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The effects of reflex stimulus intensity and stimulus onset asynchrony on prepulse inhibition
and perceived intensity of the blink-eliciting stimulus

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Abstract

Prepulse inhibition of the blink reflex is widely applied to investigate information processing deficits in schizophrenia and other psychiatric patient groups. The present experiment investigated the hypothesis that prepulse inhibition reflects a transient process that protects preattentive processing of the prepulse. Participants were presented with pairs of blink-eliciting noises, some preceded by a prepulse at a variable stimulus onset asynchrony (SOA), and were asked to rate the intensity of the second noise relative to the first. Inhibition of blink amplitude was greater for a 110 dB(A) noise than for a 95 dB(A) noise with a 120 ms SOA, whereas there was no difference with a 30 ms SOA. The perceived intensity was also lower for the 110 dB(A) noise than for the 95 dB(A) noise with the 120 ms SOA, but not with the 30 ms SOA. The parallel results support a relationship between prepulse inhibition of response amplitude and perceived intensity. However, the prepulse did not reduce intensity ratings relative to control trials in some conditions, suggesting that prepulse inhibition is not always associated with an attenuation of the perceived impact of the blink-eliciting stimulus.

Keywords: startle reflex, blink reflex, sensory gating, prepulse inhibition, intensity

The effects of reflex stimulus intensity and stimulus onset asynchrony on prepulse inhibition and perceived intensity of the blink-eliciting stimulus

In the prepulse inhibition paradigm, a prepulse stimulus is presented at a stimulus onset asynchrony (SOA) of 30 to 500 ms prior to a more intense blink-eliciting stimulus. The blink reflex elicited on trials preceded by the prepulse is inhibited in comparison to trials in which the blink reflex is elicited in the absence of the prepulse. This *prepulse inhibition* is thought to reflect sensorimotor processes that gate perceptual analysis and protect the preattentive processing of the prepulse (Braff, Grillon, & Geyer, 1992; Graham, 1975). The protection of processing interpretation of prepulse inhibition is finding wide application in applied research. For instance, reduced prepulse inhibition relative to healthy control participants has been taken as evidence that sensorimotor gating deficits exist in adults with schizophrenia (Braff et al., 1992), obsessive-compulsive disorder (Swerdlow, Benbow, Zisook, Geyer, & Braff, 1993), Huntington's disease (Swerdlow, Paulsen, Braff, Butters, Geyer, & Swenson, 1995), and in children with Tourette's syndrome (Castellanos, Fine, Kaysen, Marsh, Rapoport, & Hallett, 1996). The prepulse inhibition paradigm has also been used for examining the clinical effectiveness of psychoactive medications (Kumari, Soni, & Sharma, 1999) and as a means to reduce the pain associated with an intense cutaneous electric shock (Blumenthal, Burnett, & Swerdlow, 2001). Applications such as these may benefit from an understanding of the processes that underlie prepulse inhibition.

Graham (1975, 1992) proposed that the onset of a prepulse stimulus elicits two automatic processes. The first is the initiation of processes that lead to the identification of the prepulse. The second consists of an engagement of inhibitory processes that serves to protect the preattentive perceptual analysis of the prepulse from disruption by the blink-eliciting stimulus. The degree of blink inhibition is thus proportional to the extent to which the protective mechanism has been activated. The protective mechanism is thought to build

up to a maximum level following the onset of the prepulse and then decay over time. The transient nature of the protective mechanism is reflected in the time course of prepulse inhibition. For instance, Neumann, Lipp, and McHugh (2004) observed that the time course followed a U-shaped function centered on an SOA of approximately 120 ms when a 70 dB(A) tone prepulse and 105 dB(A) white noise blink-eliciting stimulus was used. The time course and magnitude of prepulse inhibition can also be influenced by sensory variables, such as the intensity of the prepulse or blink-eliciting stimulus (Blumenthal, 1996).

Blink reflex inhibition can be assessed by measuring response magnitude (inclusion of zero amplitude responses), response amplitude (exclusion of zero amplitude responses), or response probability. Blumenthal (1996) suggested that the distinction between response amplitude and response probability is particularly informative when examining the protection of processing model of prepulse inhibition. In particular, several investigators have suggested that blink reflexes reflect the activation of two partially different neural processes: one that determines the blink initiation and one that determines the blink amplitude once it has been initiated (Blumenthal & Berg, 1986; Manning & Evinger, 1986). This distinction is supported by observations that some experimental manipulations, such as increasing the intensity of the blink-eliciting stimulus, have different effects on blink amplitude and blink probability (Blumenthal, 1996; Blumenthal & Creps, 1994). In addition, Blumenthal (1996) found that there was no significant correlation between blink probability and blink amplitude, although blink probability was correlated with blink magnitude. The blink probability measure may be particularly informative with regards to the hypothesised neural process that determines blink initiation. In contrast, the blink amplitude measure will be informative with regards to the hypothesised neural process that determines the size of the blink reflex after its initiation.

