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To blink or not to blink: inhibition and facilitation of reflex blinks

Received: 14 March 1996 / Accepted: 24 July 1996

Abstract A reflex blink typically inhibits subsequent blinks. In this study, we investigated whether the nature and time course of this inhibition vary when different combinations of blink-evoking stimuli are used. We used the paired stimulus paradigm, in which two blink-evoking stimuli — a conditioning stimulus followed by a test stimulus — are presented with a variety of interstimulus intervals, to examine the interactions between blinks evoked by trigeminal and acoustic stimuli in rats and humans. In addition, we studied the effect of a blink-evoking trigeminal stimulus on subsequent gaze-evoked blinks in humans. The results revealed that long-lasting inhibition occurred when the conditioning and test stimuli were within the same modality. A shorter period of inhibition followed by facilitation occurred when the stimuli were in different modalities. The data demonstrate that a blink-evoking stimulus initiates a lengthy period of inhibition in its own sensory pathway and a shorter period of inhibition in the reticular formation and/or in blink motoneurons. In addition, the results show that the blink-evoking stimulus also initiates a facilitatory process. Thus, the magnitude of a blink reflects a balance between inhibitory and facilitatory processes.

Key words Reflex blinks · Trigeminal · Auditory · Startle · Prepulse

Introduction

A critical feature of the blink motor program is that it must inhibit itself following a blink. With each lid movement of a blink, air races through the eyelashes and the lid rubs against the cornea. Presentation of either of these stimuli is sufficient to elicit a reflex blink. Thus, if a blink or the stimulus that evokes it fails to initiate a period of inhibition, then each blink will elicit a reflex blink, starting blepharoclonus or a spasm of lid closure. The current study investigates the duration and sites of this inhibition by pairing reflex blinks elicited by stimuli in the trigeminal and acoustic modalities and gaze-evoked blinks.

The paired stimulus paradigm provides a measure of the blink refractory period. For example, presenting pairs of identical stimuli to the supraorbital branch of the trigeminal nerve evokes two responses that normally differ markedly in amplitude. With interstimulus intervals less than 1500 ms, the blink evoked by the second (test) stimulus is smaller than the blink evoked by the first (conditioning) stimulus in humans (e.g., Kimura 1973a,b) and rodents (Basso et al. 1993; Pellegrini and Evinger 1995). Pellegrini and Evinger (1995) demonstrated that the suppression of the blink evoked by the second SO stimulus occurs within the trigeminal complex. If blink inhibition takes place only within the sensory nucleus active in producing a reflex blink, then there will be no inhibition of subsequent blinks elicited through a different stimulus modality.

In the present study, we investigated the interactions between blinks evoked by SO stimuli, acoustic stimuli, and gaze-evoked blinks. The results revealed that the conditioning stimulus or the blink it elicited caused a long-lasting inhibition of subsequent blinks evoked by test stimuli in the same modality. In contrast, the same conditioning stimulus or blink caused only a short-lasting inhibition of subsequent blinks evoked by a test stimulus in a different sensory modality. These data showed that there are at least two sites of blink inhibition. A
The subjects participated in every condition. The four classes of pairing were: (1) A long-lasting inhibition within the sensory nucleus; (2) A short-lasting inhibition probably acting on reticular interneurons; and (3) A facilitation possibly acting on facial motoneurons. These data revealed that the effects of a blink-evoking stimulus on subsequent blinks reflect a balance between inhibition and facilitation.

**Subjects and methods**

All human experiments were approved by the SUNY Stony Brook Human Subject Committee. All rat experiments were approved by the SUNY Stony Brook Institutional Animal Care and Use Committee and performed with strict adherence to all federal, state, and university regulations regarding the use of animals in research.

**Electrode placement**

**Humans**

We recorded the electromyogram of the lid-closing, orbicularis oculi muscle (OOemg) and stimulated the supraorbital branch of the trigeminal nerve (SO) in a total of nine unpaid volunteers (age 21–51 years; four female, five male). To record the OOemg, the skin around the eye was cleaned with alcohol, and two Grass gold cup electrodes filled with electrode paste were taped over the orbicularis oculi. One electrode was placed over the lateral canthus, and the second was centered immediately beneath the palpebral portion of the lower lid. To stimulating the SO nerve, one electrode was taped over the supraorbital notch and the second attached 1 cm above the first. A fifth electrode, taped to the center of the forehead, served as a ground.

