

Background noise decreases both prepulse elicitation and inhibition of acoustic startle blink responding

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Abstract

Prepulse inhibition of startle (PPI) has proved to be useful in distinguishing between schizophrenia patients and normal controls, although not all studies in this area find such group differences. One reason for this inconsistency may be the fact that some research labs present the startle eliciting and inhibiting stimuli over a steady background noise (70 dB), whereas others present stimuli in ambient noise conditions (30–56 dB). The present study tested the impact of background noise (30, 50, and 70 dB) on PPI in normal college adults, with prepulses at intensities of 75, 80, and 85 dB, and with prepulse rise times of 1 or 10 ms. Background noise decreased the amount of PPI caused by the prepulses, and also decreased the ability of the prepulses to themselves elicit blink responses. We conclude that background noise interferes with the processing of the prepulse, attenuating its effect as both an elicitor and inhibitor of the startle reflex. By elevating the difficulty of prepulse processing, this attenuation may be a necessary condition for observing differences in PPI between patient and control groups.

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Prepulse inhibition of the startle response (PPI) has been found to be a useful measure in the study of a variety of disorders, including schizophrenia, obsessive-compulsive disorder, tourette's, and post-traumatic stress disorder (Cadenhead and Braff, 1999; Braff et al., 2001). PPI is often found to be less pronounced in patients than in healthy control participants. However, some studies fail to find such a difference, and Wynn et al. (2004) have suggested that differences in background noise may underlie some of the inconsistencies in studies investigating PPI deficits in schizophrenic patients. The present paper is an attempt to evaluate the impact of a specific methodological difference that exists between clinical and nonclinical studies of PPI, the issue of background noise during the testing session.

The startle response is a rapid defensive reaction that can be elicited by sudden acoustic, visual, tactile, or electrical stimuli, and is usually measured by quantifying limb extension in rats or eyeblink electromyographic (EMG) responding in humans (Yeomans et al., 2002; Blumenthal et al., 2005). This response can be inhibited by a stimulus presented before the eliciting

stimulus (at lead intervals of 15–500 ms for acoustic prepulses preceding acoustic startle stimuli), an effect referred to as prepulse inhibition of startle (PPI) (Blumenthal, 1999; Graham, 1975). This prepulse can be in any sensory modality, and need only be above detection threshold to have an effect. Discrete prepulses, which begin and end before the startle stimulus begins, are more effective inhibitors than are continuous prepulses, which begin before the startle stimulus and stay on until or after startle stimulus onset (Blumenthal and Levey, 1989; Braff et al., 2001b; Putnam and Vanman, 1999; Wynn et al., 2000). Prepulses that are initiated at the same time as the startle stimulus have been shown to increase startle reactivity (prepulse facilitation), probably due to temporal summation (Boelhouwer et al., 1991; Sarno et al., 1997).

In studies that compare PPI in human schizophrenic patients and controls, the prepulse and startle stimuli are usually presented above a continuous background noise in the 60–75 dB range (most often 70 dB). Background noise is on throughout the testing session, unlike continuous prepulses, which are initiated either before or at startle stimulus onset on each trial, with a silent period between trials. Background noise was originally used in animal startle research by Hoffman and Fleshler (1963) to mask unpredictable environmental sounds and thereby reduce variability in startle responding.

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However, Hoffman discovered that this background noise increased startle reactivity in the rat, a finding that has been replicated many times (see Hoffman, 1999, for historical context). Further, Palmer et al. (2000) showed that PPI in rats was impaired to a greater extent when background noise was present than when background noise was absent. Miyazato et al. (1999) also showed that PPI in the rat was reduced when background noise was increased from 50 to 60 dB.

Studies in which PPI deficits are found in schizophrenia patients generally use background noise at an intensity of 70 dB (Braff et al., 2001a). In the absence of this background noise, PPI deficits are generally not seen in patients unless the prepulse is a target in an attention task (Filion et al., 1993). In this situation, PPI to ignored prepulses is equivalent in schizophrenia patients and controls, and PPI is more pronounced to target prepulses in controls, but not in patients. It may be that the attentional task increases prepulse processing, and the background noise impairs prepulse processing, leading to less effective processing for ignored prepulses or prepulse embedded in background noise, in all participants. This increased difficulty may have more of an impact in schizophrenic patients and, thereby, relatively less PPI is seen in schizophrenia patients than in normal controls in these situations.

