Review

The psychological significance of human startle eyeblink modification: a review

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Abstract

The human startle eyeblink reflex is reliably modified by both cognitive and emotional processes. This review provides a comprehensive survey of the current literature on human startle modification and its psychological significance. Issues raised for short lead interval startle inhibition include its interpretation as a measure of protection of processing, sensorimotor gating and early attentional processing. For long lead interval effects, interpretations related to attentional and emotional processing are discussed. Also reviewed are clinical applications to information processing dysfunctions in the schizophrenia spectrum disorders, and to emotional processing disorders. Finally, an integrative summary that incorporates most of the cognitive findings is presented and directions for future research are identified regarding both cognitive and emotional modification of startle. © 1998 Elsevier Science B.V.

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1. Introduction

According to historical accounts of startle research by Hoffman and Ison (1980), Ison and Hoffman (1983), the fact that reflexes can be reliably modified by antecedent changes in the sensory environment was first documented in animals in the mid 1860s by Sechenov (1965). However, it was not until the mid 1970s, when Graham reviewed literature documenting similar effects with the human startle eyeblink reflex, that interest in research on human reflex modification began to show dramatic growth. At that time Graham suggested that the study of startle modification might “provide a powerful technique for probing what underlies the normal processing of information and especially for probing processing characteristics of relatively inaccessible subjects…” (Graham, 1975, p. 238). As shown in Fig. 1, in the years since Graham’s suggestion the number of published articles on startle reflex modification in humans, as indexed by the MedLine and PsycLIT computerized databases, has increased exponentially.

The high level of interest in the startle modification technique is a clear indication that researchers believe the technique indeed yields valuable information about human attentional and affective processes. The focus of this review is on the nature of that information. For what seems to be a rather simplistic measure, interpretations of startle eyeblink modification (SEM) are varied and complex, as SEM has been reported to index various levels of cognitive and emotional processing.

Much of the complexity associated with the psychological interpretation of SEM is due to the fact that SEM is affected by many factors including the nature of the startling and startle modifying stimuli, the temporal configuration of these stimuli, the instructions given to the research participant, and the characteristics of the participants themselves. The purpose of this review is to sort through these methodological and theoretical complexities in order to provide a survey and integration of the startle modification literature, with the goal of describing the

![Fig. 1. Number of published articles on human startle eyeblink modification based on the PsycLIT and MedLine computerized databases.](image-url)
Fig. 2. An illustration of typical startle eyeblink modification paradigms. Panel A shows a baseline condition in which only a startle-eliciting stimulus is presented. Panel B illustrates a short lead interval lead stimulation condition resulting in startle inhibition. Panel C illustrates a long lead interval lead stimulation condition resulting in startle facilitation.

current state of knowledge concerning what can be learned from SEM. There have been three major reviews written regarding human SEM (Anthony, 1985; Graham, 1975; Lang et al., 1990) as well as an edited book devoted to this topic (Dawson et al., in press). The purpose of this paper is to review what we have learned about SEM and from SEM in recent years. This review is focused on the human startle modification literature. Brief referrals to the extensive literature on startle modification in nonhuman animals will be made for the interested reader where appropriate. Neurophysiological circuits for both startle and its modification are reasonably well developed in nonhuman animals, and referrals to this literature will also be given.

2. The basic startle eyeblink modification paradigm

The typical SEM paradigm involves the presentation of a series of trials in which a startle-eliciting stimulus (e.g. sudden loud noise) is presented in the absence of any other stimulus (Fig. 2, panel a), intermixed with trials in which the startle-eliciting stimulus is presented closely following a non-startling stimulus called a ‘lead stimulus’ (Fig. 2, panels b and c). The interval between the onset of the lead stimulus and the startle-eliciting stimulus is called the ‘lead interval’. The dependent measure most commonly reported in human startle research is a change or percent-change score reflecting the difference in size of the startle eyeblink elicited under these conditions.
Procedures for recording and quantifying startle eyeblink amplitude have been discussed by Anthony (1985), Balaban et al. (1986), Clarkson and Berg (1984) and Lang et al. (1990). (See Berg and Balaban, in press, for a review). Startle amplitude inhibition refers to cases in which the startle eyeblink is smaller in the lead stimulation condition than in the baseline condition (Fig. 2, panel b), startle amplitude facilitation refers to cases in which the startle reflex is larger in the lead stimulus condition than in the baseline condition (Fig. 2, panel c), and startle latency facilitation refers to cases in which the latency of the startle reflex is shorter in the lead stimulus condition than in the baseline condition.

The nature of the modifying effect of a lead stimulus on startle depends in large part on the lead interval. Generally speaking, there are two main classes of SEM effects in humans, (1) modification of amplitude and latency with lead intervals of up to approximately 500–800 ms, which will be referred to as ‘short lead interval effects’, and (2) modification of amplitude with lead intervals longer than 500–800 ms, which will be referred to as ‘long lead interval effects’. In each of the major sections of this paper, we will first review the typical reflex modification effects and their interpretations and then we will discuss the exceptions to these generalities.

3. Short lead interval effects

There are three main types of lead stimulation startle modification effects observed at short lead intervals. The first is an amplitude facilitation effect which has been shown to occur reliably for acoustic startle with vibrotactile lead stimuli at 25, 50, and 100 ms lead intervals (e.g. Blumenthal and Gescheider, 1987; Blumenthal and Tolomeo, 1989; Flaten and Blumenthal, 1996), for electrically-elicited startle with acoustic lead stimuli at a lead interval of 10 ms (e.g. Boelhouwer et al., 1991), and has also been observed for acoustic startle with visual and electrotactile lead stimuli at lead intervals of 30 and 60 ms (Graham, 1980). To date the main focus of research on this amplitude facilitation effect has been on its physiological significance (e.g. Boelhouwer et al., 1991) and it has received relatively little empirical attention or discussion in terms of its psychological significance.

The second short lead interval startle modification effect is a latency facilitation that is observed at lead intervals of approximately 100 ms or less, regardless of the modalities of the lead and startle stimuli (e.g. Graham, 1975; Graham and Murray, 1977; Braff et al., 1978; Blumenthal and Gescheider, 1987; Blumenthal and Tolomeo, 1989). The psychological significance of this latency facilitation effect has also received relatively little attention, the effect has been reported inconsistently (many reports do not include the latency measure at all), and is often reported as merely co-occurring with amplitude inhibition effects (discussed below). However, there is considerable evidence suggesting that latency facilitation and amplitude inhibition are independent processes that show a different developmental course (e.g. Anthony and Graham, 1985; Ornitz et al., 1986, 1991), are affected differently by various startle and lead stimulus parameters (e.g. Graham and Murray, 1977; Silverstein et al., 1981; Blumenthal and Levey, 1989), and psychopathological states
(e.g. Braff et al., 1992). Thus latency facilitation effects may deserve greater attention in future research, particularly in future research involving clinical populations.

The main focus of this section is the third and most robust short lead interval effect, inhibition of startle amplitude, an effect also referred to in the literature as prepulse inhibition (PPI). Excluding the conditions described above known to produce amplitude facilitation, amplitude inhibition is produced by a wide range of lead stimuli and occurs within a lead interval range of approximately 30–500 ms. The startle amplitude inhibition effect is quite robust, typically in the range of 50–80% inhibition, and is quite reliable, occurring in 90–100% of normal adult participants who show reliable eyelink reflexes. Startle inhibition can be produced by visual, acoustic, olfactory and vibrotactile lead stimuli, and their inhibitory effect is seen even when the modalities of the lead and startle stimuli differ. Moreover, an increase or a decrease in stimulus energy can also serve as an effective lead stimulus. Startle inhibition has been obtained in infants (e.g. Balaban et al., 1989; Graham et al., 1981), though the inhibitory processes do not appear to be fully developed until around the age of eight (Ornitz et al., 1986, 1991). (See Ornitz, in press, for a review). Startle inhibition is well documented in nonhuman animals (see review by Ison and Hoffman, 1983). In nonhuman animals the neural substrates of both the acoustic startle reflex (e.g. Davis et al., 1982; Koch et al., 1992; Lee et al., 1996; Davis et al., in press) and its inhibition at short lead intervals (e.g. Geyer et al., 1990; Leitner and Cohen, 1985; Swerdlow et al., 1992) are also well documented (for current reviews of this work see Dawson et al., 1997; Swerdlow and Geyer, in press).

As noted by Blumenthal (in press), “Short lead interval modification of startle is a response measure that has several obvious advantages, including: (1) availability of animal models, leading to an understanding of the neurological mechanisms underlying the effect; (2) availability of developmental models; (3) minimal compliance and motivation required of the subject; (4) sensitivity to manipulations of the sensory, cognitive, social, and pharmacological environment; (5) an effect size that is great enough that even rather large changes in methodology cannot obscure this effect; (6) functional significance in the life of the organism. What more can we ask of a response measure?”

In the following sections we will discuss the current views of the psychological interpretation and functional significance of this inhibitory effect in humans.

3.1. Protection of processing

In the first review of startle inhibition effects in humans, Graham (1975) raised the possibility that the inhibition may reflect “a wired-in negative feedback which reduces the distraction produced by reflexes such as startle, and thus protects what has been called pre-attentive stimulus processing” (p. 246). Graham’s view is that the onset of low-intensity changes in sensory stimulation evokes a ‘transient detecting reaction’ that automatically triggers a sensory-gating mechanism which momentarily prevents or attenuates extraneous reactions such as startle until the
perceptual analysis of the lead stimulus is completed. According to Graham (1975, 1979, 1992) two parallel processes occur when a stimulus is perceived: one is the encoding and perceptual analysis of the stimulus, and the other is a protective process which attenuates all subsequent stimulation until the perceptual/encoding processes have been completed. Two primary lines of evidence supporting the protection-of-processing hypothesis are discussed below.

3.1.1. Startle inhibition and startle stimulus perception

The first line of support consists of two studies that examined the perceived intensity of the startle stimulus. These studies tested the hypothesis that the startle stimulus would be perceived as less intense if its impact on the system were reduced by the lead stimulus. In these studies, the primary dependent variables were measures of startle response magnitude elicited under baseline and lead stimulus conditions and participant ratings of the intensity of the startle-eliciting stimulus under the same conditions. Using an 80 dB tone as a lead stimulus and a tap to the forehead (glabellar tap) as the startle-eliciting stimulus, Cohen et al. (1981) found that the presence of the lead stimulus decreased both the size of the eyeblink elicited by the tap as well as the estimated intensity of the tap itself. The same pattern of results was obtained by Perlstein et al. (1993), using a 75 dB tone as a lead stimulus and a 110 dB tone as the startle-eliciting stimulus. Although these studies appear to support the protection-of-processing hypothesis, Anthony (1985) has suggested that in the Cohen et al. and by extension, the Perlstein et al. studies, participants’ estimates of startle stimulus intensity may have been biased by the perception of their own reduced startle response magnitude. Blumenthal et al. (1996), however, recently demonstrated that with high intensity startle-eliciting stimuli (i.e. 100 dB or greater) both startle response magnitude and ratings of startle stimulus intensity are reduced by lead stimulation, but the amount of reduction between these measures is not correlated across participants. In any event, it may be as important to protect processing from disruption by efferent motor responses to the startle stimulus as it is to protect it from disruption by afferent sensory input itself.

