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Cardiac modulation of startle: Effects on eye blink and higher cognitive processing

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ABSTRACT

Cardiac cycle time has been shown to affect pre-attentive brainstem startle processes, such as the magnitude of acoustically evoked reflexive startle eye blinks. These effects were attributed to baro-afferent feedback mechanisms. However, it remains unclear whether cardiac cycle time plays a role in higher startle-related cognitive processes, as well. Twenty-five volunteers responded first by 'fast as possible' button pushes (reaction time, RT), and second, rated perceived intensity of 60 acoustic startle stimuli (85, 95, or 105 dB; 50 ms duration; binaural; instantaneous rise time), which were presented either 230 or 530 ms after the R-wave, and eye blink responses were measured by EMG. RT was divided into evaluation and motor response time according to previous research. Increasing stimulus intensity enhanced startle eye blink, intensity ratings, and RT components. Eye blinks and intensity judgments were lower when startle was elicited at a latency of R + 230 ms, but RT components were differentially affected: the evaluative component was attenuated, and the motor component was accelerated when stimuli were presented 230 ms after the R-wave. We conclude that the cardiac cycle affects the attentive processing of acoustic startle stimuli.

1. Introduction

Perception of bodily states plays an important role in the subjective experience of emotion (Wiens, 2005), consciousness (Damasio, 2003), and symptom genesis (Eley, Stirling, Ehlers, Gregory, & Clark, 2004). Cardiac modulation of startle eye blink (CMS) has been established as a 'background' methodology to assess cardio-afferent traffic, since it relies on intact baro-afferents and does not require active cooperation from participants (Schulz, Lass-Hennemann, Nees, et al., 2009; Schulz, Lass-Hennemann, Richter, et al., 2009). In this paradigm, the increased baro-afferent feedback during the early cardiac cycle phase attenuates startle responsiveness compared with the late cardiac cycle phase. Neural circuits for both startle (Davis, 2006) and the baroreceptor reflex (Jänig, 2006) have been identified and found to be relayed at the level of the brainstem, with only three synapses in each circuit. However, it is yet unclear whether the pre-attentional modulation of startle responses during the early cardiac cycle phase is also reflected by an altered cognitive evaluation of these eliciting stimuli.

In earlier studies, the impact of startle on parameters of cortical signal processing was substantiated by the finding that stimulus preferences of startling noises may be reflected by different response patterns in the electroencephalographic P300 component (Davis & Heninger, 1972; Hirano, Russell, Ornitz, & Liu, 1996; Putnam & Roth, 1990), which indicates a cognitive evaluation of the incoming stimulus. In another common pre-attentive startle modulation paradigm, the prepulse inhibition (PPI) of startle responsiveness (Blumenthal, 1999), in which weak pulses prior to the startle noise attenuate the startle response, the EMG responsiveness converges with subjectively perceived intensity (Blumenthal, Schicatano, Chapman, Norris, & Ergenzinger, 1996; Swerdlow, Blumenthal, Sutherland, Weber, & Talledo, 2007; Swerdlow, Geyer, Blumenthal, & Hartman, 1999; Swerdlow et al., 2005). To our knowledge, baroreflex-modulated reflex responsiveness is neither reflected by subjective aversiveness ratings of the eliciting stimulus itself (Edwards, Ring, McIntyre, & Carroll, 2001; Edwards et al., 2003), nor by ratings of emotional pictures that are presented within different cycle phases (Nyklicek, Wijnen, & Rau, 2005), although baro-afferent traffic has been found to reach higher cortical structures, such as the right anterior insula in the temporal cortex (Henderson et al., 2004; Kimmerly, O'Leary, Menon, Gati, & Shoemaker, 2005).

The simple response time to a startling stimulus may represent another measure for assessing higher cortical processing. Response times to non-startling stimuli are known to be affected by a long-term increase of baroreceptor loading, as was found in hypertensive patients (Harrington, Saxby, McKeith, Wesnes, & Ford, 2000;

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Karla, Jackson, & Swift, 1993) and by phasic variation of baroreceptor simulation across the cardiac cycle (Stewart, France, & Suhr, 2006; Weisz & Adam, 1996). A distinction between the stimulus evaluation component and the motor execution component of the response time revealed that the evaluation component is more likely responsible for the prolongation effect (Edwards, Ring, McIntyre, Carroll, & Martin, 2007).

However, the startle reflex is a defensive reflex that prepares the organism for an evasive motor response (Koch, 1999). A more intense startle stimulus shortens sensorimotor response time, regardless of whether the startle stimulus itself is the go-stimulus (Carlsen, Dakin, Chua, & Franks, 2007) or it is presented together with a go-stimulus (Lipp, Alhadad, & Purkis, 2007; Lipp, Kaplan, & Purkis, 2006; Valls-Sole et al., 1995). Thus, we assume that a dampening effect of baroreceptor feedback on startle responsiveness may impair both the evaluation and the motor component of the response time, if the go-stimulus is a startle-eliciting stimulus.

