An Analysis of Startle Responses in Patients with Panic Disorder and Social Phobia

By

Derrick K. Larsen

A Thesis
Submitted to the Faculty of Graduate Studies
In Partial Fulfilment of the Requirements
For the Degree of

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Department of Psychology
University of Manitoba
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ABSTRACT

Initial results from startle response studies indicate that patients with anxiety disorders exhibit larger baseline startle responses than healthy controls (Butler et al., 1990; Morgan III, Grillon, Southwick, Davis, & Charney, 1995), have normal startle response habituation (Butler et al., 1990; Morgan III et al., 1995; Shalev, Orr, Peri, Schreiber, & Pitman, 1992), and more pronounced fear-potentiated startle during presentation of disorder-specific fear stimuli via slides or imagery (Hamm, Cuthbert, Globisch, & Vaitl, 1991; P. J. Lang, personal communication, August, 1995). The purpose of this study was to systematically replicate (see Sidman, 1960) and extend these findings by examining baseline startle responses, startle response habituation, prepulse inhibition, and fear-potentiated startle to physical threat-related, social threat-related, and non-threatening words in 12 patients with panic disorder, 22 patients with social phobia, and 15 healthy controls. Results indicated that patients with panic disorder exhibited significantly larger startle responses than healthy controls during baseline, pulse alone, prepulse inhibition and fear-potentiated trials. Although patients with social phobia consistently exhibited larger startle responses than healthy controls during all the trials a statistically significant difference was only found during the pulse alone trials. Implications and limitations of the study are discussed and it is suggested that future studies should examine the relationship between startle responses and all forms of anxiety disorders.

AN ANALYSIS OF STARTLE RESPONSE IN PATIENTS WITH PANIC DISORDER AND SOCIAL PHOBIA

In the past, numerous researchers (e.g., Schneirla, 1959; Konorski, 1967; Dickinson & Dearing, 1979) have proposed biphasic theoretical models of emotion. In general, these theoretical models submit that all emotions can be located along an appetitive-aversive dimension. Hence, the term biphasic. More recently, Lang and his associates (Lang, 1995; Lang, Bradley, & Cuthbert, 1990, 1992) have introduced a biphasic model which suggests that emotions are organized around two strategic dimensions: affective valence, and arousal. The affective valence dimension refers to the organism's disposition and is driven by two primary motivational systems: the appetitive system (consummatory and nurturant), and the aversive system (defensive and protective). The arousal dimension refers to the strength of the dominant motivational system. Therefore, according to Lang's model, emotions are not only distinguished by their affective valence, but also by their level of arousal. For instance, pleasurable emotions, like relaxed (low) and excited (high), and unpleasant emotions, such as depressed (low) and fearful (high), can be distinguished from each other by their level of arousal. In addition, Lang's model suggests that one's current emotional state can modulate concurrent but independently evoked behaviours. For instance, a defensive reflex (e.g., startle response) initiated during a defensive emotional state will be augmented. However, the same defensive reflex will be attenuated if it is initiated during a pleasant state. Therefore, a reflex can be either augmented or inhibited depending on whether it matches one's current emotional state. Most of the research in this area has examined the modulatory effects of fear (an aversive motivational state) on the

startle response (a defensive reflex).

Fear-Potentiated Startle in Rats

The startle response is a series of rapid flexor movements that surge throughout the body and is triggered by any sudden sensory event such as a loud noise (Landis & Hunt, 1939). In 1951, Brown, Kalish, and Farber hypothesized that a highly motivated aversive drive state, like fear, could result in augmentation of startle response magnitude. To test their hypothesis, they first conditioned rats to be fearful of a light-buzzer compound by pairing it with electric shock. Then, after conditioning, they recorded rats' startle responses to toy pistol shots during exposure to light-buzzer stimulus alone. Brown et al. (1951) found that the rats exhibited larger startle responses to startle probes (pistol shot) presented in the context of the conditioned stimuli, compared to neutral stimuli (i.e., never paired with electrical shock). Brown et al.'s (1951) findings have subsequently been replicated by others (e.g., Ross, 1961; Spence & Runquist, 1958; Miller & Barry, 1960; Berg & Davis, 1985). This particular phenomenon has since been termed *fear-potentiated startle* (Davis, 1989a). Intrigued by this finding, some researchers have focused their attention towards understanding the neural mechanisms underlying fear-potentiated startle reflex in rats (e.g., Davis, 1989a; Davis, Hitchcock, & Rosen, 1987; Lang, 1995).

The Rat Brain's Fear-Startle Circuit

The neural basis of fear-potentiated startle in the rat is well understood. A diagram of the rat brain's startle circuit is presented in Figure 1. The basic obligatory auditory startle circuit in the rat brain begins with the stimulation of the cochlear nucleus by a startle probe (i.e., loud noise). The activated cochlear nucleus sends impulses to the lateral lemniscus and then to the

reticular formation. From there, the efferent connections proceed through the spinal cord neurons to the reflex effectors (Davis, 1989a; Davis et al., 1987). This primary reflex pathway is effected by stimulus parameters such as stimulus intensity and frequency (Lang, 1995).

The occurrence of fear-potentiated startle suggests that this basic reflex is modulated by a secondary circuit. Numerous lines of evidence indicate that the amygdala is a principal structure in this modulatory pathway (Davis, 1992, 1989a; Davis et al., 1987; Lee, Lopez, Meloni, & Davis, 1994; Fendt, Koch, & Schnitzler, 1994). For instance, researchers have found that there are monosynaptic projections from amygdala nuclei to the principal reticular site. Furthermore, it has been observed that producing a lesion in the amygdala nullifies conditioned startle enhancement (Hitchcock & Davis, 1986) and has resulted in the reduction of innate fear (Blanchard & Blanchard, 1972; Ursin, Jellestad, & Cabrera, 1981; Werka, Skar, & Ursin, 1978). In addition, it has been shown that electrical stimulation of the amygdala (below the level of kindling) elicits fear behaviours and defensive reactions in animals (Applegate, Kapp, Underwood, & McNall, 1983; Ursin et al., 1981), and augments the startle response (Lang, 1995). It has also been shown that anxiolytic drugs which have been shown to affect benzodiazepine action in the amygdala, such as diazepam (Berg & Davis, 1984; Davis, 1979), buspirone (Kehne, Cassel'a, & Davis, 1988), and clonidine (Davis, Redmond, & Baraban, 1979) block fear-potentiated startle. Finally, it has been found that amygdala-lesioned animals exhibit deficits only in aversive learning tasks and not in appetitive learning tasks (Cahill & McGaugh, 1990). Thus, it appears that the amygdala plays a pivotal role in the modulation of the obligatory startle circuit in rats.

Fear-Potentiated Startle in Humans

Similar fear-potentiated startle responses have been reported in studies using human subjects (e.g., Spence & Runquist, 1958; Hamm, Greenwald, Bradley, & Lang, 1993; Cook, Hawk, Davis, & Stevenson, 1991; Butler et al., 1990). It is, therefore, believed that a comparable fear-startle circuitry exists in both rats and humans (Lang, Bradley, Cuthbert, & Patrick, 1993). The methodology for recording the startle response in humans is slightly different than the methods used for rats. Typically, whole body startle responses are recorded in rats, whereas the eyeblink component of the startle response is measured in humans (Lang, 1995). Nevertheless, analogous results have been obtained.

One of the earliest fear-potentiated startle studies on human beings was conducted by Spence and Runquist (1958). They conditioned humans to be fearful of a light stimulus by pairing it with an electric shock. After acquisition training, it was found that probe startle responses (evoked by an airpuff) were augmented during the light cue. This study was later replicated by Ross (1961). Furthermore, comparable results have also been obtained in studies in which photographic slides were paired with mild electric shocks (Hamm et al., 1993; Greenwald, Bradley, Cuthbert, & Lang, 1990; Hamm et al., 1991). Fear-potentiated startle responses have also been observed in humans exposed to nonlaboratory "conditioned" fear. For instance, augmented startle responses have been observed in people while viewing naturally fear-provoking pictures (e.g., mutilated bodies or faces, spiders, a coiled snake)(Vrana, Spence, & Lang, 1988; Bradley, Cuthbert, & Lang, 1990), and films depicting climatic scenes of horror movies, bloody bodily mutilations, and frightening facial expressions (Jansen & Frijda, 1994),

and while imagining naturally fear-provoking events (Cook et al., 1991).

Startle and Fear-Potentiated Startle in Patients with Anxiety Disorders

Recently, there have been a number of studies that have examined exaggerated startle and fear-potentiated startle in patients with anxiety disorders. For instance, Butler et al. (1990) recorded eye blink startle responses in individuals with combat-related post-traumatic stress disorder. They found that patients with post-traumatic stress disorder exhibited larger baseline startle responses than controls. However, habituation of the startle response in patients with post-traumatic stress disorder did not differ from habituation rates in healthy controls. Similarly, Morgan III et al. (1995) found that patients with post-traumatic stress disorder showed greater startle amplitude during baseline compared to healthy controls, but no differences in habituation. Morgan III, Grillon, Southwick, Davis, and Charney (1996) also found that Gulf War veterans with post-traumatic stress disorder exhibited larger startle amplitude, compared to combat and civilian controls, and no differences in habituation. Increased baseline startle responses has also been reported in women with sexual assault-related post-traumatic stress disorder (Morgan III, Grillon, Hedar, & Southwick, 1997). More recently, several studies have found increased startle responses in patients with post-traumatic stress disorder only in experiments in which stressful procedures were used. For example, Grillon, Mogan III, Davis, and Southwick (1998) found that Vietnam veterans with post-traumatic stress disorder only exhibited increased baseline startle responses when aversive shocks were anticipated. Similar contextual effects have been found in Gulf War veterans with post-traumatic stress disorder (Grillon and Morgan III (1999) and in Vietnam veterans with post-traumatic stress disorder during dark conditions (Grillon, Morgan

III, Davis, & Southwick, 1998). The exaggerated startle response typically found in patients with post-traumatic stress disorder was not obtained by Shalev et al. (1992). They also found no significant differences in habituation between normal controls and post-traumatic stress disorder patients. Grillon, Ameli, Goddard, Woods, & Davis (1994) examined baseline and fear-potentiated startle (threat of shock) in patients with panic disorder. They found that young patients with panic disorder exhibited larger startle responses throughout the testing compared to young healthy controls. Significant differences only occurred during the fear-potentiated startle phase.