3.1.2. Startle inhibition and lead stimulus perception

The second line of investigation testing the protection of processing hypothesis consists of four studies that have examined the impact of a startle-eliciting stimulus on participants’ perceptions of the lead stimulus. If startle inhibition serves to protect the perceptual processing of the lead stimulus, then perception of the lead stimulus should be more accurate when it is effective in producing startle inhibition.

In each of two studies, (Filion and Ciranni, 1994; Perlstein et al., 1993, experiment 2), participants were presented with three stimulus conditions relevant to the present discussion: a lead stimulus alone, a startling stimulus alone, and the lead stimulus followed by the startling stimulus at a lead interval of 500 ms (Perlstein et al., 1993) or 120 ms (Filion and Ciranni, 1994). The primary dependent measures were startle-eyeblink amplitude and participant ratings of lead stimulus intensity recorded under the paired and non-paired conditions. In terms of startle responding, both studies confirmed the basic inhibition effect in the lead stimulus condition.
In terms of the lead stimulus intensity ratings, the lead stimulus in the paired condition was rated as slightly, but significantly, louder than it was in the non-paired condition, indicating that in the paired condition, the startling stimulus interfered with the perceptual analysis of the lead stimulus. This is a well-documented phenomenon known as loudness assimilation. This result suggests that inhibition of the startle response in the lead stimulation condition did not result in perfect protection of the perceptual analysis of the lead stimulus. However, as a further test of the relationship between startle inhibition and lead stimulus perception, Filion and Ciranni (1994) also computed the correlation between the amount of startle inhibition produced by the lead stimulus and the amount of interference in lead stimulus perception produced by the startling stimulus. In support of the protection-of-processing hypothesis, a significant correlation was obtained indicating that participants showing greater startle inhibition had a more accurate perception of the lead stimulus. Similarly, using the same paradigm, Perlstein, Fiorito, Simons, and Graham (1989) discussed in Graham (1992) found that college students who scored abnormally high on a perceptual aberration scale exhibited significantly less startle inhibition as well as significantly greater startle-produced interference with lead stimulus perceptions than did a normal control group.

Finally, following the same logic but taking a slightly different strategy, Norris and Blumenthal (1995) required participants to indicate after each trial whether a high-pitched lead stimulus, a low-pitched lead stimulus, or no lead stimulus had been presented. Because the tone pitches were difficult to discriminate, these investigators were able to use the number of hits and misses for the target lead stimulus as a measure of the accuracy of lead stimulus perception. Consistent with the protection-of-processing hypothesis, results revealed that greater startle inhibition was produced on trials in which the lead stimulus was correctly identified than on trials in which the participant’s response was incorrect.

3.1.3. Protection of processing and sensorimotor gating

Taking a view quite similar to the protection-of-processing hypothesis, Braff, Geyer, and colleagues (e.g. Braff and Geyer, 1990) have suggested that startle inhibition may serve as an operational measure of sensorimotor gating, “reflecting the ability to effectively buffer or screen out the potentially chaotic flow of information and sensory stimuli” (Cadenhead et al., 1993, p. 1862). In their view, startle inhibition indexes a basic inhibitory process which regulates sensory input to the brain and allows the early stages of information processing to occur without disruption. What sets this view apart from the protection-of-processing view is the suggestion that startle inhibition reflects a general ability to inhibit external stimuli (auditory, visual, tactile, etc.) as well as internal stimuli such as thoughts and impulses (e.g. Geyer et al., 1990).

In support of the sensorimotor gating view, there is a rapidly growing literature documenting startle inhibition deficits in clinical populations characterized by inhibitory deficits and an inability to regulate internal stimulation (to be reviewed in a later section). To date, startle inhibition deficits have been reported in schizophrenia patients (Braff et al., 1978, 1992; Dawson et al., 1993; Grillon et al.,
1992), schizotypal patients (Cadenhead et al., 1993), college students scoring high on psychosis-proneness scales (Perlstein et al., 1989; Schell et al., 1995; Simons and Giardina, 1992; Swerdlow et al., 1995a; but see Blumenthal and Creps, 1994 and others to be reviewed later for exceptions), obsessive-compulsive disorder patients (Swerdlow et al., 1993), individuals with Huntington’s Disease (Swerdlow et al., 1995b), and children with attention-deficit disorder (Anthony, 1990) and nocturnal enuresis (Ornitz et al., 1992). In addition, Perry and Braff (1994) reported a significant positive relationship between startle inhibition deficits and independent measures of thought disorder in a population of individuals with schizophrenia. Taken together, these findings suggest that startle inhibition may indeed index an inhibitory ability that generalizes beyond specific time-locked inhibitory effects following the onset of external stimuli.

3.2. Protection of processing: summary

The studies above are generally supportive of the protection-of-processing hypothesis and suggest that startle inhibition may be mediated by a partial sensory blockade of the startle stimulus. One direction for future tests of the protection-of-processing hypothesis may be to design studies that assess more independent measures of startle stimulus impact. For example, Foss et al. (1989) found that presentation of a weak lead stimulus 100 ms prior to a startle-eliciting stimulus significantly reduced startle-produced errors in rifle-aiming, suggesting that lead stimulation does reduce the impact of the startle-eliciting stimulus on motor output. Further work is needed to determine whether startle responses can be shown to disrupt performance on non-motor tasks, and whether presentation of a lead stimulus can reduce such disruption. Finally, although it is consistent with the sensory gating view that several clinical populations characterized by reduced inhibition also show SEM deficits, further research is needed to determine whether these deficits signify a common cognitive impairment, share a common underlying neurophysiology, or both. Although the bulk of the research described above supports the protection-of-processing hypothesis, many questions remain as to the nature of the protective process.

3.3. Early attentional processing

One question raised by the protection-of-processing and sensorimotor gating views concerns whether the protection of lead stimulus processing occurs automatically or whether it is dependent upon controlled attentional processing.

3.3.1. Evidence for automatic processes

Recall that Graham (1975, 1979) originally suggested that short lead interval startle inhibition might reflect the protection of pre-attentive processing, implying that the inhibitory effect should be attention invariant. This suggestion was based on the findings that startle inhibition is observed in nonhuman animals, and in fact in decorticate rats (Ison et al., 1991), as well as in infants (Graham et al., 1981),
sleeping human adults (Silverstein et al., 1980), and that it is observed on the first presentation of a lead stimulus-startle stimulus pairing (Graham, 1975). Moreover, the fact that pre-habituation of the lead stimulus does not affect startle inhibition in either nonhuman animals (Wu et al., 1984) or humans (Wynn et al., 1996) suggests that this inhibition reflects the action of automatic processes. Clearly, evidence indicates that short lead interval startle inhibition is at least partially an automatic effect. However, this does not preclude the possibility that this startle inhibition might be modulated by controlled attentional processes. The following section describes several studies designed to examine the modulatory effects of attention on startle inhibition.

3.3.2. Evidence for attentional processes

The possibility that attention may have a modulatory influence on SEM was raised initially by studies documenting an increase in startle inhibition in conditions in which a warning stimulus predicted the presentation of the lead stimulus (e.g. DelPezzo and Hoffman, 1980; Hackley and Graham, 1983; Ison and Ashkenazi, 1980). In the DelPezzo and Hoffman (1980) studies, for example, the eyeblink eliciting stimulus was a tap to the forehead and the lead stimulus was a light presented at a lead interval of 150 ms that could appear in one of several possible locations on a grid located directly in front of the participant. Participants were instructed to maintain their gaze at a position in the center of the grid. In the first experiment, participants were warned on half of the trials as to the location where the lead stimulus would be presented, and were given no information about the lead stimulus on the remaining trials. The result of interest is that startle inhibition was greater on trials in which the participants knew the location of the upcoming lead stimulus than when they did not. This finding suggests that directing attention toward the location of a visual lead stimulus increases the amount of inhibition produced by that lead stimulus. The second experiment tested the hypothesis that instructing participants to direct their attention away from a visual lead stimulus would decrease the amount of inhibition produced by that lead stimulus. In this experiment, the lead stimulus consisted of a light that was always presented at the center position of a grid located directly in front of the participant. While maintaining visual fixation on this center location, participants were instructed prior to half of the light presentations to attend to the central location, and prior to the other half of the trials to attend to grid location 40° to the left or right of the center location. The results of this procedure revealed that the presentation of the visual lead stimulus produced the expected startle inhibition, and that the inhibition was greater when attention was directed to the location of the lead stimulus than when attention was directed away from the lead stimulus.

Consistent with this finding, McDowd et al. (1993) found greater startle inhibition at a lead interval of 120 ms during a trial block in which participants were required to press a response key whenever they detected a lead stimulus than during a trial block in which there were no task instructions. Taken together these studies suggest that, contrary to what would be expected with a purely automatic process, directing attention toward a lead stimulus increases the amount of startle inhibition
it produces. However, the attention effects may be attributed to generalized attentional/arousal processes rather than selective attentional processes because attention was manipulated across blocks of trials (Harbin and Berg, 1986).

In an attempt to address the question of whether the attentional effects on startle inhibition are general or selective, Acocella and Blumenthal (1990) employed an intense white noise as the startle eliciting stimulus and a low pitched tone, a high tone, and a less intense white noise as three unique lead stimuli. On one block of trials participants were instructed to attend to the lead stimuli and to press a response key whenever a particular stimulus was presented (e.g. press whenever you hear a low tone). On another block of trials, participants were instructed to ignore all lead stimuli. Results indicated that the three lead stimuli all produced startle inhibition, and that inhibition was greater when participants were attending to the lead stimuli than when the lead stimuli were ignored. Within the attention block of trials, however, there were no differences observed between the amount of inhibition produced by the lead stimulus that signalled a motor response and the other two lead stimuli. These results suggest a generalized attentional/arousal effect rather than a selective attention effect.