According to Graham's (1975, 1992) conceptualization, the processing of the prepulse is protected from the interruption caused by the blink-eliciting stimulus. As noted by Blumenthal (1996), this protection could result from preventing a blink response altogether (inhibiting blink probability) or from reducing the size of an already initiated response (inhibiting blink amplitude). This distinction does not necessarily exclude a protection of processing view in which the protective mechanism varies along a continuum from no response to a maximal response with all possible levels of responses in between. Rather, it aims to localise the underlying neural process that is most closely associated with the protection of processing view (i.e., blink initiation/maximal blink amplitude inhibition vs. blink amplitude when a response cannot be prevented; Blumenthal & Berg, 1986; Manning & Evinger, 1986). Experimental manipulations that produce different effects on blink probability and amplitude measures may, therefore, be particularly useful when examining the protection of processing model of prepulse inhibition. For instance, if prepulse inhibition reflects a protective process that attenuates or eliminates the impact of the blink-eliciting stimulus, the degree of prepulse inhibition should be associated with an independent measure of the impact of the blink-eliciting stimulus. If the independent measure is more closely associated with the inhibition of response amplitude than with the inhibition of response probability, it would suggest that the protection of processing mechanism largely reflects a neural process that is associated with determining blink amplitude, not blink initiation.

An independent measure of the impact of the blink-eliciting stimulus used in past research has been subjective ratings of the perceived intensity of the blink-eliciting stimulus (Cohen, Hoffman & Stitt, 1981; Blumenthal, Schicatano, Chapman, Norris, & Ergenzinger, 1996; Perlstein, Fiorito, Simons, & Graham, 1993; Perlstein, Simons, & Graham, 2001; Swerdlow, Geyer, Blumenthal, & Hartman, 1999; Swerdlow, Stephany, Talledo, Light, Braff, Baeyens, & Auerbach, 2005). Initial research established that stimulus arrangements that

produced prepulse inhibition also reduced the perceived intensity of the blink-eliciting stimulus (e.g., Cohen et al., 1981), but not in all cases (Perlstein et al., 1993). Experimental manipulations that modulate prepulse inhibition also appear to modulate the perceived intensity of the blink-eliciting stimulus. For instance, Swerdlow et al. (1999) varied the intensity of a prepulse noise that was presented prior to a noise blink-eliciting stimulus. Prepulse inhibition of blink reflex magnitude to a 118 dB(A) blink-eliciting stimulus increased as the intensity of the prepulse increased from 74 dB(A) to 86 dB(A), when all stimuli were presented over a 70 dB(A) background noise. Perceived intensity ratings of the blink-eliciting stimulus paralleled these effects and showed a greater reduction as the intensity of the prepulse increased. Blumenthal et al. (1996) used prepulse tones of 60 and 70 dB(A) and blink-eliciting noises of 80, 90, and 100 dB(A), although unlike Swerdlow et al. (1999) no background noise was present. Prepulse inhibition of response amplitude and response probability increased with both prepulse intensity and blink-eliciting stimulus intensity. When participants were asked to rate the intensity of the blink-eliciting stimulus, prepulses had no effect on the ratings when blink-eliciting stimuli were either 80 or 90 dB(A). However, when blink-eliciting stimuli were 100 dB(A), both the 60 and 70 dB(A) prepulses significantly decreased intensity ratings. Perlstein et al. (2001) examined blink reflexes to a 110 dB(A) tone presented over 60 dB white noise that was preceded by an air puff at 60 and 360 ms SOAs. Blink magnitude and perceived intensity ratings were reduced during the paired prepulse trial in comparison to blink-eliciting stimulus alone trials and the reduction was greater at the 360 ms SOA than at the 60 ms SOA. Swerdlow et al. (2005) examined the relationship between prepulse inhibition and intensity ratings in several experimental sessions. One session used a 105 dB(A) noise blink-eliciting stimulus and a 86 dB(A) noise prepulse presented over 70 dB(A) background noise. Prepulse inhibition of blink reflexes and of perceived stimulus intensity ratings showed a similar, but not identical,

pattern across SOAs of 10, 20, 30, 60, and 120 ms. One difference between the two measures was the blink magnitude was inhibited at the 30, 60, and 120 ms SOAs, whereas perceive stimulus intensity ratings was inhibited only at the 60 and 120 SOAs.

The previous research has generally confirmed a close relationship between prepulse inhibition and intensity ratings, although some differences have also been found (e.g., Swerdlow et al., 2005). The present experiment aimed to investigate the relationship further as it has important implications for research that uses the prepulse inhibition paradigm as a measure of protective preattentive processing. We examined the interaction between two factors on intensity ratings and prepulse inhibition and in doing so was able to investigate a dissociation between the measures of response amplitude and response probability. These two factors were blink-eliciting stimulus intensity and SOA. As blink-eliciting stimulus intensity increases, the amount of prepulse inhibition of blink amplitude increases (Blumenthal, 1996; Blumenthal & Creps, 1994). Prepulse inhibition of response amplitude and probability also varies across SOAs and tends to be greater for a SOA of 120 ms than for SOAs of 30 ms or 60 ms (Blumenthal & Creps, 1994; Neumann et al., 2004). Interestingly, Blumenthal and Creps (1994) observed an interaction between 60 and 120 ms SOAs and 85 and 100 dB SPL blink-eliciting stimulus intensities. The interaction appeared to reflect that there was greater prepulse inhibition of response amplitude for 100 dB SPL blink-eliciting stimuli than for 85 dB SPL blink-eliciting stimuli at the 120 ms SOA, whereas there was no difference at the 60 ms SOA. In contrast, no interaction between SOA and blink-eliciting stimulus intensity was observed for response probability.