Other studies have provided prefatory evidence that individuals with anxiety disorders exhibit more pronounced fear-potentiated startle to disorder-specific fear stimuli than to nondisorder-specific fear stimuli. For example, Hamm et al. (1991) presented startle probes to phobic patients and nonphobics while they viewed slides of pleasant, neutral, unpleasant, and phobic objects (e.g., spiders, snakes, mutilated bodies). They found that both groups (phobic and nonphobic) exhibited augmented startle responses while viewing unpleasant slides. However, the phobic group, compared to the nonphobic group, exhibited significantly greater startle potentiation while viewing phobic objects. Similar findings have been reported by Lang (1995). In this study, startle responses between four different anxiety groups (i.e., patients with panic disorder, social phobia, post-traumatic stress disorder, and simple phobias) were measured. Startle probes were presented to the subjects while they imagined four different scenes containing neutral, dangerous, embarrassing, and clinical content (i.e., an event directly relevant to their specific clinical problem). All four anxiety groups exhibited larger startle responses to

probes presented while imagining fear scenes (i.e., dangerous, embarrassing, and clinical) than during neutral scene imagery. More importantly, patients with simple phobia, panic disorder, and post-traumatic stress disorder showed the largest augmentation of startle while imagining disorder-specific related scenes. For example, patients with panic disorder showed greatest augmentation of startle while imagining dangerous scenes. Patients with social phobia, on the other hand, did not follow this trend and exhibited their largest startle responses while imagining dangerous scenes. However, compared to the other anxiety groups (patients with simple phobia, panic disorder, and post-traumatic stress disorder) the patients with social phobia showed the largest startle responses while imagining embarrassing social scenes.

Prepulse Inhibition

The startle response is not only modulated by the emotional context in which a startle probe occurs, but it also can be modulated by a pre-startle stimulus (prepulse). When a nonstartle-eliciting stimulus precedes a startle probe by a *short* duration and a decrement in startle amplitude is observed this is called *prepulse inhibition* (PPI; see Graham & Hackney, 1991 for a review). Prepulse inhibition is well established in animal and human populations (e.g., Bradley, Cuthbert & Lang, 1993; Hoffman & Wible, 1970; Ison & Leonard, 1971; Buckland, Buckland, Jamieson, & Ison, 1969). It is theorized that the inhibitory effect of a prepulse stimulus on the startle response is credited to attentional mechanisms (Graham, 1980; Graham & Hackney, 1991). That is, the sensory system restricts reactions to new input until the processing of previous information is complete.

Clinical observations have indicated that patients with schizophrenia typically exhibit

deficits in performance on attention and information processing tasks (Braff, Grillon, & Geyer, 1992). To empirically assess this phenomenon, researchers have examined the effects of prepulse stimuli on the startle response in patients with schizophrenia (e.g., Braff et al., 1992; Grillon, Ameli, Charney, Krystal & Braff, 1992). Their results indicate that patients with schizophrenia do exhibit deficits in PPI. That is, the prepulse stimulus does not reduce startle amplitude. To the best of my knowledge, prepulse inhibition has not been investigated in any other psychiatric populations. Nevertheless, there is good reason to believe that patients with anxiety disorders may also exhibit deficits in PPI. For instance, it has been argued that anxious individuals are preoccupied with their anxiety. This preoccupation is believed to inhibit their ability to focus on other tasks (Cloitre, Heimberg, Holt, & Liebowitz, 1992). In fact, results from cognitive experiments (e.g., Stroop and Dot-probe studies) suggest that patients with anxiety disorders may suffer from a deficit in performance on attention and/or information processing tasks (McNally, 1990; Eysenck, 1991; Mathews, May, Mogg, & Eysenck, 1990; Asmundson, Sandler, Wilson, & Walker, 1992; Martin, Williams, & Clark, 1991; McNally, Kaspi, Reimann, & Zeitlin, 1990; McNally, Reimann, & Kim, 1990). In addition, these studies and others have indicated that anxious individuals also display cognitive processing biases toward disorder-specific stimuli. Evidence for this selective processing bias is provided below.

Cognitive Processing Biases in Anxiety Disorders

Cognitive psychologists have studied cognitive processing biases in human beings via dichotic listening, modified stroop colour-naming, dot-probe, and skin conductance orienting response paradigms. These cognitive paradigms have been adopted and modified to study

selective processing of disorder-specific threat stimuli in people with anxiety disorders.

Dichotic Listening Paradigm

The dichotic listening paradigm is based on the premise that stimuli that are particularly threatening to an individual will be noticed more readily, whereas non-threatening material may be ignored (Foa & McNally, 1986). In this paradigm, subjects are concurrently presented with two prose passages, one in each ear. They are told to repeat aloud (shadow) a prose passage delivered to one ear, while ignoring a simultaneous passage presented in the other. Furthermore, they are asked to detect certain target words embedded in each prose passage. If the target words are threatening to the subject, they are detected more readily in the unattended channel relative to non-threatening material (Treisman & Geffen, 1967). Dichotic listening paradigm studies have consistently shown that anxious subjects more readily detect disorder-specific threatening than non-threatening words. For instance, patients with agoraphobia and social phobia have been shown to detect more fear-related words (i.e., fear words specific to their particular phobia) than neutral words in the unattended channel (Burgess, Jones, Robertson, Radcliffe, & Emerson, 1981). Similar results have been obtained in studies examining patients with generalized anxiety disorder (Mathews & MacLeod, 1986) and obsessive-compulsive disorder (Foa & McNally, 1986). Studies using the modified Stroop Colour-Naming paradigm have yielded comparable results (see below).

Stroop Colour-Naming Paradigm

In a typical colour-naming task, subjects are shown a series of words of varied emotional significance and are asked to indicate the colours in which the words are presented while

ignoring the word meaning. Interference can be inferred from delays in colour-naming which seem to occur when the meaning of the word attracts the subject's attention despite efforts to attend to and name the colour of the word (McNally, 1990). Overall, the results obtained in studies employing colour-naming paradigms with anxious subjects are similar to those found with dichotic listening paradigms. That is, patients with spider phobia (e.g., Watts, McKenna, Sharrock, & Trezise, 1986), social phobia (Hope, Rapee, Heinberg, & Dombeck, 1990; Mattia, Heimberg, & Hope, 1993), generalized anxiety disorder (e.g., Mogg, Mathews, & Weinman, 1989; Mathews & MacLeod, 1985), panic disorder (e.g., Ehlers, Margraf, Davies, & Roth, 1988; McNally et al., 1990), and post-traumatic stress disorder (Foa, 1989) were slower at colour-naming lists of threatening material relevant to their respective disorders than at colour-naming lists of non-threatening material. Furthermore, patients with panic disorder, social phobia, and post-traumatic stress disorder respond slower to all classes of words, showing a generalized deficit in performance on attentional tasks (McNally, 1990; Mathews et al., 1990; Asmundson et al., 1992; McNally, Kaspi, et al., 1990; McNally, Reimann, et al., 1990). Parallel results have been obtained in studies using the dot-probe latency paradigm created by MacLeod, Mathews, and Tata (1986).

Dot-Probe Paradigm

It is unclear whether the Stroop interference is an index of attentional direction, or of some other bias in later stages of information processing (e.g., rumination over word meanings, biases in the production of appropriate verbal responses). In an attempt to address these issues MacLeod et at. (1986) developed the dot-probe paradigm. In this paradigm, subjects are asked to

pay attention to a series of threat-neutral word pairs (order of word types are varied) displayed on a computer screen. One word appears above the other and subjects are asked to initially focus their attention to the top word. Visual attention is measured by recording reaction time to a neutral stimulus (a computer generated dot-probe). The probe periodically appears in the same visual space previously occupied by the upper or lower word. The premise behind this paradigm is that words that are threatening to the subject will attract the subject's attention and as a result subjects will respond quicker (taking into account word position) to probes that appear in the visual space previously occupied by threatening word compared to non-threatening word. In 1986 Macleod et al. demonstrated that patients with anxiety responded quicker to probes that followed either physically or socially threatening words. Asmundson et al., (1992) reported similar results for patients with panic disorder. That is, patients with panic disorder responded more quickly to probes following physically threatening material than to probes following socially threatening or neutral material. These results have been replicated by Beck, Stanley, Averill, Baldwin, and Deagle (1992). Recently, Asmundson and Stein (1994) found that patients with social phobia also differentially attended to social threat words. Similar results have been obtained in studies that have used physiological measures of attention.

Skin Conductance Orienting Response (SCOR)

The orienting response is regarded as a correlate of information processing mechanisms of stimulus analysis, encoding and selective attention (Ohman, 1979; Filion, Dawson, Schell, & Hazlet, 1991). Several studies have shown that the SCOR in various psychopathological groups are abnormal. For instance, larger skin conductance responses to anxiety-relevant, compared to

neutral content, stimuli have been found in individuals suffering from various anxiety disorders, such as obsessive compulsive disorder (Foa & McNally, 1986), specific fears (Klorman, Wiesenfeild, & Austin, 1975), post-traumatic stress disorder (McNally et al., 1987), generalized anxiety disorder (Mathews, Richards, & Eysenck, 1989), and panic disorder (Roth, Ehlers, Taylor, Margraf, & Agras, 1990; Roth, et al., 1986).

