Prepulse inhibition of startle and its moderation by schizotypy and smoking

LISA H. EVANS, NICOLA S. GRAY, AND ROBERT J. SNOWDEN

Abstract

The influences of smoking status and schizotypy on prepulse inhibition (PPI) of the startle eyeblink response were assessed in 71 healthy volunteers, across a wide range of prepulse-to-pulse intervals (50–2020 ms). Multiple regression analyses revealed that nonsmoking participants high in cognitive disorganization showed reduced PPI between 50 and 260 ms, whereas at prepulse intervals of 80 and 140 ms individuals high in introvertive anhedonia had greater PPI compared to their low-scoring counterparts. Moreover, there were positive associations in nonsmokers between introvertive anhedonia and latencies to onset and peak response. In contrast, for those individuals who smoked these associations were attenuated or abolished. The results suggest that PPI is altered differentially in psychosis-prone populations who display different symptom profiles, and that these relationships are moderated by smoking status.

Descriptors: Prepulse inhibition, Startle, Schizotypy, Schizophrenia, Smoking, Sensorimotor gating

Disruptions in information processing and attention have long been thought of as one of the hallmarks of schizophrenia (e.g., McGhie & Chapman, 1961). A psychophysiological paradigm that provides an operational measure of the ability to screen out extraneous stimuli is prepulse inhibition (PPI) of the startle response. This refers to the attenuation of the startle response if a startling stimulus (e.g., a loud noise) is first preceded, by around 30–500 ms, by a weaker stimulus (Graham, 1975). At intervals of greater than approximately half a second the participant exhibits facilitation of the startle response, prepulse facilitation. However, this phenomenon has not been investigated as extensively as PPI within the same paradigm. Braff et al. (1978) were the first to demonstrate that patients with schizophrenia have decreased PPI compared to normal controls at prepulse-to-pulse intervals of 60 and 120 ms. Importantly, the patients did not differ from the healthy participants in their amplitude response to the pulse alone trials, so it is not the case that this deficit in schizophrenia merely reflects a faulty reflex system.

Braff and Geyer (1990) hypothesize that the inability to “gate-out” extraneous stimuli, as measured by PPI, may cause the person suffering from schizophrenia to become overwhelmed with excessive exteroceptive (i.e., externally generated), and maybe even interoceptive (i.e., internally generated) information, which could lead to sensory overload and possible cognitive disintegration. Hence it is conceivable that this deficit could lead to some of the symptomatology seen in schizophrenia. However, evidence on this issue has been mixed. Braff, Sweidlow, and Geyer (1999) examined the symptom correlates of PPI in male patients with schizophrenia and found that PPI at the 60-ms prepulse interval was negatively associated with both positive and negative symptoms. Weike, Bauer, and Hamm (2000) also found a negative relationship between PPI at 60- and 120-ms intervals and the positive symptoms of schizophrenia. However, a number of other studies (e.g., Kumari, Soni, Mathew, & Sharma, 2000; Parwani et al., 2000) have failed to find any relationship between symptoms of schizophrenia and a deficit in PPI. Interestingly, when researchers have examined whether PPI is related to any specific symptoms found in schizophrenia they have met with some success. Negative relationships have been found with distractibility (Karper et al., 1996) and thought disorder (Perry & Braff, 1994; Perry, Geyer, & Braff, 1999). Both of these latter symptoms might relate to the third symptom cluster of cognitive disorganization or thought disorder (Liddle, 1987) as opposed to the positive and negative symptoms clusters investigated by the other research.

Two other potential reasons for the discrepant results in the literature are the influence of smoking status and medication. A number of studies have now demonstrated in both healthy volunteers and people with schizophrenia that smoking a cigarette prior to being tested enhances PPI (Della Casa, Hofer, Weiner, & Feldon, 1998; Kumari, Checkley, & Gray, 1996; Kumari, Cotton, Checkley, & Gray, 1997; Kumari, Soni, & Sharma, 2001). In addition, it has also been found that there is a positive correlation between both positive and negative psychotic symptoms and smoking status (Goff, Henderson, & Amico, 1992), which has been interpreted by some researchers as an attempt by people with schizophrenia to self-medicate (e.g., Dalack & Meador-Woodruff, 1996). Thus, given the large number of individuals

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DOI: 10.1111/j.1469-8986.2005.00280.x

