery aneurysm, repair of the aneurysm resulted in right hemiparesis, left occipital lobe and left thalamus infarcts and bilateral cranial nerve III palsies</td>
<td>Right hemifield defect with some paracentral sparing superior to the horizontal meridian</td>
</tr>
<tr>
<td>AH/F/43 (3 years 7 months)</td>
<td>Resection of oligodendroglioma in right occipital lobe</td>
<td>Inferior left quadrantanopsia with paracentral sparing</td>
</tr>
<tr>
<td>AD/F/18 (2 years 2 months)</td>
<td>Intraparenchymal and subarachnoid hemorrhage with right to left midline shift secondary to motor vehicle accident, subsequent craniotomy with clipping of right middle cerebral artery aneurysm</td>
<td>Superior left hemifield defect with some sparing of the superior aspect along the vertical meridian, inferior left hemifield defect with paracentral sparing</td>
</tr>
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static perimetry tests, a .43° spot of light was presented at varied intensities at random locations within a radius from fixation of either 24 or 30°. The background illumination of the hemispheric screen was 315 mL. Participants pressed a button each time they detected the onset of one of the spots of white light. Stability of gaze was confirmed by very low or zero response rates for stimuli projected to the natural blind spot. The procedure was repeated to obtain separate visual field maps for both eyes.

At the psychophysics laboratory participants were given a general description of the experiment and instructed that they were to squeeze with one hand if they received an air puff and with the other if they received a noise burst. The task required close attention because the air puff made a sound qualitatively similar to the noise burst. Hand-stimulus assignment in this choice reaction time task was counterbalanced across participants. Participants were told that the gratings would sometimes be illuminated just before the imperative/reflexogenic stimulus. They were also asked to maintain fixation on the LED, but were told that they could rest their eyes for a few seconds after each air puff or noise burst. The minimum intertrial interval of 8 s was explained, along with the importance of having the eyes open and fixated on the LED by the beginning of the trial. Gaze direction and task compliance were monitored via electro-oculography and ambient-light video.

The procedure consisted of 6 blocks of 32 trials. A brief rest break was given after each block of trials and a longer break was provided after half of the blocks had been completed. There were three general types of trials: A blink-eliciting stimulus preceded by a prestimulus (N = 24 per block), a prestimulus delivered in isolation (N = 2), and a blink-eliciting stimulus in isolation (hereafter referred to as a control trial, N = 6). There were two possible prestimulus locations, blind and intact hemifield, and two possible blink-eliciting stimulus modalities, acoustic and cutaneous. The prestimulus-alone condition confirmed that the slow rise-time gratings were nonreflexogenic, and these trials will not be further discussed. Trials with both a prepulse and a reflexogenic stimulus used one of six SOAs that were chosen based on a pilot study. The asynchronies were 80, 120, 200, 400, 600, and 1000 ms. Trials were selected randomly without replacement.

By using two modalities for the blink-eliciting stimuli, a rapid presentation rate could be maintained without concern of excessive habituation. Thus, the intertrial intervals were unusually short for a startle experiment, ranging from 8 to 20 s (rectangular distribution). As noted above, the air puff was actually a bimodal acoustic-cutaneous compound. The presence of an early R1 component (discussed below) confirms that the somatic modality did contribute to the eyeblink EMG response.

Participants were asked a short series of questions at the conclusion of the experiment, while the electrodes were being removed. These questions concerned whether the patients ever saw the prestimuli in their blind hemifield and, if so, what the estimated brightness was as compared to the gratings in the intact hemifield.

2.4. Recordings and analyses

Electrophysiological activity was recorded using Ag/AgCl surface electrodes filled with Grass EC-2 paste. Reflexive EMG bursts were recorded from the agonist muscle for eye closure, m. orbicularis oculi. Two electrodes were centered below the pupil on the lower lid of each eye for these recordings. EMG bursts associated with voluntary hand-grip responses were recorded with two electrodes located on the dorsal surface of the forearm. To monitor gaze stability, horizontal electrooculograms (H-EOGs) were obtained using electrodes placed approximately 2 cm lateral to the outer canthus of each eye. Vertical electrooculograms (V-EOGs) were recorded using the more medial of the electrodes on the bottom lid of the right eye paired with an electrode placed on the forehead directly above the pupil. Care was taken to avoid excessive abrasion, but electrode impedances were always less than 15 kΩ. The bandpass settings were 30–300 Hz for forearm and eyelid EMG and .01–100 Hz for both H-EOG and V-EOG.