Hackley and Graham (1987, experiment 2) also examined attentional effects on startle inhibition, but employed a task that did not require a motor response from the participant. Instead, startle inhibition was examined under conditions in which to-be-attended and to-be-ignored lead stimuli were presented within the same trial block in an unpredictable sequence. In this experiment, a warning signal was presented, followed by the presentation of a tone to either to the left ear, the right ear, or to both ears simultaneously. Participants were required to judge the durations of the tones presented to one spatial location while ignoring tones presented to the other locations. A subset of these to-be-attended and to-be-ignored tones served as lead stimuli for a startle-eliciting air puff. The results indicated that the lead stimuli reliably produced startle inhibition, and the attended lead stimuli produced greater startle inhibition than the ignored lead stimuli when the discrimination was between lateralized stimuli.

Expanding upon these results, Filion et al. (1993) conducted an experiment in which participants were presented an unpredictable intermixed series of tones of two different pitches and were instructed to count the number of longer than usual occurrences (i.e. 7 rather than 5 s) of one tone pitch and to simply ignore the tones of a different pitch. This differential attention paradigm was originally devised and employed to study attentional processes associated with the orienting response (Dawson et al., 1989; Filion et al., 1991). Specifically, it requires participants to perform a series of cognitive operations beginning with the onset of a tone: (1) to first pre-attentively detect and discriminate the to-be-attended tone from the to-be-ignored tone; (2) to then allocate additional controlled processing resources necessary to confirm the identity of the to-be-attended tone and begin the duration judgment task; and (3) finally, to sustain selective attention to the to-be-attended tone throughout its duration in order to determine its length and perform the required timing task (Dawson et al., 1997).
In the Filion et al. (1993) study, the two tones served as lead stimuli for a startle-eliciting noise burst presented at short lead intervals of 60, 120, and 240 ms. The results, re-presented in Fig. 3, revealed significant startle inhibition at each of these short lead intervals, and that for the 120 ms lead interval, the attended lead stimulus produced significantly greater startle inhibition than the ignored lead stimulus. These basic results have since been replicated and extended in six independent samples: unselected college students (Filion et al., 1994; Jennings et al., 1996; Seljos et al., 1994), college students selected to serve as normal controls for high-risk populations (Schell et al., 1995), and non-college students selected to serve as normal controls demographically matched to schizophrenia outpatients (Dawson et al., 1993; Hazlett et al., 1995).

In another recent study relevant to the discussion of attentional effects on SEM, Hazlett et al. (1993) presented startle stimuli at short lead intervals following the onsets of digits presented in a memory load version of a continuous performance task. In this task, participants viewed a series of rapidly presented digits on a computer screen and were asked to press a response key whenever they detected the digit ‘7’ immediately following the digit ‘3’. A startle eliciting noise burst was presented at lead intervals of 120 and 240 ms following the onset of a subset of the digits assumed to be associated with high attentional processing (e.g. the target digit ‘3’), as well as digits assumed to be associated with relatively low attentional processing (e.g. non-target digits temporally distant from both 3 and 7’s). Results of this procedure revealed significantly greater startle inhibition at the 120 ms lead interval following the target lead stimuli than non-target lead stimuli. Consistent with these results for target and non-target stimuli, Bradley et al. (1996) found greater startle inhibition at a lead interval of 300 ms by lead stimuli consisting of positively and negatively valenced pictures than by neutral pictures, which were presumably less arousing, interesting, and/or attention-demanding.

Fig. 3. Short lead interval startle eyeblink modification results from an active attention paradigm (adapted from Filion et al., 1993).
Together, these results demonstrate that attention can modulate startle inhibition at short lead intervals in a variety of paradigms, and that the effects can be observed cross-modally, with visual lead stimuli and acoustic startle-eliciting stimuli. It should be noted, however, that Vanman et al. (1996, experiment 1) observed no difference in inhibition at a lead interval of 250 ms between affective pictorial lead stimuli that were to be attended compared to affective pictures that were to be ignored. Although this finding appears inconsistent with the above studies, an interpretation suggested by Vanman et al. (1996) is that the affective/arousing nature of the pictures used in this experiment may have overwhelmed the effect of the instructional attentional manipulation.

The studies just described suggest that attentional manipulations may have a selective, stimulus specific effect on the startle inhibition produced by a to-be-attended lead stimulus, although a nonspecific arousal/activational effect may have contributed to the SEM observed to the to-be-ignored lead stimulus as well. To date, however, only one study has examined the relative contributions of attentional effects that are due to non-specific increases in arousal/activation versus effects that are due to selective stimulus processing. Jennings et al. (1996) tested participants in one group with the tone-length judgment task of Filion et al. (1993) and tested participants in a second group with identical stimuli but with no task to perform. Using this design, selective attentional effects can be examined by comparing the amount of inhibition produced by the to-be-attended and to-be-ignored lead stimuli in the selective attention group, whereas non-specific activational effects can be examined by comparing the startle inhibition produced by the to-be-ignored lead stimulus in the selective attention group to the amount of inhibition exhibited by the group given no explicit instructions regarding the lead stimuli and no task to perform.

In this experiment, lead stimuli were high and low pitched tones which preceded a startle-eliciting noise burst at a short lead interval of 120 ms. Results for the active attention group revealed that the to-be-attended lead stimulus produced greater startle inhibition than the to-be-ignored lead stimulus. In addition, greater inhibition was produced by the to-be-attended prepulse in the active attention group than by the comparable lead stimulus in the passive attention group, whereas the amount of inhibition produced by the to-be-ignored lead stimulus in the active attention group did not differ from the inhibition produced by the comparable lead stimulus in the passive attention group. These results suggest that the attentional instructions had a selective effect in that they increased startle inhibition to the to-be-attended lead stimulus, whereas there was no evidence of a non-specific arousal effect because the inhibition produced by the to-be-ignored lead stimulus in the attention group and the comparable lead stimulus in the no-task group did not differ.

3.4. Early attentional effects: summary and conclusions

Taken together, the studies just reviewed suggest that startle inhibition at short lead intervals may reflect not only the automatic protective and/or sensorimotor
gating system, but that it may also index the early stages of controlled attentional processing. As discussed further in the concluding section of this paper, the automatic and controlled processes appear to follow different time courses and may be separable by studying the effects of the task-imposed attentional demands of the lead stimulus. That is, findings from several studies indicate that attentional modulation of startle inhibition occurs only at and after approximately 120 ms, and not during the earlier portion of the time window of short lead interval inhibition, suggesting that controlled attentional processes develop more slowly. However, it is also important to note that in several of these studies, the attentional enhancement of startle inhibition occurred at a 120 ms lead interval, but not at a 240 ms lead interval, suggesting that the attentional processes underlying this effect have an extremely short duration or that the attentional processes may interact with the processes underlying the transition from short lead interval startle inhibition to long lead interval startle facilitation. Thus, further research is needed to determine which stage(s) or type(s) of attentional processing are indexed, as well as the relationship between attentional effects and more non-specific arousal effects.

3.5. Relationship to other measures

3.5.1. Behavioral measures

As reviewed by Filion et al. (in press), another strategy for assessing the psychological significance of short lead interval startle inhibition is to examine its relationship to behavioral measures of inhibition such as performance on backward masking, negative priming, and Wisconsin Card Sorting Tasks. Although attempts to correlate these behavioral measures with startle inhibition on a within-participant basis have yielded inconsistent results, psychopathological populations (particularly those with schizophrenia spectrum disorders) who exhibit reduced startle inhibition have been shown to exhibit consistent patterns of deficits in these tasks. These results suggest that the inhibitory processes reflected by these measures may be different, occur at different stages of information processing, and/or have different neural substrates. Further research is needed to determine more precisely the nature and generality of the inhibitory processes reflected by short lead interval startle inhibition.

3.5.2. Event-related potentials

Another line of investigation possibly related to the significance of the short lead interval startle inhibition effect involves the examination of event related potentials in lead stimulation paradigms. Although few studies have examined evoked potentials in what would be considered a typical startle inhibition paradigm (e.g. a low intensity lead stimulus followed by a high intensity startle-eliciting stimulus), there is a large literature in which the P50 component of the cortical evoked potential has been recorded during presentation of pairs of moderately loud auditory clicks separated by approximately 500 ms. The P50 amplitude elicited by the second test click is normally suppressed compared to the P50 elicited by the first member of the pair. This P50 suppression effect is interpreted as indexing an inhibitory sensory
gating process similar to the processes thought to be indexed by startle inhibition at short lead intervals (Freedman et al., 1987).

In one attempt to examine the relationship between short lead interval startle inhibition and P50 suppression, Schwarzkopf et al. (1993) tested the same participants using the typical protocols for each measure. The two test protocols, with a lead interval of 100 ms for startle inhibition and 500 ms for P50 suppression, were separated by 20 min. Only a modest trend for a positive association was found between P50 suppression and startle inhibition. Moreover, the fact that the optimal lead interval for P50 suppression is longer than the optimal interval for startle inhibition further calls into question whether the two measures are tapping the same inhibitory processes. In order to obtain measures of startle inhibition and modification of evoked potential concurrently within exactly the same paradigm, Perlstein et al. (1993) recorded evoked potentials and startle eyeblinks simultaneously under four conditions: low intensity tone alone (75 dB(A), 40 ms 800 Hz tone); high intensity tone alone (110 dB(A), 40 ms 800 Hz tone); low intensity-low intensity pair separated by a fixed lead interval; and low intensity high-intensity pair separated by the same lead interval. Significant inhibition of the startle eyeblink occurred at both a 120 ms (experiment 1) as well as a 500 ms (experiment 2) lead interval in both of the paired-stimulus conditions compared to the single stimulus controls. The results revealed that the P30 component of the evoked potential was unaffected by stimulus pairing, but that the P50, N100, and P200 components were significantly smaller in response to the second tone in the paired stimulus conditions compared to the single tone baseline. Extending this work, Sugawara et al. (1994) examined lead stimulation effects on the P300 by comparing the P300 elicited by a startle stimulus alone (104 dB SPL, 50 ms, white noise), and by lead stimulus (75 dB SPL, 25 ms, 1000 Hz tone)-startle stimulus pairings at lead intervals of 60 and 120 ms. Startle inhibition as well as a significant reduction in the P300 occurred to the startle-eliciting stimulus presented in the lead stimulation conditions compared to the response to the startle-eliciting stimulus alone. These results demonstrate that conditions producing startle inhibition also produced reductions in evoked potential components occurring in the mid to long latency range (50–300 ms). These reductions would generally be expected if sensorimotor gating processes are reducing the effective intensity of the startle eliciting stimulus. (For a further analysis of parallels and differences between lead stimulation effects on startle and on ERP components, see Ford and Roth, in press).