The intensity rating procedure used in the present experiment followed that developed by Swerdlow et al. (1999). Participants were asked to rate the intensity of the blink-eliciting stimulus in comparison to an identical stimulus presented 6-sec earlier. The blink-eliciting stimulus was preceded on some trials by a prepulse at SOAs of 30 and 120 ms. The blink-

eliciting stimulus was presented at 95 dB(A) or 110 dB(A). It was expected that inhibition of blink amplitude would be greater for the 110 dB(A) blink-eliciting stimulus than for the 95 dB(A) blink-eliciting stimulus at the 120 ms SOA, but not at the 30 ms SOA (Blumenthal & Creps, 1994). No interaction between blink-eliciting stimulus intensity and SOA was expected for response probability. However, inhibition of response probability was predicted to be greater at the 120 ms SOA than at the 60 ms SOA (Blumenthal, 1996; Blumenthal & Creps, 1994). If prepulse inhibition reflects the protection of preattentive processing of the prepulse, the perceived intensity of the blink-eliciting stimulus will be rated as lower on prepulse inhibition trials than on blink-eliciting stimulus alone trials. Moreover, the perceived intensity ratings should parallel the effects of the experimental manipulations on blink reflex modulation. However, different predictions hold for blink amplitude and probability inhibition with regards to the interaction between blink-eliciting stimulus intensity and SOA. The degree to which the intensity ratings are associated with blink amplitude or probability will determine whether perceived intensity is associated with the attenuation of the elicited blink response or the prevention of the response altogether.

Method

Participants

Thirty-four male and 35 female students from The University of Queensland participated after providing informed consent. The ages ranged from 17 to 34 years, with a mean age of 20.5 years. The participants were instructed to refrain from smoking tobacco for one hour prior to the experiment and from consuming caffeine-containing drinks for three hours prior to the experiment.

Apparatus

The blink reflex was recorded by measuring electromyographic (EMG) activity of the orbicularis oculi muscle with a pair of 4mm diameter Ag/AgCl domed electrodes filled with

Surgicon E10 electrolyte. One electrode was placed under the pupil of the right eye, and the second was placed approximately 10 mm lateral. A ground electrode was strapped to the inside of the participants' right forearm. The raw EMG signal was amplified with a Grass 7P3C AC preamplifier using a 0.5 amplitude high-pass cutoff of 10 Hz and a low-pass cutoff of 3000 Hz. The raw EMG signal was displayed on a Grass 7D polygraph (calibration: 100 μ V/cm pen deflection) using a paper speed of 2.5 mm/s for visual verification. In addition, the raw signal was digitized and sampled online with an IBM-compatible (486) computer. A sampling rate of 1000 Hz was used in a 500 ms time window that began 100 ms prior to the onset of the blink-eliciting stimulus and continued a further 400 ms after the onset of the blink-eliciting stimulus. The computer that sampled the EMG also controlled the stimulus sequence, stimulus duration and the intertrial intervals.

The blink-eliciting stimuli were 95 dB(A) and 110 dB(A) bursts of white noise presented with a duration of 50 ms and an instantaneous rise time. A 1000 Hz pure tone presented at an intensity of 70 dB(A) and a 30 ms rise time served as the prepulse stimulus. Prepulse stimulus offset coincided with blink-eliciting stimulus onset. No background noise was presented during the experiment. All auditory stimuli were generated by a custom-built tone generator and presented via stereophonic headphones (Sennheisser HD25-1). These stimulus parameters were selected for the following reasons. First, it was aimed to replicate the interaction between SOA and blink-eliciting stimulus intensity and the dissociation between response amplitude and response probability measures reported by Blumenthal and Creps (1994). These investigators used a white noise blink-eliciting stimulus of 50 ms duration and no background noise during the experiment. Second, the lower intensity blink-eliciting stimulus level (95 dB(A)) was selected on the basis that a relatively large difference in intensity between the prepulse and blink-eliciting stimulus intensity is needed to observe reductions in perceived intensity ratings (Blumenthal et al., 1996). The higher intensity

blink-eliciting stimulus level (110 dB(A)) was selected to maintain a difference of 15 dB(A) between the blink-eliciting stimuli (Blumenthal & Creps, 1994). Ethical considerations and equipment limitations did not allow higher blink-eliciting stimuli intensities (e.g., 100 dB(A) and 115 dB(A)) to be used. Third, a continuous tone prepulse, rather than discrete white noise prepulse, were used to enhance the differentiation between the noise blink-eliciting stimulus (which was to be rated for intensity) and the prepulses (which were not to be rated, but can influence blink reflexes and intensity ratings). The use of a continuous tone prepulse was considered to have minimal effects on the measures used because prepulse inhibition does not differ between discrete and continuous prepulses (Graham & Murray, 1977) and does not differ between 1000 Hz, 2000 Hz, and white noise prepulses (Acocella & Blumenthal, 1990). A rating scale was located 1.5m directly opposite the participant and at eye level. The scale was divided into one unit gradations ranging from -9 to +9. The text “more loud” and “less loud” was placed under the numbers +9 and -9, respectively. In addition, the text “slightly more loud” and “slightly less loud” was placed below +6 and -6, and “very slightly more loud” and “very slightly less loud” was placed below +3 and -3.