These results suggest several similarities between startle research and the cognitive studies. For example, the current fear state of an individual modulates both startle responses and responses to dichotic listening, stroop, dot-probe, and orienting tasks.

Purpose and Hypotheses

Initial results from startle response studies indicate that patients with anxiety disorders exhibit larger baseline startle responses than healthy controls (Butler et al., 1990; Morgan III et al., 1995, Grillon et al., 1994), have normal startle response habituation (Butler et al., 1990; Morgan III et al., 1995; Shalev et al., 1992), and more pronounced fear-potentiated startle during the presentation of disorder-specific fear stimuli via slides and imagery (Hamm et al., 1991; Lang, 1995). The purpose of this study was to systematically replicate (see Sidman, 1960) and extend these findings by examining baseline startle responses, startle response habituation, PPI, and fear-potentiated startle to physical threat-related, social threat-related, and non-threatening words in patients with panic disorder, social phobia and healthy controls.

This study is important for a number of reasons. First of all, it will be the first study to use words as potential startle augmenting stimuli. This is significant for several reasons: (1) this study can potentially extend the range of stimuli that have been shown to augment startle

responses in a disorder specific way, and (2) significant results would make it possible to tie the effects of startle and other procedures (e.g., Stroop tests) together. Thus, if the same words used in the Stroop studies (etc.) are effective in augmenting startle responses, this would indicate that linguistic factors may be an important component of human fear systems. Secondly, this study is significant because it compared potential startle enhancing, and startle decrementing stimuli within the same session. Although many studies have shown exaggerated startle responses in individuals with anxiety disorders (Butler et al., 1990; Hamm et al., 1991, Lang, 1995, Grillon et al., 1994) this will be the first study to examine whether or not the individuals with panic disorder and social phobia also suffer from an inability to inhibit startle responses.

Based on the results from startle response and cognitive studies presented thus far, it is hypothesized that: (1) patients with panic disorder and social phobia will display larger baseline startle responses compared to controls, (2) patients with panic disorder and social phobia will show reduced PPI compared to healthy controls, but will not differ from one another, (3) there will be no differences in startle response habituation between patients with panic disorder, social phobia, and healthy controls, and (4) patients with panic disorder will exhibit the largest fear-potentiated startle responses in the presence of physical threat-related words and patients with social phobia will show the largest fear-potentiated startle responses in the presence of social threat-related words.

Method

Subjects and Subject Selection

The sample consisted of 49 individuals (35 female, 14 males, mean age = 33.6 years, SD

= 9.2). There were twelve patients with panic disorder, 22 patients with social phobia, and 15 healthy controls. Groups did not significantly differ on age ($F(2, 48) = 1.09$, $p = .346$) or gender ($\chi^2(2) = 1.1$, $p = .573$). Patients and controls were recruited through the St. Boniface General Hospital Anxiety Disorders Research Program, the St. Boniface General Hospital Anxiety Disorders Clinic, and through media advertisements. The diagnosis of panic disorder and social phobia was made by experienced psychologists and psychiatrists using Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV; American Psychiatric Association, 1994) criteria (see Table 1). Control subjects were free of lifetime psychiatric illnesses. Patients with panic disorder or social phobia who had any other comorbid anxiety disorder, current major depressive disorder, psychoses or substance abuse were excluded from the study.

Visual Stimuli

Thirty words (15 related to physical threat, 15 related to social threat) extracted from a study by MacLeod et al. (1986) and fifteen non-threatening words obtained from a study by Asmundson et al. (1994) were used as stimuli for the fear-potentiated startle trials (see Appendix A). The physical and social threat-related words were originally chosen by MacLeod et al. (1986) from descriptions of anxiety disorders given by Beck, Emery, and Greenberg (1985) and Hibbert (1984). The threatening and non-threatening words have been used in the past to show consistent attentional differences between patients with panic disorder, social phobia and healthy controls (MacLeod et al., 1986; Hope et al., 1990; Beck et al., 1992; Asmundson et al., 1992; Asmundson & Stein, 1994). In addition, the threatening and non-threatening word pairs were matched for length and frequency of use in the English language (Kucera & Francis, 1967).

Words were presented individually on a computer monitor situated two feet in front of the subjects. Each word was centered on the computer monitor, measured one inch in height, was white in colour, and presented on a black background.

Procedure

This experiment was conducted in two parts. A schematic representation of the sequence of the procedure is presented in Figure 2. During the first visit subjects viewed a short video illustrating the procedure of the study. In addition, subjects were allowed to examine the room in which the experiment was held and asked any questions they had regarding the study - this took approximately 10 minutes. This first visit aided in familiarizing the subjects with the experimental room and procedures, thus reducing any "experimental" anxiety they might have experienced if not given this initial visit. Subjects were then scheduled for their second appointment.

During the second visit, subjects were met by a researcher who sat them in a comfortable chair and ask them to read and sign the informed consent form (see Appendix B). Subjects were then given a short hearing test with a Beltone 10D audiometer. Individuals who demonstrate problems detecting 30db signals were excluded from the study - none were excluded. Following the hearing test, three silver\silver electrodes were placed around the subjects' right eye via adhesive collars. The first was placed 1 cm lateral and 0.5 cm below the lateral canthus. The second was placed 1.5 cm below and slightly medial to the first electrode. The third, was placed behind the right ear over the mastoid and served as a ground. Electrode resistance measurements read at or below 5 kohms. After the electrodes were connected, and resistance measurements

were satisfactory, subjects were given instructions for the startle experiment. Essentially, they were told that they will be hearing a series of loud, but not painful, tones through the headphones and occasionally a word will appear on the computer screen in front of them. Finally, headphones (Telephonics TDH-39P) were placed on the subject's head.

Subjects were given a ten minute adaptation period which allowed them to relax. Following the ten minute adaptation period there was a five minute acclimation period. This acclimation period consisted of subjects listening to 70-dB[A] white noise - which will also served as background for the experiment.

Acoustic startle stimuli had a near instantaneous rise time and was presented binaurally through the headphones. Subjects received 80 trials in which startle is elicited by a 116-dB[A] noise burst 40 ms in duration. The first 5 trials were pulse-alone (block 1) followed by 75 trials consisting of 5 blocks of 15 trials each. The first block served as a habituation procedure that acquainted subjects with the startle stimuli. The remaining five blocks included three pulse alone, three pre-pulse, and nine "fear-potentiated" trials (three physical threat-related, three social threat-related, and three non-threatening words). The pulse alone, prepulse, and fear-potentiated trials were randomly ordered as was the physical threat-related, social threat-related, and non-threatening words within the fear potentiated trials. In other words, trials and words were randomly generated; however, the ordering of the trials and the words were such that no trial class nor word category occurred more than twice in a row. The prepulse trials consisted of 74-dB[A] sound bursts, 20 ms in duration and had a prepulse-to-pulse interval of 100 ms. The fear-potentiated trials consisted of 116-dB[A] sound bursts that occur either 2.5, 3.5, or 4.5 sec after

the onset of the visual stimuli (i.e., physical threat-related, social threat-related, and non-threatening words). Once a word appeared on the screen it remained for six seconds. Only six of the nine fear-potentiated trials for each block were followed by a startle stimulus. This aided in the unpredictability of startle stimuli in the fear-potentiated trials. Inter-trial intervals (ITI) were 16, 20, and 24 sec in duration.

Startle Recording

Eye-blink Component of Startle

Eye blink activity was recorded by electrodes placed through an electromyographic (EMG) amplifier to a computerized startle response monitoring system (SR-LAB, San Diego Instruments Inc., San Diego, California) for digitization and analysis. To eliminate 60 Hz interference a 60 Hz notch filter was used.

A detailed description of the methodology for measuring the startle reflex has been presented elsewhere by Grillon, Ameli, Woods, Merikangus, and Davis (1991). In short, peak eyeblink amplitudes were determined in the 21-120 milliseconds after stimulus onset. Responses were excluded if onset and peak latency differ by more than 95 milliseconds and/or if an eyeblink was detected within 20 milliseconds following stimulus onset.

Data Reduction and Analyses

The independent variables for this study are group (i.e., panic disorder, social phobia and Healthy Controls), block (1-5), and word type (physical threat-related, social threat-related, and non-threatening). In general, the dependent variable can be conceptualized as eyeblink amplitude. The nature of the study, however necessitates that eye blink be used in a more

specific fashion as follows: a) baseline startle amplitude (mean of first five pulse-alone eye-blink EMG amplitudes), b) prepulse data will be calculated in two ways: (1) startle amplitude during prepulse trials (mean of all pre-pulse inhibition EMG amplitudes) and (2) prepulse effect (mean of pulse alone amplitudes - mean of prepulse amplitudes)], c) habituation (mean of each pulse-alone amplitude for each block), and d) "fear-potentiated amplitude" (mean of all eye-blink EMG amplitudes occurring when a pulse is in the presence of a physical threat-related, social threat-related or non-threatening word). All startle amplitudes are expressed in arbitrary units (au).

The general design of the study includes one between-groups factor (group: panic disorder vs social phobia vs Control) and 5 within-groups factors, including block, word type, baseline, prepulse, and habituation. To measure group differences in baseline EMG measures a one-way ANOVA (analysis of variance) was used. The pulse alone EMG and pre-pulse EMG data was analyzed with separate 3 (group) x 5 (block) repeated measures ANOVAS. The repeated measurements for these analyses were block. A 3 (group) x 5 (block) x 3 (word type) repeated measures ANOVA was used to analyze the fear-potentiated EMG data. The repeated measures were block and word type.