4. Long lead interval effects

In contrast to the unidirectional inhibitory effects discussed above, at lead intervals greater than approximately 800 ms, startle amplitude can exhibit either inhibitory and facilitatory effects, depending on stimulus conditions and participant instructions (see reviews by Anthony, 1985; Graham, 1992; Lang, 1995; Putnam, 1990; Putnam, in press). In addition, in contrast to the homogeneous interpretation of short lead interval effects involving the protection-of-processing/sensorimotor
gating frameworks, at long lead intervals there are two main classes of modification
effects, modification by attentional processes and modification by emotional pro-
cesses, and each is interpreted within a different theoretical framework and appar-
ently involves different neural pathways. In the following sections we first review
each class of modification effect and its interpretation, and then review a small
literature consisting of experiments designed to examine the relative contributions
of attentional and emotional processes to SEM within the same participants and
within the same paradigm.

4.1. Modulation by attention

Research with nonhuman animals has demonstrated that the amplitude of the
startle reflex is facilitated when startle is elicited after a relatively long lead interval
(e.g. 2000 ms) if the lead stimulus is sustained throughout the lead interval
(Hoffman and Wible, 1969; see Graham, 1975, pp. 243–246, for a review). Graham
(1975) suggested that the mechanism underlying startle facilitation with continuous
lead stimulation may be “a classical activation effect mediated by the reticular
activating system”. Graham et al. (1975) replicated these effects with human startle
eyeblink and found, unlike the earlier findings with rats, that startle facilitation also
occurred with discrete lead stimuli (those that offset before the end of the lead
interval) as well as with continuous lead stimuli. The human participants also
showed strong and persistent heart rate orienting responses during the lead interval,
particularly when the onset of the startle-eliciting stimulus was unpredictable,
suggesting that orienting and attention were playing a role in SEM in addition to
the effects of ‘classical activation’. These observations led to a systematic series of
investigations and hypothesizing about attentional factors influencing human SEM
at long lead intervals.

Early investigations of attentional influences on SEM at long lead intervals
focused primarily on modality-specific selective attention effects. Studies have
shown that at long lead intervals startle is facilitated when participants are
instructed to focus their attention on the startle-eliciting stimulus or on the same
sensory modality as the startle-eliciting stimulus (Bohlin and Graham, 1977; Bohlin
et al., 1981; Hackley and Graham, 1983). When instructions direct attention toward
a modality different from that of the startle-eliciting stimulus, startle is inhibited
(Anthony and Putnam, 1985; Putnam, 1990; Silverstein et al., 1981). These effects
are interpreted as being due to a process of selective sensory pathway enhancement
whereby paying attention to a sensory modality primes the sensory pathway for
that modality, thereby facilitating sensory processing of all input in that modality,
and simultaneously inhibiting sensory processing of other modalities. Thus, atten-
tion to the startle eliciting stimulus is viewed as turning up the gain in certain
anatomical structures which overlap those involved in the elicitation of the startle
blink (Anthony, 1985).

One implication of this view is that SEM effects, both facilitatory and inhibitory,
should be enhanced in situations in which the degree of attention as well as the
direction of attention is manipulated. This notion was tested explicitly in a series of
Fig. 4. Startle responses to auditory eliciting stimuli presented during the 6000 ms warning interval of an anticipation task (adapted from Putnam, 1990).

studies by Putnam and colleagues (see Putnam, 1990 for a review), who presented startle-eliciting stimuli during the warning interval of a speeded simple reaction time task. Since this type of task requires participants to attend to the modality of the imperative stimulus and to ‘pay closer attention’ as the end of the warning interval approaches, this paradigm allows examination of the effects of both the direction and degree of attention on SEM. Consistent with the view that long lead interval SEM is sensitive to both the direction and degree of attention, not only were startle responses facilitated when the modalities of the startle-eliciting stimulus and the expected imperative stimulus matched, and were inhibited when the modalities were different, these attentional effects were stronger for startle-eliciting stimuli presented later compared to earlier in the warning interval. These findings are illustrated in Fig. 4.

In another set of studies examining attentional influences on long lead interval SEM, Anthony and Graham (1983, 1985) presented one group of participants with a set of visual lead stimuli, half consisting of light-coloured blank slides (considered dull), and half consisting of slides of human faces (considered interesting). A second group of participants received auditory lead stimuli consisting of either tones (considered dull), or music-box melodies (considered interesting). The startle-eliciting stimulus for both groups, presented after a lead interval of 4000 ms, was auditory (a noise burst) on half of the trials, and was visual (a light flash) during the remaining trials. The results of this procedure with infants indicated that for each startle stimulus modality, startle responses were larger when the lead and startle-eliciting stimuli matched than when they were different. In addition, attention effects were observed within modalities such that when the modalities of the
lead and startle-eliciting stimuli matched, startle responses were larger when the lead stimulus was interesting than when it was dull. This same pattern of results was obtained with adult participants except that the attentional effects were observed in the latency of the startle responses rather than the amplitude. Anthony and Graham (1985) argue that the modality specific effects suggest that SEM is due to modification in specific afferent pathways rather than to modification in a final common motor pathway. Findings consistent with this viewpoint were reported by Simons and Zelson (1985), who found that startle responses elicited by auditory stimuli were smaller when presented during interesting compared to dull visual lead stimuli, and by Zelson and Simons (1986), who found that performance of a visual vigilance task resulted in significant inhibition of the acoustic startle response, and that a difficult vigilance task produced greater inhibition than a less difficult vigilance task.

Also consistent with these findings, Filion et al. (1993, 1994), in the studies described earlier, presented participants with a series of intermixed high and low pitched tones which varied between 5 and 7 s in duration and instructed them to keep a count of the number of seven second tones of one pitch and to ignore the tones of the other pitch. Results revealed that both to-be-attended and to-be-ignored tones produced startle facilitation at a lead interval of 2000 ms, and that there was greater facilitation following the attended than the ignored tones. This pattern of findings using this paradigm has been replicated several times in our laboratory (Dawson et al., 1993; Jennings et al., 1996; Schell et al., 1995; Seljok et al., 1994). The greater startle facilitation following the attended than the ignored lead stimulus has been interpreted as reflecting greater allocation of attentional resources to the attended tone.

This interpretation was supported by Jennings et al. (1996) in which the same task was used and startle-eliciting stimuli were presented at lead intervals of 2000, 4500, and 6000 ms. This tone length judging task should result in increasing attentional demands across the lead stimulus window (that is, participants should pay closer attention toward the end of the tone when the critical length judgment is to be made). Therefore, Jennings et al. (1996) predicted that if startle facilitation reflects the allocation of attentional resources, then startle facilitation should show a commensurate increase across the lead intervals. An additional feature of this study was that for half of the trials involving the 6000 ms lead interval, the lead stimulus duration was 5 s and for half it was 7 s. This allowed an additional test of the attentional resource hypothesis, by comparing facilitatory effects when the startle-eliciting stimulus is presented at a time point when attention was assumed to be high and at a time point when attentional processing was assumed to be completed. Fig. 5 shows the long lead interval results from this experiment. Consistent with the attentional resource hypothesis, the results revealed that both the attended and ignored tones produced startle facilitation with greater facilitation produced by the attended tone, and that during the attended tone greater facilitation was observed at the 4500 ms lead interval than the 2000 ms lead interval. There was greater facilitation at the 6000 ms lead interval during the 7 s lead stimuli than at the 2000 ms lead interval, but there was no facilitation at the 6000 ms lead
interval during the 5 s lead stimuli. Thus, the results of Jennings et al. (1996) indicate that the amount of startle facilitation at long lead intervals is a function of the degree of attentional processing.

In order to investigate the generality of these effects, two studies have employed the length judging task to determine whether the long lead interval attentional modulation effects are modality specific (Böhmelt et al., 1996; Lipp et al., 1997 experiment 2; Lipp and Siddle, in press). Lipp et al. examined the effects of lead stimulus modality as a between-groups factor by presenting an acoustic startle stimulus at lead intervals of 3500 or 4500 ms during to-be-attended and to-be-ignored lead stimuli that were acoustic for one group of participants and visual for a second group. The results revealed greater startle facilitation during to-be-attended than to-be-ignored lead stimuli in both groups. Böhmelt et al. (1996) examined the effects of lead stimulus modality as a within groups factor by presenting participants with two classes of auditory lead stimuli (high pitch tones and low pitch tones), and two classes of visual stimuli (horizontal and vertical bars). Participants were instructed to count the number of occurrences of one of the auditory and one of the visual stimuli that had a longer than usual duration (e.g. count the number of high tones and vertical bars that are of longer than usual duration). These stimuli served as lead stimuli for a startle eliciting noise burst presented at a long lead interval of 4500 ms. The results revealed that the to-be-attended tone produced greater startle facilitation than the to-be-ignored tone and also that the to-be-attended visual stimulus produced greater startle facilitation than the to-be-ignored visual stimulus. Thus, the findings of Lipp et al. (1997) and Böhmelt et al. (1996) suggest an attentional effect on long lead interval SEM that is independent of stimulus modality.

Fig. 5. Long lead interval startle eyeblink modification results from an active attention paradigm (adapted from Jennings et al., 1996).
Together, the studies reviewed in this section demonstrate that attentional processes can have bi-directional effects on the startle reflex at long lead intervals. Further research is necessary to determine whether the attentional processes have effects that are modality specific, modality independent, or both, depending upon the nature of the attentional task. A related question is whether this modulation of startle occurs in afferent pathways, efferent pathways, or both.

4.2. Modulation by emotion

Another important type of SEM effect observed at long lead intervals is that seen in the processing of affective stimuli. In nonhuman animals, the whole body startle response is reliably facilitated by presenting the startle-eliciting stimulus at a long lead interval following a stimulus that has previously been predictive of an aversive event such as a shock (e.g. Brown et al., 1951; Davis and Astraehan, 1978), a phenomenon termed the fear-potentiated startle effect. This effect has been observed over a wide range of lead intervals but appears to be maximal when the lead interval matches the interval used between the predictor and aversive stimuli (Davis et al., 1989; Siegel, 1967). The neural circuits underlying fear potentiation of animal startle have been well described (see Davis, 1996). Fear potentiation can be observed when the lead stimuli and the startle stimuli are in different modalities, which is not what would be expected viewing startle from an attentional framework. Affectively valenced stimuli appear to have unique effects on the startle response.

In the first examination of affective processing and SEM in humans, Vrana et al. (1988) presented participants with a series of six second pictorial slides depicting affectively positive (e.g. smiling baby), negative (e.g. mutilated body) and neutral (e.g. basket) images, and acoustic startle-eliciting stimuli were presented during the slides at lead intervals of 500, 2500, and 4500 ms. These pictures, as well as those used in the studies throughout this section, are from a standardized library of images that have been calibrated for valence and arousal level (The International Affective Picture System (IAPS); Center for the Study of Emotion and Attention, 1995; Lang et al., 1995). Thus it is important to note that the positive and negative pictures were equally arousing and attention-demanding, based on these calibrations and on findings that heart rate orienting responses and free viewing time did not differ between the affective picture categories. The results, re-presented in Fig. 6, revealed a significant linear trend at long (but not short) lead intervals over picture valence, with the largest startle responses occurring during unpleasant pictures and smallest during pleasant pictures.