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with schizophrenia who smoke (Dulack, Healy, & Meadow-Woodruff, 1998) it is possible that there is an interaction between smoking status and psychotic symptomatology that is affecting PPI. Unfortunately, in the studies examining psychotic symptoms and PPI the smoking status of the participants is not reported (Braff et al., 1992; Grajcar, 1978; Grillon, Ameli, Charney, Krystal, & Braff, 1992) the majority of patients were presumably taking atypical antipsychotic medication and robust deficits in PPI were observed. Thus it seems likely that if typical antipsychotics do have any effect on PPI it is only marginal and does not produce any substantial improvements. The effect of atypical antipsychotic medication is more controversial. A number of studies by Kumari and colleagues (Kumari, Soni, & Sharma, 1999; Kumari et al., 2000) suggested that the PPI deficit that is usually seen at short-intervals in individuals with schizophrenia can be normalized by atypical antipsychotic medication. Furthermore, two independent laboratories have replicated this effect (Leumann, Feldon, Volkmann, & Ludewig, 2002; Oranje, Van Oel, Gispen-De Wied, Verbaten, & Kahn, 2002). However, further research, using a more informative within-participants longitudinal design, has not replicated these findings (Duncan et al., 2003; Mackeprang, Kristiansen, & Glenthoj, 2002). It seems likely that one of the reasons for the ambiguity in results is the wide range of atypical antipsychotics that have been examined, all of which might not be as effective in the reinstatement of PPI. Furthermore, there are a number of serious confounds in some of the studies that have assessed the effects of medication on PPI. For example, Mackeprang et al. tested patients after 4 h of smoking withdrawal, which, as was highlighted above, is known to be associated with disrupted PPI. Finally, this area of research is further complicated by the finding that procyclidine, one of the most commonly prescribed anticholinergic drugs used to treat extrapyramidal symptoms, can also significantly impair PPI at the 60-ms prepulse interval (Kumari et al., 2003).

To summarize, the inconsistent research literature linking psychotic symptoms to a deficit in PPI could be due to (a) different studies focusing on different symptom clusters, (b) differential smoking status or time since last cigarette between the studies, (c) the patients taking different classes and combinations of medication between studies (typical vs. atypical antipsychotics and anticholinergics), or (d) an interaction between these three factors. These factors are extremely difficult to disentangle. First, accurately measuring psychotic symptoms in patients with schizophrenia is very difficult, as they are often motivated to hide their true symptoms to prevent their medication being increased, which can be associated with unpleasant side effects. Furthermore, these individuals are often incapable of full and accurate disclosure of their symptoms, especially if they are thought disordered, due to poor insight. Second, as the vast majority of patients with schizophrenia smoke and are strongly resistant to remaining nicotine free for any reasonable length of time, investigating this variable and its interactions with psychotic symp-
Gray, Jones, and Gray (1997) found a positive relationship between an asocial component of schizotypy and PPI at prepulse intervals of 120, 240, and 500 ms, whereas Swerdlov, Filion, Geyer, and Braff (1995) found a negative relationship between an MMPI (Minnesota Multiphasic Personality Inventory; Hathaway & McKinley, 1943) subscale and PPI at the 60-ms interval. In contrast, no relationship was found between a positive or negative aspect of schizotypy and PPI at 30-, 60-, or 120-ms prepulse intervals by Cadenhead, Kumar, and Braff (1996).

A possible explanation for these discordant results was provided in a study by Kumari, Toone, and Gray (1997), who also took into consideration participants’ smoking status. It was found that nonsmoking individuals high in psychoticism (EPQ; Eysenck & Eysenck, 1975) demonstrated a reduced PPI response, particularly at prepulse intervals of 60 and 120 ms. However, in the smoking group there were no effects of psychoticism on PPI. In addition, latencies to onset and peak were recorded. The main applications of these latency measures to PPI are (a) to determine whether abnormalities in reflex latency present in certain groups may contribute to an artifact in the measurement of startle magnitude, and (b) to determine whether there is a reduction in the latency of response in the presence of a prepulse. This latter issue is important as a deficit in reflex latency facilitation provides some evidence that there has been diminished detection of the prepulse, and so PPI deficits need to be interpreted in this context (Braff et al., 1992). Kumari, Toone, et al. (1997) found normal latency facilitation at short-lead intervals for all participants. However, there were differences in the latencies to onset and peak as a function of psychoticism but only in the nonsmoking group. Those individuals high in psychoticism who were nonsmokers responded faster across all trial types than those low in this trait. Kumari, Toone, et al. argue that “smoking/nicotine may to some extent act to restore cognitive attentional deficits indexed by habituation and PPI of the acoustic startle in the smoking population scoring high on the psychometric measures of psychosis-proneness” (p. 189). Thus this study suggests that if a sample is composed of predominately smokers then no relationship will be found between schizotypy and PPI.

