



Sex differences in prepulse inhibition of the acoustic startle response

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Abstract

The startle response is inhibited when the startle-eliciting stimulus is preceded 30–500 ms by a prepulse. This effect, known as prepulse inhibition (PPI), is believed to represent a sensorimotor gating mechanism, which protects the brain from experiencing sensory overload. PPI is disturbed in many psychiatric disorders. Within healthy populations, women show less PPI than men. This study employed a new PPI paradigm with a single prepulse or two prepulses to measure PPI in 15 men and 15 women. Startle stimuli were preceded on some trials by a single discrete prepulse with a 120-ms prepulse-to-pulse interval. On other trials, a second discrete prepulse preceded the first with 30–480-ms prepulse-to-prepulse intervals. Women showed less PPI than men with a single prepulse. PPI, however, was quantitatively identically reduced (greatest reduction when the second prepulse preceded the first with a 120-ms interval) in the two sexes by two-prepulse trials, relative to that with a single prepulse. Women showed a smooth transition from reduced PPI to an observed prepulse facilitation (PPF) with two prepulse trials. We conclude that sex difference consists in a general shift of the inhibition/facilitation curve in the direction of facilitation in women relative to men.

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1. Introduction

Modulation of the startle response represents a cross-species non-invasive psychophysiological model which is widely applied to evaluate information processing and emotional deficits in a wide variety of human and animal populations (Kumari & Sharma, 2000). The simple startle reflexive response is known to show several forms of plasticity, including prepulse inhibition (PPI) and habituation. PPI refers to a reliable reduction in the amplitude of the startle response to a strong sensory stimulus (pulse) if this is preceded by 30–500 ms by a weak stimulus (prepulse) (Graham, 1975). It is thought to reflect an automatic sensorimotor gating mechanism: while resources are directed at the prepulse, any other incoming information is attended to at a reduced level thereby safeguarding the processing of the initial event (Graham & Murray, 1977). Deficits in the ability to avoid such stimulus interference may cause sensory over-stimulation and behavioral confusion (Braff & Geyer, 1990), as seen for example in patients with schizophrenia who also show reduced PPI (Braff, Stone, Callaway, Geyer, Glick, & Bali, 1978; Braff, Grillon, & Geyer, 1992; Braff, Swerdlow, & Geyer, 1999; Perry, Geyer, & Braff, 1999).

Sex differences are characteristic of many behaviours and are also observed with regards to PPI. Women consistently show reduced PPI compared to men (Swerdlow, Auerbach, Monroe, Hartson, Geyer, & Braff, 1993; Swerdlow, Hartson, & Auerbach, 1997; Swerdlow, et al., 1999) even after controlling for differences in personality characteristics (Corr, Tynan, & Kumari, *in press*) or cigarette smoking status (Swerdlow et al., 1999). Changes in PPI in normal women may, in part, reflect cyclic changes in mesostriatal dopamine activity (Becker, 1990) as PPI is reduced during periods of elevated estrogen levels (Swerdlow et al., 1997). Highest levels of PPI are found in women during the luteal phase of the cycle (Swerdlow et al., 1997), but even then they show lower PPI than men (Abel, Waikar, Pedro, Hemsley, & Geyer, 1998). More work is needed to understand the precise nature and cognitive meaning of reduced PPI in women who, although they have less PPI, manifest lower incidence and less severe forms of schizophrenia compared to men (Castle & Murray, 1991; Faraone, Chen, Golstein, & Tsuang, 1994).

To explore further the influence of sex in human PPI within the context of the theory that PPI is protective of prepulse processing (Graham, 1975), this study investigated whether the response to a prepulse can be modulated by another prepulse of similar intensity and, if so, how is this influenced by sex. The experimental paradigm employed was different from previous studies which examined the startle response (Blumenthal & Berg, 1986) or its inhibition (Blumenthal, 1995) as an indicator of temporal summation using brief single or paired pulse-s/prepulses. Given that a prepulse supposedly interferes with the normal processing of the pulse, it was assumed that the first prepulse would interfere with the effects of the second prepulse (i.e. the prepulse preceding the pulse) and so would disrupt PPI. A greater disruption of PPI was expected in men than women as they on average show more PPI (i.e. greater inhibitory mechanism) and thus likely to suffer more from disruption of the processing of the prepulse preceding the pulse in dual prepulse trials. Women were expected to show less disruption of PPI by two prepulse trials relative to that seen with single prepulse trials, assuming that the disruption by additional prepulse would be proportionate to inhibition (PPI) seen with a single prepulse.

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