This affective modification effect has been interpreted within a theoretical framework focused on motivational priming (Lang et al., 1990). According to this framework, reflexive responding is dependent on two factors: the classification of the reflex as appetitive or defensive, and the affective valence of the individual’s ongoing emotional state. Defensive reflexes such as startle will be enhanced if elicited in the context of a negative emotional state, whereas appetitive reflexes will be enhanced if elicited in a positive emotional state. According to Lang (1995), “In
Fig. 6. Affective modulation of startle. Blink magnitude to startle-eliciting stimuli presented while participants view emotional pictures (adapted from Vrana et al., 1988).

an unpleasant stimulus foreground the brain is processing negative affective information; the relevant subcortical, aversive system circuitry is contacted; and a defensive reflex is augmented... when appetitive information is the focus of processing, the startle reflex is expected to show relative diminution.” (p. 379)

Over the past decade the affective modulation of startle in humans has been replicated in numerous studies and has gained much attention in the study of human emotion, as evidenced by several recent reviews of the extensive emotional modification of startle literature (Bradley et al., in press; Lang, 1995; Lang et al., 1990, 1992, 1993). Affective modulation of startle has been shown to be quite ubiquitous, occurring as early as 5 months of age (Balaban, 1995), and generalizing to a variety of other lead stimulation conditions which affect the emotional state of the participant, including pleasant and unpleasant film clips (Jensen and Frijda, 1994), pleasant and unpleasant odours (Ehrlichman et al., 1995; Miltner et al., 1994), as well as fear-potentiation conditions in which the lead stimuli signal an upcoming aversive event such as electric shock (e.g. Grillon et al., 1991; Hamm et al., 1993). Moreover, in the fear-potentiation paradigm, startle facilitation has been shown to increase as a function of anticipatory anxiety, with the largest facilitation occurring just prior to delivery of the aversive stimulus (Grillon et al., 1993). In addition, affective modulation of startle has also been demonstrated in situations in which the lead stimulus serves as a cue for participants to engage in an affective task such as rehearsing sentences with differing affective tone (Vrana and Lang, 1990) or imagining pleasant versus unpleasant scenes (Cook et al., 1991). Although fear appears to have been the negative emotion most often studied, other negatively valenced emotions such as sadness, anger, and disgust also produce potentiated startle (Cook et al., 1991; Witvliet and Vrana, 1995; Vrana, 1994).

Consistent with the motivation priming hypothesis, Bonnet et al. (1995) found no affective modulation of the spinal tendinous reflex, a reflex that is not inherently defensive. The effect also seems to be particularly resistant to habituation (Bradley et al., 1993a), and appears to be most robust in the context of highly arousing stimuli (Cuthbert et al., 1996). In addition, Bradley et al. (1991, 1996) have reported
evidence suggesting that this emotion modification effect may be lateralized. In these studies, participants were presented with startle-eliciting stimuli consisting of left and right ear monaural noise bursts at lead intervals of 2000–6000 ms while viewing positive, negative, and neutral images. The results revealed that startle stimuli presented to the left ear (activating predominantly the right hemisphere) produced a significant pattern of modulation by the affective nature of the pictures whereas reflexes elicited by startle stimuli presented to the right ear (activating predominantly the left hemisphere) showed no significant emotional modulation. This finding is consistent with current theories suggesting that the right hemisphere plays a dominant role in the processing of emotional information (e.g. Bowers et al., 1993). However, Hawk and Cook (1997) found no laterality effect with tactile startle stimuli.

Finally, as was the case with the short lead interval effects, in which startle inhibition deficits in various clinical populations appear to validate the protection of processing/sensorimotor gating hypothesis, there are also clinical data which appear to validate the motivational priming interpretation of the emotional modulation effects. As will be discussed in more detail later, Patrick et al. (1993) found that criminal psychopaths failed to show the typical linear relationship between lead stimulus valence and SEM, with the lack of emotional modulation observed specifically in prisoners who, at interview, showed emotional indifference and lack of remorse. Also, individuals with specific phobias have been reported to exhibit a larger startle facilitation effect while viewing pictures of their own phobic objects than do non-phobic individuals viewing these or other unpleasant pictures (Hamm et al., 1997).

The studies reviewed in this section clearly illustrate that the emotional context in which startle is elicited can modulate the amplitude of the startle reflex. Although this phenomenon has been replicated many times across a variety of experimental protocols, several important questions remain unanswered. For example, what are the roles of arousal and attention in affective modulation of startle? These questions are particularly germane in light of recent reports that affective modulation of the startle amplitude occurs only with affective stimuli that are highly arousing. Pictures which were rated lower in arousal, although they differed in affective valence as much as did the high arousal pictures, did not produce affective modulation of startle (Cuthbert et al., 1996). The research of Cook and his colleagues, reported in detail below, which indicates greater emotional modulation of startle among high fearful than low fearfulness individuals, is also relevant to this issue. For instance, Cook et al. (1991) reported that low fear participants, for whom arousal during negatively valenced imagery would presumably be lower than for high fear subjects, did not show significant emotional modulation of startle. On the other hand, Witvliet and Vrana (1995) reported affective modulation of startle using sentences having emotional content that were low in arousal as well as high in arousal. Paradigms that allow the simultaneous measurement of both affective and arousal/attentional processes are relevant to these issues and are beginning to be published, as discussed in the following section.
4.3. Attentional and affective effects compared

The studies reviewed above examining the effects of attentional processing on SEM provide support for the attentional resource framework in explaining/predicting long lead interval SEM effects. Likewise, the studies reviewed above examining the effects of emotional processing on SEM provide support for the motivational priming framework in explaining/predicting long lead interval SEM effects in situations in which the lead stimuli possess a strong affective valence. Thus, the attentional resource framework suggests that the size of the startle reflex will be determined by the amount of attention allocated to the modality of the startle stimulus, and the motivational priming framework suggests that the size of the startle reflex will be determined by the affective valence of the lead stimulus. What is not well understood at this point is the relationship between these frameworks. Are both frameworks necessary or is it possible that one of these frameworks may be capable of accounting for both sets of findings? To date, five studies have addressed this issue.

In the first study, Bradley et al. (1990) noted that the basic attention-related effect of the Anthony and Graham (1983, 1985) studies of smaller acoustic startle responses during interesting visual lead stimuli could be easily accounted for by the motivational priming framework by simply making the assumption that the interesting lead stimuli had a high positive affective valence. In addition, they noted that the basic emotional modulation findings with acoustic startle reflexes could be accounted for within the attentional resource framework by making the assumption that the negative lead stimuli resulted in attention being directed away from the visual modality. Based on this latter assumption, they designed an experiment in which the attentional hypothesis and the motivational priming hypothesis made competing predictions. This experiment involved lead stimuli consisting of positive, negative, and neutral pictures and both acoustic and visual startle-eliciting stimuli. Based on the assumption that lead stimuli consisting of unpleasant pictures would result in attention being directed away from the visual modality, the attentional resource hypothesis predicts that for visual startle stimuli, unpleasant pictures should produce smaller reflexes than positive pictures. In contrast, the motivational priming hypothesis predicts the opposite. The results supported the motivational priming hypothesis; over lead intervals ranging from 2500 to 5500 ms, startle eyeblinks were largest during the unpleasant pictures and smallest during the pleasant pictures (showing the same pattern as shown in Fig. 6), regardless of the modality of the startle-eliciting stimulus.

In a second study, Bradley et al. (1993a) tested the hypothesis that the startle reflex may be sensitive to both attentional and emotional processes, but that the time course of these processes may differ. Participants were again presented with positive, negative, and neutral pictures and auditory startle-eliciting stimuli, but instead of presenting the startle stimulus at lead intervals ranging from 2500 to 5500 ms, the startle stimulus was presented at lead intervals of 300, 800, 1300, and 3800 ms following picture onset. The results revealed a significant effect of attention at the 300 ms lead interval; i.e., startle responses were smaller during both pleasant
and unpleasant pictures than during the neutral pictures. Bradley et al. (1993a) interpreted this effect as due to attentional processes, not emotional processes, because positive and negative pictures, which were both more interesting than the neutral pictures, had identical effects. Emotion effects were observed at all three of the long lead intervals, with startle responses smaller during pleasant pictures than unpleasant pictures. Bradley et al. (1993a) concluded that these results provide support for the motivational priming hypothesis in accounting for long lead interval SEM effects, and suggested that attentional influences account for short lead interval effects.

In a third study, Robinson and Vrana (1995) noted a critical difference in the way attention was defined in studies with affectively loaded stimuli (e.g., Bradley et al., 1993a) and those with neutral stimuli (e.g., Filion et al., 1993). In the Bradley et al. (1993a) study, attention was determined by the affective arousal properties of the pictures themselves, with both pleasant and unpleasant pictures assumed to be more attention-engaging than the neutral pictures. In the Filion et al. (1993) study, attention was manipulated by instructing participants to estimate the duration of one class of affectively neutral lead stimulus and to ignore another class. Robinson and Vrana noted that one way to manipulate attention and emotion independent of the qualities of the lead stimulus is to use a neutral lead stimulus as a signal for an emotional task. Participants, therefore, were presented three tones varying in pitch with the high and low tones serving as signals to generate pleasant and unpleasant images, and auditory startle probes presented at short and long lead intervals following tone onsets. Tones signalling emotional imagery produced greater inhibition of startle at the short 120 ms lead interval than did tones not signalling the imagery task, consistent with a short lead interval attention effect, but the two tones signalling pleasant and unpleasant imagery did not produce differential short lead interval inhibition. However, the tone that cued negatively valenced emotional imagery did produce larger startle magnitude at long intervals of 1400 ms than the tone signalling positively valenced emotion. Thus the results corroborate earlier findings that attention can influence startle at short intervals and affective modulation occurs later.