An additional limitation of the vast majority of studies examining the association between schizotypy and PPI is that they have focussed on short-lead intervals, generally 30–120 ms, and there has been a paucity of research examining the longer intervals. This is unsatisfactory because Ludewig, Geyer, and Vollenweider (2003) have reported that individuals with schizophrenia exhibit less prepulse facilitation when there is a 2000-ms prepulse interval compared to healthy volunteers. This suggests that as well as having the well-reported deficit in inhibition, individuals with schizophrenia can also have a problem with the excitatory processes of facilitation that are evoked by this paradigm. However, in schizotypy and schizophrenia studies, intervals this long have very rarely been examined, due primarily to reasons of time. Therefore the first aim of this study was to elucidate the sensorimotor deficits that could be seen across a wide range of prepulse intervals, by measuring startle inhibition and facilitation from 50 ms (when inhibition occurs) through to 2020 ms (when facilitation typically occurs).

The second aim was to determine if any schizotypy dimensions were associated with deficits in inhibition or facilitation at any of the prepulse intervals. In the schizophrenia literature studies have found a link between PPI and the positive symptoms of psychosis (Braff et al., 1999; Weike et al., 2000), whereas other
The distributions of scores on each of the dimensions can be seen in Table 1 for both the nonsmoking and smoking groups. In addition, the original norms established by Mason et al. (1995) have been included for comparative purposes. As can be seen from Table 1 our sample statistics were very similar to those found by Mason et al., which suggests a representative sample in terms of schizotypy scores. A series of independent sample t tests indicated that there were no significant differences between the nonsmoking and smoking groups on any of the schizotypy dimensions (p > .1).

**Table 1. Descriptive Statistics for Each of the Schizotypy Dimensions Obtained by the Smoking Group (n = 30) and the Nonsmoking Group (n = 41)**

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unusual Experiences</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>9.70</td>
<td>7.15</td>
<td>0–27</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>7.27</td>
<td>5.17</td>
<td>0–19</td>
</tr>
<tr>
<td>Mason et al. (1995)</td>
<td>9.7</td>
<td>6.7</td>
<td>3–19</td>
</tr>
<tr>
<td>Cognitive Disorganization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>11.83</td>
<td>6.10</td>
<td>1–21</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>13.29</td>
<td>5.44</td>
<td>2–23</td>
</tr>
<tr>
<td>Mason et al. (1995)</td>
<td>11.6</td>
<td>5.8</td>
<td>–</td>
</tr>
<tr>
<td>Introvertive Anhedonia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>4.17</td>
<td>3.43</td>
<td>1–17</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>3.93</td>
<td>3.37</td>
<td>0–13</td>
</tr>
<tr>
<td>Mason et al. (1995)</td>
<td>6.1</td>
<td>4.6</td>
<td>–</td>
</tr>
<tr>
<td>Impulsive Nonconformity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
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<td>3.68</td>
<td>1–18</td>
</tr>
<tr>
<td>Nonsmokers</td>
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<td>3.73</td>
<td>2–16</td>
</tr>
<tr>
<td>Mason et al. (1995)</td>
<td>9.1</td>
<td>4.3</td>
<td>–</td>
</tr>
</tbody>
</table>

*In addition, the original norms gathered by Mason et al. (1995) are displayed for comparative purposes.

**Measurement of Startle Response**

The methodology for measuring PPI was very similar to Braff et al. (1992). Each participant was seated in a moderately lit sound-proof room. They were told that they would hear a variety of sounds and that all they had to do was to look at a point approximately at eye level on the wall in front of them. Participants were reminded to keep their eyes open and to try and blink as normally as possible. Startle response was measured by EMG activity from the right orbicularis oculi muscle using two 6-mm silver/silver chloride electrodes filled with electrode gel. These were positioned approximately 1 cm below the pupil and 1 cm below the lateral canthus. The ground electrode was placed over the right mastoid. All resistances were less than 5 kΩ.