To evaluate the potential cortical impact of cardiac modulated startle we conducted a within-subject experiment with 25 healthy volunteers who received 60 randomized acoustic startle probes. The startle probes had an intensity of 85, 95, and 105 dB(A) and were presented with a latency of 230 ms and 530 ms after the participants' R-wave, identical to an earlier study protocol (Schulz, Lass-Hennemann, Nees, et al., 2009). The definition of R + 230 ms as the early cardiac cycle phase was based on the fact that (i) at this delay relative to the R-wave reflex responsiveness is maximally attenuated by baroreceptor feedback (Edwards et al., 2001), suggesting that neural output of arterial baroreceptors is at maximum around R + 230 ms (Edwards, Ring, McIntyre, Winer, & Martin, 2009), and (ii) simultaneous judgments of heartbeats and exteroceptive signals (Ring & Brener, 1992; Ring, Liu, & Brener, 1994) suggest effective bottom-up transmission of cardio-afferent signals at this latency. At R + 530 ms, the neural baro-afferent traffic should be minimal (e.g., Mancia & Mark, 1983; Milnor, 1990). The participants were asked to hold a home button pressed until they heard a startle sound, then to release it and to press a response button as fast as possible. After that they rated the subjective intensity of the startle sound. This procedure may clarify whether the cardiac modulation effect of startle is also reflected by modulation of cognitive evaluation processes such as stimulus evaluation and simple response times.

2. Method

2.1. Participants

Twenty-five young healthy undergraduate students (fourteen women) participated to receive course credit. Physical health status was assessed by a health questionnaire. Hearing problems (impairments, tinnitus), regular use of contact lenses, any actual health complaints, abuse of illicit drugs within the last six months, medication other than occasional pain killers and oral contraceptives, confirmed somatic or psychiatric diseases within the last six months other than banal infections or minor injuries, or a BMI lower than 19 or higher than 25 kg/m^2, were exclusion criteria. One individual was rejected before data collection due to acute psychopharmacologic medication. Furthermore, we excluded potential participants with a resting heart rate of higher than 85 bpm to prevent startle stimuli from extending into the next cardiac cycle. Mean age of the participants was 25.2 (range: 19–30; SD = 4.1) years, mean resting heart rate was 75.6 (SD = 7.1) bpm, and mean BMI was 21.4 (SD = 1.4) kg/m^2. All participants gave their written informed consent and were made aware of their right to discontinue participation in the study at any time. The study procedure was approved by the local ethics committee.

2.2. Apparatus

2.2.1. Stimulus intensity scores

Subjectively perceived stimulus intensity was assessed by an Electronic Visual Analog Scale (EVAS). This customized EVAS device consists of a continuously turning knob, whose activity is displayed on the internal LCD screen (13 cm × 4 cm). Additionally, anchoring adjectives can be presented onto that screen. In this study, the anchors were "very low intensity", "medium intensity", and "very high intensity". Response resolution of the EVAS device is 256-point. Recent studies confirmed the validity of electronic VAS devices in judging the intensity of startle stimuli (e.g., Swerdlow et al., 2007). We standardized the judgments by the scale resolution and thus provided %EVAS scores.

2.2.2. Data recording parameters

Physiological data were collected via a Biopac® MP150 system (Biopac Systems, Inc.) with 16 bit resolution and a sampling rate of 1 kHz. EMG startle responses were recorded via Tyco Healthcare H124SG electrodes (diameter: 24 mm) placed below the left eye with an inter-electrode distance of 1.5 cm to assess EMG-activity of the Musculus orbicularis oculi. Hardware band-pass filter settings (Biopac EMG100C) were 10–500 Hz, followed by software filtering (28 Hz high-pass cutoff: van Boxtel, Boelhouwer, & Bos, 1998). The raw signal was rectified and integrated online with a time constant of 10 ms (Blumenthal, 1994). Electrodes for ECG measurement (ECG Tyco Healthcare H34SG Ag/AgCl electrodes of 45 mm diameter) were placed according to a standard lead II configuration. The ECG signal was high-pass filtered (Biopac ECG100, HPF: 0.5 Hz) and stored to disk (1 kHz), as well. R-waves were identified online by a fast DASYLAB-8.0 (National Instruments, Inc.) algorithm running on a different CPU, based on a gradient detection, the threshold of which was set separately for each participant. Accuracy of R-wave detection in sines rhythm was higher than 99.8%, with a latency below 3 ms (internal lab report).

2.2.3. Stimulus presentation

Acoustic startle stimuli (intensities: 85, 95, and 105 dB(A), 50 ms duration, instantaneous rise time, binaural presentation) were presented via headphones (Sennheiser Electronic GmbH & Co. KG, Wedemark, Germany). Experimental instructions were displayed by an E-Prime 1.1 (PST Software, Inc.) based platform onto a LCD monitor at a distance of 80 cm from participant to screen.

2.2.4. Response times data collection

A home button and a response button were located on a PST E-Prime Serial Response Box (PST Software, Inc.) with a distance of about 1 cm. While the middle key of the Response Box was always defined as the home button, the response button was located left or right of the home button, each for half of the participants. As in past studies (Doucet & Stelmack, 1999, 2001; Jensen & Munro, 1979), the time from onset of stimulus presentation to lifting off the home button was defined as reaction time ('RT'), representing the central component of the response time. The interval between lifting off the home button and pressing the response button was defined as movement time ('MT'), representing the motor component of the response time. Median values were calculated for each condition in a particular participant and included in the statistical model due to the non-linearity of response times. Means of medians over participants are reported in the results section.

2.3. Analysis of physiological data

A customized C++ based semi-automated PC program was used to analyze EMG-responses. The algorithm identified response peaks in the rectified and integrated signal during a time interval