In a fourth study, Vanman et al. (1996, experiment 2) devised an ‘affect-directed attention’ paradigm to independently manipulate attentional and emotional modulation of startle with affectively loaded pictures. Participants were instructed to either count the longer than usual occurrences of all the pleasant pictures and ignore all unpleasant pictures or the opposite, with the attended valence counterbalanced across participants. Thus the emotion quality of the picture became an attentional cue to perform or not perform the duration judgment task. Therefore, across participants, startle was recorded during attended and unattended pictures with both positive and negative affective tone. Auditory startle probes were presented at lead intervals of 250, 750, and 4450 ms following picture onsets, as well as 950 ms following picture offsets. Affective modulation, with larger startle blinks following the unpleasant pictures than following the pleasant pictures, was found at the both short lead intervals (250 and 750 ms) and the long lead interval (4450 ms). In contrast, the only evidence of attentional modulation occurred at the lead
interval 950 ms following picture offset, where the offset of the attended pictures produced greater startle inhibition than the offset of the ignored pictures. This is the first study to demonstrate affective modulation of the human eyeblink at short lead intervals, although a similar effect has been reported with rats in a fear conditioning paradigm (Davis et al., 1989). Vanman et al. (1996) concluded that both affective and attentional modulation of startle can occur at both short and long lead intervals depending upon task requirements and stimulus parameters.

Taking a very different approach, Haerich (1994) also examined the relative contributions of attentional and affective processes to SEM. In this experiment, participants were presented with a series of trials in which a visual warning stimulus was followed at a lead interval of 6 s by either an eyeblink-eliciting air puff or an eyeblink-eliciting noise burst, with presentation order unpredictable from the participant’s point of view. For half of the trials, participants were instructed to focus their attention on and judge the length of one of these two startle-eliciting stimuli and ignore the other, with the instruction reversed on the remaining trials. In this way, the influences of attentional focus on startle responding could be assessed. In addition, half of the participants in this experiment heard descriptions of the air puff stimulus that suggested a negative emotional context, (i.e. ‘the air puff will be directed toward your eye’), whereas the remaining participants received neutral information (i.e. ‘the air puff will be directed near your ear’). This manipulation allowed an assessment of the effect of emotional context on SEM, although in fact the location of the air puff was identical in both groups. The results revealed that in the neutral-context group, startle responding varied directly with attentional focus, with larger responses elicited when the startle-eliciting stimulus was presented in the attended modality. In contrast, participants in the negative context group showed larger startle responses to the airpuff eliciting stimulus, regardless of the focus of attention.

The five studies reviewed above demonstrate that both affective and attentional modulation of startle can be observed within the same participants within the same paradigm. Paradigms such as these may provide a window on the interactions and temporal relationships between affective and attentional processes, potentially disentangling their mutual effects. For example, this line of research may be able to determine whether certain types of stimuli elicit emotions pre-attentively (i.e. Zajonc, 1980), or whether the elicitation of emotions requires prior attention and cognitive evaluation of the stimulus (i.e. Lazarus, 1984).

5. Application of startle modification in clinical research

SEM paradigms are being increasingly applied in clinical research. Although these applications have involved a wide variety of clinical populations, we will focus here on the use of the short lead interval inhibition paradigm in the study of schizophrenia spectrum disorders, and on the use of the long lead interval affective modulation paradigm in the study of affective disorders and psychopathy.
5.1. Short lead interval startle inhibition

As described earlier, short lead interval startle inhibition is widely viewed as a measure of the protection of early stimulus processing. For this reason, startle inhibition measures have been of particular interest in the study of schizophrenia because deficits in early stimulus processing are believed to represent core characteristics of the disorder, possibly related to underlying vulnerability factors (Cadenhead and Braff, in press). To date, there are five published reports of startle inhibition in schizophrenia (Bolino et al., 1994; Braff et al., 1978, 1992; Dawson et al., 1993; Grillon et al., 1992).

In the earliest of these studies (Braff et al., 1978), hospitalized inpatients with schizophrenia were tested in a passive attention paradigm (participants were given no explicit task to perform) involving a continuous pure-tone lead stimulus and a white noise startle-eliciting stimulus presented at short lead intervals ranging from 30 to 500 ms. The results revealed that the schizophrenia patients exhibited significantly less startle inhibition than controls at a 60 ms lead interval. Braff et al. (1992), also studying inpatients, employed a similar paradigm using a discrete white noise burst as the lead stimulus and found significantly reduced startle inhibition in the schizophrenia inpatients at lead intervals of 30, 60, and 120 ms. Grillon et al. (1992) also observed reduced startle inhibition in schizophrenia patients at a 120 ms lead interval using a discrete white noise lead stimulus presented at intensities ranging from 75 to 90 dB(A). In addition, in order to determine whether this schizophrenia-linked deficit is modality specific, Braff et al. (1992) included a condition in which the startle-eliciting stimulus was tactile rather than acoustic and found that the schizophrenia patients exhibited deficient startle inhibition in the tactile condition as well. These results have been interpreted as indicating that patients with schizophrenia have poor automatic, pre-attentive sensorimotor gating that can lead to sensory overload, thought disorder, and perhaps the cognitive fragmentation associated with severe psychotic symptoms (e.g. Braff et al., 1995).

Two more recent studies, however, have revealed a more complex pattern of results. Bolino et al. (1994) examined SEM in hospitalized schizophrenia inpatients using an electrocutaneous startle-eliciting stimulus (shock to the forehead activating the trigeminal nerve) and discrete electrocutaneous lead stimuli at short lead intervals of 30, 60, and 120 ms. With electrocutaneous stimuli, two distinct EMG components are generally observed: R1, generally occurring in a latency window less than 25 ms, and R2, occurring later and typically showing an inhibitory effect of lead stimulation that is most closely associated with the eyeblink measured to acoustic and visual eliciting stimuli. In contrast to the previously reviewed findings (e.g. Braff et al., 1978), Bolino et al. found no differences between schizophrenia and control participants in terms of the inhibition of the R2 component of the startle response. However, there was a difference between the groups in the temporal pattern of R1 facilitation. Both groups showed facilitation of R1 magnitude at the 60 ms lead interval, but only the control group sustained that facilitatory effect at the 120 ms lead interval. The authors conclude that the facilitatory neural pathways are abnormal in schizophrenia patients.
Dawson et al. (1993) tested patients with schizophrenia and matched normal controls in the active attention tone-length judgment paradigm described previously (e.g., Filion et al., 1993). The schizophrenia participants were outpatients and were or had been participants in a longitudinal study of the early phases of schizophrenia (Nuechterlein et al., 1992). These patients were in the relatively early phases of schizophrenia without a long history of medication and institutionalization and were relatively asymptomatic at the time of testing, as assessed by independent ratings on an expanded version of the Brief Psychiatric Rating Scale (Overall and Gorham, 1962; Lukoff et al., 1986) Normal control participants also were drawn from participants in the longitudinal research project and were matched to the outpatients on age, sex, race, and educational level.

In this active attention paradigm, participants were presented an intermixed series of tones of two different pitches and were instructed to count the number of longer than usual occurrences of one particular tone and to simply ignore the other tone. In addition to the tone stimuli, a startle-eliciting noise burst was presented at short lead intervals of 60, 120, and 240 ms following the to-be-attended tones and the to-be-ignored tones. Recall that, using this task, college student participants have been reported to exhibit significantly greater inhibition following the attended tone than the ignored tone at the 120 ms lead interval, and significant but non-differential inhibition during the attended and ignored tones at the 60 ms lead interval (e.g., Filion et al., 1993). This pattern of results led Dawson et al. (1993) to suggest that startle inhibition at the 60 ms lead interval reflects predominantly automatic sensorimotor gating, whereas inhibition at the 120 ms lead interval reflects the additional allocation of controlled attentional resources. The results of the Dawson et al. (1993) study revealed that the schizophrenia patients failed to show attentional modulation of startle inhibition at 120 ms but exhibited normal inhibition at 60 ms, leading to their conclusion that “relatively asymptomatic outpatients are not measurably deficient in the early pre-attentive stimulus detection and evaluation process—rather, they are deficient in the allocation of controlled resources at 120 ms to evaluate the to-be-attended prepulse…” (p. 639).

Although these results and conclusions, as well as those of Bolino et al., appear inconsistent with those of the earlier studies, there are several key methodological differences that may account for the apparent discrepancies, including the characteristics of the research participants. The deficits in automatic startle inhibition observed in the Braff et al. (1978, 1992) studies were observed in chronic hospitalized inpatients, whereas deficits in automatic startle inhibition were not observed by Dawson et al. (1993) in their sample of remitted outpatients.

One strategy for increasing our understanding of the information processing deficits associated with schizophrenia that reduces the complication of chronicity and hospitalization is to examine SEM in ‘at-risk’ populations (individuals who are considered to be vulnerable to psychosis but who are not psychotic). This strategy was employed by Swerdlow et al. (1995a), who examined startle inhibition in ‘normal’ participants recruited from the community whose profile on the
Minnesota Multiphasic Personality Inventory (MMPI) is considered ‘psychosis-prone’ based on previously published theoretically and empirically derived criteria (Butler et al., 1993). Using a passive attention startle modification paradigm with a lead interval of 60 ms, Swerdlow et al. reported that the MMPI-defined ‘psychosis prone’ group exhibited significantly less startle inhibition compared to controls. A similar strategy was also employed by Cadenhead et al. (1993), who examined startle inhibition in individuals meeting the DSM-III-R criteria for schizotypal personality disorder. These patients manifest symptoms in the schizophrenia spectrum, but to a less severe degree than those diagnosed with schizophrenia. Cadenhead et al. (1993) also employed a passive attention paradigm with acoustic lead and startle-eliciting stimuli and found that individuals with schizotypal personality disorder exhibited significantly less startle inhibition than controls at lead intervals of 30, 60 and 120 ms. In contrast to the findings of Braff et al. (1992) with schizophrenia patients, however, no differences between groups were observed in a condition involving a tactile startle-eliciting stimulus.

A third putatively vulnerable ‘psychosis-prone’ population includes individuals who experience extreme Perceptual Aberrations and/or Magical Ideation (Chapman and Chapman, 1987; Chapman et al., 1994). Individuals who score high on true-false questionnaires designed to evaluate these characteristics are called ‘Per-Mags’, and these individuals have been shown to exceed normal scoring control participants on rate of diagnosis of psychosis at a 10 year follow up (Chapman et al., 1994). There have been six studies to date that have examined startle inhibition in Per-Mag individuals (see Dawson et al., 1995 for a review).