The acoustic stimuli were delivered, recorded, and scored by a computerized startle response system (SR-Lab, San Diego Instruments). The system recorded a 250-ms EMG signal epoch starting at the onset of the startling stimulus, which was sampled at a rate of 1000 Hz. In addition, EMG activity was band-pass filtered (10–1000 Hz) and rectified. Amplifier gain was kept constant for all participants. Onset latency is reported in milliseconds and was defined as a shift of 6 μV from the baseline value occurring 18–100 ms after the startling stimulus. The baseline value was defined as the average EMG activity recorded at the beginning of the sampling window for 18 ms. Startle response magnitude was defined as the maximal (peak) amplitude occurring within 18–50 ms from the startling stimulus; the point at which this occurred was recorded as the peak latency. If the onset and peak latencies differed by more than 95 ms or if the baseline values shifted by more than 40 μV then the trial was excluded, as responses were deemed to be spontaneous or unstable. Very few trials were excluded using these criteria (< 5%). Startle response amplitudes that did not exceed the response threshold level were scored as zero. In these instances the participant’s mean onset and peak latency values for that particular type of trial were substituted for the missing latency data. This was also the technique used to deal with missing startle amplitude and latency measures due to trial rejection. No participant had more than one trial of each prepulse type per PPI trial block rejected.

**Startle Session**

Acoustic stimuli were presented binaurally through headphones (TDH-39-P, Maico). Each participant completed three PPI trial blocks, each lasting 8 min. This format was adopted to reduce participants’ boredom and to reduce the effects of habituation. Between blocks participants completed a filler attentional task for 10 min. The electrodes were kept fixed to the participant. Each block started with a 2-min acclimatization period consisting of 70 dB[A] SPL white noise that continued as the background noise for the session. Participants received 25 trials in each block, hence 75 trials in all. A PPI block contained four pulse alone trials (and always began with this type of trial) and three trials of each of the following prepulse intervals: 50, 80, 140, 260, 520, 1020, and 2020 ms, which were presented in a random order that was identical for all participants. The prepulse intervals were measured from the onset of the prepulse to the onset of the pulse. The startling stimulus was a 40-ms burst of 116 dB[A] SPL white noise, with a rise and fall time of 12–15 μs. The prepulse was a 20-ms burst of white noise, 86 dB[A] SPL. The intertrial interval (measured from the end of recording of one trial to the beginning of recording the next trial) had a range of 9 to 23 s, with a mean of 15 s.

**Data Analysis**

PPI was calculated by subtracting the mean amplitude of the prepulse trials from the mean amplitude of the pulse alone trials and dividing this by the mean amplitude of pulse alone trials, then converting the obtained ratio to a percentage. The response to the first pulse alone in each session was not used in this calculation as it was typically much larger than all subsequent responses.

As outlined in the Participants section, 11 participants were classified as nonresponders, and therefore excluded from analyses. These were defined as individuals whose mean amplitude to the pulse alone trials was less than 30 μV in any of the PPI blocks. The PPI and latency data were then screened using graphical and
statistical methods at the group level to ensure that the dependent measures were normally distributed and linear (see Tabachnick & Fidell, 2001, for more details). These revealed that 2 individuals’ data (2 women; 1 smoker and 1 nonsmoker) were causing excessive skewness to the PPI data at most prepulse intervals (their z scores were more than 3 standard deviations from the mean). By omitting these individuals’ data the distributions were within acceptable limits. Thus the decision was taken to exclude these 2 individuals, as this resulted in a better solution than applying transformations. It is important to note that although all the results reported have been conducted with these 2 individuals excluded, analyses have also been conducted with these participants included (not reported). Identical results were obtained. Thus the conclusions being drawn from this study have not been affected by the exclusion of these participants. The total sample size for this study was therefore 69 participants (57 women and 12 men), of which 40 were nonsmokers and 29 were smokers.

Analyses were conducted to determine whether participants who were excluded from the study systematically differed in their smoking status or O-LIFE scores from those participants who were included in the study. Second, to confirm that any deficit in PPI that might be seen in schizotypy or as a function of smoking status was not merely a function of a faulty reflex system, reactivity to the pulse alone was inspected to see if there were any significant associations with any of the schizotypy dimensions or smoking status. Third, repeated-measures ANOVAs were completed on the PPI and latency data to examine the effect of the various prepulse intervals on these measures and also the effect of smoking status. In the ANOVA examining PPI the within-participants variable trial block was also added. The Greenhouse–Geisser correction was utilized in these analyses due to a violation of the assumption of sphericity, and where post hoc analyses were necessary classical Bonferroni corrections were applied. Finally, it was assessed whether there were any relationships between the schizotypy dimensions and PPI deficits or latency characteristics and whether these relationships were dependent on smoking status.

