



## Anxiety and prepulse inhibition of acoustic startle in a normative sample: The importance of signal-to-noise ratio

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### ABSTRACT

Previous studies have used prepulse inhibition of the startle response (PPI) to investigate the anxiety spectrum, primarily in patient samples, with mixed results. The inconsistency in findings may be due, in part, to the use of non-optimal signal-to-noise ratios (SnRs: the difference between background noise intensity and prepulse intensity) in some studies. We proposed that, as SnR approaches +15 dB, anxiety spectrum variables will be negatively correlated with PPI, even in a normative sample. Thus, we used the MCMI-III to measure levels of trait anxiety, posttraumatic stress disorder (PTSD), and the three Cluster C personality disorders in a sample of 53 undergraduate females, and then correlated their scores with their PPI levels at SnRs of +5, +10, and +15 dB. All of the anxiety constructs except obsessive-compulsive personality disorder (OCPD) were correlated with PPI, but only in the +15 dB condition. Although OCPD symptomatology was not correlated with PPI, it was negatively correlated with PTSD and may have been indicative of adaptive functioning in this normative sample. The present study demonstrates that PPI is a sensitive index of anxiety symptomatology even in the normative range, and that a SnR near +15 dB may be necessary to reliably detect associations between PPI and these psychological variables.

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### 1. Introduction

The acoustic startle reflex is a defensive reaction that occurs in response to a sufficiently sudden and intense sound (Blumenthal et al., 2005). Although this response can involve a full-body reaction, it is most often quantified as electromyographic (EMG) activity of the orbicularis oculi, the muscle that controls eyeblinking, because the eyeblink component is the most sensitive and is the most resistant to habituation. Prepulse inhibition (PPI) of the acoustic startle response occurs when a stimulus (i.e. the prepulse) is presented 30–500 ms before the startle-eliciting stimulus, and causes a decreased startle response relative to non-prepulse trials (Blumenthal, 1999). PPI traditionally has been theorized to be a psychophysiological index of information processing (e.g. Graham, 1975) and sensorimotor gating (Swerdlow, Braff, & Geyer, 2000), such that less PPI is associated with poorer information processing, and with impairments in sensorimotor gating that are characteristic of schizophrenia spectrum disorders. PPI is due to an inhibitory projection from the tegmentum to the startle center in the brainstem (Swerdlow et al., 2000), and variations in PPI can be used to index variations in functioning of a variety of brain areas. Specifically, frontal lobe deficits may cause less activation of the midbrain

inhibitory center responsible for PPI, and therefore a reduction in PPI in this condition.

Although most of the PPI research in clinical populations has focused on the schizophrenia spectrum, with findings of decreased PPI across most of the spectrum (e.g. Cadenhead, Swerdlow, Shafer, Diaz, & Braff, 2000; Duncan et al., 2006; Swerdlow, Filion, Geyer, & Braff, 1995), over the past decade there has been an increasing focus on the anxiety spectrum. Findings indicate decreased PPI in post-traumatic stress disorder (PTSD; Grillon, Morgan, Southwick, Davis, & Charney, 1996; Grillon, Morgan, Davis, & Southwick, 1998; Ornitz & Pynoos, 1989), obsessive-compulsive disorder (OCD; Hoenig, Hochrein, Quednow, Maier, & Wagner, 2005; Swerdlow, Benbow, Zisook, & Geyer, 1993), and panic disorder (Ludewig, Ludewig, Geyer, Hell, & Vollenweider, 2002; Ludewig et al., 2005), and in college students with high trait anxiety (Duley, Hillman, Coombes, & Janelle, 2007). Five other studies, however, did not find any association between anxiety spectrum constructs and PPI (Butler et al., 1990; Grillon, Dierker, & Merikangas, 1997; Larsen, Norton, Walker, & Stein, 2002; Lipschitz et al., 2005; Morgan, Grillon, Lubin, & Southwick, 1997).

Although many of the anxiety spectrum PPI studies that yielded null findings had small sample sizes and, therefore, may not have possessed sufficient power to detect PPI differences, many of these null findings also may be explained, in part, by other methodological issues, such as non-optimal signal-to-noise ratio (SnR). The SnR of a PPI study is the difference between the background noise intensity

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and prepulse intensity (because sound intensity is usually measured in decibels, which are on a logarithmic scale, taking the difference between two intensities yields a ratio). Many PPI labs traditionally have used background noise levels around 70 dB in order to mask variable ambient noise; however, Wynn et al. (2004) posited that if background noise was not used, it may be more difficult to detect associations between PPI and psychological variables. Blumenthal, Noto, Fox, and Franklin (2006) supported this position by finding that PPI decreased as background noise increased above 50 dB, and concluded that when background noise is not used, the prepulse may be so salient that PPI deficits do not appear in clinical populations. It should be noted, however, that ambient noise levels may sometimes approach 70 dB, and these ambient sounds may act like prepulses in some cases, or may mask prepulses in other cases. Based on this and other research (e.g. Franklin, Moretti, & Blumenthal, 2007; Swerdlow, Blumenthal, Sutherland, Weber, & Talledo, 2007), we propose that the optimal SnR may be +15 dB because the effects of prepulses at SnRs below this level may be obscured by sensory masking effects, and the effects of prepulses at SnRs above this level may be obscured by ceiling effects of prepulse salience.