Employing a passive attention paradigm, Simons and Giardina (1992) found that Per-Mag college students exhibited less startle inhibition than normal controls at a lead interval of 120 ms, but exhibited comparable inhibition at a lead interval of 60 ms. Perlstein et al. (1989) found no Per-Mag deficit at a lead interval of 120 ms but did observe reduced startle inhibition at a 500 ms lead interval. In contrast to these positive results, no differences in startle inhibition between Per-Mags and control participants were observed by Cadenhead and Braff (1992) at 30, 60 or 120 ms lead intervals, nor by Blumenthal and Creps (1994) at lead intervals of 60 or 120 ms, nor by Lipp et al. (1994) across a wide variety of lead intervals, including 120 ms. Finally, Schell et al. (1995) tested Per-Mag college students in the active attention tone-length judging paradigm described previously with short lead intervals of 60, 120 and 240 ms. As in the previous studies, the normal controls exhibited startle inhibition at each of the short lead intervals and enhanced startle inhibition at the 120 ms lead interval following the attended compared to the ignored lead stimulus. In contrast, the Per-Mag participants failed to show this attentional modulation of startle inhibition at 120 ms although they did show enhanced startle inhibition during the attended lead stimulus at 240 ms, suggesting that attentional processing may follow a slower time course in these individuals. The Per-Mags also showed no evidence of deficits in automatic startle inhibition (i.e. startle inhibition was normal at the 60 ms lead interval).
5.2. Clinical applications of short lead interval SEM: conclusions

Together, the short lead interval SEM studies described above present a complex picture regarding the nature of information processing dysfunctions in schizophrenia and at-risk populations. Although some of the apparent discrepancies in the studies of schizophrenia appear to be at least partially due to the characteristics of the participants (i.e. chronic/acute, psychotic/remitted), there are also apparently discrepant findings in the at-risk populations, even within similarly defined participants. For example, five of the studies reviewed above examined SEM in Per-Mag college students utilizing a passive attention paradigm. Three of these studies observed no Per-Mag deficit in startle inhibition across lead intervals of 30, 60, and 120 ms (Blumenthal and Creps, 1994; Cadenhead and Braff, 1992; Lipp et al., 1994), whereas the other two did observe deficits, one at a lead interval of 120 ms (Simons and Giardina, 1992), and one at a lead interval of 500 ms (Perlstein et al., 1989). Moreover, Schell et al. (1995), utilizing an active attention paradigm, observed no Per-Mag deficit in automatic startle inhibition, and observed that attentional modulation of startle inhibition followed a different time course for the Per-Mag group than the control group, with controls exhibiting the attentional effect at a 120 ms lead interval and the Per-Mag group showing the effect at a lead interval of 240 ms.

Thus it is clear that differences in characteristics of the research participants are not sufficient to account for all of the complexities in this literature, and that characteristics of the lead and startle-eliciting stimuli as well as of the tasks and lead intervals are also critical factors. For example, Braff and colleagues have reliably observed a schizophrenia-related deficit using acoustic and tactile startle-eliciting stimuli, whereas Bolino et al. observed no such deficit using an electrically elicited R2 response. In addition, in terms of the characteristics of the SEM paradigm used, deficits in automatic startle inhibition were observed using a passive attention paradigm in the studies by Braff and colleagues, whereas only deficits in the attentional modulation of startle inhibition were observed by Dawson et al. (1993). One possible explanation for this latter discrepancy suggested by Dawson et al. (1997) is that “Requiring active attention may alter the underlying processes such that automatic deficits are no longer detectable; instead only controlled processing impairments are apparent”. Thus it may be the case that schizophrenia involves deficits in both automatic sensorimotor gating and controlled processing, but that the introduction of a task increases the overall activation level of schizophrenic patients and subsequently increases the level of ‘automatic’ startle inhibition. Moreover, it may be possible that the nature of the SEM deficit in schizophrenia changes over the developmental course of the disorder. An important direction for future research into SEM and schizophrenia will be to clarify these factors.

5.3. Long lead interval startle modification

As described earlier, SEM at long lead intervals has been shown to be sensitive to emotional processes; negative or unpleasant lead stimuli produce startle facilita-
tion, whereas positive/pleasant lead stimuli produce startle inhibition. (See review by Cook, in press). For this reason, affective SEM paradigms are becoming increasingly popular in the study of affective disorders and psychopathy. Current research in these areas will be discussed below.

One application of the affective modulation paradigm has been focused on the study of anxiety states such as fearfulness, phobias, and stress disorders. In the first of such studies, Cook et al. (1991) examined SEM in college students classified into high-fear and low-fear groups based on their responses to a version of the Fear Survey Schedule. Participants performed an imagery task in which they were cued on different trials to imagine joyful, relaxing, fearful, angry, sad, and neutral scenes/activities, and a startle-eliciting noise burst was presented at lead intervals ranging from 8 to 13 s into the imagery period. The results revealed that startle responses were significantly larger during negative than positive imagery, and that this effect was greater in high-fear than low-fear participants. Startle potentiation was not specific to fear; rather it occurred during all of the negative affect imagery (sadness, anger, and fear). In a second study, Cook et al. (1992) examined startle responding in participants viewing a series of intermixed neutral (plants, household objects, etc.) and aversive (wounds, mutilated bodies, etc.) pictures. A warning stimulus informed participants as to the content of each picture presented, and a startle-eliciting noise burst was presented while participants were viewing the pictures. The results revealed that high fear participants exhibited significantly larger startle responses while viewing the aversive pictures than did the low fear participants. Together, these results suggest that startle facilitation can discriminate high and low fear participants on the basis of their differential responding to positive and negative stimuli, but may be limited in discriminating specific emotions within the negative category such as fear, anger, and sadness.

A related area of research in which the affective modulation of SEM technique has been utilized is in the study of phobias. Hamm et al. (1997) have reported that individuals show a significantly larger startle facilitation effect when viewing pictures of their specific phobic object than when viewing other unpleasant pictures and greater facilitation while viewing the phobic objects than non-phobic individuals viewing the same or other unpleasant pictures. Moreover, this phobia-related facilitation effect is so robust that it has been proposed as an instrument for evaluating the effectiveness of specific phobia therapies (de Jong et al., 1993). de Jong et al. (1991) measured startle responses while spider phobics were viewing live spiders or food items before and after one exposure and modelling treatment session. Initially, startle responses were greater during viewing of the spiders than the food items, as would be expected. After the treatment session, although responses were still larger during spider viewing, the degree of emotional modulation of startle had declined significantly. Similar results were obtained in two case studies by Vrana et al. (1992), who found that a series of systematic desensitization treatments eliminated the initial difference in startle response during phobic and neutral imagery. A somewhat different pattern of results was obtained by de Jong et al. (1993), who reported that after one treatment, startle responses during viewing of phobic, pleasant, and neutral items all declined. Emotional modulation
of startle was not significant before or immediately after treatment, but was at a one-week follow-up. The initial absence of emotional modulation of startle was attributed to a generalized fear-induced potentiation, since participants were aware that phobic objects (live spiders) would be viewed.

Although Hamm et al. (1997) found that persons with specific phobias show larger startle facilitation when viewing their phobic objects that other unpleasant pictures, results from an investigation that included participants with simple phobias, social phobia, post-traumatic stress disorder (PTSD), and panic disorder suggest that not all anxiety states exhibit this same pattern of results (Lang, 1995).

In this study, participants read a sentence that involved either routine and affectively neutral events, anxiety evoking social situations (an embarrassing act or speech performance), situations involving threat or danger (an auto accident or a night time intruder), or situations directly relevant to their specific problem. Participants were instructed to imagine themselves in the situation described by the sentence. Startle-eliciting stimuli were then presented at long lead intervals during the imagery task. The results revealed that all participants showed startle potentiation in the threat-danger condition compared to the neutral condition. However, whereas the participants with simple and social phobias also showed startle potentiation during imagery involving their specific phobic object situation, participants in the panic and PTSD groups did not exhibit startle potentiation during imagery involving their specific traumatic events. These data suggest that the startle facilitation measure may be valuable in understanding the dynamics of anxiety disorders.

A third area of anxiety research in which the SEM paradigm has been applied is in the area of fear-potentiation in PTSD. In order to test the hypothesis that individuals with PTSD might show an exaggerated fear-potentiated startle response, Morgan et al. (1995) conducted an experiment in which startle-eliciting stimuli were presented to PTSD and control participants first during a simple habituation series and then during alternating shock-threat and no-threat anticipatory intervals. During the latter intervals participants were presented with two coloured lights, one of which reliably predicted the presentation of a shock to the forearm, the other of which signalled a no shock-threat period. Each light was presented for 50–60 s, and startle-eliciting stimuli were presented at lead intervals ranging from 5 to 45 s. Participants were instructed that when a shock was presented it would always be presented during the last 10 s of a trial. The results of this experiment revealed that both PTSD and control participants exhibited startle facilitation during the shock-threat intervals, with the amount of facilitation increasing as the likelihood of shock increased. Contrary to prediction, the individuals with PTSD did not show an exaggerated facilitation of startle during the shock-threat condition, but rather exhibited significantly larger startle responses than controls across all three conditions (habituation, threat, and no-threat conditions). One possibility suggested by Morgan et al. (1995) is that the increased baseline responding may have been due to an increase in generalized anxiety in the PTSD individuals brought on by the stress of participating in an experiment involving an aversive stimulus.
Another promising avenue for SEM research and affective processes is the area of psychopathy. Cleckley (1976) provided the classic description of the psychopath and emphasized the importance of general poverty of affect in this disorder (e.g. lack of remorse, absence of nervousness, inability to love, and failure to establish close relationships). Therefore, one would predict that psychopathy would be characterized by poor affective modulation of SEM. Patrick et al. (1993) (see also Patrick and Lang, in press) tested this prediction by examining SEM in prison inmates while they viewed pictures of pleasant, neutral, and unpleasant pictures. The results for inmates without a psychiatric diagnosis were comparable to those typically observed with this paradigm; startle responses were largest during the unpleasant pictures and smallest during the pleasant pictures. In contrast, the criminal psychopaths showed no significant startle facilitation during the viewing of unpleasant pictures. Moreover, this lack of emotional modulation was observed specifically in prisoners who, at interview, showed emotional indifference and lack of remorse as opposed to only a history of criminal behaviour. Thus the lack of affective modulation of startle responding confirmed the clinical assessment of reduced emotional reactivity. Patrick (1994) has reported a replication of these results.