Multiple regression was utilized to assess the relationship between the four schizotypy dimensions (unusual experiences, cognitive disorganization, introverted anhedonia, and impulsive nonconformity) and PPI or latency measures. One major advantage of multiple regression is that given that some of the schizotypy dimensions are significantly correlated with each other (see Mason et al., 1995, for more details) it can assess the unique contribution of each of the schizotypy dimensions to the prediction of the dependent variable. The alpha level for significance (two-tailed) was set at $p < .05$, unless specified otherwise.

### Results

**Excluded Participants**

In total 11 nonsmoking (21.5%, 8 women and 3 men) and 5 smoking individuals (14.7%, 4 women and 1 man) were excluded from this study. These individuals were comparable with the included participants in terms of smoking status, which was confirmed by a chi-square analysis, $\chi^2(1) = 0.63$, $p > .05$. A further concern with the individuals excluded was whether they differed from the included individuals on any of the O-LIFE dimensions. Therefore a series of independent sample t tests were run examining if there was a difference on any of the schizotypy dimensions between these two groups. All of these tests proved to be nonsignificant.

**Pulse Alone Amplitude**

Startle amplitude to the pulse alone was analyzed by multiple regression, using the four schizotypy dimensions as the predictor variables and the mean amplitude to the (a) first pulse (a measure of initial reactivity) and (b) other pulse alone trials, as the dependent variables. For both of these analyses it was found that there were no significant relationships with any of the schizotypy dimensions. Furthermore, two independent t tests revealed that there were no significant differences in the mean amplitude to the (a) initial pulse or (b) other pulse alone trials between the smoking and nonsmoking groups. Thus there were no differences between different scores on the schizotypy dimensions, or between smoking status groups, in initial reactivity or baseline startle response, so any differences in PPI that may be found in relationship to the schizotypy dimensions, or between smoking status groups, are not due to a faulty reflex system.

**Prelude Inhibition**

A repeated-measures ANOVA was conducted on PPI examining the effects of the within-participants variable prepulse interval (seven intervals: 50, 80, 140, 260, 520, 1020, and 2020 ms), the within-participants variable trial block (three levels: blocks 1, 2, and 3), and the between-participants variable smoking status (nonsmoker or smoker). There was a main effect of prepulse interval, $F(6,402) = 61.34, p < .001, \epsilon = .67$, with significant negative linear, $F(1,67) = 138.35, p < .001$, and negative quadratic, $F(1,67) = 18.21, p < .001$, trends (Figure 1). There was no significant main effect of trial block. There was however a significant interaction between prepulse interval and trial block, $F(12,804) = 3.87, p < .001, \epsilon = .65$. When followed up with simple effects tests it was found that there was a significant difference between blocks 1 and 2 at the 50-ms prepulse interval (2 > 1) and between blocks 1 and 2 and 1 and 3 at the 140-ms prepulse interval (1 > 2 and 3, $ps < .05$, with Bonferroni adjustment).

Furthermore, there was a tendency toward a significant main effect of smoking status, $F(1,67) = 3.56, p = .06$. By examining Figure 1 it can be seen that there appears to be a difference in the linear trend component between nonsmokers and smokers. To examine this further the linear regression lines for both nonsmokers and smokers were found and the t statistic was used to determine if there was a significant difference between their slopes. To maximize the fit of the regression lines the logarithm of prepulse interval was used as the independent variable (nonsmokers, $R^2 = 98$%; smokers, $R^2 = 96$%). Prepulse inhibition was the dependent variable. There was a significant difference between the slopes of the nonsmokers and smokers’ regression lines, $t(65) = 6.66, p < .001$. Finally, there was no significant three-way interaction, nor significant interactions between trial block and smoking status, or between prepulse interval and smoking status.