Given that animal studies have clearly shown that background noise can facilitate startle and impair PPI, and given that hundreds of PPI studies have been conducted with humans, some using background noise and others not, it is noteworthy that no reports investigating the impact of background noise on human startle and PPI had been published until very recently (Flaten et al., 2005; Hsieh et al., 2005). Flaten et al. presented a 70 dB pure tone prepulse before a 94 dB noise startle stimulus, in the presence of background noise intensities of 28 dB (ambient), 40, and 60 dB, and found that increasing background noise from 28 to 40 dB increased startle reactivity. Increasing background noise from 40 to 60 dB resulted in reduced PPI, an effect that Flaten et al. attribute to a reduction in the signal-to-noise ratio (the intensity of the prepulse relative to the intensity of the startle stimulus). That is, as background noise level increased, the difference between background noise intensity and prepulse intensity (signal) decreased, making prepulse detectability more difficult. Hsieh et al. (2005) found that increasing background noise from 54 dB (ambient) to 70 dB resulted in reduced PPI, similar to the finding of Flaten et al. (2005). Hsieh et al. also conclude that the important parameter in determining PPI is signal-to-noise ratio between the prepulse and the background. This signal-to-noise explanation was also proposed by Gewirtz and Davis (1995) to explain reduced PPI in the presence of background noise in rats.

In a second experiment, Flaten et al. (2005) used an airpuff prepulse to the hand, stating that the signal-to-noise explanation should not apply when the prepulse and background noise are in different sensory modalities. In support of their hypothesis, the background noise level had no impact on PPI caused by the tactile prepulse. In a third experiment, Flaten et al. used an acoustic prepulse and a tactile startle stimulus, an airpuff directed to the temple. PPI was seen when 28 dB (ambient)

background noise was used, but no PPI was seen when background noise was 60 dB, showing that the background noise effect could be seen even when the prepulse and startle stimulus were not in the same modality, as long as the prepulse and background noise are in the same modality. This supports the conclusion that using background noise and acoustic prepulses can reduce the signal-to-noise ratio of those prepulses enough to impair PPI. An interesting test of this hypothesis (not included in the present paper) would be the use of prepulses and “background noise” in a non-auditory modality.

The present study extends the findings of Flaten et al. (2005) and Hsieh et al. (2005) in several ways. Whereas the highest background noise intensity used by Flaten et al. was 60 dB, and the lowest used by Hsieh et al. was 54 dB, the present study used background noise intensities of 30, 50, and 70 dB, with 70 dB being the level most often used in schizophrenia—PPI research (Braff et al., 2001a). The present study also used prepulses at three intensities, to further evaluate the impact of signal-to-noise ratio at the background noise level most often used in the clinical research in this area. Finally, the signal-to-noise hypothesis was tested in a second manner in this study, by evaluating the ability of the prepulses themselves to elicit blink reflexes (Blumenthal and Goode, 1991). If decreased PPI in the presence of background noise is due to a lowering of the signal-to-noise ratio, then prepulses presented in the context of background noise should also be less able to elicit blinks themselves. These two effects would converge on the conclusion that background noise interferes with the processing of the prepulse, decreasing its effectiveness as both an elicitor and an inhibitor of the blink response. To increase the information available in this study, prepulses with rise times of either <1 or 10 ms were used, since prepulse rise times within this range should affect the ability of the prepulse to elicit a blink response without affecting the PPI caused by these prepulses (Reilly and Hammond, 2001; Blumenthal and Goode, 1991; Blumenthal and Levey, 1989).

1. Methods

1.1. Participants

Participants were randomly selected from a group of introductory psychology students earning extra credit. All participants responded to the startle stimulus in each background noise condition, but two participants were excluded due to equipment problems, leaving a sample of 45 participants, 33 females and 12 males, ranging from 18 to 21 years of age. All participants reported no hearing loss or psychiatric disorders. All procedures in this study were approved by the Institutional Review Board of Wake Forest University.

1.2. Stimuli

Startle stimuli were 105 dB (A) broadband noise (20 Hz–20 KHz), with a 50 ms duration and a rise/fall time of <1 ms. Background noise was 30, 50, and 70 dB (A) broadband noise. Prepulses were 75, 80, and 85 dB (A) broadband noise, with a duration of 40 ms. Participants were tested in two groups according to the rise/fall time of the prepulses, either <1 ms ($N = 21$) or 10 ms ($N = 24$). All stimuli were generated by Coulbourn noise generators, gated through Coulbourn rise/fall gates, amplified by Coulbourn audio mixer amplifiers, and presented to the participant via 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.

