Physiology & Behavior 165 (2016) 179–186

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Effect of stress and attention on startle response and prepulse inhibition

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HIGHLIGHTS

- Prepulse inhibition was reduced by induced stress.
- Directing away attention from the pulse reduced startle response magnitude.
- Startle reflex and prepulse inhibition are useful tools to study the effects of emotional and attentional processes.

ARTICLE INFO

Article history:
Received 27 April 2016
Received in revised form 26 July 2016
Accepted 29 July 2016
Available online 30 July 2016

Keywords:
Startle
Prepulse inhibition
Stress
Attention

ABSTRACT

The startle reflex magnitude can be modulated when a weak stimulus is presented before the onset of the startle stimulus, a phenomenon termed prepulse inhibition (PPI). Previous research has demonstrated that emotional processes can modulate PPI and startle intensity, but the available evidence is inconclusive. In order to obtain additional evidence in this domain, we conducted two experiments intended to analyze the effect of induced stress and attentional load on PPI and startle magnitude. Specifically, in Experiment 1 we used a between subject strategy to evaluate the effect on startle response and PPI magnitude of performing a difficult task intended to induce stress in the participants, as compared to a group exposed to a control task. In Experiment 2 we evaluated the effect of diverting attention from the acoustic stimulus on startle and PPI intensity. The results seem to indicate that induced stress can reduce PPI, and that startle reflex intensity is reduced when attention is directed away from the auditory stimulus that induces the reflex.

1. Introduction

The startle reflex is an involuntary response consisting of flexion of certain muscle groups, most marked in the upper half of the body, that is produced when an intense stimulus appears. From a functional point of view, this reflex serves as a protective function against any signal strong enough to indicate a circumstance which might endanger the life or integrity of the individual, since it provides fast muscle activation that can support a defensive response if necessary [5,16].

Even though the startle response represents a seemingly unalterable reflex reaction, there are several circumstances that may modulate its intensity, either by intensifying or reducing the reflex response. Thus, for example, the startle reflex increases when a sensitization process (e.g., [56]) or a prepulse facilitation process (e.g., [86]) is induced. Conversely, a reduced response is observed after stimulus habituation (e.g., [58] or prepulse inhibition (e.g., ([25,38]).

The startle modulation process that has probably received the most attention in the recent scientific literature is the so-called Pre-Pulse Inhibition (PPI), a phenomenon that was operationally defined in 1965 by Hoffman and Searle as the reduced startle reflex to an intense sound (named Pulse) that appears when it is preceded by a weaker sound (named Prepulse) presented between 30 and 500 ms before the Pulse. Since the phenomenon was described for the first time, a large amount of research has been conducted intended to analyze PPI from physiological, psychological, or even psychiatric perspectives (see, for reviews, [5, 10,47]).

From a functional perspective, Graham [25] proposed that PPI has the purpose of protecting the processing of current information. Specifically, a pre-attentional brain inhibitory process intended to prevent current processing from interference will be active until the attended stimulus is fully processed. Such inhibition impedes the interference that would be induced by mobilization of the attentional resources that usually occurs when new stimuli are detected, and the intensity or the nature of the stimulus that follows is independent of the stimulus that is currently being processed. This PPI interpretation has been complemented by a physiological perspective proposing that any new stimulus presentation activates an inhibitory process involving limbic cortico-striato-pallido-pontine circuitry that minimizes the processing of other stimuli during a "gate" that ranges from 30 to 500 ms (e.g., [65]). From this perspective, PPI is considered to reflect the functioning of a central process, that has been labeled sensorimotor gating, that is responsible for protecting the processing of the first stimulus (the

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http://dx.doi.org/10.1016/j.physbeh.2016.07.022
0031-9384/

Prepulse) from the interference of other incoming stimuli (e.g., [70,71]). Since the integrity of the sensorimotor gating process ensures an adequate organization of our cognitive resources, it has been proposed that PPI can be employed as a neurobiological marker for those pathologies characterized by inadequate motor or sensory gating such as, for example, schizophrenia (e.g., [11,32,51,81]). Also, PPI deficits have been reported in cases of obsessive-compulsive disorder (e.g. [37]), patients with Huntington's disease [75], and many other pathologies (see, for a recent review, [44]). In fact, the relationship between PPI and psychopathology has largely favored the use of such phenomena as an experimental paradigm in psychophysiological research and, particularly, in the field of study of psychiatric disorders [15].

Since a common factor in many psychopathologies is the existence of high anxiety levels, this should be a relevant aspect to be specially considered when analyzing startle reflexes or PPI in pathological populations (e.g., [26,40]). In fact, there is experimental evidence indicating that the induction of positive or negative emotional states in participants without pathologies during startle or PPI induction modulates both responses (e.g., [17,84]).