Procedure

The experimental procedure was granted ethics approval by the relevant human research ethics process at the University of Queensland. The participants were seated in a semi-reclining chair opposite the rating scale and the experiment was monitored via a closed circuit video system from an adjoining room. Following electrode placement, participants received one or more warned presentations of the 110 dB(A) blink-eliciting stimulus to check placement of electrodes. The participants were next given a 3-min acclimatization period during which they were instructed to relax with their eyes open.

Following the acclimatization period, a prepulse inhibition assessment phase began during which participants were given an opportunity to familiarize themselves with the

experimental stimuli. The participants were informed that they would be presented with some sounds over the headphones, and that some will be louder than others. The participants were instructed to listen to the sounds and to refrain from excessive motor movements. During this phase, the participants received two blocks of trials. Each block consisted of two presentations of the blink-eliciting stimulus alone and four presentations of the blink-eliciting stimulus preceded by the prepulse stimulus. Stimulus onset asynchronies of 30 ms and 120 ms were used, evenly divided in each block. In all trials, the blink-eliciting stimulus was presented at an intensity of 110 dB(A). The intertrial intervals were varied at random between 16, 20 and 24 seconds with a mean of 20 seconds. Trial order was randomized in each block such that six different trials sequences were developed and were allocated to participants in random fashion. At the completion of the prepulse inhibition assessment phase, the participants were asked whether they had heard white noise presentations alone and immediately preceded by a short tone. All participants reported that they could distinguish between the tone and noise presentations.

The rating phase began next during which participants were informed that they would be presented with a series of noise presentations and that they would be required to rate the perceived intensity of some of the noises. The participants were told that the noises would be presented in pairs, such that one noise would be presented and followed six seconds later by a second noise. They were instructed to mentally assign the first noise of every pair a rating of zero and to rate the intensity of the second noise in comparison to the first noise. The participants were directed to the rating scale and informed that they should give a positive rating when the second noise seemed louder than the first and a negative rating when the second noise seemed less loud than the first, according to the ranges on the scale. If the two noises seemed to be of equal intensity, the participants were told that the proper rating assignment would be zero. In addition, the participants were told that they may hear

presentations of the tone prior to the noises on some trials but that they should ignore this tone in determining the ratings. Moreover, the participants were asked to ignore their own bodily reactions to the noises when providing the intensity rating.

The rating phase consisted of 10 unique trial types. Each trial consisted of paired presentations of the blink-eliciting stimulus, such that one stimulus was presented initially (S1) and followed six seconds later by a second stimulus (S2). The paired presentation of the blink stimuli is designated as one trial. It is important to note that on all trials, the intensity of the blink-eliciting stimulus was the same for both S1 and S2. Different trial arrangements were possible depending on the presence of the prepulse stimulus. Reference trials consisted of presentations of the blink-eliciting stimulus and no presentations of the prepulse stimulus. On prepulse inhibition trials, one presentation of the blink-eliciting stimulus was preceded by the prepulse stimulus. Trials in which the prepulse stimulus preceded the second blink-eliciting stimulus were designated Order A and those in which the prepulse stimulus preceded the first blink-eliciting stimulus were designated Order B. Ten unique trial types were presented depending on the presence of the prepulse stimulus and the combination of blink-eliciting stimulus intensity, SOA, and order. Two were reference trials, in which no prepulse stimulus was presented, and they differed depending on whether the blink-eliciting stimulus was presented at an intensity of 95 dB(A) or 110 dB(A). Eight types of prepulse inhibition trials were presented, by crossing the SOA (30 ms or 120 ms), the blink-eliciting stimulus intensity (95 dB[A] or 110 dB[A]), and the trial order (Order A or Order B), for instance, 30 ms/95 dB(A)/Order A. Throughout the experiment, the two types of reference trials were repeated four times and the eight types of prepulse inhibition trials were repeated twice to result in a total of 24 trials. Following the presentation of S2 in each trial, the participant called out his or her rating and the experimenter noted it down. The experimenter then presented the next trial, but ensured that there was at least 15 seconds between the times the

participant called out the rating and the presentation of the first stimulus in the trial. The participants were debriefed at the conclusion of the experiment.

Scoring and response definition

Offline, the digitized raw EMG activity was rectified and smoothed using a Butterworth filter with a time constant of 80 ms. Blink amplitude was obtained from the integrated signal. Amplitude was measured as the difference between the value of the integrated signal at the peak of the response and the value at the onset of the response. Response peak was defined as the maximum value of the integrated response curve that corresponded to the blink response within 200 ms following blink-eliciting stimulus onset. Response onset was defined as the point on the integrated response curve at which 10% of the maximum slope was reached. Amplitude could not be scored for trials in which no response onset was detectable within 20 to 60 ms following blink-eliciting stimulus onset. A trial was discarded if the integrated signal was not stable within 100 ms before the blink-eliciting stimulus onset. The data from a participant was not included if the number of missing or zero responses for response amplitude exceeded one-third of all trials. Following the data processing, there were 40 participants in the final sample. Analysis with and without the excluded participants yielded the same pattern of results.