1.3. Response measures

Eyeblink EMG responses were measured from the orbicularis oculi by surface recording electrodes (Ag/AgCl, 11 mm outer diameter, 4 mm diameter contact surface) placed on the face below the left eye. EMG activity of the muscle was amplified with a Biopac EMG amplifier and sampled (1000 Hz) by a Biopac MP150 workstation which stored four versions of the EMG input: raw unfiltered EMG, filtered EMG in a passband of 30–500 Hz, a rectification of the filtered EMG signal, and a rectified and smoothed (five sample Boxcar filter) derivation of the filtered signal. The data reported in this paper are based on the smoothed EMG signal.

1.4. Procedure

Participants read and signed an informed consent form and filled out a brief medical history questionnaire. The skin below the left eye was cleaned with a cotton swab dipped in rubbing alcohol. Surface recording electrodes were filled with synapse conducting paste and then attached to the skin overlaying the left orbicularis oculi, one electrode directly below the center of the pupil but below the lower lid, and the center of the other electrode approximately 15 mm lateral and slightly higher than the center of the first. The procedure was explained to the participant, who was asked to sit still and look forward. Headphones were placed on the participant, and three blocks of trials were presented. Each block started with 5 min of background noise at either 30, 50, or 85 dB (A), with the order of background noise level counterbalanced across participants. With the background noise still on, three startle stimuli were presented with an average intertrial interval of 20 s (range = 15–24 s) to prehabituate the startle response. Then 32 startle trials were presented (eight sub-blocks of four trials each, each including a 105 dB (A) startle stimulus presented alone or preceded at a lead interval of 120 ms by a prepulse of 75, 80, or 85 dB (A), in random order). This was followed by 5 min of the next background noise intensity, then 32 startle and prepulse trials, then 5 min of the third background noise intensity, and 32 more startle and prepulse trials. This resulted in the control and three prepulse trial types being presented eight times in the context of each background noise intensity. Prepulse rise/fall time was <1 ms for one group of participants ($N = 21$; seven males) and 10 ms for the other group ($N = 24$; five males).

1.5. Data analysis

Dependent variables were blink response probability, magnitude, and onset latency, within each stimulus condition. Response amplitude was also scored, but the outcomes were generally similar to those for response magnitude, so those analyses have been omitted. Response probability was the ratio of the number of trials on which a response was detected divided by the number of trials on which a response could have been detected (number of trials minus trials contaminated by artifact; 5.4% of trials were deleted due to movement artifacts or unstable baselines). Response onset latency was the time between stimulus onset and response onset, within a window of 20–120 ms after stimulus onset, for all trials on which a response was actually detected (those trials with a probability of 1.0). Response magnitude was the average of the difference between peak and baseline voltage of the smoothed EMG voltage, within a window of 20–150 ms after stimulus onset, for all trials on which a response could have been detected (those trials not contaminated by artifact), with trials on which no response was seen assigned a magnitude of zero.

PPI was calculated as the proportion of the difference from control ((control condition – prepulse condition)/control condition) for response magnitude, and as difference from control (control condition – prepulse condition) for response probability and onset latency, as recommended by Blumenthal et al. (2004). For each of these measures, the 95% confidence interval was calculated, and PPI was said to be present if the particular cell in the $3 \times 3 \times 2$ design matrix did not include zero. In a similar fashion, the 95% confidence interval was used to determine whether the prepulse elicited a response, with only intervals above zero meeting this requirement.

2. Results

2.1. Responses to startle stimuli on control trials

ANOVA were conducted on the startle response magnitude, probability, and onset latency recorded on control (no-prepulse) trials, with background noise level as a within-participants variable (30, 50, and 70 dB). Post-hoc pairwise comparisons were conducted with Bonferroni reduction of degrees of freedom. Background noise had a significant effect on startle magnitude, $F(2, 88) = 4.88, p < .025$. Response magnitude was lower in the 30 dB noise condition than in the 50 or 70 dB noise condition ($p < .025$; mean response magnitudes of 28.33, 38.16, and 35.97 μV , respectively). No effect of background noise level was found for response probability or onset latency ($F < 1.0$).

