ABNORMAL EMOTIONAL REACTIVITY AMONG ALCOHOLICS: DELINEATING ANTISOCIAL PERSONALITY DISORDER

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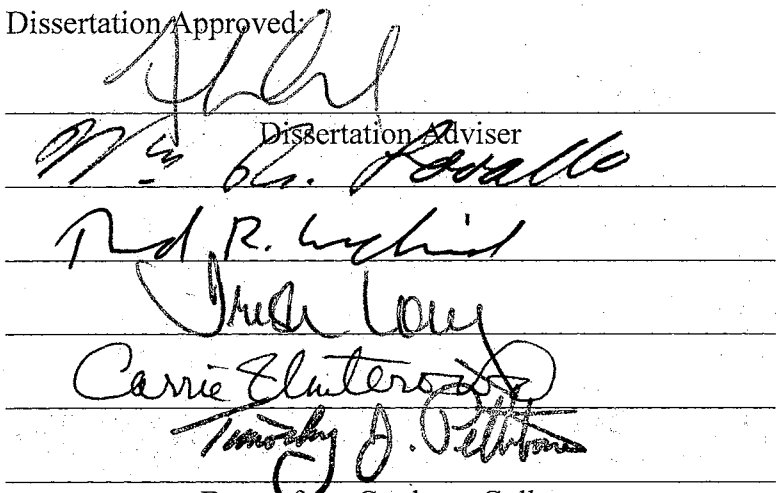

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Chapter One: OVERVIEW

Alcoholism is a longstanding societal problem. Impacting the lives of nearly 35 million Americans, alcoholism has an estimated annual cost of $148 billion dollars (Grant et al., 1994; NIH, 1998). The epidemic proportion of alcohol use disorders in the U.S. has motivated legislators to devote considerable resources toward improving our understanding of alcohol addiction. A substantive focus of recent work has been to delineate factors that confer liability for developing and sustaining maladaptive drinking behavior. Advances in affective neuroscience suggest that dysfunction in the neural circuitry that regulate emotion may be associated with alcoholism and risk for the disorder.

Despite historical debate regarding the centrality of emotion in governing behavior (Freud, 1938; Skinner, 1953), contemporary theorists agree that emotion holds an important position in determining how the brain generates and regulates behavioral responses. As a field, affective neuroscience has undergone considerable growth over the past decade and markedly advanced our understanding of addiction. Animal models have elucidated emotion-related brain sites affected by acute drug administration and identified neuropharmacological mechanisms involved in addiction (Koob & Le Moal, 2001), while human research has begun to advance our understanding of individual differences associated with phenotypic variations in alcoholism and other substance use disorders (Tarter & Vanyukov, 1994).

An emotion-based model of alcoholism holds the potential of integrating the multitude of addiction theories proposed by various disciplines (Quirk, 2001). Because brain systems that regulate emotion serve as the interface between an individual and his environment, this domain of investigation holds relevance for all contemporary theories

of maladaptive behavior. Moreover, variations in emotional responsiveness and self-regulation are shown to be at the core of individual differences in temperament and personality, both of which confer liability to addiction. Coupled with the well-established fact that the neural circuitry that governs emotion are the primary sites of action for all drugs of abuse, including alcohol, this points to the potential utility of studying emotion in relation to alcoholism.

Though existing research clearly underscores the importance of examining affective dysfunction in addiction, our present understanding of the relationship between abnormal emotional reactivity and alcohol dependence is limited. A notable limitation of previous research has been the bias toward studying alcohol dependent individuals as a homogeneous group. This approach disregards developmental research showing that alcohol dependence has a myriad of etiological pathways and maintaining factors. Remarkable convergence in the literature indicates that antisocial traits are highly comorbid with alcoholism and play an important role in the development of the disorder. From a developmental psychopathology perspective, researchers have identified a subtype of alcoholism characterized by these antisocial traits, earlier onset, and a more severe course with poorer prognosis. Moreover, electrophysiological and linguistic studies, as well as mounting brain-imaging work, have clearly identified deficient emotional reactivity among individuals who exhibit pervasive antisocial tendencies. Given the high co-occurrence of antisocial personality disorder (ASPD) and alcoholism, failure of previous studies to assess for ASPD when examining emotional reactivity among alcoholics precludes clear interpretation of existing work.

The work presented here provides a review of the existing literature implicating abnormalities in emotional regulation in alcoholism. Limitations of previous work will

be discussed and a study will be described in which emotional reactivity among alcohol dependent males was examined and the role of ASPD delineated. Findings from this study further support the need to extricate ASPD when discussing emotional dysregulation in relation to alcoholism. Implications of this work are discussed within an individual difference and interdisciplinary framework.

It is important to note that alcoholism, a term commonly used in the addiction literature, is not a diagnostic category of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*; American Psychiatric Association, 1994). Although generally used as an equivalent term for alcohol dependence, this usage is not ubiquitous. The classification system outlined in the *DSM-IV* is currently the most widely used nomenclature for psychopathology among both behavioral scientists and clinicians. Because of this, classifying maladaptive alcohol-related behavior in accordance with this system has practical utility in that it facilitates communication and the dissemination of knowledge. In the current document, the terms *alcoholic* and *alcoholism* will be used interchangeably with the *DSM-IV* diagnosis of alcohol dependence except in reviews of other work and unless otherwise specified.

Chapter Two: REVIEW OF THE LITERATURE

Emotion, Temperament, and Theories of Alcohol Addiction

Though oftentimes implied rather than specifically stated, emotion holds a central position in nearly all contemporary theories of alcoholism. Traditionally, the inclusion of emotion in addiction theory has capitalized on the ability of alcohol and other substances to modify or regulate mood states. Psychological and sociocultural theorists have emphasized the potential for alcohol to regulate affective states and have stressed the relevance of alcohol expectancies in the development of drinking motives (Goldman, Brown, & Christiansen, 1987; Gusfield, 1987; MacAndrew & Edgerton, 1969; Orcutt, 1993). Others have concentrated on the biphasic neurochemical effects of alcohol on mood during the ascending and descending limbs of intoxication (for review see Lang, Patrick, & Stritzke, 1999). Though the anxiolytic and mood setting properties of alcohol have pervaded theories of alcoholism, emerging evidence points to a broader role of emotion in addiction.

Advances in affective neuroscience suggest that dysfunction in the neural circuitry that regulates emotion may be associated with alcoholism and risk for the disorder. Emotions are conceptualized from a neuroscience perspective as a constellation of specific physiologic responses triggered by affect-laden stimuli that prompt an organism to avoid harm and approach pleasure (Damasio, 2000). These visceral responses are assumed to be set by the genome and reflect adaptive evolution (Damasio, 2000; Darwin, 1859/1964, 1872/1955). Within this framework, emotional reactivity is central to generating advantageous behavioral responses and inhibiting behavior that will lead to negative consequences (Tranel, 1994; Damasio, Tranel, & Damasio, 1990, 1991). For example, emotional responses to unpleasant stimuli (e.g., a conditioned punishment

cue) inhibit appetitive behaviors, whereas responses to pleasant stimuli facilitate appetitive behaviors.

Acquired or inherent abnormalities in the neural substrata that regulate emotional responsiveness have been shown to disable emotional signaling and impede behavioral response selection, such that maladaptive behavioral choices are consistently made (Bechara, Damasio, Damasio, 2000; Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Damasio, & Lee, 1999; Damasio, 1994; Tranel, 1994). As will be emphasized here, abnormalities in emotional reactivity have been associated with antisocial behavior and impaired decision-making, and empirical support linking emotional underresponsiveness to alcoholism has begun to accumulate. Interpretations of this literature have proposed that emotional underresponsiveness serves as a catalyst for alcohol misuse via fearlessness, self-regulatory deficits, and a myriad of uninhibited behaviors (i.e., social deviance). It follows that individuals with such alterations in temperament have difficulties learning to drink responsibly because of fundamental neurologic deficits in their ability to adaptively regulate their behavior (Finn, Kessler, & Hussong, 1994; Finn, Sharkansky, Brandt, & Turcotte, 2000).

Contemporary theorists have adopted a two-factor motivational model of emotion, wherein emotions are conceptualized as action dispositions that prime an organism to avoid harm and attain rewards. This two-factor model, derived from work on animal learning and motivation (Estes, 1969; Konorski, 1967; Mowrer, 1960), postulates that emotional reactivity activates hypothesized appetitive and aversive motivational systems of the brain. The appetitive motivational system, also known as the behavioral activation system, stimulates approach or reward seeking behavior in response to positive or pleasant conditioned stimuli. In contrast, activation of the postulated aversive

motivational system, or the behavioral inhibition system, inhibits approach behavior in the face of conditioned cues signaling punishment. Because these two systems are theorized to be mutually antagonistic, the probability and directionality of a behavioral response depends on the relative dominance of one of these systems (Fowles, 2001).