Statistical analyses

Two measures of the blink reflex were examined, response amplitude and response probability (Blumenthal, 1996; Blumenthal, Cuthbert, Filion, Hackley, Lipp, & Van Boxtel, 2005). Response amplitude was the averaged value for a particular trial type after the exclusion of trials in which no response occurred or trials in which the response was discarded such as due to movement artifact. Response probability was expressed as the percentage of trials for a particular trial type in which a response occurred and a response was possible to occur (i.e., discarded trials were not used in the calculation of response

probability). For the prepulse inhibition trials, response amplitude and probability inhibition were reflected as a percent change from baseline. The calculation used the formula $(\text{baseline trial} - \text{prepulse inhibition trial}) / \text{baseline trial} * 100$. A positive percent change thus indicates the inhibition of response amplitude or a less probable response. The calculations for response amplitude are referred to as prepulse amplitude inhibition and the calculations for response probability are referred to as prepulse probability inhibition. The 95% percent confidence intervals were inspected to determine if the inhibition was significantly different from baseline. Significant inhibition was indicated when zero was outside the confidence interval. The baseline trial for the prepulse inhibition assessment phase was the mean of those trials in which the blink-eliciting stimulus was presented alone. Prepulse amplitude and probability inhibition during the prepulse inhibition assessment phase was examined with a repeated-measures *t*-test to determine the effect of SOA on inhibition.

Blink amplitude and probability during the rating phase were averaged separately across each unique trial type for responses to S1 and S2. Response amplitude and probability to S1 and S2 during the reference trials was examined with a 2 x 2 (Stimulus x Intensity) repeated-measures ANOVA. For the prepulse inhibition trials, prepulse amplitude and response probability inhibition were calculated for each unique trial type. The baseline trial was taken as the response to the commensurate blink-eliciting stimulus during the reference trials for that blink-eliciting stimulus intensity (e.g., the baseline trial for the 95 dB(A) prepulse inhibition trials for Order A was the response to the 95 dB(A) S2 during the reference trials). Prepulse amplitude and probability inhibition were subjected to separate 2 x 2 (SOA x Intensity x Order) repeated-measures ANOVAs.

The perceived intensity rating to the reference trials were averaged separately for each blink-eliciting stimulus intensity and analyzed with a repeated measures *t*-test. The 95% confidence intervals of the mean were also examined to determine if the mean ratings were

significantly different from zero. In an analogous manner to the blink reflex data, the effect of the prepulse on perceived intensity ratings were calculated as the numerical difference between the ratings during the reference trials and the ratings when one of the S1 or S2 stimuli was preceded by a prepulse stimulus. This calculation is referred to as prepulse inhibition of intensity ratings. The calculation that was used differed, however, depending on the order of the trials. For Order A, the effect of the prepulse in reducing the perceived intensity of the blink-eliciting stimulus would be reflected in relatively lower ratings because the participants always rated the intensity of the second stimulus in relation to the first. Likewise, a reduction in the perceived intensity of the blink-eliciting stimulus following a prepulse inhibition trial would be reflected in relatively higher ratings for Order B. For Order A, prepulse inhibition rating = [reference rating] – [Order A rating] and for Order B, prepulse inhibition rating = [Order B rating] – [reference rating]. Thus, a positive prepulse inhibition rating value indicates that the prepulse reduced the perceived intensity of the blink-eliciting stimulus.

Following Swerdlow et al. (1999), analyses were also conducted in which the prepulse inhibition ratings were range corrected by taking into account the participant's total range of ratings using the formula, [prepulse inhibition rating / rating range] x 100. However, since the results of the statistical analyses were identical with both calculation methods, only the data for the non-corrected prepulse inhibition ratings are reported. The prepulse inhibition rating values were calculated separately for each trial order, blink-eliciting stimulus intensity, and SOA and analyzed with a 2 x 2 x 2 (SOA x Intensity x Order) ANOVA. The 95% confidence intervals were also examined to determine if the mean inhibition rating was significantly different from baseline.

Pair-wise comparisons were used for further investigation of all significant interactions. The comparisons used *t*-tests that were adjusted for the accumulation of Type I

error by using Šidák's multiplicative inequality (Games, 1977). The minimum level of significance for all statistical tests was set at .05.

Results

Prepulse amplitude inhibition during the prepulse inhibition assessment phase was greater for the 120 ms SOA ($M = 62.23\%$, $SD = 29.83$) than for the 30 ms SOA ($M = 28.52\%$, $SD = 30.82$), $t(39) = 6.37$, $p < .001$. Response probability inhibition for the 30 ms ($M = 1.04\%$, $SD = 8.89$) and 120 ms ($M = 1.67\%$, $SD = 9.47$) SOAs did not differ, $t < 1$.

Figure 1 shows the blink amplitude and perceived intensity ratings for S1 and S2 during the reference trials of the rating phase. As can be seen, blink amplitude did not differ as a function of blink-eliciting stimulus repetition, but was smaller when the blink-eliciting stimulus intensity was 95 dB(A) than when it was 110 dB(A), Main effect for Intensity, $F(1, 39) = 129.20$, $p < .001$. All other effects were not significant, all $F_s < 1.41$. Although there was a tendency for response probability to be lower for the 95 dB(A) blink-eliciting stimulus ($M = 89.38\%$, $SD = 16.04$) than for the 110 dB(A) blink-eliciting stimulus ($M = 93.96\%$, $SD = 13.04$), this effect was not significant, all $F_s < 1.73$. The intensity of S2 was rated as neither more or less loud than S1 for the 95 dB(A) blink-eliciting stimulus condition. In contrast, S2 was rated as louder than S1 for the 110 dB(A) blink-eliciting stimulus condition. Inspection of the confidence intervals showed that the intensity rating was significantly different from zero only for the 110 dB(A) blink-eliciting intensity condition. The difference between the blink-eliciting stimulus intensity conditions was also confirmed by the statistical analysis, $t(39) = 9.19$, $p < .001$.