Results

Preliminary Analyses

In order to identify outliers, means and standard deviations of startle amplitudes for each group and dependent variable (i.e., baseline, pulse alone, prepulse, and fear-potentiated startle amplitudes) were calculated. According to Emerson and Streino (1983) any deviation below the twenty fifth percentile value or above the seventy fifth percentile value by more than 1.5 times

the interquartile range is considered an outlier. Subjects startle amplitudes that met this criteria were eliminated from specific analysis. This resulted in 3 healthy controls and 1 patient with social phobia being dropped from the baseline analysis, 2 healthy controls being dropped from the pulse alone analysis, 1 healthy control being dropped from the prepulse analysis, and 2 healthy controls and 1 patient with social phobia being dropped from the fear-potentiated startle analysis.

It has been found that large doses of diazepam blocked fear-potentiated startle (Patrick, Berthot, & Moore, 1996). A number of patients were on low doses of anxiolitic drugs and when anxiolytic drugs were entered as a covariate in the analyses it did not effect the results. Therefore, all results are reported without the anxiolytic drug covariate.

A 3(group) x 5(condition) ANOVA was used to assess the effectiveness of the different conditions (i.e., fear-potentiated startle, prepulse, and pulse alone) on startle responses. The analysis revealed a significant difference between conditions [$F(4, 44) = 16.61$, $p < .000$]. Post hoc analysis revealed that startle responses were significantly larger in the physical-threat related condition (35.95 ±26.38) compared to the prepulse condition (24.85 ± 22.49)[$t(90) = 2.17$, $p = .032$]. Startle responses were larger in the social-threat conditon (34.27 ● 25.03) compared to the prepulse condition but did not reach statistical significance [$t(90)$ 1.90, $p = .061$]. There were no other significant differences.

Baseline Startle

A one-way ANOVA was used to measure group differences in baseline EMG amplitude measures. The analysis revealed a significant difference between groups [$F(2,40) = 4.425$, $p <$

.018]. The means are shown in figure 3. Post hoc analysis indicated that patients with panic disorder (66.75 ± 37.24) had significantly larger baseline startle amplitudes compared to healthy controls (37.45 ± 10.19; Tukey HSD, $p < .018$). There were no other significant differences.

Pulse Alone Startle

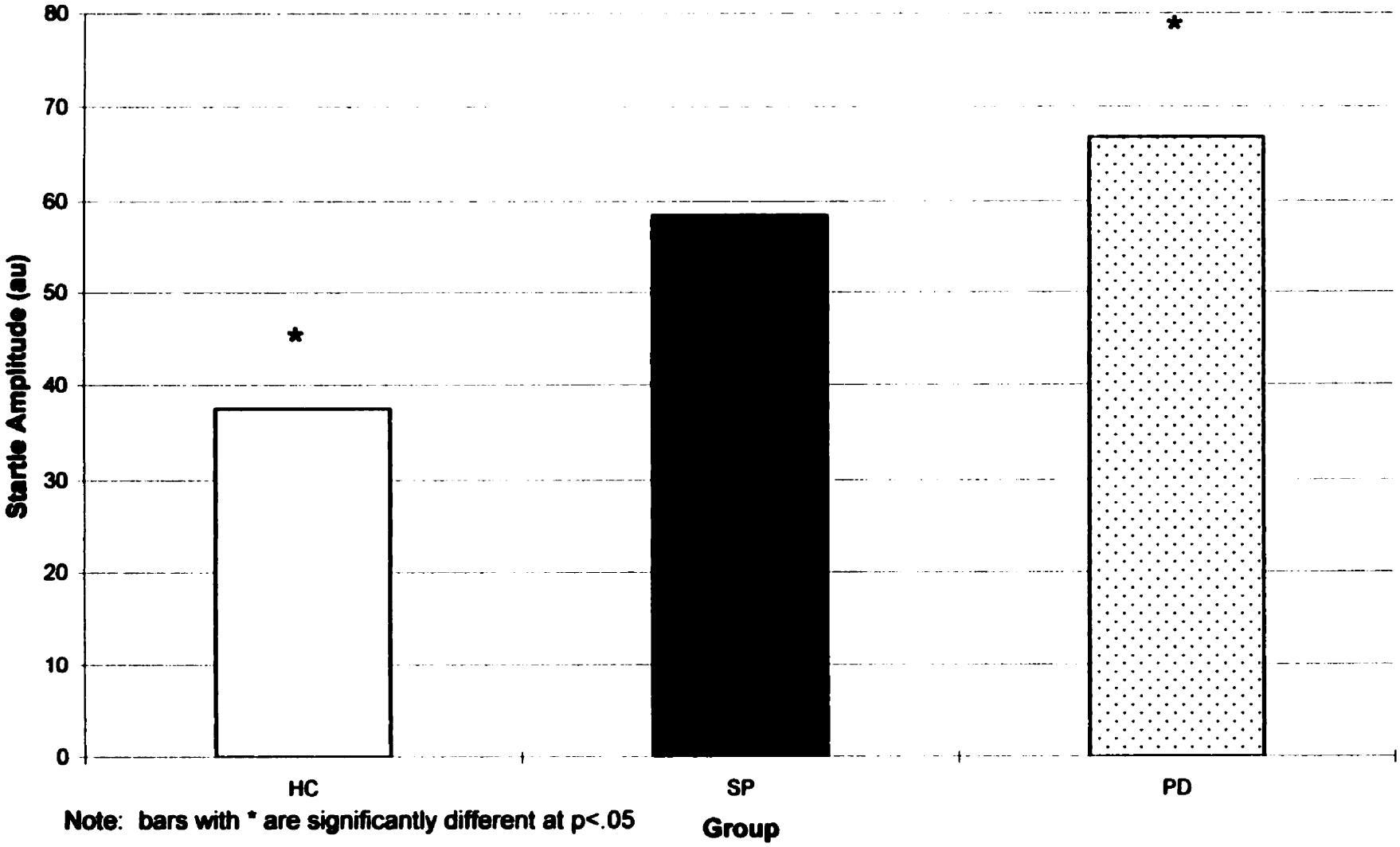
A 3 (group) x 5 (block) repeated measures ANOVA was used to analyze differences in pulse alone EMG amplitude. The repeated measurement for this analysis is block. The analysis of between subjects variables was significant [$F(2,44) = 5.52$, $p < .007$]. The means are shown in figure 4. Post hoc analysis revealed that the patients with panic disorder (42.78 ± 33.00) had significantly greater pulse alone startle amplitude compared to healthy controls (15.31 ± 12.07; Tukey HSD, $p < .009$), and that patients with social phobia (36.09 ± 19.21) also had significantly greater pulse alone startle amplitude compared to healthy controls (Tukey HSD, $p < .027$). Patients with panic disorder and social phobia did not differ from each other. The analysis for the within subjects effect revealed a significant main effect of block [$F(4,176) = 15.21$, $p < .000$]. There was no significant group by block interaction, indicating that the rate of habituation of startle amplitude did not differ between groups.

Prepulse Startle

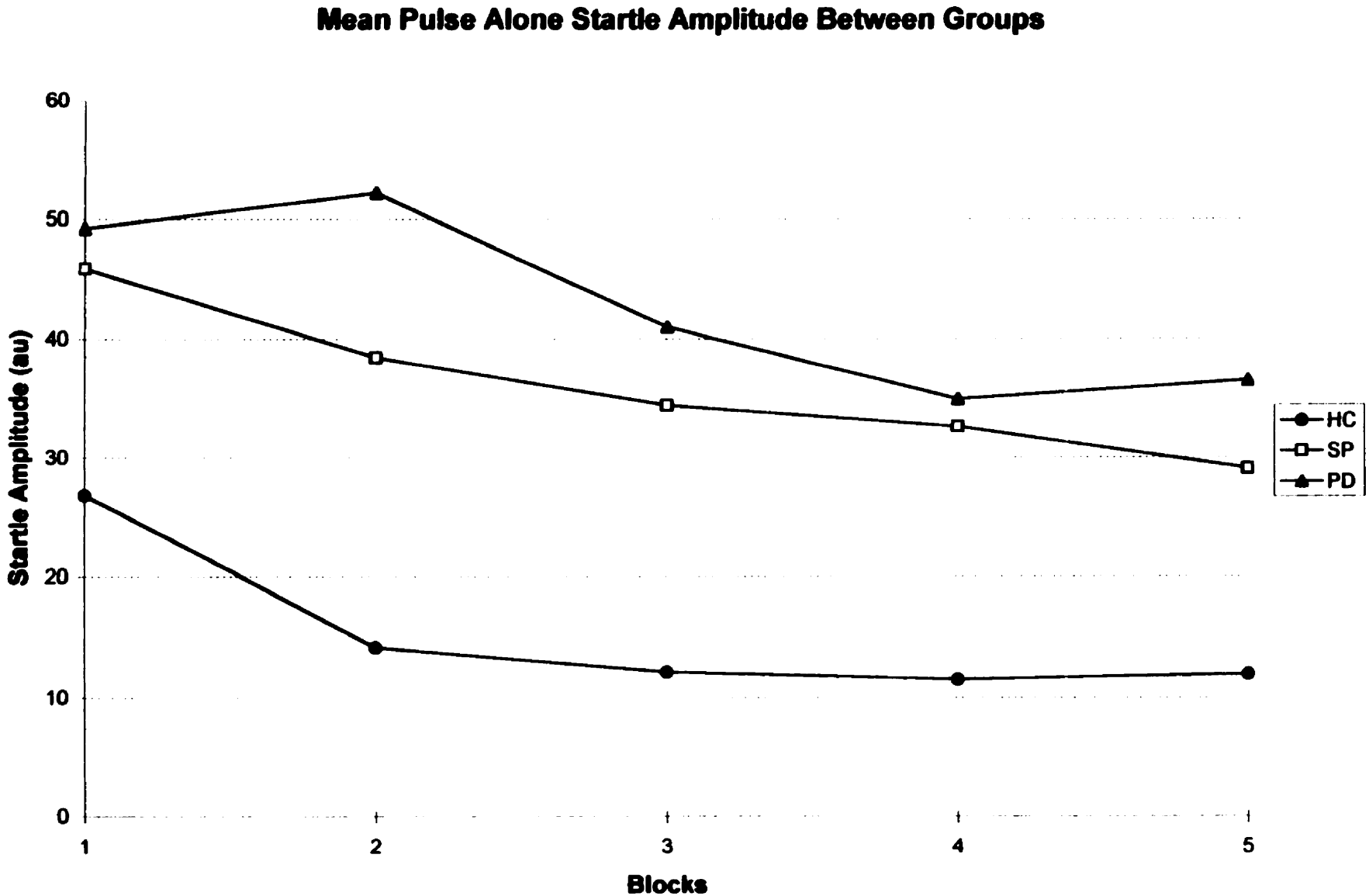
A 3 (group) x 5 (block) repeated measures ANOVA was used to analyze differences in: 1) startle amplitude during prepulse trials (mean of all prepulse inhibition EMG amplitudes) and 2) prepulse effect (mean of pulse alone amplitudes – mean of prepulse amplitudes). The repeated measurement for these analyses is block.