Individual differences in emotional responsiveness and activation of motivational brain systems have been associated with variations in temperament, which confer liability for psychopathology (Kendler, Neale, Kessler, Heath, & Eaves, 1992). Family prevalence, twin and adoption studies suggest that alcoholism risk includes both inherited and environmental contributions (Schukit, 1994; Tarter et al., 1999). Inherited factors include biologically rooted individual differences in behavioral tendencies and self-regulation (Thomas & Chess, 1977). As stated above, it has been postulated that such dispositions may be related to variations in affective responsivity to environmental cues and are associated with different temperamental styles (Bates, 2000; Strelau, 1983, 1994). Within this conceptual framework, alterations in affective responsiveness may impede central inhibitory processes (i.e., the behavioral inhibition system) and lead to poor behavioral control and a generally disinhibited temperament (Finn et al., 1994; Gorenstein and Newman, 1980; Gray, 1991). A variety of evidence has shown that individuals at risk for developing alcohol use disorders based on a family history of alcoholism exhibit poor impulse control, antisocial tendencies, negative affectivity, and sensation seeking (Finn et al., 1997; Sher, Walitzer, Wood, & Brent, 1991), and these, in part, mediate the relationship between a familial background and the development of alcohol use disorders (Chassin, Pitts, Delucia, & Todd, 1999; Finn et al., 2000).

Deficits in Emotional Responsiveness and Alcoholism: Empirical Findings

Studies have shown that alcohol dependent individuals have alterations in neural systems that regulate physiological responsiveness to emotionally charged stimuli. Cortisol is a stress hormone that assists in normal metabolic and cellular functions and is secreted when an individual is exposed to an aversive situation that subsequently evokes negative emotions, such as anxiety, anger, depression, and confusion (Lovallo, Pincomb, Brackett, & Wilson, 1990; al'Absi et al., 1997; Buchanan, al'Absi, & Lovallo, 1999). In recent decades, researchers have begun to measure affective modulation of cortisol secretion as an objective physiologic indicator of emotional response patterning (Lovallo, 1997). To date, several studies have examined cortisol secretion to laboratory psychological stress tasks in relation to alcohol dependence.

Lovallo and his colleagues have conducted a series of four studies in which alcohol dependent individuals showed a significantly reduced stress cortisol response relative to nonalcohol dependent controls. Across studies, participants were patients from 28-day treatment programs and were tested following 21 to 28 days of abstinence. All participants met *DSM third edition, revised* (*DSM-III-R*; American Psychiatric Association, 1987) or *DSM-IV* criteria for alcohol dependence or alcohol dependence with comorbid cocaine or amphetamine dependence. Control participants did not meet diagnostic criteria for any substance use disorder and consumed fewer than 14 drinks per week. Groups were matched for age and had normal liver enzymes at the time of participation. In addition, depressive symptomatology was measured and was within the normal range.

The first study contrasted stress endocrine responsivity of male alcohol dependent individuals relative to controls in a protocol that included 22 minutes of exposure to

mental arithmetic and a 90-second cold pressor test (Errico, Parsons, King, & Lovallo, 1993). The groups did not differ in blood cortisol levels prior to or immediately following the stressors. Results indicated, however, that 20 minutes poststress induction, controls showed a significant increase in stress endocrine response while alcoholics did not. In a set of follow-up studies, stress responses in alcohol dependent individuals and controls were investigated using urinary cortisol levels collected over the 2-hour period prior to stress induction and at the end of the protocol. The first follow-up study compared 42 male alcohol dependent individuals and 14 controls. Testing consisted of: a) resting baseline, b) mental arithmetic, and c) isometric handgrip for 5 minutes at 20% maximum grip strength (Bernardy, 1996). Prestress cortisol levels were similar in both groups, however, at posttest the alcohol group failed to show the typical cortisol response. In the second study, female participants diagnosed with alcohol dependence or alcohol and comorbid stimulant dependence ($n = 32$) and controls ($n = 16$) were tested using the same methods as outlined in the previous study, except that public speaking, in conjunction with the isometric grip task, were used for stress induction (Bernardy, King, Parsons, & Lovallo, 1996). Urine was collected three times: a) before the study, b) immediately poststress, and c) one hour later. The results paralleled those of the previous study in that cortisol levels did not differ before or immediately following stress induction. However, the final urine sample showed significantly higher cortisol levels among control participants relative to the alcohol group. It is noteworthy that among this sample of alcohol dependent women, 70% met diagnostic criteria for ASPD.

The final study published by this group to date was designed to test the aforementioned relationships with better control over the cortisol cycle (Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000). Cortisol functions on a diurnal rhythm,

reaching its apex at approximately 6:00 a.m., with an overall decrease throughout the day. Examination of the cortisol cycle allows for a more detailed analysis of an individual's stress response. To accomplish this, cortisol was measured on separate rest versus stress days in three groups of participants: 10 controls, 10 alcohol dependent individuals, and 10 alcohol-stimulant dependent individuals. On the rest day, participants sat quietly in the lab from 7:30 a.m. to 10:00 a.m. Salivary cortisol samples were taken at 8:00, 8:30, 9:00, and 10:00 a.m. in the laboratory, and 9:00 p.m. at home. On the stress day, participants were exposed to a 20-minute public speaking stressor that began at 8:30 a.m. All groups had comparable basal cortisol curves on the rest day, with a morning to evening decline of 2.0ng/mL, indicating normal diurnal cortisol regulation among alcohol dependent individuals and alcohol-stimulant abusers. Two responses measures were used, change from baseline to speech on the stress day and the difference between rest day and stress day for the 9:00 a.m. cortisol level. Control participants had significant elevations of cortisol on both measures. The alcohol group had a nonsignificant rise on the speech day but a significant elevation relative to the rest day. The alcohol-stimulant group failed to produce a significant cortisol response using either response index.

Others have observed a stress cortisol hyporesponsiveness in boys, ages 10 to 12 years, with a family history (FH+) of substance use disorders relative to family-history-negative (FH-) peers. Moss, Vanyukov, and Martin (1995) studied a sample of prepubescent sons of fathers diagnosed with a substance use disorder. The primary purpose of this study was to test for FH group differences in salivary cortisol concentrations during stressful anticipation of a medical procedure (venipuncture). Results indicated that FH+ boys showed reduced cortisol responsivity to the anticipated stressor relative to FH- boys. Differences in cortisol responsiveness were not due to

variations in subjective state anxiety. Findings of this study further indicated that the observed hyporesponsiveness among FH+ boys was associated with more impulsive and aggressive behavior.

In an extension of this work, Moss, Vanyukov, Yao, and Kirillova (1999) completed a 4-year follow-up of a subsample of these boys. Consistent with findings from the previous study, relative to FH- controls, FH+ youth exhibited decreased salivary cortisol responses to the anticipated stressor. Notably, boys identified as endocrine nonresponders in the initial study were more likely to smoke nicotine and marijuana by ages 15 to 16 (Moss et al., 1999). In addition, there was a trend toward a significant relationship between diminished prepubescent stress cortisol concentrations and regular alcohol use during adolescence ($p = .12$).

In a related program of study, others have postulated that alcohol dependent individuals have underlying deficits in their ability to differentiate the emotional quality of socially relevant information. Philipot et al. (1999) examined emotional facial expression decoding skills among 25 alcohol dependent individuals and an equal number of control volunteers matched for age, sex, and education. Facial expressions were presented along a continuum of emotional intensity: neutral, mild, moderate, or strong. Results indicated that, relative to control participants, individuals with alcohol dependence demonstrated significant deficits in their ability to recognize emotions. Specifically, alcohol dependent participants were more likely to make errors in decoding facial expressions with a special bias for anger and contempt, as well as to overestimate the intensity of emotional expressions. Interestingly, despite significant deficits in emotional detection, when queried alcohol dependent individuals reported no difficulties with the task. Kornreich et al. (2001) replicated these findings and demonstrated that the

deficits evidenced among alcohol dependent individuals were not found among patients with obsessive compulsive disorder, suggesting that deficits in emotional facial expression decoding are specific to alcohol dependence and not related to psychopathology in general. Comparison work with other psychopathological groups has not been conducted.

In similar work, Monnot, Nixon, Lovallo, and Ross (2001) hypothesized that individuals with alcohol dependence would also demonstrate deficits in their ability to comprehend affective prosody. Affective prosody is the nonlinguistic component of language that conveys information regarding emotional quality. This important aspect of communication is achieved through acoustic features such as pitch, intonation patterns, stress, timing, rhythm, and differential pausing. These authors investigated affective prosody among 32 individuals with alcohol dependence, 11 with fetal alcohol exposure, and 41 control volunteers. Results showed that the alcohol dependent group scored two standard deviations below the control mean, indicating significant impairment in their ability to distinguish affective qualities in speech. Individuals in the fetal alcohol exposure group scored five standard deviations below the control mean.

Lastly, in an elegant study involving risk for alcoholism and classical conditioning to signals for punishment, Finn et al. (1994) found that nonalcoholic FH+ males (n = 16) were deficient in their ability to discriminate between conditioned stimuli and tones that were not paired with shock relative to matched FH- controls (n = 16). Specifically, this study measured skin conductance responses to conditioned and non-conditioned stimuli during an acquisition phase and a discrimination test. Notably, underresponsiveness to the conditioned stimuli was significantly related to more alcohol-related problems. Consistent with Fowles (1987), the authors interpreted their findings as

evidence for a relationship between risk for alcoholism, altered emotional reactivity and weak behavioral inhibition system processes.