Supporting this hypothesis, most of the anxiety spectrum PPI studies that have used SnRs between +10 dB and +16 dB have detected significantly decreased PPI in anxiety groups (Duley et al., 2007; Hoenig et al., 2005; Ludewig et al., 2002, 2005), with two exceptions: Butler et al. (1990), which used a SnR of +15 dB, but may have possessed limited power because of a small sample size and a combat veteran control group, and Swerdlow et al. (1993), which found that a SnR of +4 dB, but not +16 dB, was associated with decreased PPI in 11 OCD patients. Nevertheless, Hoenig et al. (2005) conducted a study similar to that of Swerdlow et al. (1993), with SnRs between +2 and +16 dB, but with a sample of 34 OCD patients, and found that only the +16 dB condition was associated with decreased PPI. The results of anxiety spectrum PPI studies that either used lower SnRs (<+10 dB), or did not report background noise intensities, have been mixed, with some finding PPI deficits (Grillon et al., 1996; Grillon et al., 1998; Ornitz & Pynoos, 1989; Swerdlow et al., 1993), and others finding no significant effects (Grillon et al., 1997; Larsen et al., 2002; Lipschitz et al., 2005; Morgan et al., 1997). Grillon et al. (1996, 1998) and Ornitz and Pynoos (1989) did not report background noise intensity but still detected PPI deficits; thus, it may be that the ambient background noise levels in these studies produced SnRs close to +15 dB, as was the case in Duley et al. (2007), which reported an ambient background noise of approximately 60 dB and a prepulse intensity of 70 dB. In any case, a systematic investigation of the effects of different SnRs on PPI in relation to various anxiety spectrum constructs may help to explain the aforementioned discrepancies of PPI findings in the anxiety spectrum.

As mentioned above, the anxiety spectrum is often associated with decreased PPI; nonetheless, it remains unknown if this association is specific to certain disorders (i.e. PTSD, OCD, panic disorder) or if this association applies more generally to the anxiety spectrum as a whole, including Axis II anxiety spectrum disorders (i.e. the Cluster C personality disorders; APA, 1994). Moreover, although Duley et al. (2007) found decreased PPI in a normative sample with high trait anxiety, no studies have explored how PTSD and other anxiety spectrum constructs are associated with PPI in a normative sample. Such an investigation would provide a rigorous test for the hypothesis that decreased PPI is generally associated with the anxiety spectrum. Therefore, one purpose of the present study was to replicate the finding of decreased PPI with increased trait anxiety in a normative sample (Duley et al., 2007), to extend the findings of decreased PPI in PTSD patients to a normative sample (Grillon et al., 1996, 1998; Ornitz & Pynoos, 1989), and to explore the relationship between PPI and traits of the three Cluster C personality disorders: avoidant personality disorder (APD),

dependent personality disorder (DPD), and obsessive-compulsive personality disorder (OCPD). It should be noted that although OCPD sounds similar to OCD, it is a distinct clinical condition.

Because each of these five constructs (i.e. trait anxiety, PTSD, APD, DPD, and OCPD) theoretically belongs to the same spectrum, we hypothesized that they should be significantly intercorrelated. In addition, based on previous studies of decreased PPI in the anxiety spectrum, we hypothesized that each of these constructs should be negatively correlated with PPI. A second purpose of the present study was to examine the hypothesis that the associations between PPI and psychological variables should be most evident at SnRs that approach +15 dB (Franklin, Bowker, & Blumenthal, 2007; Swerdlow et al., 2007). Accordingly, we posited that, as the SnR approaches +15 dB (in this study, the 85 dB prepulse intensity condition), the associations between anxiety spectrum constructs and PPI would become stronger. The findings of the present study should help to elucidate the relationship between PPI, SnR, and the anxiety spectrum, and would provide strong support for the position that many of the null findings of PPI in the anxiety spectrum may be explained, in part, by the use of non-optimal SnRs. In addition, the findings of this study should demonstrate that PPI is generally sensitive to elevations in anxiety, even in a subclinical normative sample.

## 2. Methods

### 2.1. Participants

Female participants ( $N = 53$ ) ranging from 18 to 22 years of age were randomly selected from a group of Wake Forest University introductory psychology students earning credit for a research participation option. As this study was part of a larger project necessitating a predominantly female sample, only females participated in this study. Participants signed an informed consent form and all procedures were approved by the Institutional Review Board of Wake Forest University. In the first portion of the experiment, participants completed the third version of the Millon Multiaxial Clinical Inventory (MCMI-III; Millon, Davis, & Millon, 1996). One to six weeks later, they completed the startle portion of the experiment. None of the participants in the startle portion indicated that they had any illness or psychiatric diagnosis, used any psychoactive medication, or used any tobacco products within four hours prior to the experiment.

### 2.2. Stimuli

Startle stimuli were 100 dB(A) broadband noises (20 Hz to 20 kHz), with a 50 ms duration and a rise/fall time of <1 ms. Prepulses were 75, 80, and 85 dB(A) broadband noises, each with a 40 ms duration and a rise/fall time of 5 ms. The stimulus onset asynchrony (prepulse to startle stimulus) for each trial was 120 ms. Background noise was a continuous 70 dB(A) broadband noise present during the entire testing session. Intertrial intervals varied randomly from 14 to 23 s. All stimuli were generated by Coulbourn S-series noise generators, gated through Coulbourn rise/fall gates, amplified by Coulbourn audio mixer amplifiers, and presented to the participants through Telephonics TDH-39 headphones. Stimulus intensities were calibrated with steady-state signals presented through the headphones and measured with a Quest sound level meter with a fitted earpiece.

### 2.3. Response measures

Eyeblink EMG responses were measured from the orbicularis oculi muscle with In Vivo Metric surface recording electrodes

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