Analysis of between subjects variables was significant [$F(2,45) = 4.65$, $p = .015$] for

Mean Baseline Startle Amplitude Between Groups



Note: bars with * are significantly different at p<.05

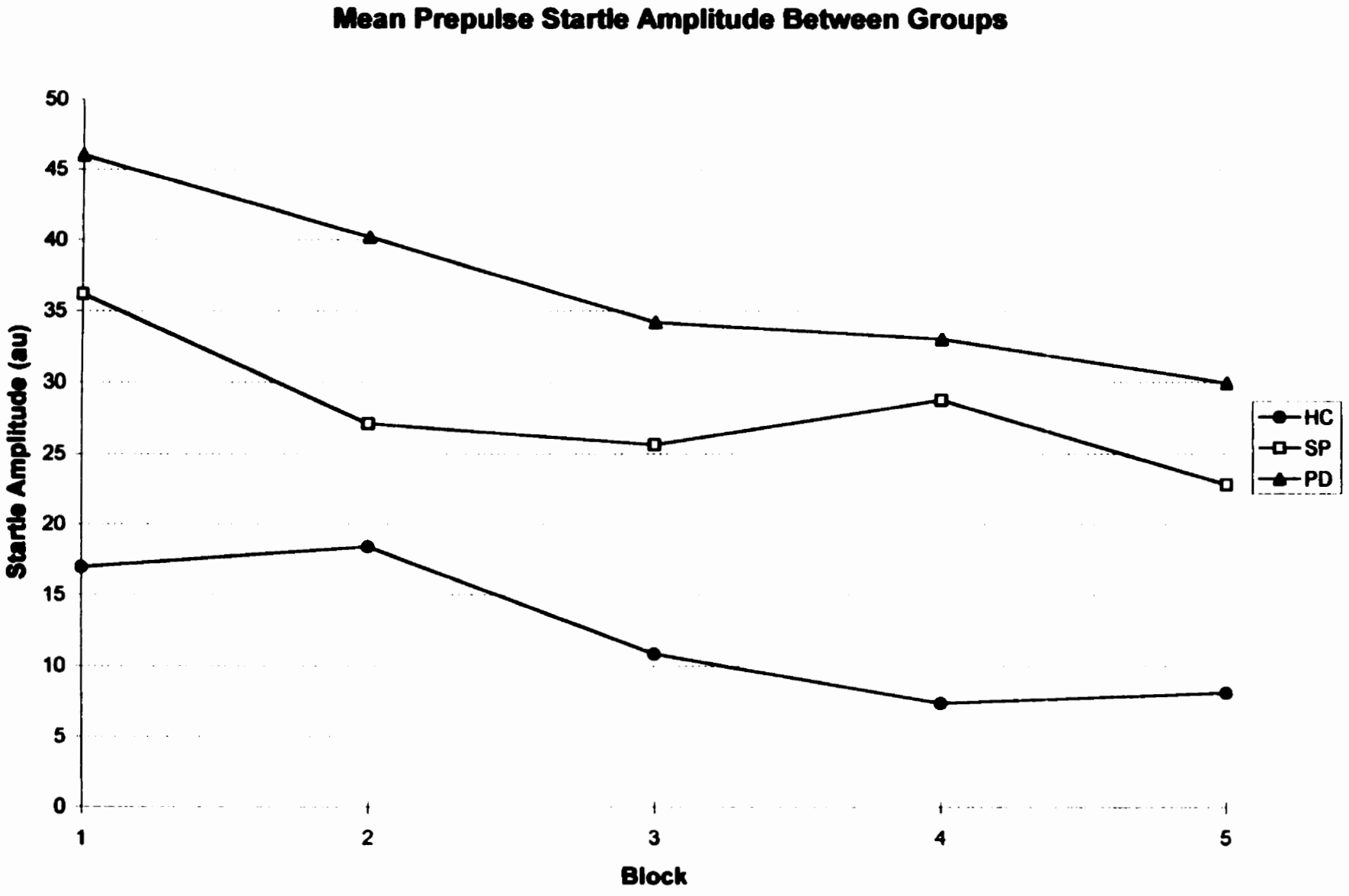

Mean Pulse Alone Startle Amplitude Between Groups
Startle Amplitude (au)
60
50
40
30
20
10
0
1
2
3
4
5
Blocks
HC
SP
PD

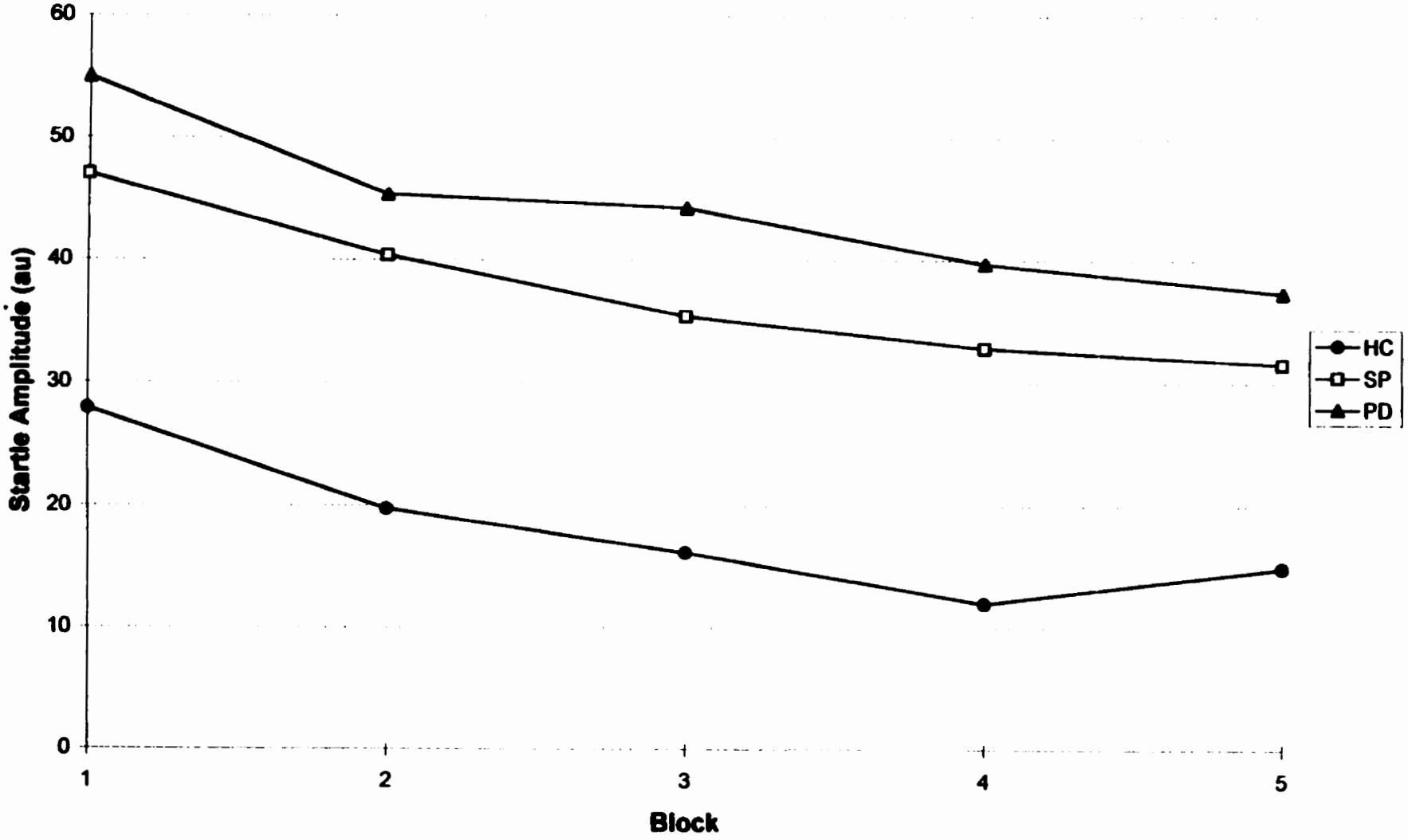
startle amplitude during prepulse trials. The means are shown in figure 5. Post hoc analysis revealed that the patients with panic disorder (36.67 ± 32.34) had significantly greater startle amplitude during prepulse trials compared to healthy controls (12.35 ± 9.23; Tukey HSD, $p < .013$). Patients with social phobia (28.10 ± 18.33) also had larger startle amplitude during prepulse trials compared to healthy controls, but did not reach statistical significance (Tukey HSD, $p = .081$). Patients with panic disorder and social phobia did not differ significantly from each other. The analysis for the within subjects effect revealed a significant main effect of block [$F(4,180) = 12.77$, $p < .000$]. There were no significant interactions.