Collectively, previous work indicates a relationship between alcoholism and deficient affective responding, particularly in response to negative or aversive stimuli. Findings suggest that despite normal diurnal secretion of cortisol, alcoholics and those at genetic risk for developing the disorder have blunted-to-absent affective modulation of cortisol secretion in response to acute psychological stress tasks relative to control individuals. These findings suggest a potentially important abnormality in the responsiveness of the hypothalamic-pituitary-adrenocortical axis to unpleasant or punishing emotionally relevant stimuli (Lovallo et al., 2000). Findings from related studies provide further support for the overall hypothesis that individuals with alcohol dependence possess alterations in central nervous system processes that regulate emotional reactivity. Specifically, alcohol dependent individuals demonstrate deficits in their ability to differentiate the emotional quality of socially relevant information. Evidence from these studies may hold important clinical significance in that poor ability to decode emotional facial expressions and accurately detect emotion in the voice of others may impair social functioning and the ability to maintain healthy interpersonal relationships.

Limitations of the Previous Work

Although research has implicated altered emotion regulation in the development and maintenance of alcoholism, further exploration is needed to clarify this relationship. At the present time, our understanding of the mechanisms by which emotion impacts alcohol addiction is limited in several important ways. First, research on alcohol and emotion has primarily investigated alcohol dependent individuals as a homogeneous

group. This methodology disregards the developmental and typological research indicating that individuals with a diagnosis of alcohol dependence constitute a heterogeneous group with differing etiological pathways and maintaining factors (Tarter & Vanyukov, 1994). Existing evidence suggests that dividing this population into more discrete subtypes may provide a more intricate and informative analysis of the relationship between emotion and alcohol addiction.

One subgroup of alcohol dependent individuals, distinguishable by the presence of ASPD, has been consistently identified (Cloninger, 1987; Babor et al., 1992). This subgroup, accounting for approximately 14% of alcoholics (Reiger et al., 1990), is characterized by an earlier onset and more rapid progression to pathological drinking (Hesselbrock et al., 1984). Characteristically, individuals with ASPD engage in numerous impulsive behaviors (i.e., gambling, violence, robbery). Conceptually, these variegated topographical behaviors may be manifestations of a common underlying emotional regulatory problem. Indeed, a variety of evidence strongly indicates abnormalities in emotional responsiveness among individuals with ASPD.

A second more general limitation concerns the overall paucity of research on alcoholism and emotion, as defined within a neuroscience framework. This dearth stems largely from philosophical and methodological problems associated with the assessment of emotion. As covert experiences, emotions are not amenable to direct observation. As such, many alcohol researchers have relied primarily on subjective self-report (i.e., negative reinforcement models) and within physiologic research investigators have primarily examined responsiveness to unpleasant stimuli. As reviewed above, work examining cortisol secretion among persons with alcohol dependence have limited their study to stress-related responsivity. While increased cortisol levels are reliably

associated with induced negative mood states, this measure has several limitations. First, emotion-modulated cortisol takes considerable time and requires strict compliance on the part of the participant (e.g., diet restriction, multiple specimen collection). Second, this measure does not appear as sensitive to positive affect induction, though studies have shown diminished cortisol secretion to pleasant film clips (Buchanan et al., 1999). This limitation inhibits the attainment of an emotion response profile across valence by measuring cortisol. To obtain a more complete understanding of emotional processes and alcohol dependence, additional work using more sensitive indices of emotional responsiveness is needed.

A third limitation of existing work is the inconsistency with which diagnostic classification systems have been applied across studies. Oftentimes the taxonomy used to categorize participants is vague or absent, and when described, reliability information regarding diagnostic decisions is infrequently provided. This use of such methods has made it difficult to confidently interpret many results and hinders the ability to blend empirical findings with diagnostic nomenclature and clinical practice.

Given the aforementioned limitations, the following review will argue for the necessity of accounting for ASPD when examining emotional reactivity among alcohol dependent populations. This position is most strongly supported by considerable evidence indicating that deficient emotional responsiveness is a hallmark feature of ASPD. Empirical support for this petition will be reviewed. Studies will also be reviewed that support the utility of developing more homogeneous diagnostic taxonomies of alcohol dependence, with special emphasis placed on a subgroup of alcoholics who present with comorbid ASPD.

Antisocial Personality Disorder and Emotional Dysfunction

Studies have indicated that approximately 2.6 to 3.3% of the U.S. population meet *DSM-IV* diagnostic criteria for ASPD (Cloninger, Bayon, & Prxybeck, 1997). As with alcoholism, the disorder is more prevalent among men (3% among males, 1% among females), with young men, ages 18 to 29, demonstrating the highest prevalence of the disorder. Notably, ASPD is the predominant personality disorder among males under 30 years of age (Cloninger et al., 1997).

A diagnosis of ASPD (APA, 1994) requires the presence of severe behavioral problems during childhood, as evidence by conduct disorder (CD) before age 15. Behavior which falls under the rubric of CD includes fighting, cruelty to humans or animals, fire setting, truancy, running away from home, and persistent disregard for authority. In addition, *DSM-IV* criteria specify that individuals with ASPD must be at least 18 years of age, display a pervasive pattern of disregard for the rights of others, and their antisocial behavior cannot be limited to psychotic or manic episodes. Of particular importance here, approximately 70% of individuals diagnosed with ASPD also met diagnostic criteria for lifetime alcohol abuse or dependence (Reiger et al., 1990).

It is important to note that existing literature on individuals with antisocial traits is permeated with numerous taxonomic schemes and participant selection procedures (Arnett, 1997; Hare, Hart, & Harpur, 1991; Widiger & Corbitt, 1993). Scientific nomenclature for antisocial pathology has spanned sociopathy (Presly & Walton, 1973; Tyrer & Alexander, 1979), dyssocial personality disorder (World Health Organization, 1990), psychopathy (Cleckley, 1941; Hare, 1985, 1991), and ASPD (APA, 1994). Presently, psychopathy and ASPD are the most widely adopted classification systems by researchers and clinicians. Though analogous to *DSM second edition* criteria for ASPD

(American Psychiatric Association, 1968), psychopathy emphasizes dysfunctional personality traits (i.e., superficial charm, grandiosity, lying and manipulativeness, absence of remorse, and a lack of empathy) while down-playing the importance of impulsive and disruptive behaviors that are now emphasized in the *DSM-IV* (Harpur, Hakstian, & Hare, 1988; Harpur, Hare, & Hakstian, 1989). Despite the distinction, psychopathic traits as measured by the Psychopathy Checklist-Revised (Factor 1; Hare, 1991) and ASPD have been shown to be highly correlated among prison (r = .54) and forensic psychiatric outpatients (r = .48; Hart, Forth, & Hare's study as cited in Hare and Hart, 1995).

Most conceptualizations of ASPD place affect-related personality traits and dispositions at the core of the syndrome (Hare, 1998a) and empirical evidence has overwhelmingly supported this position. Studies of autonomic arousal have consistently shown that antisocial individuals show poor conditionability to fearful or aversive cues and have difficulty avoiding punishment in passive avoidance learning tasks (for review see Hare, 1978, 1998a; Lykken, 1995; Newman & Wallace, 1993). Within this framework, deficient electrodermal responsivity to emotion-charged cues has been the most widely studied and well-documented abnormality among psychopaths. Transitory or phasic increases in electrodermal activity (EDA) produced in response to various physical and emotional stimuli reflect activation of the sympathetic nervous system. Studies have shown that psychopaths have blunted anticipatory EDA to stimuli signaling punishment (Hare, Frazelle, & Cox, 1978; Ogloff & Wong, 1990; Tharp, Maltzman, Syndulko, & Ziskind, 1980; Ziskind, Syndulko, & Maltzman, 1978) and poor reactivity to actual punishment stimuli (i.e., aversive tone; Hare et al., 1978).

Dinn and Harris (2000) evaluated neurocognitive function and electrodermal responsivity to affectively valenced stimuli among males with ASPD (n = 12) and a control group (n = 10) matched for age, educational level, handedness and gender. Each participant completed a neuropsychological test battery including the Stroop color-word test, a visual go/no-go discrimination task and an object alternation test as measures of orbitofrontal dysfunction. They also completed a word fluency test and a divergent thinking task as measures of executive functioning. Following the test battery, each participant underwent a laboratory procedure in which electrodermal activity was recorded during presentation of 30 pleasant, neutral, and unpleasant words. Results indicated that, despite nonsignificant differences in participants' subjective evaluation of word pleasantness, individuals with ASPD were electrodermally hyporesponsive to unpleasant stimuli as compared to individuals in the control group. Results further revealed that although individuals with ASPD performed similarly on tests on executive function, they demonstrated significantly greater deficits on tests of orbitofrontal function associated with decision-making and the processing of reward and punishment. Studies have shown that the orbitofrontal and other prefrontal regions are intimately involved with emotional behavior and that lesions to these brain regions produce marked abnormalities in emotional reactivity (for review see Zald & Kim, 2001).