 Insert Figure 1 about here

The mean prepulse amplitude inhibition during the rating phase is shown in Figure 2. Amplitude inhibition was significantly different from baseline in all conditions, although the amount of inhibition varied as a function of SOA, blink-eliciting stimulus intensity, and order. Prepulse amplitude inhibition was greater for Order A than for Order B, Main effect for Order $F(1, 39) = 5.68, p < .05$ and was greater at the 120 ms SOA than at the 30 ms SOA, Main effect for SOA $F(1, 39) = 28.13, p < .001$. Prepulse amplitude inhibition also varied as a function of blink-eliciting stimulus intensity, Main effect for Intensity, $F(1, 39) = 7.53, p < .01$, and this factor interacted with SOA, Intensity x SOA interaction, $F(1, 39) = 6.14, p < .05$. The interaction was due to significantly greater prepulse amplitude inhibition for the 110 dB(A) blink-eliciting stimulus than for the 95 dB(A) blink-eliciting stimulus at the 120 ms SOA, $t(39) = 5.15, p < .01$, whereas there was no significant difference at the 30 ms SOA, $t(39) = 1.64, p > .05$. All other effects were not significant, all $F_s < 1$.

The findings for prepulse probability inhibition differed in some respects from that of amplitude inhibition (see Figure 3). Prepulse probability inhibition was significantly different from baseline for all conditions with the 95 dB(A) blink-eliciting stimulus, except for the 30 ms SOA at Order B. Significant response probability inhibition was observed for the 110 dB(A) blink-eliciting stimulus only for the 120 ms SOA at Order B. Prepulse probability inhibition was also greater for the 95 dB(A) blink-eliciting stimulus than for the 110 dB(A) blink-eliciting stimulus, Main effect for Intensity, $F(1, 39) = 6.67, p < .05$, and greater at the 120 ms SOA than at the 30 ms SOA, Main effect for SOA, $F(1, 39) = 17.29, p < .001$. Unlike the amplitude findings, there was no interaction between SOA and blink-eliciting stimulus intensity, all other $F_s < 1.27$.

 Insert Figures 2 and 3 about here

Prepulse inhibition of intensity ratings is shown in Figure 4. Contrary to expectations, no rating inhibition was observed at the 30 ms SOA for either blink-eliciting stimulus intensity or at the 120 ms SOA for the 95 dB(A) blink-eliciting stimulus intensity. Indeed, the ratings were significantly less than zero, indicating that the blink-eliciting stimulus was perceived as being more intense when the prepulse preceded it. Prepulse inhibition of intensity ratings at the 120 ms SOA for the 110 dB(A) blink-eliciting stimulus intensity was significantly reduced relative to baseline. Despite the relative lack of inhibition that was found at some combinations of SOA and blink-eliciting stimulus intensity, the effects of the experimental manipulations on prepulse inhibition of intensity ratings paralleled that obtained with the prepulse amplitude inhibition. The blink-eliciting stimulus was perceived as being less intense for the 120 ms SOA condition than for the 30 ms SOA condition, Main effect for SOA $F(1, 39) = 15.27, p < .001$. A Main effect for Intensity $F(1, 39) = 37.70, p < .001$ and a Intensity x SOA interaction, $F(1, 39) = 28.50, p < .01$ was also found. Further comparisons showed that prepulse inhibition of the intensity ratings was greater for the 110 dB(A) blink-eliciting stimulus than for the 95dB(A) blink-eliciting stimulus at the 120 ms SOA, $t(39) = 5.91, p < .001$, but not at the 30 ms SOA, $t(39) = 1.68, p > .05$.

 Insert Figure 4 about here

Discussion

The main findings of the experiment were as follows. Blink amplitude inhibition and blink probability inhibition yielded a different pattern of results during the rating phase. Blink amplitude inhibition was greater for the 110 dB(A) blink-eliciting stimulus than for the 95 dB(A) blink-eliciting stimulus at the 120 ms SOA, whereas there was no difference at the 30 ms SOA. In contrast, there was no interaction between blink-eliciting stimulus intensity

and SOA for blink probability inhibition. Blink probability inhibition was greater for the 95 dB(A) blink-eliciting stimulus than for the 110 dB(A) blink-eliciting stimulus. The different pattern of results indicates that the experimental manipulations differentially affected the occurrence (probability) and the attenuation (amplitude) of the elicited blink reflex. In this situation it is particularly informative to examine whether the perceived intensity of the blink-eliciting stimulus is associated with the amplitude or probability measure. The present findings showed that the effects of the experimental manipulations on perceived intensity ratings paralleled those obtained for blink amplitude inhibition. Prepulse inhibition of intensity ratings was greater for the 110 dB(A) blink-eliciting stimulus than for the 95 dB(A) blink-eliciting stimulus at the 120 ms SOA, whereas there was no difference at the 30 ms SOA. However, the perceived intensity of the blink-eliciting stimulus was not reduced relative to baseline for some combinations of SOA and intensity, suggesting that prepulse inhibition is not always associated with a reduction in the perceived intensity of the blink-eliciting stimulus.