The analysis of between subjects variables for the prepulse effect (mean pulse alone amplitudes - mean prepulse amplitudes) revealed no main effect for group. Analysis of within subject variables showed no main effect for block, and no significant interactions. Thus, the prepulse effect was equal for all groups and across all blocks.

Fear-potentiated Startle

A 3 (group) x 3 (word) x 5 (block) repeated measures ANOVA was used to analyse differences in fear-potentiated EMG amplitude. The repeated measurements for this analysis is word and block. The analysis of between subjects variables was significant [$F(2,43) = 4.46$, $p < .017$]. The means for group are shown in figure (6). Post hoc analysis revealed that patients with panic disorder (44.32 ± 6.68) had significantly greater overall startle compared to healthy controls (18.16 ± 6.42; Tukey HSD, $p = .019$). The difference in startle amplitude between patients with social phobia (37.43 ± 5.05) and healthy controls approached significance (Tukey HSD, $p = .058$). There were no significant differences between patients with panic disorder and


Mean Prepulse Startle Amplitude Between Groups
Startle Amplitude (au)
50
45
40
35
30
25
20
15
10
5
0
1
2
3
4
5
Block
HC
SP
PD


Mean Fear-potentiated Startle by Group
Startle Amplitude (au)
60
50
40
30
20
10
0
1
2
3
4
5
Block
HC
SP
PD

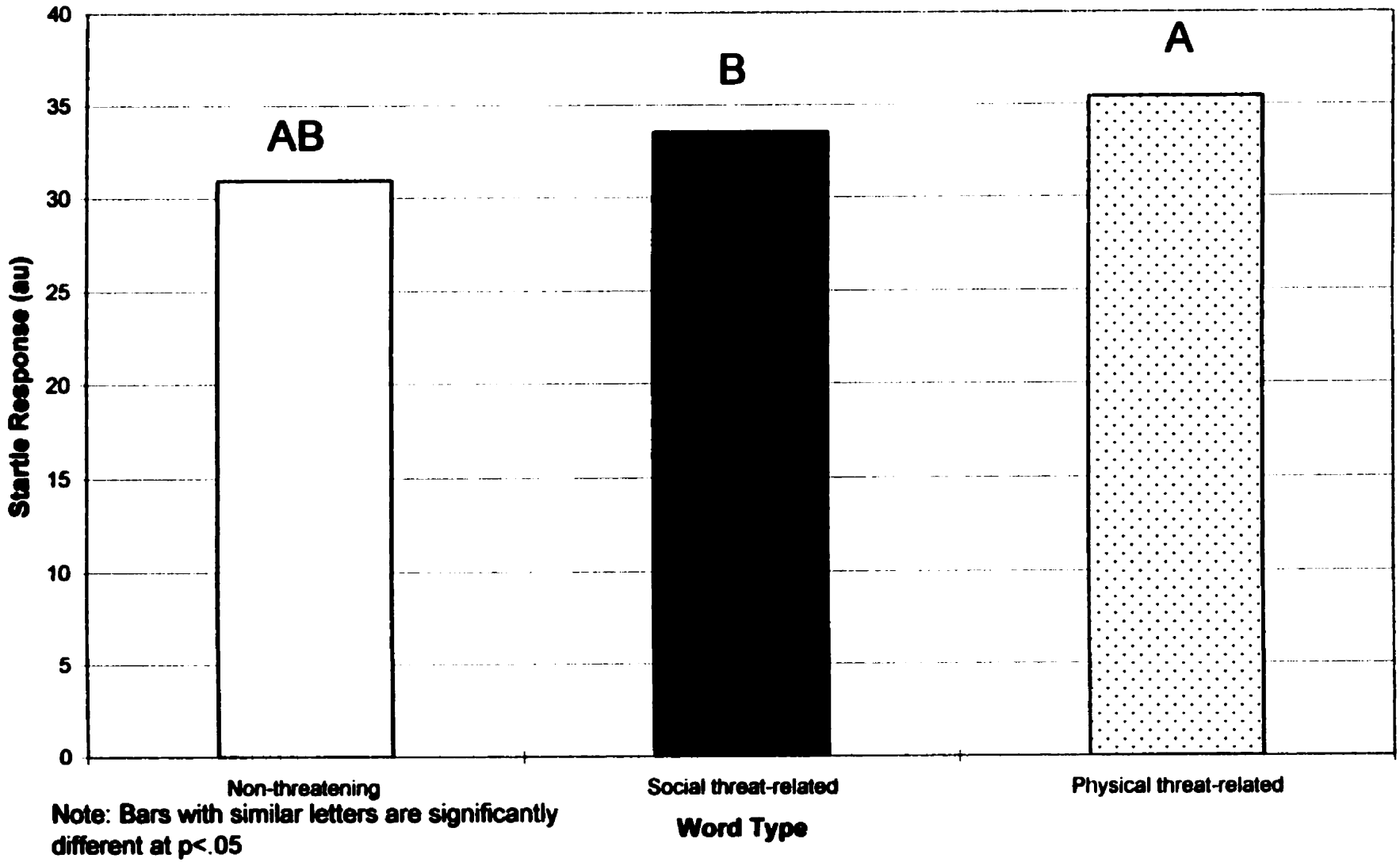
social phobia. The analysis for the within subjects effects revealed a significant main effect of word [$F(2,86) = 9.57$, $p < .000$] and block [$F(4,172) = 25.82$, $p < .000$]. There were no significant interactions. Pairwise comparisons indicated that subjects exhibited significantly larger startle responses to physical threat-related words (35.44 ± 3.74) compared to non-threatening words (30.94 ± 3.41; $p = .001$) and also significantly larger startle responses to social threat-related words (33.53 ± 3.56) compared to non-threatening words (30.94 ± 3.41) ($p = .004$). Differences between startle responses towards physical threat-related words and social threat-related words did not differ significantly, but did approach significance ($p = .058$: see figure 7).

Discussion

The present study investigated baseline startle responses, startle response habituation, PPI, and fear-potentiated startle to disorder-specific threat stimuli in patients with panic disorder and social phobia. To the best of my knowledge, this is the first study to implement words as potential startle augmenting stimuli.

Overall, the results indicate that an exaggerated startle response may be characteristic of panic disorder and to a lesser extend social phobia. Specifically, during baseline, pulse alone, PPI, and fear-potentiated trials patients with panic disorder exhibited significantly larger startle responses than healthy controls, but did not differ significantly from patients with social phobia. This result is in agreement with findings from Grillon et al. (1994) that patients with panic disorder exhibit an exaggerated startle response. Although patients with social phobia consistently exhibited larger startle responses than healthy controls during all the trials a statistically significant difference was only found during the pulse alone trials. A number of

Mean Fear-potentiated Startle Amplitude by Word Type



Note: Bars with similar letters are significantly different at $p<.05$

hypotheses may account for the exaggerated startle response found in anxious patients. It is important to note that the exaggerated startle in patients with panic disorder and social phobia are not due to a failure to habituate since there were no differences in habituation rate between the groups. One potential explanation that has been proffered by others (e.g., Morgan III et al., 1996; Grillion, Morgan, Southwick, & Charney, 1996) to account for the exaggerated baseline startle responses in patients with post-traumatic stress disorder, is that it may reflect a persistent sensitization of the startle reflex (i.e., severe and prolonged trauma-induced stress may cause a pronounced increase in startle amplitude). For instance, for war related post-traumatic stress disorder, an exaggerated startle response may reflect a sensitization produced by the trauma of war. It is possible that similar factors may account for exaggerated startle in patients with panic disorder and social phobia. For example, Gorman, Liebowitz, Fyer, and Stein (1989) indicated that repeated panic attacks that occur "out of the blue" may lead to a "kindled" state of chronic elevated anxiety. Furthermore, they indicate that this chronic state may result in a reduced threshold of responsivity to a number of related and unrelated stressors (e.g., startle). Similar reasoning could be applied to patients with social phobia who are repeatedly exposed to social stressors. However, social anxiety would be restricted to social situations. Therefore, the sensitization effect may not be as strong as in patients with panic disorder. However, there is little empirical evidence to support the "sensitization" theory. Animal studies have shown that prior stress has had little to no effect on startle in rats (Davis, 1989). However, other studies increased startle amplitudes in rats due to previous exposure to footshock, but these effects are relatively short in duration (e.g., 4 days)(Servatius et al., 1994). Nevertheless, it is plausible that

the exaggerated startle response may be due to a sensitization effect. This theory is supported by the association between the amygdala and fear and anxiety (Davis, 1992; Gloor, 1960; Kapp et al., 1984; Mishkin & Aggleton, 1981; Sarter & Markowitsch, 1985) and that it appears that the amygdala plays a central role in the neural pathway in which fear is conditioned and expressed (LeDoux, 1987, 1990, 1992; Davis, Hitchcock, & Rosen, 1987; Davis, 1992; Kapp et al., 1984, 1990, 1992; Gentile et al., 1986).

A second possibility is that the stress of the experimental context produced higher levels of anxiety in the anxiety disorder patients. Studies that have examined startle in Vietnam veterans with post-traumatic stress disorder have found evidence of exaggerated startle throughout testing in which stressful procedures were used (Morgan, Grillon, Southwick, Davis & Charney, 1995; Morgan et al., 1995; Grillon, Morgan III, Davis et al., 1998; Grillon, Morgan III, and Davis, 1998; Grillon & Morgan, 1999), but not in the absence of experimental stress (Grillon et al., 1996). Although this is possible, every effort was taken to reduce any 'experimental anxiety' by allowing participants to visit and familiarize themselves with the experimental room and procedures (i.e., watch a short video tape illustrating the procedure of the study) prior to participating in the experiment proper. Nevertheless, this procedure may have produced the opposite effect by priming "experimental anxiety" for the experiment proper.