Event-related potentials were recorded from Fz, Pz, and Oz, but these data will not be presented. Contingent negative variations were not obtained even with intact-hemifield prestimuli, presumably due to the use of variable SOAs that made onset of the imperative stimulus difficult to predict. Also, there were too few trials per condition to generate interpretable visual evoked potentials.

EMG activity from both eyelids and forearms were full-wave rectified and then signal averaged. Trials with excessive EMG activity during the baseline period (e.g., due to spontaneous blinks), with suspected shifts in gaze, or with errors in the RT task were excluded from the averages. The data of participants who failed to manifest a particular response (e.g., the acoustic blink reflex) were excluded from analyses of that measure. EMG responses on control trials were required to be at least three times larger than background noise levels for a participant’s data to be accepted for analysis. Blinks were also recorded using V-EOG, which reflects suppression of the blink antagonist muscle, levator palpebrae, and passive forces (e.g., viscosity, elasticity) in addition to activation within the agonist muscle, orbicularis oculi.

Signal averaged waveforms for each condition were measured for onset latency, defined as the first point at which 25% of peak amplitude was reached, and mean amplitude, defined as the average voltage level within a specified latency window relative to the 30-ms prestimulus baseline. For the cutaneous blink reflex, separate measurement windows were employed for the disynaptic (R1) and polysynaptic (R2) EMG components (15–30 and 60–130 ms, respectively). Means for each subject for each condition were subjected to repeated measures analysis of variance (ANOVA). Planned comparisons at each SOA
used factors of ipsilesional/contralesional eyelid and either blind-hemifield prepulse versus control or intact-hemifield prepulse versus control. Significant modulatory effects on EMG were confirmed using percent change scores \((\text{Pre-pulse} - \text{Control})/\text{Control} \times 100\). For V-EOG measures of blink, the ipsi/contra factor was omitted because vertical electro-oculograms were only recorded from one eye. Effects are reported as significant if they lay within the conventional rejection region of \(p < .05\) and if a similar effect was also observed (1) for the same dependent measure at an adjacent SOA, or (2) for a different measure at the same SOA, or (3) for the same dependent measure and SOA but for a different stimulus condition. This procedure controls Type I error rate in the face of multiple comparisons without simultaneously increasing Type II error rate, which is not possible with Bonferroni-style corrections (Burke and Hackley, 1997).

3. Results

3.1. Phenomenological report

During postexperimental questioning, two of the 13 participants reported some ability to see the prepulses within their field defect. For one of these patients, additional testing was then performed to establish the extent to which she could see the gratings when actually trying to do so. The patient was asked to hold her gaze on the fixation light while shifting her attention to the blind hemifield. Under these presumably more favorable conditions, she claimed not to be able to perceive any of the blind-hemifield gratings. This follow-up testing was not performed with the second participant who reported seeing the blind-hemifield prestimuli. However, that individual reported only fleeting awareness (“Maybe just a flicker a few times”). The other 11 participants insisted that they were never able to see the blind-hemifield gratings. Their electrophysiological data were similar to those of the two participants with partial awareness.

3.2. Voluntary response latency

As noted above, onset latency was quantified as the first point in the signal averaged forearm EMG waveform to reach 25% of peak amplitude. In comparisons of blind-hemifield prepulse versus control trials and of intact-hemifield prepulse versus control trials at each SOA, the only significant effect in the acoustic conditions \((N = 12\) participants) was latency shortening at the 80 ms lead time for intact-hemifield prestimuli, \(F(1,11) = 19.69, p < .001\). A similar pattern was obtained for reactions to the cutaneous stimulus \((N = 11\) participants): Only when the prepulse was displayed in the intact hemifield and preceded the air puff by 1000 ms did it effectively serve as a warning signal and speed reaction time, \(F(1,10) = 16.89, p < .001\). None of the blind-hemifield conditions yielded effects that met our criteria for statistical significance.

3.3. Acoustic reflex magnitude

The data concerning modulation of acoustic blink EMG are depicted in Fig. 1. The top panel gives percent change scores as a function of SOA and shows that the size of the acoustically elicited blink tended to be facilitated at 80 ms and inhibited at all other asynchronies. Signal averaged waveforms collapsed across the 200-, 400-, and 600-ms conditions are shown in the bottom panel, illustrating that the presentation of the prepulse within the intact hemifield resulted in amplitude inhibition and latency facilitation whereas its presentation in the blind hemifield produced neither effect.