2.2. Prepulse modification of startle reactivity

ANOVA were conducted on the PPI magnitude, probability, and onset latency data, with background noise level (30, 50, 70 dB) and prepulse intensity (75, 80, 85 dB) as two within-participant variables, and prepulse rise time (1 or 10 ms) as a between-groups factor. PPI was significant ($p < .05$) in all conditions for response magnitude, but inhibition of response probability was significant only when background noise level was 30 or 50 dB, not at 70 dB. For response onset latency, prepulse inhibition (longer latency) was significant for 85 dB prepulses presented with 30 dB background noise, and significant response facilitation was seen when 80 or 85 dB prepulses were presented with 70 dB background noise.

For PPI of response magnitude, significant effects of background noise level and prepulse intensity were found, $F(2, 86) = 9.53$ and 18.50, respectively, $p < .001$ (see Fig. 1). The amount of inhibition decreased as background noise increased from 50 to 70 dB, ($p < .05$). PPI increased marginally as prepulse intensity increased from 75 to 80 dB ($p = .078$), and significantly as prepulse intensity increased from 80 to

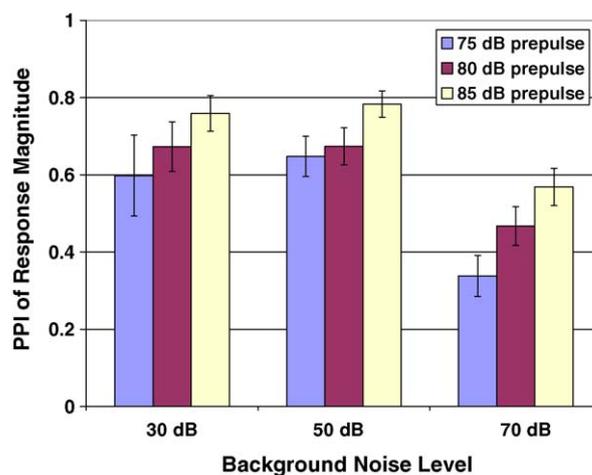


Fig. 1. PPI of response magnitude (proportion of difference from control) as a function of background noise level and prepulse intensity. Bars represent S.E.M.

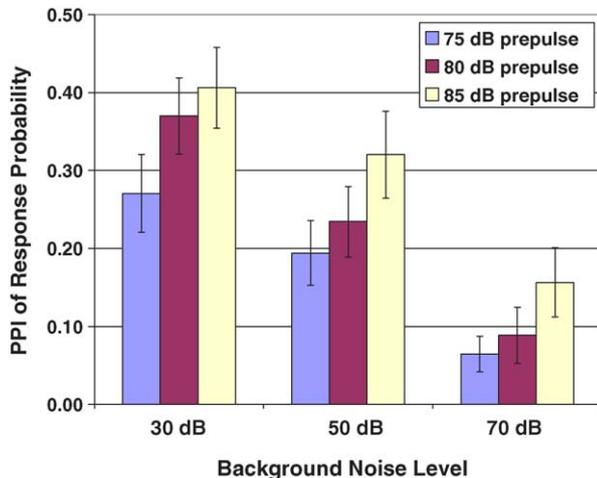


Fig. 2. PPI of response probability (difference from control) as a function of background noise level and prepulse intensity. Bars represent S.E.M.

85 dB ($p < .01$). No other main effects or interactions reached significance.

For PPI of response probability, significant effects of background noise level and prepulse intensity were found, $F(2, 86) = 16.13$ and 23.25 , respectively, $p < .001$ (see Fig. 2). The amount of inhibition decreased as background noise increased from 30 to 50 to 70 dB ($p < .05$), and increased as prepulse intensity increased from 75 to 80 to 85 dB ($p < .001$). No other main effects or interactions reached significance.

Since zero is not an acceptable value for response onset latency, failure to respond to at least one presentation in each prepulse condition resulted in the exclusion of a participant's data from the ANOVA for response onset latency. This failure is most likely due to the fact that the prepulse resulted in a total inhibition of the response on all trials in one condition, such that the people whose data are excluded are actually those who showed the most pronounced PPI. Therefore, conclusions based on the remaining participants are more conservative, but less powerful. Since 13 participants failed to respond to at least one presentation of all prepulse conditions, PPI of response onset latency was based on 32 of the 45 participants. A main effect of background noise level was found for response onset latency, $F(2, 60) = 5.78$, $p < .005$, with a prepulse inhibiting onset latency by 1.99 ms in the 30 dB background noise condition, but facilitating onset latency by 2.33 ms in the 70 dB condition, with no effect of prepulses on onset latency in the 50 dB background noise condition ($p < .05$). That is, prepulses slowed responding when background noise was low, but speeded responding when background noise was high. No other main effects or interactions were significant.

