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Research report

The blink reflex magnitude is continuously adjusted according to both current and predicted stimulus position with respect to the face

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ABSTRACT

The magnitude of the hand-blink reflex (HBR), a subcortical defensive reflex elicited by the electrical stimulation of the median nerve, is increased when the stimulated hand is close to the face ('far–near effect'). This enhancement occurs through a cortico-bulbar facilitation of the polysynaptic medullary pathways subserving the reflex. Here, in two experiments, we investigated the temporal characteristics of this facilitation, and its adjustment during voluntary movement of the stimulated hand. Given that individuals navigate in a fast changing environment, one would expect the cortico-bulbar modulation of this response to adjust rapidly, and as a function of the predicted spatial position of external threats. We observed two main results. First, the HBR modulation occurs without a temporal delay between when the hand has reached the stimulation position and when the stimulus happens (Experiments 1 and 2). Second, the voluntary movement of the hand interacts with the 'far–near effect': stimuli delivered when the hand is far from the face elicit an enhanced HBR if the hand is being moved towards the face, whereas stimuli delivered when the hand is near the face elicit an enhanced HBR regardless of the direction of the hand movement (Experiment 2). These results indicate that the top-down modulation of this subcortical defensive reflex occurs continuously, and takes into account both the current and the predicted position of potential threats with respect to the body. The continuous control of the excitability of subcortical reflex circuits ensures appropriate adjustment of defensive responses in a rapidly-changing sensory environment.

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1. Introduction

The eye blink elicited by electrical stimulation of the median nerve at the wrist hand-blink reflex (HBR) is a defensive reflex subserved by an entirely subcortical circuit at brainstem level (Miwa, Nohara, Hotta, Shimo, & Amemiya, 1998; Valls-Solé, Valldeoriola, Tolosa, & Marti, 1997). Human electromyographic (EMG) recordings from the *orbicularis oculi* muscles show that the HBR consists of a bilateral response with an onset latency of ~45 msec. The HBR is functionally similar to the R2 component of the trigemino-facial blink reflex (Cruccu & Deuschl, 2000).

The magnitude of the HBR increases when the proximity between the stimulated hand and the face is reduced (Sambo, Forster, Williams, & Iannetti, 2012; Sambo, Liang, Cruccu, & Iannetti, 2012). Such increase has allowed the identification of a portion of space surrounding the face with a protective function, the defensive peripersonal space (DPPS) (Bufacchi, Liang, Griffin, & Iannetti, 2015; Sambo & Iannetti, 2013; Sambo, Liang, et al., 2012). Similarly to what has been observed in non-human primates (Graziano & Cooke, 2006), potentially harmful stimuli occurring within this space elicit stronger defensive responses compared to stimuli located outside of it (Sambo & Iannetti, 2013; de Vignemont & Iannetti, 2015).

The HBR enhancement is consequent to a tonic, cortico-bulbar facilitation of the polysynaptic medullary pathways that relay the somatosensory input to the facial nuclei at pontine level (Sambo, Forster, et al., 2012). The strength of this facilitation is determined by a number of cognitive factors, which demonstrates its defensive value; for example, the HBR magnitude increase is finely adjusted depending on the estimated probability that the threatening stimulus will occur, as well as on the presence of defensive objects near the face (Sambo, Forster, et al., 2012). These observations highlight the behavioural relevance of such fine top-down modulation of this subcortical reflex.

In contrast, the temporal dynamic of this top-down modulation has not been explored. Indeed, in previous experiments the eliciting stimuli were delivered using a long temporal interval (i.e., more than 20 sec) after the hand was placed at the target distance from the face (Sambo, Forster, et al., 2012; Sambo & Iannetti, 2013; Sambo, Liang, et al., 2012). Therefore, the only information about the temporal profile of the cortico-bulbar facilitation underlying the HBR increase is that it is exerted *tonically*, well before the eliciting stimulus is delivered (Sambo, Liang, et al., 2012).

Given that individuals navigate in a fast changing environment, one would expect the cortico-bulbar facilitation to adjust within a time frame appropriate to minimise the potential for harm of sudden external events (i.e., within tens of milliseconds), and as a function of the predicted spatial position of external threats. Here, in two experiments we investigated the temporal characteristics of the cortico-bulbar facilitatory effect (*Experiment 1*), and its adjustment depending on the predicted position of the stimulus (*Experiment 2*). In *Experiment 1* we exploited the well-established HBR enhancement observed when the stimulated hand is located inside the DPPS of the face (position 'Near') compared to when it is located outside (position 'Far'). We tested whether the HBR enhancement is modulated by the length of the time interval between when the hand reached the target position and the subsequent delivery of the eliciting stimulus. In *Experiment 2* we exploited the ability of the nervous system to accurately predict limb positions during voluntary movement: participants continuously moved their hand between the 'Far' and 'Near' positions and the stimulus was automatically delivered either inside or outside the DPPS, when the hand was moving either towards or away from the face. We therefore tested whether the HBR facilitation depends on the *direction* of the movement of the stimulus with respect to the body.

2. Methods

2.1. Participants

Sixty six healthy participants were screened for this study, to identify HBR responders (Miwa et al., 1998). All participants gave written, informed consent before taking part in the study. All procedures were approved by the local ethics committee.

2.2. Stimulation and recording

Electrical stimuli were delivered to the right median nerve at the wrist using a bipolar surface electrode (inter-electrode distance: ~2 cm) attached to a Digitimer constant current stimulator (model DS7A). Stimulus duration was 200 μsec. Stimulus intensity was adjusted, in each participant, to elicit a clear HBR in at least three consecutive trials (3.5–70 mA, mean ± SD: 16.7 ± 16.3 mA). The definition of a clear HBR was subjective, and based on the visual inspection of the EMG recording, as in previous HBR experiments (Sambo, Liang, et al., 2012; Valls-Solé et al., 1997). EMG activity was recorded from the orbicularis oculi muscle, bilaterally, using pairs of surface electrodes. The active electrode was located ~1 cm below the lower eyelid, and the reference electrode ~1 cm laterally of the outer canthus. Signals were amplified and digitized at a sampling rate of 10 kHz (Neuroscan 4.5). In *Experiment 2*, the position of the hand was continuously monitored using a 3D localizer (Polhemus Fastrak) programmed to trigger a stimulus when the hand reached two pre-defined positions, one inside and one outside the DPPS (see next section for details). This device allows localizing the position and orientation of the hand, and consists of an alternating current static magnetic transmitter that emits an electromagnetic dipole field. Tracking sensors were attached to the moving hand and to the forehead, and their positions were located relative to the position of the static transmitter.

2.3. Experimental procedures

2.3.1. Preliminary recordings

Participants sat in a comfortable chair with their forearms resting on a pillow laying on a table in front of them. In each participant we first determined whether they were 'responders', by increasing the stimulus intensity until a clear HBR was elicited in three consecutive trials, or the participant