Planned comparisons for acoustic reflex EMG magnitude (60–130 ms measurement window, \(N = 12\) participants) at each of the SOAs for the intact-hemifield versus control conditions documented reliable inhibition at 120, 200, and 400 ms, \(F(1,11) = 14.16, 23.03,\) and 6.55, respectively; all \(p\)'s < .05. There were no main effects for the factor of ipsilesional vs. contralesional eyelid. However, at the 200 ms lead time both the intact-vs.-control and blind-vs.-control analyses showed ipsilesional/contralesional X prepulse/control interactions \([F(1,11) = 5.49\) and 6.44, respectively,

![Fig. 1. Acoustic blink reflex (EMG). (Top panel) Percent change in reflex magnitude as measured from signal averaged electromyograms from the orbicularis oculi (oo) muscle as a function of prepulse-reflexogenic stimulus onset asynchrony for trials in which the prepulse was delivered to the blind or the intact hemifield. (Bottom panel) Grand average EMG waveforms for responses to the acoustic reflexogenic stimulus. The solid line indicates control trials on which there was no prepulse. Long dashed lines are for trials in which the visual prepulse was delivered to the blind hemifield at onset asynchronies of 200, 400 or 600 ms. Fine dashed lines are for the analogous condition but for which prestimuli were presented within the patients’ intact hemifield.](image-url)
$p's < .05$] such that prepulse-control differences tended to be larger at the eyelid contralateral to the patients’ lesion.

Blinks measured from the V-EOG recordings (mean voltage, 70–170 ms) showed reliable inhibition by intact-hemifield prepulses at the 200, 400, and 600 ms asynchronies, $F(1,11) = 8.01$, $16.35$, and $4.90$, respectively; all $p's < .05$. Again, blind-hemifield prepulses had no effect.

## 3.4. Cutaneous reflex magnitude

In EMG recordings, the cutaneous blink reflex exhibits two major components that are modulated in different ways by a prepulse (Sanes and Ison, 1979). The early, disynaptic component, R1, is only manifest in the eye on the same side as the reflexogenic stimulus. It shows amplitude facilitation at essentially all nonzero lead times. The later, polysynaptic, bilateral component, R2, is similar to the acoustic blink reflex. It can exhibit facilitation at short and long asynchronies, but is inhibited at intermediate ones. In the present experiment, R1 amplitude was measured within a window of 15–30 ms, and R2 amplitude, from 60 to 130 ms.

The line graph in the top panel of Fig. 2 portrays percent change in R2 reflex amplitude as a function of SOA ($N = 13$ participants). Comparisons of the intact-hemifield prepulse conditions revealed statistically significant inhibition at the 120- and 200-ms lead times, $F(1,12) = 6.72$, $p < .05$. $F(1,12) = 9.63$, $p < .01$, respectively. This trend continues with the 400 and 600 ms asynchronies which were nearly significant, $F(1,12) = 4.72$, $p = .051$; $F(1,12) = 4.17$, $p = .064$, respectively. The blind-prepulse versus control comparisons returned no significant main effects at any SOA. A significant interaction was obtained between the ipsilesional/contralesional and blind/control factors at the 120 ms lead time, $F(1,12) = 4.94$, $p < .05$. As for the acoustic blink reflex, prepulse-control differences tended to be larger for the eyelid contralateral to the lesion.

Electrooculographic measures of blink appeared to be more sensitive than EMG. They indicated that the intact-hemifield prepulses generated significant inhibition in all but the 1000-ms condition (80 ms: $F(1,12) = 6.82$, $p < .05$; 120 ms: $F(1,12) = 10.42$, $p < .01$; 200 ms: $F(1,12) = 28.32$, $p < .001$; 400 ms: $F(1,12) = 18.90$, $p < .005$; 600 ms: $F(1,12) = 12.23$, $p < .005$). Again, blind-hemifield prepulses had no effect.

As expected, the disynaptic R1 component of the EMG behaved quite differently than did R2 and the acoustic blink reflex. Fig. 3 illustrates the fact that R1 amplitudes in the intact prepulse condition appeared to be greatly facilitated at all asynchronies above 80 ms. (R1 modulation can be seen in the 15–25 ms region of the waveforms in Fig. 2, lower panel.) Due to the small number of participants manifesting this component ($N = 6$), only the 200 ms condition yielded statistically significant results, $F(1,5) = 11.18$, $p < .05$. The 120, 400, and 600 ms intact-hemifield conditions were marginally significant, $F(1,5) = 4.66$, 5.44, and 5.55, respectively; all

![Fig. 2. Cutaneous blink reflex (EMG). (Top panel) Percent change in R2 reflex magnitude as measured from signal averaged electromyograms (EMG) from the orbicularis oculi muscle as a function of prepulse-reflexogenic stimulus onset asynchrony for trials in which the prepulse was delivered to the blind or the intact hemifield. (Bottom panel) Grand average EMG waveforms for responses to the cutaneous reflexogenic stimulus. The solid line indicates control trials on which there was no prepulse. Long dashed lines are for trials in which the visual prepulse was delivered to the blind hemifield at onset asynchronies of 200, 400 or 600 ms. Fine dashed lines are for the analogous condition but for which prestimuli were presented within the patients’ intact hemifield. Activity in the 10–30 ms region shows facilitation of the R1 component. The R2 component seen at 30–100 ms was inhibited by intact-hemifield prepulses.](image)