Multiple regressions were completed initially for both nonsmokers and smokers together at each of the PPI intervals to evaluate any relationships with the schizotypy dimensions. These are reported in Table 2, section A. Multiple regressions were then

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1Studies have indicated that PPI is moderated by gender (Swerdlow, Auerbach, Monroe, & Hartston, 1993) and menstrual cycle (Swerdlow, Hartman, & Auerbach, 1997); thus it is possible that these factors could have influenced O-LIFE scores, which in turn had an effect on PPI. To rule out this possibility we examined whether there were any associations between these variables (menstrual cycle was measured using the same criteria as Swerdlow et al., 1997) and O-LIFE scores; none were found ($p > .05$). This suggests that our results are due to schizotypy rather than mediated via effects of gender or menstrual cycle.
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**Figure 1.** Mean percent prepulse inhibition or facilitation exhibited by nonsmoking (n = 40) and smoking (n = 29) participants at each of the prepulse-to-pulse intervals. Error bars represent ± 1 standard error of the mean.

Conducted separately for nonsmokers and smokers to analyze the hypothesized interaction between schizotypy and smoking status. These are reported in Table 2, section B.

**All participants.** Negative relationships were found between cognitive disorganization and PPI at the 80-, 140-, and 260-ms prepulse intervals. In contrast, positive associations were found between introvertive anhedonia and PPI at the 80- and 140-ms intervals.

**Nonsmokers.** When the multiple regressions were completed with the smokers excluded the relationships that were found for the nonsmokers were stronger than for the group as a whole. Thus for cognitive disorganization there were negative associations with PPI at prepulse intervals of 80 and 140 ms and a tendency toward negative associations at intervals of 50 (p = .06) and 260 (p = .08) ms. However, for introvertive anhedonia there were positive relationships with PPI at 80 and 140 ms. The only other significant result was a positive relationship between unusual experiences and PPI at the 50-ms interval.

**Smokers.** In contrast to the nonsmoking group, where the relationships between PPI and the schizotypy dimensions of cognitive disorganization and introvertive anhedonia got stronger, for the smoking group most of these associations were abolished. Only two tendencies toward significant results remained: At the 80-ms interval there was a positive relationship with introvertive anhedonia (p = .09) and at the 260-ms interval a negative relationship with cognitive disorganization (p = .08).

**Onset and Peak Latencies**
Repeated-measures ANOVAs were conducted examining the effects of prepulse interval (eight levels: pulse alone, 50, 80, 140, 260, 520, 1020, and 2020 ms) and smoking status on onset and peak latency. There was a significant main effect of prepulse interval on both onset, F(7,469) = 26.08, p < .001, ƞ² = .64, and peak latency, F(7,469) = 24.46, p < .001, ƞ² = .74 (Figure 2). There were no main effects of smoking on either onset or peak latency and no interaction was found between prepulse interval and smoking status.

Multiple regression analyses revealed that in the nonsmoking participants the dimension of introvertive anhedonia showed a significant positive relationship, or a tendency toward a significant positive relationship, with onset latency at prepulse intervals of 80 to 2020 ms. A parallel result was found with this dimension and peak latency, with a significant positive relationship, or a tendency toward a significant positive relationship, at prepulse intervals of 140 to 2020 ms. In contrast, for the smoking individuals there were no associations between any of the schizotypy dimensions and onset or peak latency at any prepulse interval. These results can be seen in Table 3.

**Discussion**
As predicted, there was an interaction between schizotypy, smoking status, and PPI. Contrary to expectation, however,

### Table 2. Beta Coefficients Obtained between the Schizotypy Dimensions and PPI at Each of the Prepulse Intervals, Conducted First (A) with All Participants and Second (B) Separately for Both Nonsmokers (n = 40) and Smokers (n = 29)

<table>
<thead>
<tr>
<th>A. All participants (nonsmokers and smokers)</th>
<th>50 ms</th>
<th>80 ms</th>
<th>140 ms</th>
<th>260 ms</th>
<th>520 ms</th>
<th>1020 ms</th>
<th>2020 ms</th>
</tr>
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<tbody>
<tr>
<td>UE</td>
<td>.06</td>
<td>.06</td>
<td>.06</td>
<td>.23</td>
<td>-.05</td>
<td>.02</td>
<td>-.08</td>
</tr>
<tr>
<td>CD</td>
<td>-.13</td>
<td>-.29*</td>
<td>-.34*</td>
<td>-.35*</td>
<td>-.10</td>
<td>-.18</td>
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<tr>
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<td>.09</td>
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<td>.29*</td>
<td>.21</td>
<td>.12</td>
<td>.13</td>
<td>.11</td>
</tr>
<tr>
<td>IN</td>
<td>-.24</td>
<td>-.14</td>
<td>-.06</td>
<td>-.02</td>
<td>.01</td>
<td>.02</td>
<td>.12</td>
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<td>.18*</td>
<td>.13</td>
<td>.10</td>
<td>.02</td>
<td>.03</td>
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<table>
<thead>
<tr>
<th>B. Separated into nonsmokers and smokers</th>
<th>NS</th>
<th>S</th>
<th>NS</th>
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<td>.48**</td>
<td>.34</td>
<td>.51**</td>
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<td>.31</td>
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<td>-.10</td>
<td>-.23</td>
<td>-.01</td>
<td>.07</td>
<td>-.16</td>
<td>.10</td>
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<td>.15</td>
<td>.30*</td>
<td>.16</td>
<td>.26*</td>
<td>.11</td>
<td>.11</td>
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</table>