Other studies have found emotion-related abnormalities among psychopaths using lexical decision tasks. During these tasks, respondents are required to indicate whether a string of letters forms a word as quickly and accurately as possible. Among control participants, responses to emotionally positive and negative words are more accurate and rapid than responses to neutral words. Williamson, Harpur, and Hare (1991) showed that

psychopaths fail to show any reaction time differences between neutral and emotional words.

Brain imaging studies have also supported the position that psychopathic individuals have deficits in processing emotion-laden stimuli. Intrator et al. (1997) tested 8 male psychopathic inpatient substance abusers, 9 male nonpsychopathic inpatient substance abusers, and 9 matched controls using single photon emission computerized tomography. Relative cerebral blood flow (rCBF) was examined while participants completed a lexical decision task involving neutral and negative emotional words. Though groups did not differ in task performance, psychopathic men showed greater rCBF to the negatively charged emotion words relative to neutral, whereas nonpsychopathic individuals showed the opposite pattern. While these findings may seem counterintuitive, previous work has shown that as cognitive operations required for task performance become well-learned, the metabolic demands on task-relevant brain regions diminish (Gur et al., 1982; Gur, Roland, & Gur, 1992). As such, these findings have been interpreted as reflecting an inefficient allocation of cognitive resources toward processing emotionally relevant information among psychopaths.

Raine, Lencz, Bihrle, LaCasse, and Colletti (2000) used structural magnetic resonance imaging to examine prefrontal function among a sample of men with ASPD relative to men with a lifetime diagnosis of substance dependence, and a control group. Autonomic activity was also assessed during a social stressor task in which participants gave a videotaped speech on their faults. Findings demonstrated a significant (11%) reduction in prefrontal gray but not white matter among the antisocial participants. Notably, reduced prefrontal gray matter volume was related to reduced autonomic arousal to the social stress task ($d = 1.04$). Importantly, ASPD and substance dependent groups

did not differ in prevalence of alcohol or other substance use disorders. Groups also did not differ in age of onset of drug use, the number of times alcohol was used in the past week and month, number of drinks consumed during drinking episodes, or the largest number of drinks consumed on one occasion. These findings implicate abnormalities in brain regions that govern emotional reactivity and fear conditioning among persons with ASPD, and failed to show such deficits among non-ASPD substance dependent individuals. Though previous investigators have found decreased prefrontal gray matter volumes among substance abusers relative to controls (Liu, Matochik, Cadet, & London, 1998; Pfefferbaum, Sullivan, Mathalon, & Kim, 1997), ASPD was not assessed in these studies.

Schneider et al. (2000) used functional magnetic resonance imaging to examine cerebral regional activation using the blood-oxygenation-level-dependent contrast effect (BOLD) among individuals with ASPD and healthy controls during a differential aversive classical conditioning paradigm. Participants were 12 males who met *DSM-IV* criteria for ASPD and 12 male controls; individuals with any comorbid psychiatric condition with the exception of substance abuse were excluded from participation. Notably, the impact of substance abuse was not specifically examined in this study. The conditioning procedure utilized an unpleasant odor as the unconditioned stimulus and neutral faces as the conditioned stimuli. Each participant underwent a habituation phase to establish a baseline for BOLD, an acquisition phase to condition neutral faces with either an unpleasant or a neutral control odor, and an extinction phase. Results indicated that participants with ASPD demonstrated altered neuronal activity in the dorsolateral prefrontal cortex and amygdala relative to controls in response to the aversive conditioned stimuli. Interestingly, no differences were found between groups in

subjective verbal evaluation of the stimuli. Overall, these findings suggest a relative insensitivity of the amygdala to negatively valenced stimuli at baseline and differential conditioning effects among ASPD individuals.

Physiologic research on individuals with ASPD have also found abnormalities in basal levels of arousal. Arousal, as defined within psychophysiology, has been associated with the intensity of an affective disposition and ranges from quiescence to vigorous activation (Bradley & Lang, 2000; Stritzke, Patrick, & Lang, 1995). Researchers have generally concluded that individuals with ASPD demonstrate chronic underarousal (Chesno & Kilmann, 1975; Hare, 1978). In this arena, the majority of work has used the electroencephelogram (EEG). Studies using this method have found that individuals with ASPD show increased theta and delta (low frequency) and decreased alpha (high frequency) waves, indicating diminished arousal, relative to controls (Mednick, Volavka, Gabrielli, & Itil, 1981). In a review of the literature on ASPD and arousal, Mednick, Pollock, Volavka, and Gabrielli (1982) reported that individuals with a history of violent crime had the highest prevalence of EEG abnormalities indicative of diminished arousal. Interestingly, recidivistic offenders showed the most severe abnormalities. It has been suggested that this cortical underarousal may be associated with poor information processing and attention, thereby making ASPD individuals susceptible to misinterpretation of environmental cues and the potential aversive consequences of their behavior (Raine, Venables, & Williams, 1995). Although such an interpretation coincides with the lower educational achievement found among individuals with ASPD (Robins, Tipp, & Przybeck, 1991), investigations of the precise mechanisms by which lower EEG patterns are related to antisocial behavior have not been done.

Another physiological measure used by researchers to investigate arousal in individuals with ASPD has been heart rate. Heart rate is a useful peripheral index of an individual's affective responsiveness. Deceleration or low basal heart rate has been associated with calm/fearless stimulus processing and the orienting response, whereas acceleration and rapid basal heart rate has been associated with anxiety and the defensive response (Brownley, Hurwitz, & Schneiderman, 2000). In 1993, Raine reviewed 14 studies on noninstitutionalized conduct disordered, delinquent, and antisocial children and adolescents and consistently found that these youth showed significantly lower resting heart rate as compared to control participants (average effect size = .84). Raine concluded that lower heart rate may be a predisposition for antisocial behavior patters later in life. Importantly, these findings did not generalize when investigating incarcerated individuals in general, but were specific to those with conduct disorder.

In addition, Raine, Venables, and Williams (1990) conducted a 9-year prospective study investigating three physiological response systems among a random sample of 101 predominantly Caucasian males, which included heart rate, electrodermal arousal, and EEG measures. Findings indicated that, collectively, these physiological measures correctly classified 74.7% of the participants as either having engaged or not engaged in antisocial behavior by age 24. Specifically, results indicated that decreased heart rate and electrodermal arousal, and excessive theta EEG (slow) waves at age 14 to 16, were significantly related to antisocial behavior at the 9-year follow-up. Furthermore, each of the response systems contributed uniquely, indicating independence in the measures. Group differences in social class, academic ability, and area of residence were not found to mediate the link between underarousal and antisocial behavior. An additional 5-year follow-up of this sample revealed similar results and indicated that not only is low

arousability a risk factor for antisocial behavior, but that high arousability functions as a protective factor against aberrant acts (Raine et al., 1995).

Taken together, remarkable convergence in the literature demonstrates that antisocial individuals have distinct abnormalities in emotional responsiveness. Evidence from electrophysiological and linguistic studies, as well as mounting brain-imaging work has specifically pointed to deficient reactivity to punishing and unpleasant stimuli among individuals with ASPD. Given the high co-occurrence of ASPD and alcohol use disorders, failure to assess ASPD in studies of emotional reactivity among alcoholics precludes clear interpretation of existing work. Further support for the importance of delineating ASPD when examining affective responding among alcoholics stems from work supporting a subtype of alcoholism marked by comorbid ASPD and a distinct etiology.

Taxonomies of Alcoholism: Support for an ASPD Subtype

Over recent decades, researchers have developed numerous classification systems for better delineating the parameters of maladaptive drinking behavior. As currently reflected in the psychiatric nomenclature of the *DSM-IV*, problematic alcohol consumption is dichotomized as either alcohol abuse or alcohol dependence. Alcohol abuse is characterized by maladaptive drinking patterns as evidenced by one or more of the following: failure to fulfill one's major obligations (e.g., work-related responsibilities, family responsibilities), use in situations potentially hazardous to self or others (e.g., operating a motor vehicle), or repeated alcohol-related legal, interpersonal, or social problems (APA, 1994). Alternatively, alcohol dependence, based on the early work of Edwards and Gross (1976), is considered a more severe alcohol-related disorder and may include: a) physiological symptomatology (e.g., tolerance, withdrawal), b) uncontrollable

duration or quantity of consumption, c) unsuccessful efforts to abstain from or reduce amounts of consumption, d) a significant portion of time spent obtaining alcohol or recovering from its aversive consequences, e) reduction or termination of participation in important activities, or f) persistent use despite negative long-term effects on one's physical and/or psychological health (APA, 1994). Though the *DSM-IV* classification system has heuristic value and generated considerable research, particularly within the realm of treatment outcome, it has been criticized for discounting the heterogeneity among individuals within a given diagnostic category (Tarter & Vanyukov, 1994). As such, researchers have worked to refine the parameters of these broader diagnostic categories by identifying more precise homogenous subtypes.