A third explanation, first posited by Grillon et al. (1996), is the possibility that exaggerated startle may be associated with anxiety disorders. Studies that have examined startle responses in healthy subjects have shown that the magnitude of startle responses vary greatly between subjects but are quite stable within individuals. Therefore, it is possible that patients

who eventually develop an anxiety disorder (e.g., post-traumatic stress disorder, panic disorder or social phobia) might be those individuals who originally had higher levels of startle. Interestingly, a recent study by Grillon, Dierker and Merikangas (1998) found elevated startle responses in offspring of parents with anxiety disorders.

Although patients with panic disorder and social phobia exhibited exaggerated startle responses no differences in PPI were found between the groups. It was argued that anxious individuals are preoccupied with their anxiety and this preoccupation may inhibit their ability to focus on other tasks (Cloitre et al., 1992). Although results from cognitive studies (e.g., stroop and dot probe) have indicated attentional deficits in patients with panic disorder and social phobia, no significant differences in PPI were found. Significant deficits in PPI have been found in patients with schizophrenia (Braff et al., 1992; Grillon et al., 1992). However, patients with schizophrenia are characterized by significant deficits in attention and information processing such as slowed processing, increased distractibility, and inefficient allocation of attentional resources. These deficits can lead to stimulus 'overload' and result in the cognitive fragmentation observed in patients with schizophrenia (Braff et al., 1992; Braff & Geyer, 1990). A possible explanation for the null result is that patients with anxiety disorders do not exhibit such extreme deficits of attention and information processing, as patients with schizophrenia do, and therefore, do not exhibit deficits in PPI.

An alternative explanation is that patients with anxiety disorders do exhibit deficits in attention and information processing but only in stressful situations congruent to their anxiety disorder. Leitner (1986) found that PPI can be reduced in rats following immersion in cold

water. Thus, demonstrating that PPI can be affected by stress. Therefore, patients with panic disorder may only exhibit significant deficits in PPI during a panic attack. Similarly, patients with social phobia may only exhibit significant deficits in PPI while under the stress of a social situation.

Lang et al.'s (1990) has indicated that startle probe modulation is attributed to emotional response priming. For example, a defensive reflex (i.e., startle response) initiated during a defensive emotional state (i.e., fear) will be augmented and if it is initiated during a pleasant state will be attenuated. Results from this study provide support for Lang's theory. It was found that all three groups (panic disorder, social phobia, and healthy controls) exhibited augmented startle responses in the presence of physical threat-related and social threat-related words compared to non-threatening words. These results support findings by Hamm et al. (1991) and Lang (1995) in which fear-potentiated startle was demonstrated in anxious populations. However, the hypothesis that individuals with anxiety disorders exhibit more pronounced fear-potentiated startle to disorder-specific fear stimuli than to nondisorder-specific fear stimuli was not supported. There are a number of possible explanations for this null result.

One possibility is that the "potency" of the threat was not strong enough. It may be that the physical threat and social threat-related words presented on the computer screen are not "potent" enough to elicit fear responses in patients with panic disorder and social phobia. Although these words have been shown to be effective in attention studies (e.g., MacLeod et al., 1986; Hope et al., 1990; Beck et al., 1992; Asmundson et al., 1992; Asmundson et al., 1994) they may not be strong enough to elicit fear responses in patients with anxiety disorders. Hamm

et al. (1991) presented pictures of phobic objects to individuals with simple phobia and Lang (1995) asked individuals with simple phobias, social phobia, panic disorder, and post-traumatic stress disorder to use imaginary techniques to imagine disorder-specific situations. The stimuli used by Hamm et al. (1991) and Lang (1995) may have been more "potent", thus producing a fear-potentiated effect to disorder-specific threat stimuli in various anxious populations.

Another possible explanation is that people in general are more fearful of physical threat than to social threat. Results from the study indicated a main effect for word. That is all subjects startled the largest following the presentation of physical threat-related words (e.g., death, injury, paralyzed), second largest to social threat-related words (incompetent, failure, embarrassed), and the smallest to non-threatening words (respectable, gentle, mild). Therefore, the physical threat-related words may be highly significant for all subjects and therefore obscure any between group differences that may have been present.

Finally, there are a number of potential limitations in this study. For instance, one plausible limitation in this study may be that the sample size was too small. Nevertheless, even with only 12 patients with panic disorder a number of significant findings were produced.

Another limitation is that prescribed and self-prescribed medications could confound the results of this experiment. Recently, Patrick et al. (1996) found that 15 mg dose of diazepam blocked fear-potentiated startle, but had little effect on overall startle magnitudes in a nonclinical sample. Initial screening procedures (via SCID interviews) should have weeded out any subjects who are on significant doses of psychoactive medication. Although urine analysis would be the best way to screen for drug usage, budget constraints did not permit the use of this screening

method. Although there are a number of limitations to this study it has provided some interesting results and raised some significant questions. Therefore, it is important to conduct future studies which will further examine the relationship between startle response and all forms of anxiety disorders.

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Appendix A

Stimuli for Fear-Potentiated Startle

Physical threat-related	Social threat-related	Non-threatening
injury	criticized	mild
ambulance	embarrassed	normal
emergency	failure	friendly
disease	stupid	quiet
cancer	foolish	honourable
fatal	inferior	gentle
mutilated	indecisive	sensible
coffin	lonely	fair
death	hated	alert
paralyzed	humiliated	respectable
coronary	incompetent	observant
harm	worthless	cautious
violence	ridiculed	typical
fracture	insecure	kind
corpse	ashamed	modern

Appendix B

INFORMATION PROCESSING STUDY

INFORMATION FOR PARTICIPANTS

PURPOSE OF THE STUDY:

The purpose of this study is to examine the way individuals with anxiety disorders process certain types of information. Some studies suggest that people with anxiety disorders may think in a different way than those who do not have anxiety disorders. A number of tests have been devised to examine brain responses to various stimuli (e.g., auditory tones and words). These tests will tell us how your brain processes new information and thus teach us more about brain functioning in anxiety disorders. This information along with future studies will help to improve our understanding of anxiety disorders.

ABOUT THE STUDY:

If you agree to participate, you will be asked to take part in a screening process to determine if you are eligible or not for the study. This will involve a 30 minute telephone interview, followed by a 90 minute in-person interview. If you have already been assessed recently by a staff member of the Anxiety Disorders Clinic information about your diagnosis and your scores on assessment forms (for example, anxiety and depression questionnaires) will be obtained so that we do not have to repeat the questionnaires and interview.

If you are eligible (that is, based on the screening procedures you suffer from a specific anxiety disorder or are a healthy control), you will be scheduled for your first session of the information processing study. **Testing will be conducted in the Clinical Research Laboratory**

(Room 4L43) at the University of Winnipeg.

During the first session you will view a short tape about the study. In addition, you will be allowed to tour the room in which the study will be held and ask any questions you have regarding the study - this will only take 10 minutes. At the end of the first session we will schedule a convenient time for your second session.

During your second visit, you will be met by a staff member who will seat you in a comfortable chair. First of all, you will be given a brief hearing test. Then two sticky pieces of tape with wires attached will be placed on the surface of your skin above and around your right eye and one behind your right ear. These are not painful and only rest on the surface of your skin to measure muscle tension.

Throughout the study you will be wearing headphone in which tones will be delivered. Some of these tones will be loud enough to startle you. The loudest volume of these tones will be 120 decibels. This is roughly equivalent to a loud clap of thunder. While this is unpleasant for most people , this volume is not harmful to you or to your hearing. You will be asked to watch the computer monitor for words to appear during the entire study. This second session will last approximately 1 hour and 15 minutes.

RISKS:

There are no anticipated risks to this study. Some individuals may find the tones to be unpleasant.

POTENTIAL BENEFITS

This study is designed to acquire information that will, in the long run, lead to an

improved understanding of panic disorder. The knowledge gained from this study will be of considerable potential benefit to the scientific community, and ultimately, we hope, to patients who suffer from anxiety disorders.

CONFIDENTIALITY:

Your participation in this study will be held in strict confidentiality. Any data from this study will be used for research purposes, and your name or other data that will identify you will not be released.

VOLUNTARY NATURE OF STUDY:

You are free to participate or not participate in the study - it is entirely voluntary. Furthermore, even if you give your consent and later change your mind, that is your right. If you choose not to participate, your treatment in the clinic or participation in other studies will not be affected.

HONORARIUM:

Upon Completion of your participation in the study you will receive a $25 honorarium as a small compensation for the time required to participate in the study.

RESEARCH PERSONNEL

This study is being conducted by Derrick Larsen, M.A. under the supervision of Dr. G. R. Norton and Dr. J. Walker. If you have any questions or concerns about the study, please contact Mr. Derrick Larsen, M.A. at 237-2805.

CONSENT FORM

I, _____, have read the attached information regarding the study entitled Cognitive Processing in Anxiety Disorders and have had any questions satisfactorily answered.

I agree to participate in the study. I understand that my participation is voluntary, and that I may withdraw my consent to participate at any time, for any reason. I understand that any information derived from this study is confidential and may only be shared with the staff involved in the study. I also understand that this information will be used for research purposes, but any details that may reveal my identity will be excluded from any research papers or presentations.

I further understand that an honorarium in the amount of $25.00 will be paid to me upon completion of my participation in the study.

I am in good health and do not have any medical conditions (e.g., heart conditions) that would be adversely affected by participating in the study.

If I have any concerns or further questions about the study, I understand that I am to contact Derrick Larsen, M.A. at 237-2805.