The close association between blink amplitude and intensity ratings supports a model of prepulse inhibition in which the protection of processing mechanism attenuates the impact of the blink-eliciting stimulus. The protection of processing mechanism does not appear to reflect the complete prevention of the impact of subsequently presented stimuli. The protection of processing mechanism hypothesized in Graham's (1975, 1992) conceptualization thus appears to protect the processing of the prepulse stimulus via an attenuation of perceptual aspects of processing. Attentional processes have been shown to modulate prepulse inhibition. For instance, prepulse inhibition is enhanced for lead stimuli that are attended to in comparison to lead stimuli that are ignored (Filion, Dawson, & Schell, 1993). This suggests that attentional processes can influence the amount of attenuation of the impact of the blink-eliciting stimulus. In the present experiment, attention to the prepulse

was not directly manipulated by instructing participants to explicitly attend to or ignore it. However, informing participants that a prepulse was presented, but should be ignored for the purpose of making the ratings, may have enhanced their attention to the prepulse more than if no reference to the prepulse was made. It would be informative to manipulate attention to the prepulse explicitly (e.g., Fillion et al., 1993) to examine whether the increased prepulse inhibition observed during attended lead stimuli is associated with an increased reduction of the perceived intensity of the blink-eliciting stimulus.

A finding that may be interpreted as being problematic for a protection of processing interpretation of prepulse inhibition was that the intensity ratings of the blink-eliciting stimulus were not reduced relative to baseline on some trials. Participants rated the blink-eliciting stimulus as more intense than those presented on the reference trials when the 30 ms SOA was used with the 95 and 110 dB(A) blink-eliciting stimuli and when the 120 ms SOA was used with the 95 dB(A) blink-eliciting stimulus. The findings for perceived intensity ratings may be problematic for a protection of processing interpretation because each of these combinations of SOA and blink-eliciting stimulus intensities produced significant inhibition of blink amplitude. A similar failure to find reductions in the perceived intensity of a blink-eliciting stimulus when it was preceded by a prepulse has been reported by Perlstein et al. (1993), Blumenthal et al. (1996), and Swerdlow et al. (1999). Indeed, Perlstein et al. (1993) reported that the perceived intensity of the blink-eliciting stimulus was more intense than baseline when a 75 dB(A) blink-eliciting stimulus was preceded by a 75 dB(A) prepulse stimulus.

It may be argued that the failure to find a reduction in the perceived intensity of the blink-eliciting stimulus during some conditions is due to methodological features of the experiment. The rating procedure followed the methods described by Swerdlow et al. (1999). Perlstein et al. (1993) asked participants to give an intensity rating after every trial of the

blink-eliciting stimulus. Like the present experiment, a reference stimulus was presented to anchor the intensity ratings. Two 90 dB(A) tones were given prior to each block of trials and participants were told that these were the standard tone to compare the subsequent presentations to. Blumenthal et al. (1996) noted that a problem could arise with the assignment of a stimulus to anchor judgments. They argued that the intensity of the anchor stimulus might affect the slope of the psychological function relating stimulus intensity to the judgments, with a larger effect being present when the intensity is very different to the rated stimulus. Due to this potential problem, Blumenthal et al. (1996) let participants freely choose an intensity rating without any reference to an anchor stimulus. Despite the differing methodologies used in the present experiment and the experiments reported by Perlstein et al. (1993) and Blumenthal et al. (1996), all studies failed to find a reduction in the perceived intensity of the blink-eliciting stimulus on some trials. This suggests that the finding is not an artifact of the procedure used to obtain the intensity ratings.

Blumenthal et al. (1996) reported that a difference of at least 30 dB(A) between the prepulse and blink-eliciting stimulus is required to observe a reduction in the perceived intensity of the blink-eliciting stimulus. This interpretation can account for the failure to find a reduction in perceived intensity for the 95 dB(A) blink-eliciting stimulus because the prepulse stimulus intensity was 70 dB(A), yielding a difference of only 25 dB(A). However, it cannot account for the failure to find a reduction when the 110 dB(A) blink-eliciting stimulus was used with a 30 ms SOA, unless the SOA represents a factor that may moderate the relationship. A 30 ms SOA lies at the minimum range at which reliable prepulse inhibition is found (Neumann et al., 2004). Although significant prepulse inhibition was observed at this SOA, it may be that it is a less reliable SOA for which to observe a reduction in the perceived intensity of the blink-eliciting stimulus. The function that relates SOA to intensity judgments may be shifted to the right relative to that for blink amplitude inhibition.

Further research that uses a wider range of SOAs than used in the present experiment may help to clarify this issue.

Alternative explanations for the relationship between prepulse inhibition and perceived intensity have been suggested in previous research. It has been suggested that participants may be influenced by their own physical reactions to the blink-eliciting stimulus (Blumenthal et al. 1996). As blink reflexes are inhibited more during prepulse inhibition trials than during reference trials, participants may inadvertently take their motor response into account when assigning an intensity rating. However, several aspects of the present findings argue against such an interpretation. First, the instructions for the present task explicitly requested participants to disregard their own bodily reactions when giving the ratings. Second, there was evidence of dissociations between blink reflexes and intensity ratings. For instance, during the reference trials the same blink-eliciting stimulus was presented as S1 and S2 without any prepulse stimulus. Blink reflex amplitude and probability did not differ between these repeated presentations. However, participants rated the intensity of S2 to be louder than S1 when the 110 dB(A) blink-eliciting stimulus was used. Third, if the participant's ratings were influenced by their physical reactions, it would be expected that the ratings should be more closely associated with the measure of response probability than with response amplitude. The inhibition of response probability would have produced a larger effect in minimizing bodily reactions as no blink response occurred. The finding that intensity ratings were associated with blink amplitude inhibition, but not blink probability inhibition is not consistent with this interpretation.