*p < .05; **p < .01.
different dimensions of schizotypy were found to have differential associations with PPI in the nonsmoking group. In particular, a negative relationship was observed in the nonsmokers between cognitive disorganization and PPI. Thus the higher the cognitive disorganization score the smaller the PPI displayed at prepulse intervals of 50 to 260 ms. In contrast, a positive association was found in the nonsmoking group between introvertive anhedonia and PPI: the higher the introvertive anhedonia score for these participants the greater the inhibition, at prepulse intervals of 80 and 140 ms. For the smoking group these associations were attenuated or abolished.

The direction of the effect of cognitive disorganization on PPI is consistent with the majority of previous research, which has found that higher scores on a psychosis-proneness measure are associated with lower PPI at short-lead prepulse intervals. For example, Simons and Giardina (1992) found that there was a negative relationship between the dimension of perceptual aberration and PPI. Consistent with this, Swerdlow et al. (1995) reported that individuals scoring highly on the MMPI Goldberg Index, a measure of psychosis-proneness, have reduced PPI. Furthermore, there is of course the large body of literature that has demonstrated reduced PPI in individuals with schizophrenia (e.g., Braff et al., 1978, 1992) and a few reports of attenuated PPI in Schizotypal Personality Disorder patients (e.g., Cadenhead, Geyer, & Braff, 1993). Moreover, this result supports the work of Perry and colleagues (Perry & Braff, 1994; Perry et al., 1999) and Karper et al. (1996) in suggesting that it is the symptoms of thought disorder and cognitive disorganization that are significantly associated with reductions in PPI.

The more surprising result occurred with the introvertive anhedonia dimension, which is thought to reflect the negative symptoms of psychosis. Nonsmoking individuals having low scores on this dimension displayed less inhibition than individuals with high scores. Although the negative dimension of schizotypy has been measured in previous studies examining the link between schizotypy and a deficit in PPI no significant associations have been found (e.g., Cadenhead et al., 1996; Simons & Giardina, 1992). This could be due to a number of reasons. First, the number of participants in these studies is typically quite small (e.g., Cadenhead et al., 1996; 7 individuals, excluding nonresponders, in the negative schizotypy group), and so they may lack the power required to detect associations. Second, most of these studies have utilized the physical anhedonia scale (Chapman, Chapman, & Raulin, 1976) to measure the negative symptoms of schizotypy. Katsanis, Iacono, and Beiser (1990) have demonstrated that psychotic patients score higher on this scale than their first-degree relatives, who in turn score higher than healthy controls. However, scores on the physical anhedonia scale did not distinguish among the four groups of patients tested (schizophrenic, schizophreniform, major depressive, and bipolar), which suggests that this scale lacks specificity. Finally, another possible reason why a positive relationship has not been found between a negative dimension of schizotypy and PPI is the smoking status of the participants in the study. If a sample was composed of predominately smokers, then from the results of this study it would be predicted that no relationship would be observed between the negative dimension of schizotypy and a deficit in PPI. This explanation could also explain why a positive association has not been found between the negative symptoms of schizophrenia and a disruption in PPI in individuals with schizophrenia. In fact, it is even more pertinent in this sample given the large number of patients with schizophrenia who smoke (Dalack et al., 1998). Thus, this is the first time increased PPI has been found in a sample of participants scoring highly on a symptom scale measuring propensity to negative symptoms of schizophrenia.