More specifically, evidence on startle response and PPI changes induced by high anxiety or stress states have been obtained in experiments both with animals and with human participants, but the results seem contradictory. Thus, for instance, [49]) found disrupted PPI in rats submitted to stress induced by a forced swim procedure, and Pijlman et al. [57] found the same results in rats receiving a foot-shock treatment, but intact PPI was found in rats submitted to psychological stress (by being witnesses to the shock treatment). In experiments with human participants, [27]) using an anticipation of electric shock procedure (that can be considered as the equivalent to psychological stress, since the participants never received the electric shock) found enhanced PPI in the stress condition as compared to a control "safe" condition that did not expect any shock, but similar PPI enhancement was found by merely indicating to the participants that they should actively attend to the different stimuli presented during the experiment. Therefore, the PPI increase can be attributed either to an emotional or to an attentional effect of the treatment (or a combination of both factors). Relatedly, when PPI has been registered in pathological populations diagnosed with anxiety disorders characterized by the presence of stress, such as Posttraumatic Stress Disorder (PTSD) or Panic Disorder (PD), PPI appeared disrupted both in medicated PD patients [54], and unmedicated PD patients [53]. However, while several experiments have reported reduced PPI in PTSD patients ([29–31,55], others revealed intact PPI in similar populations ([13,39,52].

The available evidence on emotional modulation of the startle amplitude is far more consistent. Thus, according to the emotional priming model proposed by Lang and his colleagues [45,46], the startle intensity is increased when it is elicited in the presence of aversive stimulation (e.g., [20,36,84]), but it is decreased when the stimuli are appetitive (e.g., [14,17,69]). Such emotional modulation of the startle response has been observed both in experiments with animals and with human participants, and is not dependent on the modality of the stimuli presented to induce the emotional state [8].

The main purpose of the Experiment 1 was to add evidence to the apparently contradictory results on the effects of stress on PPI. To this end, we registered the startle response in healthy participants who were submitted either to a stress condition by being engaged in a very difficult task (Stress Group), or to a very easy task (Control Group). Previous evidence evaluating the effect of stress on PPI makes it difficult to anticipate a result, but based on the results from rats and from PTSD patients, we expect a reduced PPI effect for those participants in the stress condition as compared to those participants in the control condition [29,30,49]. As for the effect of stress on startle magnitude, our hypothesis is clearer: we anticipate an enhanced startle reflex in the Stress Group as compared to the Control Group.

Since performing a difficult task requires a great amount of attentional resources, and some studies have demonstrated the effect of attentional manipulations on startle response and PPI (e.g., [4,63,66,78]), we also analyzed the possible effect of attentional demands on startle and PPI. More specifically, using an "attention-to-prepulse" paradigm that involves instructions to attend to one of two prepulses differing in pitch and duration while ignoring the other, it has been demonstrated that PPI was higher to the attended as compared to the non-attended prepulse (e.g., [3,22]). Therefore, the stress-mediated reduction of PPI we anticipated in Experiment 1 could be also related to reduced attention to the prepulse. To check this possibility, we employed in Experiment 2 the same parameters and stimuli from Experiment 1 to induce the startle response and PPI, but the participants were faced with a very simple task that required the allocation of a high amount of attentional resources (High Load [HL] Group) or to a task that did not require such effort (Low Load [LL] Group). If attention plays a role in PPI modulation in the first experiment, we would expect reduced PPI in the HL Group, but PPI should remain unchanged in the LL Group. As for the startle response, we expect a reduction of intensity in the HL as compared to the LL condition (e.g., [4]).

2. Experiment 1

Stress corresponds to an emotional state that has been traditionally associated with relevant changes in learning and behavior, but it is a concept of difficult definition since it is composed of multiple components [50]. From a physiological point of view, stress produces changes in the activity of the mesolimbic dopaminergic system (e.g., [24,77]), and in the opioid system (e.g., [82]). Both physiological processes seem to be involved in startle and PPI modulation [27,57] that has favored the study of the relationship between stress, startle, and PPI ([21,27,29–31].

A common definition of a stressful situation implies that the requirements or demands of such situations threaten or exceed the capacities of the individual [48]. Accordingly, it is a common practice to induce situational stress in experimental situations by instructing the participants to solve intelligence-related tasks such as arithmetic tasks (e.g., [12,19]) or tests specifically designed to evaluate IQ as the Raven's progressive matrices test (e.g., [60,85]). In our first experiment, we manipulated stress by differentially threatening participant's self-esteem by facing half of them (those in the Stress Group) to the most difficult items from the Advanced Progressive Matrices test [59]. The remaining half of participants (those in the Control Group) were simply instructed to attend to a series of neutral images appearing on the computer screen, a common procedure used in our laboratory to minimize potential distractions in participants (e.g., [18]). To induce startle and PPI the experimental treatment alternated trials involving presentations of an intense tone by itself (the Pulse, that allowed the startle reflex to be registered), and Prepulse-Pulse trials, consisting of the same intense tone preceded by a weaker sound.

2.1. Method

2.1.1. Participants

Twenty-two volunteers ($n = 11$ per group), 8 males and 14 females, participated in this experiment for course credits. Their ages ranged between 17 and 25 years. None of the participants reported any visual or hearing problem. All participants were informed of the type of stimulation used in the experiment, and provided signed informed consent before to start the experimental manipulations. Seville University's ethical committee approved the study.

2.1.2. Materials

2.1.2.1. Questionnaire. Levels of induced affect and arousal were assessed using the Mood Grid Scale [61] that consists of a square divided in 81 cells organized in 9 rows and 9 columns, with the horizontal dimension representing emotion (from extremely unpleasant to extremely