Signature of Participant	Date
Signature of Witness	Date
Signature of Investigator	Date

Table 1

DSM-IV PRIMARY DIAGNOSTIC CRITERIA FOR PANIC DISORDER AND SOCIAL PHOBIA

Panic Disorder

A. recurrent unexpected panic attacks

B. at least one of the attacks has been followed by a month (or more) of: (a) persistent concern about having additional attacks; (b) worry about the implications of the attack or its consequences; or (c) a significant change in behaviour related to the attacks

C. the panic attacks are not due to the direct effects of a substance or a general medical condition

D. the anxiety is not better accounted for by another mental disorder

Social Phobia

A. a persistent fear of performance or social situations in which embarrassment may occur

B. exposure to social or performance situations usually provokes anxiety (sometimes in the form of a situationally bound or situationally predisposed panic attack)

C. recognition that this fear is unreasonable or excessive (adults only)

D. social or performance situations are avoided or endured with intense anxiety

E. diagnosis is only appropriate when avoidance, anxious apprehension, or fear of social or performance situations significantly interferes with the individual's life or causes marked distress

F. symptoms must persist for at least 6 months for individuals under the age of 18

G. fear or avoidance is not due to the direct effects of a substance or general medical condition and is not better accounted for by another mental disorder

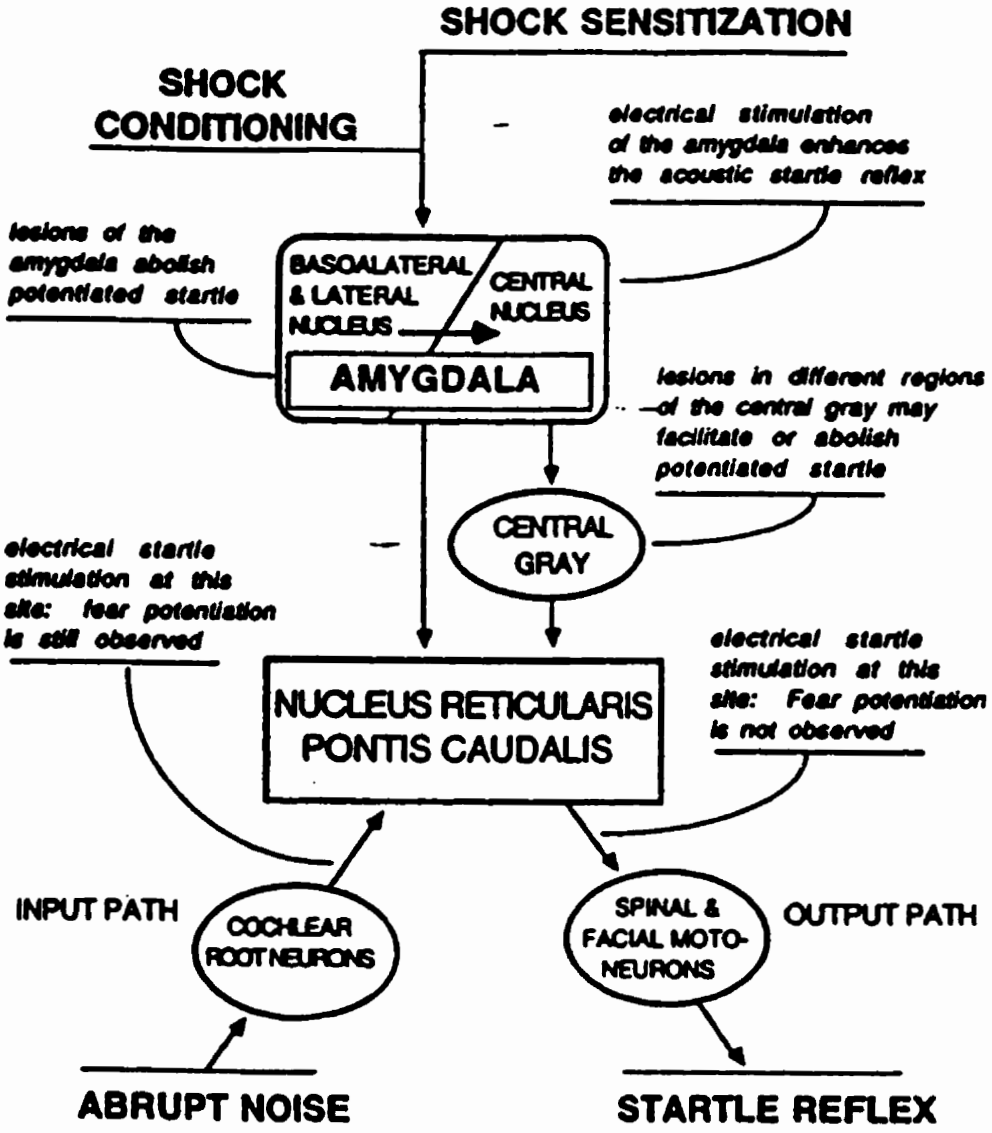
H. if a general medical condition or other mental disorder exists, the fear is unrelated to it

---

Figure Caption

Figure 1. Schematic representation of the primary neural path between a startle stimulus input and its effector output.

Schematic Representation of the Primary Neural Path Between a Startle Stimulus Input and Its Effector Output

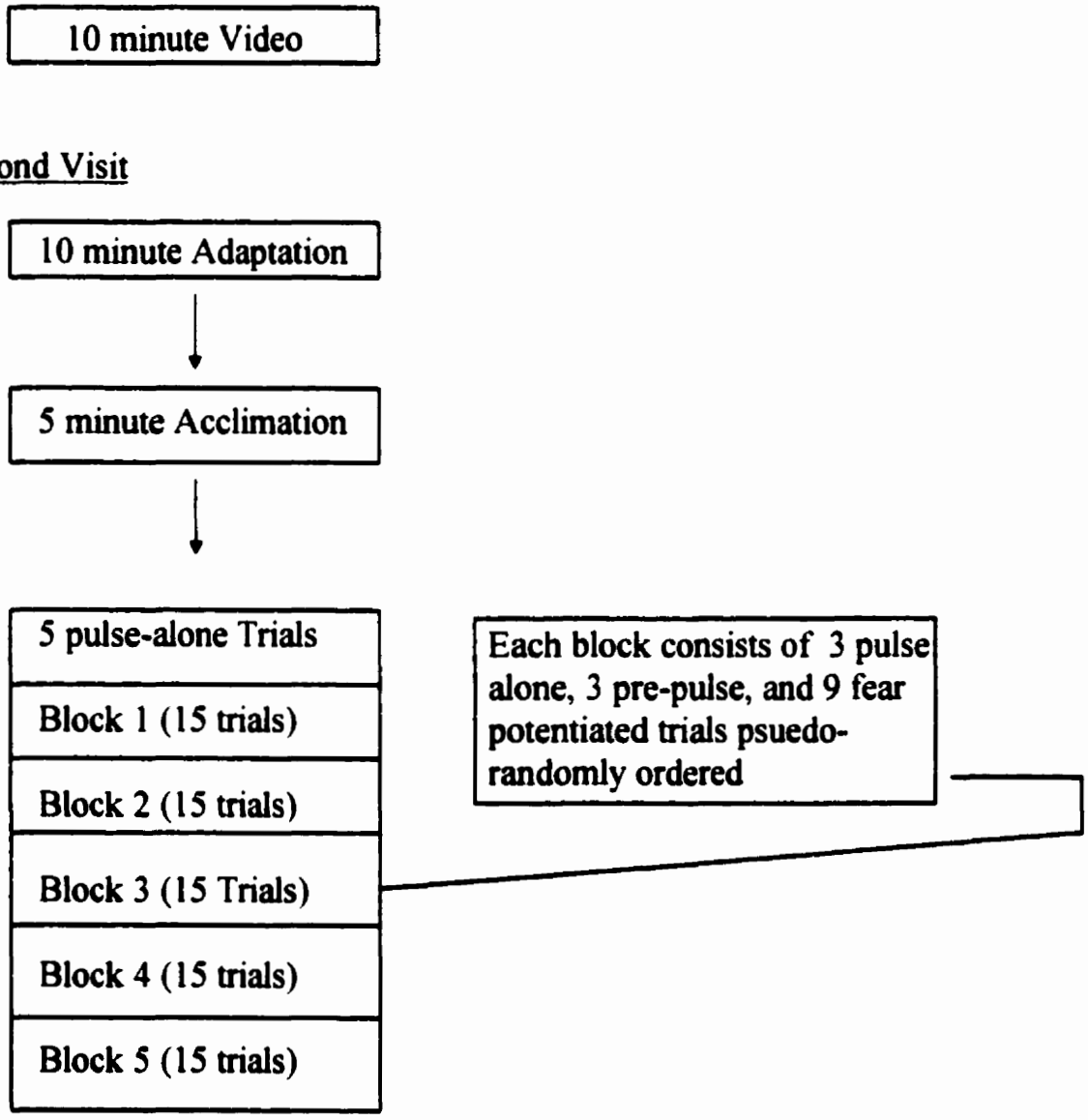


Note. From "The emotion probe: Studies of motivation and attention" by P. J. Lang, 1995, American Psychologist, 50, p.378. Copyright 1995 by the American Psychological Association. Reprinted with permission of the author.

Figure Caption

Figure 2. Schematic representation of the sequence of the procedure.

First Visit


10 minute Video
Second Visit
10 minute Adaptation
5 minute Acclimation
5 pulse-alone Trials
Block 1 (15 trials)
Block 2 (15 trials)
Block 3 (15 Trials)
Block 4 (15 trials)
Block 5 (15 trials)
Each block consists of 3 pulse alone, 3 pre-pulse, and 9 fear potentiated trials psuedo-randomly ordered