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Relationship of prepulse inhibition of the startle reflex to attentional and executive mechanisms in man

Panos Bitsios*, Stella G. Giakoumaki

Department of Psychiatry and Behavioural Sciences, Faculty of Medicine, University of Crete, Heraklion, Crete, Greece

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Abstract

Prepulse inhibition (PPI) of the startle reflex at short lead intervals is thought to reflect the operation of a preattentive "sensorimotor gating" mechanism, which suggests that processing of the prepulse stimulus should not be modulated prior to its inhibitory effects on startle. To test this hypothesis, we examined whether PPI is affected following habituation to the prepulse. PPI was measured in two sessions associated with either the presence (habituation condition) or the absence (control condition) of prepulse repetition. There was a trend for prepulse repetition to reduce the effectiveness of that prepulse in inhibiting the startle response. We also explored the relationship of PPI to scores in tests of selective and sustained attention and planning ability. Overall PPI performance was correlated to performance indices of planning ability and there was a trend level correlation with scores in selective but not sustained attention tests. These preliminary results merit further investigation.

Keywords: Prepulse inhibition; Startle reflex; Habituation; Stroop; CANTAB; Healthy humans

1. Introduction

The startle reflex consists of contraction of the skeletal and facial musculature in response to a sudden intense stimulus, e.g. a loud noise. The startle reflex is a primitive, cross-species reflex mediated by a pontine-based, ear-to-spinal outflow, simple neural circuit that has been specified in animals by the work of Davis and colleagues (Lee et al., 1996). The blink reflex component of the startle response is a convenient measure of startle in man and refers to the electromyographic response of the orbicularis oculi muscles in response to a sudden intense stimulus (e.g. a loud noise) (Graham, 1975; Braff et al., 1978). It is well established that the amplitude of the startle reflex response is attenuated when the strong startle-eliciting stimulus is preceded 30–500 ms by a weaker stimulus, or prepulse. This phenomenon is termed prepulse inhibition (PPI) and has been observed across a wide range of stimulus intensities and modalities in animals (Hoffman and Ison, 1980,

* Corresponding author. Tel.: +30 2810 394610; fax: +30 2810 394617.
E-mail address: pbitsios@med.uoc.gr (P. Bitsios).

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1992) and humans (Graham, 1975; Filion et al., 1998 for review). PPI varies with different prepulse intensities being generally more pronounced for more intense prepulses (Graham and Murray, 1977; Schwarzkopf et al., 1993; Blumenthal and Creps, 1994; Blumenthal, 1995), and it is most robust for 60- and 120-ms lead intervals (i.e. when the prepulse precedes the pulse stimulus by 60 or 120 ms). Graham (1975) proposed that PPI reflects the operation of an automatic preattentive sensory gating process that momentarily protects the processing of the prepulse from distractions such as a startling loud sound. PPI of the startle reflex is thus used as an operational neurobiological measure of a central process termed "sensorimotor gating" (Swerdlow et al., 1992).

The operation of a preattentive sensory gating mechanism is assumed to precede any general or selective attentional process, and thus there should be no attentional selection of sensory information for further processing prior to the operation of such a mechanism (Deutch and Deutch, 1964). Therefore, if the phenomenon of PPI reflects the operation of a preattentive "sensory gating" mechanism, independent from a selective attentional mechanism, then processing of the prepulse stimulus should not be modulated prior to its inhibitory effects on startle. Consequent to this idea is the hypothesis that PPI of the startle reflex should not diminish with prepulse habituation. Indeed, animal (Wu et al., 1984; Ison et al., 1973; Russo et al., 1975; Hoffman et al., 1969) and human [Abel et al., 1998; Lipp and Krinitzky, 1998; Schell et al., 2000] studies showed that repetitive preexposure to a prepulse does not produce any observable habituation of PPI of the startle reflex.

In the above studies, startle was measured over intermixed blocks of trials consisting of the startle stimulus alone and of the startle stimulus preceded by the prepulse, either following extended repetition of the prepulse or not. It is possible that habituation of PPI at the end of the phase of preexposure to the prepulse may have dissipated as a result of presentations of the startle stimulus (itself a potent dishabituating stimulus) at test. Gewirtz and Davis (1995) minimised the potential impact of dishabituation over the course of testing for PPI, using a relatively small number of startle stimuli presented at long regular intervals, interspersed among a much larger number of auditory prepulse-alone stimuli. These procedures unmasked a reduction of the effectiveness of an auditory prepulse in inhibiting the startle response, leading to the conclusion that PPI in the rat, is subject to the influences of general attentional mechanisms. The primary aim of this study was to examine whether PPI in human subjects, could habituate as a result of prepulse repetition, using a protocol based on the optimal procedures mentioned above.

The dominant theoretical interpretations of the phenomenon of PPI, at least at short lead intervals, is that it reflects (a) a "low-level" inhibitory mechanism that serves to protect processing of the prepulse (Graham, 1975) and also (b) a more general inhibitory process (sensorimotor gating). The latter is regarded as a critical component for intact cognitive processing that involves filtering out irrelevant sensory, motor, and cognitive information in the early stages of information processing (Braff and Geyer, 1990). Despite these widely accepted theoretical interpretations, the study of the relationship between PPI and more specific aspects of cognitive processing in normal subjects has received little empirical attention to date. One approach has been the investigation of the relationship of PPI to other measures of cognition, which share a similar "inhibition-based" theoretical interpretation. Indeed, such studies comparing PPI with the backward masking and negative priming (measures reflecting low-level inhibitory processes) and with the Wisconsin Card Sorting Test and Ego Impairment Index (neuropsychological and clinical measures reflecting high-level inhibitory processes) reveal several intriguing similarities (see Filion et al., 1999 for a review of this evidence). However, there are also important differences, which weaken the argument of a shared, common underlying inhibitory process (for a review of this evidence, see Filion et al., 1999) and leave this issue still inconclusive.

A secondary aim of this study was therefore to collect preliminary empirical evidence about the relationship of PPI to behavioral measures of attention, which are "inhibition-based" (Stroop Interference Test) and others, which are not (Rapid Visual Information Processing test) in the same group of normal subjects. This aim also extends in the collection of preliminary empirical evidence about the relationship of PPI to planning ability, a measurable aspect of cognition, central to many aspects of