2.3. Responses to prepulses

ANOVA were conducted on the magnitude, probability, and onset latency of responses to the prepulses, with background noise level (30, 50, 70 dB) and prepulse intensity (75, 80, 85 dB) as two within-participant variables, and prepulse rise

time (1 or 10 ms) as a between-groups factor. Although, the response criteria used to identify prepulse responses were the same as those used to identify responses to the 105 dB startle stimulus, no-stimulus catch trials were also scored, to identify the noise floor of the scoring procedure. These catch trials were actually the no-prepulse control trials, inspected for responses in the window beginning 100 ms before the startle stimulus. The probability of response identification on catch trials was .0878, .0504, and .0996 when background noise was 30, 50, and 70 dB, respectively. If the 95% confidence interval included the value for the no-stimulus response probability, then the prepulse could not be said to have elicited a reliable response. In fact, all response probabilities were well above this noise floor for 17 of the 18 prepulse conditions, with only the fast-rising 75 dB prepulse in a 70 dB background failing to elicit responses at a level above the noise floor (response probability in this condition was .0900, with a noise floor of .0996). Swerdlow et al. (2004) also found that fast-rising prepulses 5 dB above background noise could inhibit startle without themselves eliciting blinks.

For response magnitude, significant effects of background noise level and prepulse intensity were found, $F(2, 86) = 13.05$ and 15.31 , respectively, $p < .001$, as was a significant effect of prepulse rise time, $F(1, 43) = 4.76$, $p < .05$ (see Fig. 3). Significant interactions were also found between background noise level and prepulse intensity, $F(4, 172) = 4.25$, $p < .01$, between background noise level and prepulse rise time, $F(2, 86) = 4.33$, $p < .025$, and between prepulse intensity and prepulse rise time, $F(2, 86) = 7.02$, $p < .001$. A significant three-way interaction was found between background noise level, prepulse intensity, and prepulse rise time, $F(4, 172) = 3.01$, $p < .05$. Responses to the prepulses decreased in magnitude as background noise increased from 50 to 70 dB, and this effect was most pronounced for the fast-rising prepulses at 85 dB.

For response probability, significant main effects of background noise level and prepulse intensity were found, $F(2, 86) = 17.10$ and 24.58 , respectively, $p < .001$ (see Fig. 4). A significant interaction between background noise level and

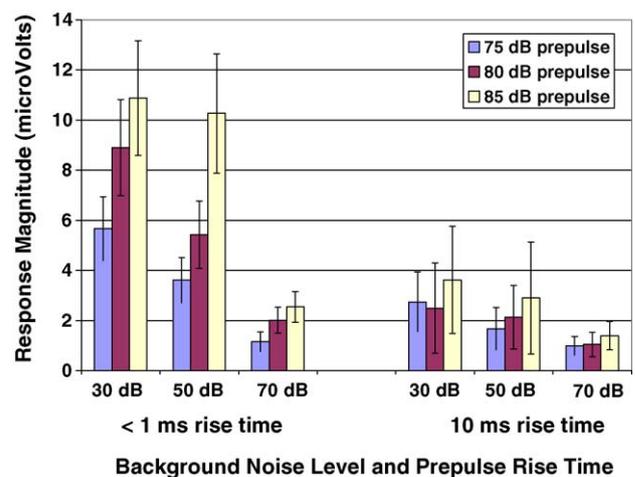


Fig. 3. Response magnitude (microvolts) to the prepulse as a function of background noise level, prepulse intensity, and prepulse rise time. Bars represent S.E.M.