Loudness assimilation has also been suggested as a mechanism by which the intensity ratings may be influenced by a factor independent to a protection of processing mechanism (Blumenthal et al., 1996; Perlstein et al., 1993). Loudness assimilation has been described as a situation in which the intensity rating for one member of a pair is shifted in the direction of

the intensity of other member of the pair (Perlstein et al., 1993). An intense blink-eliciting stimulus is thus rated as less intense when it is preceded by a moderate prepulse stimulus. Loudness assimilation may influence intensity ratings when both members of a stimulus pair are presented in the same stimulus modality, as in the present experiment. However, loudness assimilation does not appear to provide a sole explanation for reductions in intensity ratings. For instance, Swerdlow et al. (1999) found a reduction of perceived intensity of an air-puff and acoustic blink-eliciting stimulus when the stimuli were preceded by an acoustic prepulse. As reductions in perceived intensity were observed for both modality match and mismatch conditions, the reductions are better explained by a process independent to loudness assimilation. In addition, loudness assimilation does not appear to account for the present findings in which no reductions in perceived intensity were found during some prepulse inhibition trials (e.g., 95 dB(A) blink-eliciting stimuli).

The present findings showed a dissociation between blink amplitude and intensity ratings during the reference trials. During the reference trials, identical blink-eliciting stimuli were presented in the absence of any prepulse stimulus. Results showed that blink amplitude did not differ between S1 and S2, but that S2 was rated as more intense than S1. Using similar methodology, a dissociation was also reported by Swerdlow et al. (1999). In their study, S2 was rated as more intense than S1 for both acoustic and air-puff blink-eliciting stimuli. Swerdlow et al. (1999) suggested that this effect might reflect that the S1 directs attention to S2 and/or a trace aftereffect of S1. The present experiment showed that there are limits to the increased perceived intensity of S2 relative to S1. The S2 stimulus was rated as more intense only when a 110 dB(A) blink-eliciting stimulus was used. There was no effect for the 95 dB(A) blink-eliciting stimulus. It would appear that the increased intensity ratings may better be explained as a trace aftereffect as the strength of this trace would be expected to be reduced in the 95 dB(A) condition relative to the 110 dB(A) condition, whereas an

attentional effect would be expected to be present at about the same magnitude in both stimulus intensity conditions.

The prepulse inhibition paradigm is increasingly finding wide application in applied research with human and nonhuman animal subjects. This application has been based on the sensory gating and protection of processing models of prepulse inhibition (Braff et al., 1992; Graham, 1975, 1992) and the observation that prepulse inhibition differs between some psychiatric groups and healthy controls (e.g., schizophrenia; Braff et al., 1992). The present findings have implications for this research. First, both prepulse inhibition of the blink reflex and perceived intensity ratings of the blink-eliciting stimulus are very sensitive to small changes in the stimulus parameters of a study, such as the intensity of the blink eliciting stimulus and the SOA. Second, prepulse amplitude inhibition, in comparison to prepulse probability inhibition, was most closely associated with perceptions of the intensity of the blink-eliciting stimulus. The protection of processing mechanism seems to serve to attenuate the impact of subsequent stimuli, rather than prevent the processing of the stimuli altogether. Third, the reduced prepulse amplitude inhibition seen in psychiatric populations such as schizophrenia (Braff et al., 1992) may reflect that these patients have an impaired ability to attenuate the processing of subsequent stimuli, rather than an impaired ability to eliminate the processing altogether. However, the relevance of the present results to research with psychiatric patients requires validation. As the present stimulus parameters differ to that used in several prior studies with psychiatric patients (e.g., we used 50 ms 95 and 110 dB(A) blink eliciting stimuli, whereas Braff et al., 1992, used a 40 ms 116 dB(A) stimulus) it would be crucial to examine the perceived perceptual impact of the prepulse in psychiatric patients. Swerdlow et al. (2005) highlighted this point as an important avenue for future research and noted that such research has the potential to provide novel information about the protection of processing mechanisms and their dysfunction in psychiatric patients.

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Figures

Figure 1. Mean blink reflex amplitude to S1 and S2 (left panels) and the intensity rating of S2 relative to S1 (right panels) for the 95 dB(A) blink-eliciting stimulus (top panels) and the 110 dB(A) blink-eliciting stimulus (bottom panels) during the reference trials in the rating phase. S1 = first blink-eliciting stimulus; S2 = second blink-eliciting stimulus.

Figure 2. Mean prepulse amplitude inhibition as a function of stimulus onset asynchrony and blink-eliciting stimulus intensity for Order A (top panel) and Order B (bottom panel) in the rating phase.

Figure 3. Mean prepulse probability inhibition as a function of stimulus onset asynchrony and blink-eliciting stimulus intensity for Order A (top panel) and Order B (bottom panel) in the rating phase.

Figure 4. Mean prepulse inhibition of intensity ratings as a function of stimulus onset asynchrony and blink-eliciting stimulus intensity for Order A (top panel) and Order B (bottom panel) in the rating phase.