In contrast to this finding, however, a recent study of schizophrenia patients found a lack of agreement between clinical/behavioral assessments of emotional reactivity and startle responding (Schlenker et al., 1995). In this experiment, schizophrenia inpatients viewed a series of pleasant, unpleasant, and neutral pictures from the IAPS, and startle-eliciting stimuli were presented during the pictures at lead intervals of 3.1 and 5.1 s. Using video tapes of clinical interviews, the patients were rated on a dimension termed ‘diminished affective expression’ based on items such as paucity of expressive gestures, unchanging facial expression, and lack of vocal expressions. Patients scoring high on this dimension were then compared to low-scorers in terms of their affective modulation of startle. The results revealed that patients rated as having a highly diminished affective expression did not differ from controls; both groups showed the typical linear response pattern of startle facilitation during unpleasant slides and startle inhibition during pleasant slides. Surprisingly, patients for whom affective expression was not diminished failed to show this pattern, instead exhibiting equally reduced startle responding during both pleasant and unpleasant pictures. Also surprising was the finding that affective modulation of startle in patients who had high scores on a self-assessed anhedonia survey did not differ from that seen in low anhedonia patients, and that neither of these subgroups displayed the typical ‘unpleasant > neutral > pleasant’ pattern of startle responding. Thus these results indicate a dissociation between behavioral assessments of emotional reactivity, subjective reports of emotional experience, and affective modulation of startle in schizophrenia. Thus SEM may provide unique information about affective processes that is not available from verbal and behavioral measures. Dissociation of expressive, experiential, and psychophysiological (skin conductance) measures of emotion also has been reported with schizophrenia patients by Kring and Neale (1996), further confirming the need for measuring multiple components of emotion.
5.4. Clinical applications of long lead interval SEM: conclusions

Together, the studies reviewed above suggest that SEM at long lead intervals is sensitive to individual differences in affective states and traits in both the normal and pathological range. High fear college students exhibit significant affective modulation of startle, with larger responses during negative affect than positive affect, to a significantly greater degree than low fear college students. Moreover, individuals with simple and social phobias, PTSD, and panic disorder all exhibit startle potentiation while viewing pictures or imagining scenes of generic threat-danger conditions, but only the phobic groups exhibit startle potentiation while viewing pictures or imagining scenes related to their specific stressful object event. Emotionally detached criminal psychopaths fail to potentiate the startle eyeblink reflex during exposure to unpleasant pictures. There is growing evidence that affective modulation of startle may provide information that is not available from verbal reports and behavioral measures (e.g. startle modulation during emotional pictures occurs in schizophrenia patients with diminished affective expression, but not in patients without this behaviourally apparent deficit). All in all, the results suggest that affective modulation of startle may be a powerful tool for detecting, quantifying, and eventually understanding affective individual differences, particularly those characterized by anxiety and negative affect.

Important directions for future research include determining to what extent affective modulation of SEM can be informative about (1) low arousal negative emotions (e.g. flat affect, anhedonia, and depression), (2) individual differences in positive emotions in addition to negative emotions, (3) identification of individuals at-risk for emotional disorders, (4) distinguishing different emotional states (e.g. fear versus anger) as well as different valences (pleasant versus unpleasant), (5) the development of emotions across the lifespan, and (6) the modifiability of emotions by learning, drugs, etc. (for work in this area, see Stritzke et al. (1995) regarding the effects of alcohol on startle and its affective modulation and Patrick et al. (1996) regarding the effects of diazepam). These directions of research can be profitably pursued by a combined study of clinical and non-clinical human populations, as well as nonhuman animals.

6. Summary, conclusions, and unanswered questions

The present paper has reviewed psychological interpretations of the significance of human startle eyeblink amplitude modification, with separate discussions of the modification that occurs at short and long lead intervals. Table 1 summarizes the principal psychological processes that have been hypothesized to mediate or influence SEM at short and long lead intervals.

Startle eyeblink modification at short lead intervals has been hypothesized to be associated with pre-attentive protection of processing (Graham, 1975, p. 246), with the pre-attentive ‘call’ for attentional processes (Filion et al., 1994, p. 76), with sensorimotor gating (Braff and Geyer, 1990), with the allocation of controlled
attentional processes (Dawson et al., 1993 p. 639), and most recently with affective modulation (Vanman et al., 1996). It is important to note that these hypotheses clearly are not mutually exclusive. Indeed, inhibition of startle amplitude at short lead intervals is probably multiply determined and numerous psychological processes may be influential depending upon the nature of the lead stimulus, the length of the short lead interval, the speedie task and state of the participants, and the characteristics of the participants.

The long lead interval effects also have been hypothesized to be modulated by a number of different processes, as summarized in Table 1: 'classical activation' (Graham, 1975, p. 243; see also Ison and Hammond, 1971, p. 449); non-specific enhancement of sensory processing (Bohlin et al., 1981, p. 609), modality-specific enhancement or inhibition of sensory processing (Bohlin et al., 1981, p. 609; Graham, 1979, p. 160, Putnam, 1990, p. 119); and match/mismatch of affect/motivation (Lang et al., 1990). As with short lead interval SEM, multiple psychological processes probably co-exist during long lead intervals, with different processes being dominant depending upon characteristics of the stimuli, the task, and the participants.

As can be seen, the psychological constructs hypothesized to mediate SEM include both cognitive and affective/motivational processes at both short and long lead intervals. The proposed cognitive processes consist of both pre-attentive automatic processes and controlled attentional processes. As shown in Fig. 7, we have previously suggested that the hypothesized effects of automatic and controlled processes can be separately evaluated at both short and long lead intervals within the differential tone length judgment task (Dawson et al., 1997). At short lead intervals, we have noted that instructionally induced attentional processes do not affect startle inhibition at 60 ms, but do have significant effects at 120 ms. Based on these observations, we have proposed that within this paradigm startle inhibition at the 60 ms lead interval represents automatic, pre-attentive processes, whereas startle inhibition at 120 ms represents a combination of automatic and controlled attentional processes. According to this interpretation, the difference in startle inhibition observed following the to-be-attended and to-be-ignored lead stimuli at 120 ms may be used to index early controlled attentional processes, as may be the enhancement of inhibition across the 60 to 120 ms lead intervals following the to-be-attended

Table 1
Psychological processes hypothesized to mediate SEM

<table>
<thead>
<tr>
<th>SEM at Short Lead Intervals</th>
<th>SEM at Long Lead Intervals</th>
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<tr>
<td>Pretentive protection of processing</td>
<td>Classical activation</td>
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<tr>
<td>Pretentive ‘call’ for allocation of controlled attention</td>
<td>Non-specific sensory enhancement</td>
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<td>Sensorimotor gating</td>
<td>Modality-specific sensory enhancement/inhibition</td>
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<tr>
<td>Allocation of controlled attention</td>
<td>Affective modulation</td>
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lead stimuli. At long lead intervals (e.g. 2000 ms), facilitation occurs following both the to-be-attended and to-be-ignored lead stimuli, with greater facilitation following the to-be-attended lead stimulus. These findings have led us to propose both a non-specific facilitation effect, as indexed by the facilitation during the to-be-ignored lead stimulus, and controlled sustained attentional processes indexed by the difference between the to-be-attended and to-be-ignored lead stimuli at the long interval.

There is much that remains to be learned about the precise cognitive processes affecting startle at short lead intervals, even within the specific differential tone length judgment task. For example, although we know that attention directed toward the lead stimulus can augment startle inhibition at the 120 ms lead interval in this paradigm, what is the precise cognitive process responsible for this effect? On different occasions, we have proposed that this effect reflects the pre-attentively initiated ‘call’ for attention (Filion et al., 1994), or the answer to that call with allocation of controlled attention (Dawson et al., 1993). These alternative hypotheses are currently being tested in our laboratory with two different strategies. First, participants are engaged in an irrelevant task during the SEM paradigm, so that the ability to answer the call with allocation of attentional resources is impaired but the
pre-attentive call is left intact (Seljö et al., 1995). Second, the controlled attentional orienting response to the prepulse is habituated by repetitive presentation prior to testing for its inhibitory power (Wynn et al., 1996).

Basic issues also remain concerning the cognitive processes affecting startle at long lead intervals. For example, does the small but significant facilitation following the to-be-ignored lead stimulus in the differential tone judgment task reflect ‘classical activation’ or non-specific sensory enhancement, and can these two hypotheses be clearly differentiated? Is the facilitation observed at long lead intervals in this paradigm following the to-be-attended lead stimulus associated with modality-specific sensory enhancement? Recall that startle facilitation occurs at long lead intervals if attention is directed toward the same modality as the startle eliciting stimulus, whereas startle inhibition has been reported if attention is directed to a modality different than that of the startle probe (e.g. Putnam, 1990). This modality-specific effect suggests that the previously observed startle facilitation following the to-be-attended acoustic lead stimulus (see Fig. 7) would become startle inhibition if visual lead stimuli were used rather than auditory lead stimuli, or if the startle reaction was elicited by visual stimuli rather than auditory stimuli. However, contrary to this prediction, startle facilitation has been found in this paradigm with both visual and acoustic to-be-attended lead stimuli (Böhmelt et al., 1996; Lipp et al., 1997). These results suggest that the long lead interval facilitation effect in this paradigm is modality-nonspecific. Results such as these demonstrate that our understanding of the basic psychological processes at long lead intervals and their relationships to startle modification, are in need of considerably more research.

Similarly, much remains to be learned about affective modulation of startle with the specific affectively loaded pictures typically used to study this phenomenon. For example, can the affective valence effects be clearly separated from the effects of arousal and attention on startle? How much of the affective modulation of startle is due to the fact that highly affective pictures are also highly arousing and highly interesting, compared to affectively neutral pictures? Is SEM differentially sensitive to different emotions, or only to the bio-dimensional affective valence (positive versus negative) associated with the emotion? That is, do all negatively valenced emotions (fear, disgust, embarrassment, depression) potentiate startle? Do all positively valenced emotions (happiness, pride, sexual arousal, interest) inhibit startle? In other words, is the critical modulating process one of motivation and valence, or does it have more to do with the varieties of emotions? Is the match between the participant’s current motivational state and the affective quality of the elicited reflex the underlying process that modulates startle? Is there independent evidence for the emotional priming process hypothesized to cause affective modulation?

Although not emphasized in this review, a distinct advantage of studying human SEM is that the same basic phenomena can also be investigated in non-humans. Research with non-humans can more readily investigate the neurophysiological and neurochemical basis of startle modification than can human research. In fact, the study of startle modification in non-humans has already produced considerable
knowledge about the neurocircuitry of the primary acoustic startle reflex (e.g. Koch et al., 1992; Lee et al., 1996), its modification at short lead intervals (e.g. see reviews by Dawson et al., 1997; Swerdlow and Geyer, in press; Swerdlow et al., 1992), and its affective modification at long lead intervals (e.g. Davis, 1996; Davis et al., in press). Any complete explanatory model of startle modification must take into account the neurophysiological and neurochemical basis of the phenomena, as well as their psychological significance. Hackley (in press) has reviewed evidence for models that incorporate cortical-subcortical pathways as well as conscious-unconscious processes. In this sense, a complete model of startle modification will be a psychophysiological model. Psychophysics lies at the interface of cognitive science, neuroscience, and clinical science (e.g. Dawson, 1990), and the study of startle modification has the potential to be a model psychophysiological system for theoretical integration across disciplinary boundaries.

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