It is possible that the associations between the different dimensions of schizotypy and PPI can be understood if the sensorimotor gating hypothesis is considered (Braff & Geyer, 1990). According to this conceptualization, in schizophrenia the patient suffers from a faulty filter that fails to gate or block excessive or trivial information, and therefore lets through into consciousness too much information. This inability to inhibit extraneous stimuli is hypothesized to lead to sensory overload and hence to cognitive deficits, such as thought disorder. This would certainly seem consistent with our results in high cognitive disorganization scorers. However it appears that this deficit only occurs around

![Figure 2](image_url)  
**Figure 2.** Mean latency to onset and peak startle response exhibited by the nonsmoking \( n = 40 \) and smoking \( n = 29 \) participants to the pulse alone trials (PA) and at each of the prepulse-to-pulse intervals. Error bars represent ± 1 standard error of the mean.

<table>
<thead>
<tr>
<th>Pulse Alone Interval (ms)</th>
<th>Onset Latency (ms)</th>
<th>Peak Latency (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NS</td>
<td>S</td>
</tr>
<tr>
<td>50</td>
<td>.24</td>
<td>.14</td>
</tr>
<tr>
<td>80</td>
<td>.26</td>
<td>.07</td>
</tr>
</tbody>
</table>

**Table 3. Beta Coefficients Obtained between the Schizotypy Dimension of Introvertive Anhedonia and Onset and Peak latency at Each of the Prepulse Intervals for Nonsmokers (\( n = 40 \)) and Smokers (\( n = 29 \)).**

Notes. PA: Pulse alone trials, NS: Nonsmoking group, S: Smoking group.  
*p < .1; *p < .05; **p < .01.
50 to 260 ms in the temporal gating window. In contrast, the finding that nonsmoking individuals high in introverted anhedonia exhibit high levels of PPI suggests that these individuals may exhibit the opposite pattern of sensorimotor gating. For these participants experience more inhibition around 80 to 140 ms after a stimulus, and so have an increased ability to inhibit information in this temporal gating window. This suggests that they may be able to process more information about the prepulse than individuals with too little inhibition.

The finding that the relationship between schizotypy and PPI is moderated by smoking status replicates the work of Kumari, Toone, et al. (1997), who found a negative association between psychoticism and PPI, but only in nonsmokers at 60- and 120-ms prepulse intervals. The results from the current study may indicate that nicotine can, to some degree, act to reinstate normal levels of PPI in smoking individuals who score highly on the disorganized dimensions of schizotypy and those who have low scores on introverted anhedonia. Finally, the fact that latencies to onset and peak were also normalized in the smoking individuals high in introverted anhedonia suggests that nicotine also has more wide-ranging benefits. Importantly although a number of studies have found that scores on certain schizotypy dimensions are higher in smokers than nonsmokers (e.g., Williams et al., 1996), this was not found in the present study. Thus these results are not confounded by differences in schizotypy scores between smokers and nonsmokers.

Importantly there was a significant difference between the pattern of inhibition/facilitation exhibited by the nonsmokers and smokers at prepulse intervals of 80 ms and greater. This is a novel finding, as previous studies, in both humans and animals, have only examined the effect of smoking/nicotine on PPI at short-lead intervals. The difference appeared to be because the smokers demonstrated facilitation at an earlier prepulse interval compared to the nonsmoking participants and also, on the whole, greater facilitation at the long-lead intervals. These are very interesting results, as they suggest that smoking reduces the temporal window in which inhibition occurs, but also increases the magnitude of facilitation at the long-lead intervals. Future research into this issue is important, as it has the potential to elucidate the behavioral, anatomical, and neurochemical actions of nicotine and sensorimotor gating. Finally, it would be informative to examine the role of smoking status in more detail. In this study the duration since the participant’s last cigarette and how many cigarettes on average they smoked a day were not controlled for. Thus the effect of these variables on PPI and the relationship between schizotypy and PPI needs to be delineated more fully.

Thus in conclusion, it has been found that different aspects of schizotypy are associated with different levels of PPI in non-smoking individuals. In particular, negative associations were found between cognitive disorganization and PPI at prepulse intervals of 50 to 260 ms, whereas positive relationships were found between introverted anhedonia and PPI at 80- and 140-ms prepulse intervals. In addition, nonsmoking individuals high in introverted anhedonia also demonstrated an increase in latencies to onset and peak response. No significant associations were found in participants who smoked. Therefore it appears that smoking plays an important role in the relationships between PPI and schizotypal experiences in healthy volunteers. It now remains to be seen whether similar relationships will be found in individuals with schizophrenia.

REFERENCES


Prepulse inhibition and schizotypy


(Received June 24, 2004; Accepted December 2, 2004)