Typologies of individuals with aberrant drinking behavior have existed since the mid-nineteenth century (Babor & Lauerman, 1986). Since that time, attempts at grouping maladaptive drinkers have evolved and become increasingly adherent to rigorous scientific standards. Morey, Skinner, and Blashfield (1984), using a cluster analytic design, examined 725 individuals seeking treatment for alcohol-related problems and identified three subtypes of alcoholics. This sample had an average age of 38.1 years and was composed of mostly male participants (79%). Participants' drinking history ranged from 1 to 49 years ($M = 19.8$; $SD = 9.8$) and they were primarily single (32%), separated (20%), or divorced/widowed (15%). Cluster analyses were computed using three self-report measures that assessed alcohol consumption patterns and consequences. Results revealed three subtypes of alcoholics, referred to as Type A, Type B, and Type C. The Type A subgroup was a fairly heterogeneous group that showed no acute symptoms of alcohol dependence and was identified by the authors as early-stage problem drinkers. Type B individuals were described as socially oriented and tended to drink on a daily

basis. This group was referred to as having affiliative moderate alcohol dependence. The third subtype, Type C, was characterized by severe alcohol dependence, more social isolation, binge drinking, and the most severe symptoms of alcoholism. Notably, the Type C subgroup consisted of individuals with the most aggressive and impulsive behavior of the three subtypes.

Cloninger, Bohman, and Sigvardsson (1981) and Cloninger (1987), using data from prospective adoption studies composed of 862 men and 913 women adopted between the years 1930 and 1949, examined the relationship between the clinical features of alcohol abusers and the interaction of genetic and environmental factors. The specific variables of interest included social, family, and medical problems, as well as core symptoms of alcohol dependence and loss of control of drinking behavior. Results of cross-fostering analyses revealed two subtypes of alcohol dependence. The first subgroup, referred to as Type I or milieu-limited, was characterized as beginning alcohol use relatively later in life, with a longer latency between initial alcohol exposure and alcohol dependence. Further, this subgroup demonstrated significantly more anxiety-related disorders, developed more psychological as opposed to physical dependence symptoms, and showed a lack of antisocial tendencies. Conversely, the Type II or the male-limited subtype, was characterized by an earlier onset, typically beginning in adolescence, a more rapid progression to diagnosable dependence, as well as more impulsive aggressive behavior and risk taking tendencies. Further, these individuals exhibited spontaneous alcohol-seeking behavior and were often socially disruptive when under the influence of alcohol. Notably, individuals with Type II alcohol dependence showed a stronger paternally-linked genetic influence and an overrepresentation of ASPD. Cloninger (1987) has proposed that dimensions of personality, based in

neurobiological substrates, account for the differentiation of these subtypes of alcohol dependence.

Zucker (1987, 1994) conceptualized four subtypes of alcohol dependence. This model differs from others in that it is a developmental-contextual theory concerned with the acquisition of alcohol dependence in the context of comorbid psychopathology. The first subtype, which he labeled "antisocial alcoholism," was described as having a genetic diathesis that is manifested in an earlier onset of the disorder and a poor prognosis. As indicated by its name, individuals with this subtype exhibited a pervasive antisocial behavioral pattern consistent with *DSM-IV* diagnostic criteria for ASPD. The second subtype, referred to as "developmentally cumulative alcoholism," stems from a culturally induced drinking pattern that culminates in alcohol dependence. Within this subtype, alcohol dependence precedes the onset of other psychiatric conditions, making them secondary to the alcohol-related disorder. In the third subtype, "negative-affect alcoholism," alcohol use primarily functions as regulatory behavior for stabilizing mood and enhancing social relationships. Finally, the fourth subtype within Zucker's classification scheme was "developmentally limited alcoholism." This subtype was characterized by frequent heavy drinking during young adulthood, which decreased to limited social drinking as the responsibilities of adulthood set-in.

More recently Babor et al. (1992), working within a biopsychosocial framework, proposed that differentiation among alcohol dependent individuals required a comprehensive analysis of the complex interaction among genetic, biological, psychological, and sociocultural factors. From this perspective, an extensive battery of self-report questionnaires, interviews, and laboratory tests was administered to 321 male (n = 228) and female (n = 85) inpatients receiving treatment for alcohol dependence. The

majority of the sample was Caucasian, with 16% African-American and most (69%) were single, divorced or separated. Ninety-six percent of the sample met *DSM-IV* criteria for alcohol dependence, with the remaining 4% meeting criteria for alcohol abuse. To differentiate subtypes of alcoholics, 17 variables were chosen based on their theoretical importance for assessing premorbid risk factors, pathological use of alcohol and other substances, chronicity and consequences of drinking, and psychiatric symptoms. These variables were assessed and subsequently analyzed using cluster analysis. Results revealed two alcohol dependent subtypes, designated Type A and Type B. The Type A subgroup was characterized by later onset, fewer childhood risk factors (e.g., conduct disorder, hyperactivity), less severe dependence, fewer alcohol-related physical and social consequences, less psychopathology, and less impairment in social and occupational functioning. The Type B subgroup was distinguished by the presence of childhood and familial risk factors (e.g., family history of alcoholism), early onset of the disorder and more severe dependence, fewer years of drinking, polysubstance abuse, more negative consequences of drinking, and comorbid psychiatric conditions. Further, individuals within this subgroup reported more experimentation with substances other than alcohol, less control over their drinking behavior, and greater levels of childhood aggression. The Type B individuals tended to be younger, though they had more extensive treatment histories. These individuals also showed an overrepresentation of ASPD.

The investigators followed this sample for 1 year and found greater alcohol consumption and symptoms of pathological drinking, and a higher degree of alcohol-related social and occupational problems among the Type B subgroup relative to Type A. Further, 64% of males in the Type B cluster relapsed and were further treated for alcohol-

related problems, in comparison to 45% of Type A males. Finally, a 3-year follow-up revealed similar results, with the only exception being that no differences were found in daily consumption of alcohol between the subtypes. The authors concluded that the Type B subgroup identified in this study, overlapped significantly with Cloninger et al.'s (1981) Type II alcoholic with regard to early onset of the disorder and the presence of strong antisocial personality traits.

The typological literature reviewed here, which has outlined the most well-cited and rigorous attempts at delineating more homogenous subgroups of alcoholics, demonstrates that conceptualizing alcohol dependence as a unitary disorder is an anachronistic view that has likely impeded scientific advancement. Further, as evidenced in this review, existing taxonomies of alcohol dependence vary in their basic subtypes. These inconsistencies may stem from differences in the theoretical foundations from which they were derived, as well as the methods used for subtype delineation (i.e., sampling biases, statistical analyses). Despite discordant subtyping among classification systems, and in spite of critics who claim that nomothetic research cannot accurately reflect the idiosyncratic nature of pathological behavior, the reliable emergence of the alcohol dependent individual who persistently engages in disinhibited and often antisocial behavior across typological systems, supports the need for research to further study this subtype. This conclusion is consistent with the well-documented observation that antisociality has the greatest symptomatic covariation with severity of alcohol dependence (Helzer, Burnam, & McEvoy, 1991; Zucker, 1994).

Summary of Previous Work

Mounting evidence suggests that dysfunction in the neural circuitry that regulates emotion may be associated with alcoholism and risk for the disorder. Specifically, a

variety of studies has found that alcoholics and those at genetic risk for developing the disorder have blunted-to-absent affective responsiveness to negative or aversive stimuli. Though this work has generated intriguing findings, failure to delineate ASPD among studied samples has significantly precluded a clear understanding of the relationship between emotion and alcoholism. A substantial body of literature, using a variety of subjective, physiologic, and neuroimaging techniques, has consistently shown individuals with ASPD to have abnormal responsiveness to affectively negative stimuli. The significant presentation of comorbid ASPD and alcohol use disorders highlights the need for investigators to use experimental designs that examine the relative contribution of each disorder to abnormal emotional functioning among alcoholics. In addition, little attention has focused on reactivity to positive emotional cues among persons either with alcoholism or ASPD. This omission is especially noteworthy given the widely theorized importance of appetitive motivational systems and conditioned incentive stimuli (i.e., drug cues) in the maintenance of substance use disorders (Fowles, 2001). To obtain a more complete understanding of emotional processes in alcohol dependence, additional work using more sensitive indices of emotional responsiveness across the spectrum of affective valence is needed.

The Present Study: Application of the Emotion-Modulated Startle Paradigm

Previous work suggests the desirability of studying other central nervous system mechanisms related to putatively altered emotion regulation among alcohol dependent individuals and highlights the necessity of delineating the influence of ASPD. The emotion-modulated startle paradigm may be useful for this purpose. One component of the human startle response is the reflexive eye blink. The eye blink component of startle is controlled by reflexive contraction of the muscle *orbicularis oculi*. According to the

two-factor model of emotion, wherein emotions are conceptualized as action dispositions that prime an organism to avoid harm and attain rewards, modulation of the startle response is postulated to vary as a function of activated motivational systems of the brain. Activation of the behavioral inhibition system prepares an organism to respond defensively and as such, protective reflex responses to aversive stimuli are potentiated. Alternatively, when the behavioral activation system is primed and dominant, an organism is prepared to respond appetitively, and reflexive responses to aversive stimuli are attenuated (Bradley & Lang, 2000).