**Rats**

Sixteen rats were prepared for chronic recording of the OOemg and stimulation of the SO nerve as described in Evinger et al. (1993). Briefly, under general anesthesia (ketamine 90 mg/kg, and xylazine 10 mg/kg) and aseptic conditions, a nerve cuff with two stimulating electrodes was placed around the SO nerve as it exited the orbit. OOemg electrodes were implanted in the orbicularis oculi muscle near the lateral and medial aspects of the eye. We also inserted a silver wire ground electrode under the skin of the neck. Wires were led subcutaneously to a dental acrylic platform, attached to the skull by four stainless steel screws, where the wires joined a connector. Rats were alert and eating within 24 h of the surgery, but at least 48 h passed before the experiments began.

**Stimulus presentation**

In both rat and human subjects, each of the four different types of stimulus pairings were presented in separate sessions. Not all subjects participated in every condition. The four classes of pairing were: (1) The subjects received a pair of identical SO stimuli (SO–SO condition). (2) The subjects received a pair of identical blink-evoking acoustic stimuli (Acoustic–Acoustic condition). (3) The subjects received a blink-evoking acoustic stimulus followed by an SO stimulus. To obtain control records, the subjects received the SO stimulus alone on alternate trials (Acoustic–SO condition). (4) The subjects received an SO stimulus followed by a blink-evoking acoustic stimulus. To obtain control records, the subjects received the acoustic stimulus alone on alternate trials (SO–Acoustic condition). Interstimulus intervals (ISIs) in the above conditions ranged from 50 to 2000 ms. To diminish habituation, trials occurred every 30±5 s. To minimize changes in attention, human subjects read during the experiments.

For both human and rat subjects, we designated the reflex blink threshold to SO stimulation as the intensity required for an SO stimulus to evoke OOemg activity on 50% of the trials. SO stimulus intensity was adjusted to approximately 2 times the blink threshold. At intensities greater than 1.25 times threshold, subjects responded on 100% of the trials. For humans, stimulus intensity ranged from 2.0 to 9.0 mA with stimulus durations of 150–200 ms. For rats, stimulus intensities ranged from 0.5 to 2.0 mA with stimulus durations of 60–100 μs. Acoustic stimuli were pure tones (1 or 2 kHz) presented through a speaker 0.5 m from the subject. Stimulus duration was 50 ms for humans and 20 or 50 ms for rats, with a rise time of 0.1 ms and an intensity measured at the subject of 95 dB.

**Gaze-evoked blinks**

To investigate a blink that did not arise via the acoustic or trigeminal modalities, we tested the interaction between SO-evoked reflex blinks and gaze-evoked blinks in humans. Gaze-evoked blinks occur because they are a component of the command for saccadic gaze shifts (Evinger et al. 1994). Subjects fixated a central target 57 cm away. At the sound of a weak tone, they used a combined eye and head movement to acquire a continuously visible peripheral target 65° away from the fixation target as rapidly as possible. This movement elicited a gaze-evoked blink. On random trials, we presented an SO stimulus after the tone but before the subject began the head movement. We measured head position with a linear, low-torque potentiometer attached to a helmet that was securely affixed to the subject’s head.

**Measurement and analysis of responses**

The OOemg was amplified and filtered (0.3–5 kHz) and fed to a computer that digitized the records at 4 kHz and stored them for off-line analysis. The off-line analysis program integrated the OOemg activity and calculated the latency for the averaged components. For the gaze-evoked blink experiments in humans, we digitized both head position and OOemg at 5000 Hz. For each trial, the computer marked the beginning and end of the gaze-evoked blink and the head movement. For a pair of identical SO or auditory stimuli, we calculated a ratio of the integrated response to the second (test) stimulus divided by the integrated response to the first (conditioning) stimulus. Data for the responses evoked by paired stimuli of different modalities were calculated as the amplitude of response to a stimulus of the same modality when it was presented alone (control). Scattered plots showing the test/condition ratio at each ISI were fitted with a logarithmic curve. Logarithmic fits were slightly better than exponential and linear fits of the same data.

**Results**

Pairs of identical stimuli

**SO–SO stimuli**

Presenting pairs of identical SO stimuli dramatically altered the response to the second stimulus relative to the