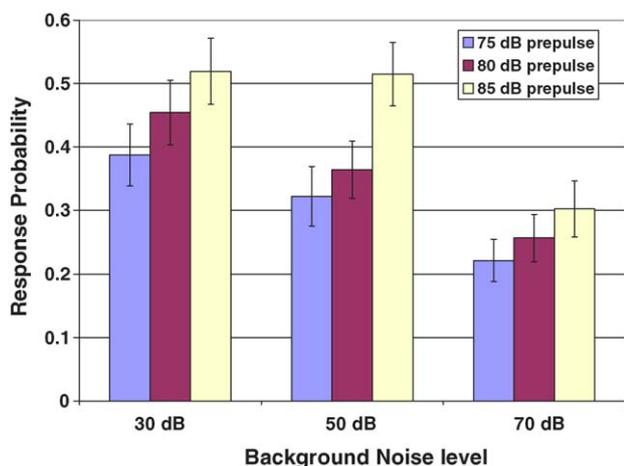


Fig. 4. Response probability (proportion) to the prepulse as a function of background noise level and prepulse intensity. Bars represent S.E.M.

prepulse intensity was also found, $F(4, 172) = 2.63, p < .05$. Reactivity decreased as background noise level increased from 50 to 70 dB, and increased as prepulse intensity increased from 75 to 80 to 85 dB, with the increase in response probability as prepulse intensity increased from 80 to 85 dB being muted by the increase in background noise level from 50 to 70 dB. A marginal interaction between background noise level and prepulse rise time was also found, $F(2, 86) = 3.16, p = .054$. Probability of responding was higher for faster rising prepulses with a 30 dB background noise, less so with a 50 dB background noise, but not with a 70 dB background noise. No other main effects or interactions were significant.

Of the 45 participants, only 17 responded to at least one prepulse in every condition. These 17 participants showed significant effects of background noise level, $F(2, 30) = 41.19, p < .001$, and a background noise level by prepulse intensity interaction, $F(2, 30) = 4.08, p < .05$, on response onset latency. Response onset latency increased as background noise level increased from 50 to 70 dB, but this effect was less pronounced as prepulse intensity increased.

The general effect of background noise on responding to the prepulse was that such responding became smaller, less probable, and later as background noise was increased from 50 to 70 dB. This suggests that detectability of the prepulse may have been interfered with, or at least was made more difficult, by the 70 dB background noise.

3. Discussion

Increasing prepulse intensity resulted in more pronounced PPI of response magnitude and probability, as seen in previous studies (e.g. Blumenthal, 1996; Blumenthal et al., 2004). However, increasing prepulse rise time to 10 ms had no effect on PPI, also replicating earlier findings (Blumenthal and Levey, 1989; Reilly and Hammond, 2001). Increasing the intensity of background noise from 30 to 50 dB resulted in a significant increase of response magnitude on control trials, but further increasing background noise to 70 dB had no additional effect.

Greater startle reactivity to increased background noise has been found in previous animal research (e.g. Hoffman and Searle, 1965) and human research (e.g. Flaten et al., 2005). Background noise had pronounced effects on PPI, with inhibition of response magnitude, probability, and onset latency decreasing as background noise intensity was increased from 50 to 70 dB. Gewirtz and Davis (1995) have suggested that decreasing the signal-to-noise ratio between a prepulse and background noise reduces PPI in rats, and Flaten et al. (2005) and Hsieh et al. (2005) make a similar suggestion for human startle responding.

Stimuli at the intensities used for prepulses in this study have been shown to be elicitors of blink responses (Blumenthal, 1988; Dahmen and Corr, 2004). In the present study, prepulses were generally more effective elicitors of blink responding as prepulse intensity increased or as prepulse rise time decreased, similar to the impact of these stimulus parameters on the eliciting power of more intense startle stimuli (Blumenthal and Berg, 1986; Berg and Balaban, 1999). For fast-rising prepulses, increasing background noise from 50 to 70 dB resulted in reduced reactivity to the prepulses, whereas reactivity was already so low for slower-rising prepulses that background noise had no further effect. Increasing background noise can interfere with the blink-eliciting power of a prepulse (also shown by Swerdlow et al., 2004), but relatively ineffective prepulse stimuli will be less impacted by background noise, due to a “floor effect”.

Psychophysical research has found that extracting a signal from background noise is impaired due to masking (Durrant and Lovrinic, 1984), such that masking may be the mechanism on which signal-to-noise effects of background noise on PPI are based. The possibility that the masking effect is peripheral to the brainstem startle center and midbrain PPI center (Koch, 1999; Davis et al., 1999; Fendt et al., 2001; Swerdlow et al., 2001) is the most parsimonious explanation for the fact that prepulses in noise are less effective as both elicitors and inhibitors of blink responses. The masking effect may begin at the basilar membrane when the frequency characteristics of the signal and noise overlap (Egan and Hake, 1950; Lockwood et al., 1999). It is also likely that masking is more pronounced at low signal-to-noise ratios, such that a background noise is more likely to interfere with the processing of a prepulse stimulus than a startle stimulus. This is evident in the present study, in that background noise reduced inhibition and elicitation caused by the prepulse, but elevated reactivity caused by the startle stimulus on control trials (when background noise was increased from 30 to 50 dB).