Consistent with this formulation, contractions of the eye blink startle reflex are enhanced by unpleasant stimuli and diminished by pleasant ones (Bradley & Lang, 2000). Startle responses to auditory probes are increased by presenting an aversive conditioned stimulus (Brown, Kalish, & Farber, 1951), viewing emotionally negative photographs and film clips (Jansen & Frijda, 1994; Lang, Bradley, & Cuthbert, 1990), and imagining emotionally negative scenes (Witvliet & Vrana, 1995). Positive pictures have been consistently shown to reduce startle magnitudes (Bradley, Cuthbert, & Lang, 1991a; Cuthbert, Bradley, & Lang, 1996). The startle reflex can be similarly elicited by acoustic, cutaneous, and photic stimulation (Landis & Hunt, 1939).

Notably, both the stress cortisol response and the eye blink startle reflex represent peripheral measures of amygdaloid functioning in relation to emotional behavior. The relationships among the amygdala, the orbital and prefrontal cortexes, the nucleus accumbens, septal nucleus, and the hypothalamus and brainstem are critically involved in different facets of emotional experience. Emotion modulation of startle is known to be controlled by inputs of the central nucleus of the amygdala (Davis, 1992). Amygdala lesions block the acquisition or expression of this reflex (Davis, 1992) and a unique

patient with amygdala lesions failed to show startle enhancement to unpleasant stimuli (Angrilli et al., 1996). Cortisol secretion in response to stressful stimuli is also under the positive control of the amygdala and amygdaloid lesions have been shown to abolish the cortisol response to emotionally distressing stimuli (Kapp, Whalen, Supple, & Pascoe, 1992). Given the common underlying neurophysioloigcal associations between stress cortisol release and the startle eye blink reflex, these measurable peripheral responses similarly serve as parallel neurophysiological indicators of emotional regulation.

Individual differences in emotion-modulated startle have been reported. Incarcerated male psychopaths (54 sex offenders) failed to show the typical potentiated startle reflex while viewing unpleasant picture stimuli and instead showed diminished startle reactivity to both pleasant and unpleasant pictures relative to neutral photographs (Patrick, Bradley, & Lang, 1993). Though this study was an important step for better understanding emotional behavior among psychopaths, it did not delineate the influence of comorbid substance use disorders. Phobic individuals, relative to nonphobic controls, have shown exaggerated startle responses while viewing pictures of phobia-specific stimuli (Hamm, Cuthbert, Globish, & Vaitl, 1997). Limited data has also suggested that persons with severe depression lack the expected diminution and instead show potentiation in the startle reflex during pleasantly valenced slides (Allen, Trinder, & Brennan, 1999). Collectively, these findings suggest that affective modulation of startle is sensitive to psychological dispositions and a useful tool for objectively comparing emotional processing across individuals and diagnostic groups (Cook, 1999).

Miranda, Meyerson, Buchanan, and Lovallo (2002) used the emotion-modulated startle paradigm to test the hypothesis that young adults with a positive paternal history of alcoholism (FH+), relative to family-history-negative controls (FH-), have altered

emotional reactivity to environmental cues. Thirty FH+ and 30 FH-, with 15 males and 15 females in each group, were tested. Participants completed self-report instruments and interviews and had eye blink electromyograms (EMG) measured to acoustic startle probes while viewing color photographs rated as affectively pleasant, neutral, and unpleasant. FH- had the expected linear increase in startle magnitude, with eye blink EMG gaining in strength from pleasant to neutral to unpleasant slides. In contrast, FH+ did not show EMG potentiation to the unpleasant slides and therefore lacked the same linear trend. Notably, FH groups rated the emotional valence and arousal of the photographs in similar ways. Self-reported negative affect partly accounted for the lack of startle potentiation in FH+, suggesting that startle modulation differences between the groups may be associated with underlying psychological characteristics. These findings implicate altered limbic outputs to the startle pathway in FH+ despite normal conscious evaluation of emotional arousal and pleasantness of the slides. This study further suggests that the emotion-modulated startle paradigm may provide a useful method for evaluating processing of emotionally relevant stimuli in relation to alcohol use disorders.

The present study compared three groups on affective modulation of startle across pleasant, neutral, and unpleasant color photographs. This measure was chosen because it is non-invasive, well-characterized in human and animal models, and has an established neurophysiological basis. Specifically, the current study compared a) alcohol dependent individuals, b) alcohol dependent individuals with comorbid ASPD, and c) a non-alcohol dependent, non-ASPD control group of social drinkers. This investigation allowed for a systematic delineation of a subgroup of alcohol dependent individuals with ASPD.

It was hypothesized that abnormal emotion priming of the startle reflex would be sensitive to antisocial differences between the groups. Specifically, alcohol dependent

individuals with ASPD were hypothesized to show greater abnormalities in affective modulation of startle relative to the two non-antisocial groups. It was hypothesized that, in contrast to alcohol dependent individuals and controls, men with ASPD would not show a significant reflex potentiation to unpleasant picture stimuli relative to neutral pictures. Because neurobiologic anomalies associated with ASPD are not specific to fear and anxiety, it was hypothesized that individuals with ASPD would also lack a significant reflex diminution to pleasant picture stimuli relative to neutral pictures. Exploratory analyses were also conducted to examine the importance of several potentially relevant variables on group differences in affective modulation of startle. Specifically, the influence of age of onset of regular alcohol use was examined because many alcoholics begin drinking in early adolescence, a neurodevelopmental period in which prominent brain transformations involving the prefrontal cortex and other emotion-related limbic brain regions and dopamine projections are taking place (Spear, 2000). The introduction of ethanol, a potent neurotoxin, during this critical neurodevelopmental period could cause notable alterations in brain regions that subserve emotional reactivity. Additionally, because previous studies have suggested the importance of psychopathy (Patrick et al., 1993), and family history of substance use disorders and subclinical depressive and anxious symptoms (Miranda, Meyerson, Buchanan et al., 2002) on startle, these variables were also examined.

Chapter Three: METHODS

Design

The primary study design included one between-subjects factor (Group) and one within-subjects factor (Valence), with eye blink electromyographic (EMG) responses as the principle dependent measure. The study was confined to males for the following reasons: a) established gender differences in emotion modulated startle have been documented (Bradley & Lang, 2000), b) the potential necessity to control for phase of menstrual cycle when conducting psychophysiological research, and c) research indicating that males and females at genetic risk for developing alcoholism have marked differences in emotional reactivity (Miranda, Meyerson, Buchanan, et al., 2002). Because of expected gender differences on the dependent measures in the present study, collapsing gender within diagnostic groups would have considerably threatened internal validity thereby placing significant limitations on the interpretation of results. A power analysis conducted in accordance with Cohen (1988) indicated that to sufficiently examine gender as a factor within the current study (3 Group × 2 Gender × 3 Valence), with a power of .80 at an alpha level of .05 and an estimated medium effect size (f = .27; Miranda, Meyerson, Buchanan, et al., 2002), 39 completers of each gender in each group for a final sample size of 195 would have been needed. Cohen's f was used for the effect size estimate as it is appropriate for analyses of variance (Cohen, 1988). Given the approximate 4:1 recruitment ratio of screened versus included individuals in the current study, an estimated 780 volunteers would have needed to be screened. Such an endeavor was beyond the resources available for present study. Given that ASPD is significantly more prevalent among males across all samples studied, this investigation examined males only.

Participants

Sixty-two adult males, 18 to 39 years of age ($M = 26.3$, $SD = 6.1$), were selected from a larger sample recruited from the greater Oklahoma City area ($n = 200$). The sample included Caucasian (89%), African American (10%), and Hispanic individuals (1%). Participants were administered structured clinical interviews based on the *DSM-IV* and categorized into the following groups: a) alcohol dependent (AD; $n = 24$), b) alcohol dependent with comorbid antisocial personality disorder (AD-ASPD; $n = 17$), or c) social drinkers with no lifetime or current substance use disorder, conduct disorder, or antisocial personality disorder ($n = 21$). Social drinking was defined as having a history of alcohol use with no current or lifetime symptoms of alcohol abuse or dependence (Zuckerman, 1999). Interviews were administered by two clinical psychology doctoral students who received systematized training in diagnostic assessment (adapted from Ventura, Liberman, Green, Shaner, & Mintz, 1998). Administration of the structured clinical interviews was audiotaped with each participant's consent. To determine the reliability of diagnostic decisions, a randomly chosen subset of taped interviews (20%) was re-rated by the second interviewer. All diagnostic decisions were based on the in-vivo interview. Interrater reliabilities (kappa) were good to excellent for all diagnostic decisions (see below).

To be eligible for this study, participants were in overall good health (i.e., body weight $\pm$ 20% of ideal by Metropolitan Life Insurance Company norms, no current or chronic medical conditions), reported no history of traumatic brain injury or hearing difficulties, and were not taking CNS acting medication for at least 30 days prior to participation. To be included, participants were literate in the English language and had at least a ninth grade education. All reported specific knowledge that their mother was

abstinent from alcohol during pregnancy. Because reflexive reactivity diminishes as a function of age, participation was restricted to individuals 18 to 39 years old. Exclusion criteria included *current or lifetime* bipolar I or II disorder, agoraphobia, a psychotic disorder, posttraumatic stress disorder, panic disorder, obsessive compulsive disorder, and eating disorders. Individuals were also excluded if they met *current* criteria for a mood disorder, generalized anxiety disorder, or an active substance use disorder. The exclusion of persons with the aforementioned psychiatric conditions was based on evidence of abnormal startle reactivity among individuals with certain psychopathologies and served to increase internal validity (Grillon & Morgan, 1999; Grillon, Morgan, Davis & Southwick, 1998; Cook, Hawk, Davis, & Stevenson, 1991; Vanman, Dawson, & Brennan, 1998). Other than group specific diagnostic criteria (ASPD, alcohol dependence), there were no significant differences in current psychopathology between groups. Tables 1 and 2 present *DSM-IV* Axis I and II diagnoses for participants across groups.