![Fig. 3. R1 component of cutaneous blink reflex. Percent change in reflex magnitude as measured from signal averaged electromyograms (EMG) from the orbicularis oculi muscle as a function of prepulse-reflexogenic stimulus onset asynchrony for trials in which the prepulse was delivered to the blind or the intact hemifield ($N = 6$ participants, see also Fig. 2, bottom panel).](image)
Another type of prepulse facilitation is the speeding of reflex onset. Latency of the acoustic blink EMG burst was shortened by intact-hemifield prepulses in the 200 ms condition of the intact-vs.-control analysis \( [N = 12 \text{ participants}; \, F(1,11) = 6.02, \, p < .05] \). The only other reflex latency effect observed in this experiment involved comparisons of the ipsilesional and contralesional eyelids. A main effect for this factor was observed in the 600-ms asynchrony condition of the intact-vs.-control analysis such that blinks tended to be slower at the eyelid contralateral to the patients’ lesion (mean delay = 6 ms; \( F(1,11) = 9.88, \, p < .01 \)). This effect also achieved significance in the 80-ms condition of the blind-vs.-control analysis (mean delay = 5 ms; \( F(1,11) = 13.42, \, p < .005 \)). Because the effect was found on control as well as prepulse trials, it is considered an efferent modulation pattern (Hackley and Johnson, 1996) and does not constitute evidence for blindsight. Whether contralesional slowing generalizes to the cutaneous blink reflex could not be ascertained because frequent and inconsistent overlap of the R1 and R2 components precluded latency measurements.

### 4. Discussion

The major finding of this study was that lesions of striate cortex eliminate prepulse inhibition and prepulse facilitation of the blink reflex when the prestimulus is located within the scotoma. With regard to inhibition, this finding confirms two previous case studies in humans (Hilgard and Wendt, 1933; Burke and Hackley, 1997) and an animal study (Ison et al., 1991). The results imply that striate cortex either mediates or modulates visual PPI.

The present data cannot distinguish these two possibilities, but a previous psychophysical study suggests the latter is more likely. Ulrich (1983, Expt. 4) found that the abrupt onset of stereoscopic contours within a random dot stereogram triggered reliable inhibition of the cutaneous R2 reflex. On the assumption that only the geniculostrate pathway can mediate stereopsis and contour detection, this well controlled experiment suggests that visual prestimuli gain access to the brainstem PPI system (i.e., the pedunculopontine and lateral tegmental nuclei; Fendt et al., 2001; Swerdlow et al., 2001) following neocortical processing.

As noted in the Introduction, the three previous anatomical studies produced varying results regarding prepulse facilitation. Ison and colleagues (1991) found that diffuse chemical lesions of cortex in rats caused PPI to be replaced by PPF at lead times ranging from about 70 to 500 ms. Using an optimal lead time of 45 ms, Hilgard and Wendt (1933) failed to observe PPF to blind-hemifield stimuli that were of low or moderate intensity. Finally, Burke and Hackley (1997) reported an apparent prepulse facilitation of latency but not amplitude in their case study. For the acoustic blink reflex, the present results were most similar to the null findings of Hilgard and Wendt. When the prepulse was delivered from within the intact hemifield, a non-significant trend toward amplitude PPF was observed at 80 ms and reliable latency PPF was documented at 200 ms. Blind-hemifield stimuli failed to trigger PPF.

Cutaneous blink reflexes had not previously been studied. For the early R1 component we found that intact-hemifield prestimuli produced a trend toward amplitude facilitation at all lead times greater than 80 ms, with statistical significance at 200 ms. Blind-hemifield prepulses had no effect. It appears that facilitation by weak visual gratings requires processing at the cortical level, at least in humans. The three earlier studies used simple luminance increments rather than gratings. Therefore, it remains possible that PPF can be triggered without cortical processing in the case of such stimuli.

Species differences might also contribute to the discrepancy between the present data and those of Ison and colleagues (1991). Because rats fear bright lights, luminance increments might activate subcortical fear pathways, leading to affect-induced reflex modulation. The modulation of startle by emotion-inducing stimuli presented within the scotoma of patients with visual cortex damage is a promising new direction for blindsight research (Hamm et al., 2003).

### References

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