Background noise is used in some research settings to mask extraneous environmental sounds, and the more intense the background noise, the more of these sounds will be masked. Being forced to increase prepulse intensity to get above the background noise intensity can result in blinks being elicited by the prepulses themselves (Blumenthal, 1988; Blumenthal and Goode, 1991; Dahmen and Corr, 2004). Therefore, researchers who use background noise in PPI studies must strike a balance between effectively masking extraneous sounds and not requiring the use of very intense prepulses. This problem is

muted somewhat by the fact that background noise also decreases the ability of the prepulses to elicit blinks.

The present study was designed to clarify inconsistent results in previous studies comparing PPI in clinical and control groups. One potential limitation in generalizing the present results to studies in which clinical and healthy control participants are compared is the fact that the stimulus parameters in this study are not identical to those often found in clinical studies (see Braff et al., 2001b, for a summary of the stimulus parameters used in human clinical studies to that date). Whereas many studies investigating differences between patients and controls use 115 dB startle stimuli, we used 105 dB startle stimuli. However, PPI deficits in patients have been seen in the presence of background noise with startle stimuli at intensities of 106 dB (Grillon et al., 1992), 105 dB (Karper et al., 1996), and 104 dB (Braff et al., 1978). Also, our prepulses were slightly longer in duration (40 ms) than those often used in clinical studies (20 ms). The impact of prepulse duration on PPI reaches asymptote between 20 and 50 ms (Blumenthal, 1995), suggesting that increasing prepulse duration from 20 to 40 ms may increase PPI, but this impact would not be expected to be pronounced. Finally, prepulse rise time is often not specified in clinical studies (it is often referred to as “uncontrolled”). In the present study, we found that prepulse rise time affected blink elicitation by the prepulses, but not PPI, both effects replicating previous findings (Reilly and Hammond, 2001; Blumenthal and Goode, 1991; Blumenthal and Levey, 1989).

Another difference between the present study and many recent clinical studies is that this study measured blink activity from the left side of the face, whereas many clinical studies measure from both sides. Some of those studies have found PPI deficits in patients only when measuring blinks from the right side of the face (e.g. Cadenhead et al., 2000), indicating less bilateral asymmetry in the PPI of patients than controls, whereas other studies do not find differences as a function of side measured (e.g. Braff et al., 2001a). This potential asymmetry should be explored in further studies with normal participants, to see if it is affected by background noise. A final factor to consider when generalizing from the present study to clinical situations is the fact that the present study had more females than males participating, whereas many clinical studies tend to include more (or only) males. This is partially due to the fact that gender differences in PPI have been reported (Swerdlow et al., 1993), and suggests that the present study be replicated with males only.

In spite of the methodological differences between the present study and some clinical studies, differences in PPI between patients and controls are rather robust, with an important exception being the sensitivity of this difference to background noise levels. When prepulses are somewhat difficult to distinguish from the background, elevating prepulse processing may be more difficult for some patient groups than for normal controls, resulting in PPI deficits in these patient groups. This has led to the finding of PPI deficits in patient groups when background noise is used (Braff et al., 2001a), but not when ambient noise is used (Wynn et al., 2004), suggesting

that these PPI decrements only occur when detection of the prepulse is relatively difficult. In the absence of background noise, differences between patients and controls are seen when an attentional task is performed, but not during passive processing (Wynn et al., 2004). Therefore, differential difficulty of prepulse processing can be imposed by either adding background noise, or by making some prepulses targets in an attentional task (nontargets are more difficult to discriminate from background noise than are targets). Patients and normal controls may be distinguishable by PPI deficits, but only when prepulse detectability (or identification) is possible but difficult.

The present results make it clear that increasing background noise intensity results in decreased effectiveness of a prepulse as both an elicitor and inhibitor of startle. These deficits may be due to the decreased signal-to-noise ratio between prepulse and background noise, based on peripheral masking, resulting in a decrease in subcortical processing of the prepulse. To the extent that PPI is useful as a possible endophenotype for clinical disorders (Hsieh et al., 2005), making prepulse processing more difficult by embedding prepulses in background noise may be a necessary condition for observing the difference in PPI between patients and controls.

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