Participants in both alcohol dependent groups were required to have abstained from alcohol and all other substances for the 30-day period prior to the laboratory session. This timeframe was chosen because the physiological effects of persistent maladaptive drinking, as well as withdrawal symptoms, are largely dissipated after a 4-week period of abstinence (Goldman, 1987). A history of other lifetime substance use disorders was permitted among alcohol dependent groups. While the inclusion of these additional lifetime substance use disorders may have reduced internal validity, the decision to include such pathology stemmed from concerns regarding the generalizability of findings and the feasibility of recruiting an adequate sample size. As stated above, control group participants could not meet current or lifetime *DSM-IV* criteria for any

substance use disorder. Table 3 presents data on lifetime substance use disorders across alcohol dependent groups. Chi-square statistics indicated that the AD-ASPD group had significantly more sedative, cannabis, and hallucinogen use disorders in comparison to the alcohol dependent group.

To be included, participants were also required to test negative for blood alcohol level using an Alco-Sensor III Breathalyzer (Intoximeters, St. Louis, MO) and provide a negative urine toxicology screen for the following substances: alcohol (< 50 mg/dl), amphetamines (< 1000 ng/ml), barbiturates (< 200 ng/ml), benzodiazepines (< 200 ng/ml), cocaine (< 300 ng/ml), cannabis (< 50 ng/ml), and opiates (< 2000 ng/ml). Urine specimens were collected on the day of participation and toxicology tests were performed by the Clinical Laboratories of the Veterans Affairs Medical Center in Oklahoma City.

Antisocial behavior was assessed using the Structured Clinical Interview for Axis II Disorders (SCID-II; First, Gibbon, Spitzer, Williams, & Benjamin, 1997). ASPD was diagnosed when the respondent met full *DSM-IV* criteria for lifetime conduct disorder (3 of 15 conduct problems identified) with onset before age 15 *and* endorsed at least 3 criteria for ASPD occurring after age 15. Based on recent work (Brown, Gleghorn, Schuckit, Myers, & Mott, 1996; Myers, Stewart, & Brown, 1998), delinquent and antisocial behaviors that were secondary to involvement with alcohol or other drugs were not included as diagnostic markers for either conduct disorder or ASPD. That is, conduct problems and antisocial behaviors that occurred exclusively during substance-induced intoxication or in an effort to obtain alcohol or other drugs were not sufficient for a diagnosis of either conduct disorder or ASPD. Though a departure from the *DSM-IV*, this primary and secondary diagnostic distinction with respect to conduct disorder, ASPD, and substance misuse has shown to be intimately related to distinct etiological pathways,

as well as differential clinical course and prognosis (Brown et al., 1996; Myers et al., 1998; Schuckit, 1985). Men in the non-ASPD groups could not meet current or lifetime diagnostic criteria for conduct disorder. To determine the reliability of diagnostic decisions for ASPD, audiotaped interviews for *all* participants were re-rated by the second interviewer. Interrater reliability (kappa) was excellent for ASPD diagnostic decisions (1.0).

All volunteers signed an informed consent form approved by the Institutional Review Boards of the University of Oklahoma Health Sciences Center, the Veterans Affairs Medical Center, and Oklahoma State University.

Procedure

Recruitment. Figure 1 shows the development of the final sample. Brochures describing the study were distributed throughout the Oklahoma City area at recreational centers, vocational schools, therapeutic residential communities and support groups for individuals with substance abuse problems, local businesses, and police and fire departments. Interested volunteers underwent a brief screening interview. Those who reported a history of symptoms suggestive of alcohol dependence and denied alcohol or other substance use within the past 30 days, and did not endorse any of the exclusionary criteria were tentatively classified as alcohol dependent. Those reporting no alcohol or other substance-related problems or a family history of substance use disorders, and did not endorse any of the exclusionary criteria were tentatively classified as controls. Screened participants who endorsed any exclusionary criteria were not further considered (see Table 4).

Of the tentatively classified individuals ($n = 95$), 84% were contacted and invited to participate in the laboratory study; the remaining 16% were lost to incontactability

following the initial screening interview (e.g., change of residence). Of those contacted and invited to participate, approximately 85% (n = 68) agreed and attended the laboratory session and 13% (n = 10) agreed, but repeatedly cancelled or failed to attend their scheduled appointment. Two men were unable to participate in the laboratory session due to involvement with the legal system.

In the laboratory session, six additional individuals were excluded due to either equipment failure (n = 2), an insufficient number of useable EMG responses (n = 1), exclusionary *DSM-IV* Axis I disorders (n = 2; i.e., psychotic disorder, bipolar I disorder), or a positive urine toxicology screen for cannabis (n = 1). Potential subjects were screened until the final sample of 62 was obtained. Individuals included in the final sample did not differ in age from the overall screening sample, $t(198) = .37, p = .71$. To test for differences in ethnic composition between the final and screening samples, chi-square analyses were used. Because the minimum expected cell count when all ethnic backgrounds were included was 1.24, and four cells (40%) had expected counts less than 5, analysis of ethnicity was limited to Caucasian, African American, and Hispanic participants and no significant difference between groups was found, $\chi^2(2, 186) = 5.14$.

Laboratory protocol. Participants arrived at the laboratory at approximately 9:00 a.m. and completed a 6.5-hour protocol. All participants were provided a meal, as well as unlimited caffeine-free beverages and snacks, and breaks from the study were taken as needed. Each participant was apprised of the procedures, provided written informed consent, and tested negative for blood alcohol using an Alco-Sensor III Breathalyzer (Intoximeters, St. Louis, MO). Urine specimens were collected for toxicology analysis. For the purposes of this study, participants underwent semistructured clinical interviews for current and lifetime psychopathology, family history of substance use disorders,

completed a self-report measure of his current affective state, and completed the emotion-modulated startle procedure. To standardize the influence of nicotine withdrawal on physiological data, all smokers had a cigarette approximately 60 minutes prior to the startle procedure. Upon completion of the protocol participants were debriefed and compensated with 50 U.S. dollars for participation. Transportation to and from the laboratory was provided.

Domains of Assessment and Measures

Psychopathology. The Structured Clinical Interview for *DSM-IV*-Research Version (SCID-I; First, Gibbon, Spitzer & Williams, 1996) was used in this study to assess and diagnose psychiatric disorders. Specifically, this measure was used to determine study group assignment and assess for exclusionary psychiatric conditions. The SCID-I is a widely used clinician-administered semistructured interview designed to assess for the presence of current and lifetime *DSM-IV* Axis I disorders. The measure consists of 10 modules and covers each of the diagnostic categories outlined in the *DSM-IV*. Empirical investigations of earlier versions of the SCID-I have revealed that the measure has good test-retest reliability (Segal, Hersen, & Van Hasselt, 1994; Strakowski, Keck, McElroy, Lonczak, & West, 1995). In the present study, interrater reliability (kappa) of Axis I diagnostic decisions was high for both current (M = 1.0) and lifetime disorders (M = .96, range = .70 - 1.0).

The SCID-II is a 140-item clinician-administered semistructured interview that assesses for personality disorders, and was used in this study to categorize participants into the appropriate study group. Items are arranged by diagnosis and assess for all personality disorders described in the *DSM-IV*. In accordance with standard protocol (First et al., 1996), administration of this measure was preceded by a self-report screening

questionnaire that guided the interview. Endorsed items on the screening instrument identify symptoms that warrant further query by the interviewer. Data from the self-report screening form were not included in any of the statistical analyses. Results from the clinical interview provide categorical diagnostic information. A number of empirical investigations have demonstrated good interrater reliability (Maffei et al., 1997), test-retest reliability (Marlow, West, Williams, & Sutker, 1989; Williams et al., 1992), and adequate validity (Hueston, Mainous, & Schilling, 1996) for the current version and its predecessors. In the present study, the interrater reliability (kappa) of Axis II diagnostic decisions was excellent (M = .98, range = .76 - 1.0).

In addition to the categorical data obtained using the SCID-I, continuous measures of subthreshold depressive and anxious symptoms were obtained using the Beck Depression and Anxiety Inventories. These measures were used to evaluate group differences in subthreshold psychiatric symptomatology. The Beck Depression Inventory- II (BDI-II; Beck, Steer, & Brown, 1996) is a 21-item multiple-choice self-report questionnaire for measuring the severity of depression. Items on the BDI are summed to provide a continuous measure of depressive symptoms, with higher scores reflecting greater levels of depression. The BDI has good validity and reliability; test-retest correlation over a one-week time period for a sample of outpatients was strong (.93; Beck et al., 1996).

The Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) is a 21-item self-report instrument used to assess severity of anxiety in respondents. The BAI has high internal consistency (α = .92) and good one week test-retest reliability (r = .75). Items are summed, with higher scores indicating greater levels of anxiety. This measure

has been shown to correlate moderately with the revised Hamilton Anxiety Rating Scale (r = .51; Beck et al., 1988).

Family history of substance use disorders. The Family History-Research Diagnostic Criteria (FH-RDC; Endicott, Andreasen, & Spitzer, 1978) for alcohol and other substance use disorders was used in this study to compare groups and evaluate the impact of familial substance use disorders on affective modulation of the startle reflex. Previous work has indicated that nonalcoholic offspring of alcohol dependent fathers have altered affective modulation of the startle reflex (Miranda, Meyerson, Buchanan, et al., 2002). The FH-RDC was administered in an interview format by a trained diagnostician. In this assessment, participants provided information regarding substance use disorders in their biological father and mother, as well as paternal and maternal grandparents. Family history (FH) status for each relative was assigned according to the guidelines of the FH-RDC manual (Endicott et al., 1978). Relatives were considered FH+ if they were reported to have problems with alcohol or drugs, not limited to isolated incidents, and which spanned one or more domains of alcohol or drug-related impairment including: marital or family difficulties, health complications, work or legal problems, poor social relations, or substance abuse treatment. The FH–RDC for alcoholism has good interrater reliability (.95; Zimmerman, Coryell, Pfohl, & Stangl, 1988) and is sensitive (.57) and specific (.96) when offspring are the informants (Thompson, Orvaschel, Prusoff, & Kidd, 1982). FH-RDC for drug abuse also has good interrater reliability (.88; Zimmerman et al., 1988) and is highly specific when offspring are the informants (1.0; Thompson et al., 1982).

For the purpose of this study, a percentage score was calculated to reflect the family density of substance use disorders for each participant. Consistent with previous

behavioral genetic research (Moss et al., 1995), a composite measure of FH status for substance use disorders that included both alcohol and drug misuse was used. This scoring method provided a continuous measure of FH density that was used in the analyses. In cases where participants reported inadequate knowledge of a specific relative, FH status for that relative was coded as negative. This approach resulted in a conservative estimate of the density of familial substance use disorders.

Cognitive and personality measures. The Shipley Institutes of Living Scale (SILS; Shipley, 1940) is a 60-item measure designed to assess general cognitive ability. This instrument is composed of two subtests, a vocabulary scale and an abstract reasoning/problem solving scale, and was used in the present study to compare groups on intellectual functioning. Age and education corrected *T*-scores for each subtest and overall performance are provided. The SILS has been widely used among populations with alcohol and other substance use disorders (e.g., Easton & Bauer, 1997; Stevens, Kaplan, & Bauer 2001; Nixon, Parsons, Schaeffer, & Hale, 1995) and normative data has been obtained for the mid-western region of the U.S.

Because previous work has suggested that psychopathy is associated with abnormal emotion-modulation of the startle reflex (Patrick et al., 1993), this construct was assessed in the current study using the Psychopathic Personality Inventory (PPI; Lilienfeld & Andrews, 1996). Higher PPI scores indicate greater psychopathic personality traits. The PPI has good internal consistencies (.90 to .93) and high test-retest reliability (.95; Lilienfeld & Andrews, 1996). Overall PPI scores are moderately to highly correlated with Factor 1 (r = .54), Factor 2 (r = .40), and total scores (r = .54) on Hare's (1991) Psychopathy Checklist-R (Poythress, Edens, & Lilienfeld, 1998). In

addition, the PPI has been shown to predict indices of aggressive behavior (Edens, Poythress, & Lilienfeld, 1999).

Alcohol and other substance use. The Cahalan Drinking Habits Questionnaire (DHQ; Cahalan, Cisin, & Crossley, 1969), formerly referred to as the Drinking Practices Questionnaire, is a 13-item measure that was used to determine levels of alcohol consumption. Using the DHQ, participants estimate how often they consume wine, beer, and/or liquor (frequency), as well as how many drinks of each are consumed during a typical drinking episode (quantity). From this information, the number of standard drinks consumed during a typical month may be calculated by multiplying the quantity by the frequency. In the current study, this instrument was clinician-administered and used to assess the number standard drinks consumed during: a) the past 30 day period and b) during a typical month when the respondent was drinking the heaviest. This measure was used in the current study to quantify and compare levels of alcohol consumption across groups.

The Fagerstrom Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) is a 6-item self-report instrument designed to assess nicotine dependence. This measure was used in the current study to assess for the severity of nicotine dependence and compare across groups. The FTND has demonstrated good test-retest reliability (r = .88; Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994) and validity (Heatherton et al., 1991; Pomerleau et al., 1994). Scoring for this measure is on a continuous scale from 0 to 10, with higher scores indicating more severe nicotine dependence. Higher scores on this measure have been shown to be related to carbon monoxide levels in breath samples and levels of cotinine in

salivary samples (Heatherton et al., 1991), as well as the number of years of smoking (Pomerleau et al., 1994).

Subjective affective ratings. To assess positive and negative affect immediately prior to the startle modulation procedure, participants completed the 20-item self-report Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). The PANAS contains two 10-item scales. The Positive Affect scale reflects enthusiasm, alertness, and full concentration. The Negative Affect scale measures general distress and negative mood states, including anger, contempt, disgust, fear, and nervousness. For both scales, higher score reflect more prominent mood states. The PANAS has demonstrated high internal consistency and 2-month test-retest reliability (Watson et al., 1988).

Using a paper and pencil version of the Self-Assessment Manikin (SAM; Lang, 1980), each participant rated his subjective experience of valence (pleasantness) and arousal to each of the slides. This measure was used to confirm the intended manipulation of the valence and arousal dimensions of emotion for each slide. This method is standard procedure when using the emotion-modulated startle technique (e.g., Patrick et al., 1993; Stritzke et al., 1995).

Demographic, employment and legal history, and substance abuse treatment. The Addiction Severity Index (ASI; McLellan et al., 1992) is a semistructured clinical interview that provides a comprehensive assessment across multiple domains of functioning. This instrument was used in the current study to gather general demographic information, as well as each participant's education and employment history. In addition, the ASI was used to obtain a detailed history of each participant's legal involvement, including previous arrests and charges, as well as the extent of previous alcohol abuse

treatment. The ASI has demonstrated good internal consistency and interrater reliability (e.g., Alterman, Brown, Zaballero, & McKay, 1994; Kosten, Rounsaville, & Kleber, 1983; McLellan et al., 1985). Notably, this instrument is a reliable measure of lifetime substance abuse and criminal behavior (Cacciola, Koppenhaver, McKay, & Alterman, 1999).

Startle modulation procedure. Participants were seated in a comfortable chair 1.5 m from a 19-inch color television, electrodes were attached, signal quality was checked, and they completed the subjective measure of state affect. Participants then viewed 60 color photographs from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 1995). The photos depict pleasant, neutral, and unpleasant objects or scenes that have been rated on valence and arousal (Lang, Bradley, & Cuthbert, 1995). Pictures with pleasant and unpleasant ratings were matched on rated arousal; both sets were previously rated as more arousing than neutral slides (Sutton, Davidson, Donzella, Irwin, & Dottl, 1997). Images were presented via a microcomputer and color television using Microsoft PowerPoint (Microsoft Corporation, Redmond, WA) for 12 s, with 12 to 16 s between pictures. They were presented in 3 blocks of 20, each block including nearly equal numbers of pleasant, neutral, and unpleasant themes. Pleasantness order was randomly determined within block and blocks were counterbalanced across participants within groups. Acoustic startle probes were administered on 15 trials in each block, and consisted of 95 dB (SPL A), 50 ms, white noise bursts with instantaneous rise time, delivered biaurally via matched Telefonics TDH 49 headphones (Farmingdale, NY). Acoustic startle probes occurred 4 to 7 s following slide onset. Variability in probe administration was randomly determined and served to decrease predictability of the acoustic probe. No background masking noise

was used during the startle procedure, however, extraneous ambient noise in the laboratory was restricted during test sessions. Ambient noise in the laboratory was sampled in three series at 500, 1000, 2000, 4000, and 8000 Hz. The range of sound pressure levels was 18.2 to 35.5 dB with an average of 27 dB. This compares favorably with a typical home environment, which averages approximately 60 dB of background noise. Because participants wore earphones, the background noise level was attenuated somewhat from the 27 dB figure.

Consistent with previous work using this procedure (Patrick et al., 1993), between each slide set participants completed affectively neutral self-report measures for 12 min as a filler activity. Following the procedure, participants viewed the slides a second time and rated each slide for valence and arousal using the Self-Assessment Manikin.

Physiological Data Acquisition and Reduction

Eye blink electomyographic (EMG) activity (μV) was recorded and scored using a commercial startle system and software (Human Startle Version 2.20; Coulbourn Instruments, Allentown, PA) from a bipolar configuration of 3 mm Ag-AgCl surface electrodes filled with Microlyte Gel (Coulbourn, Allentown, PA) and placed in an inferolateral position over the muscle *orbicularis oculi* of each participant's left eye with a reference minielectrode placed over the right mastoid process (Fridlund and Cacioppo, 1986). Skin was prepared using a gauze square treated with PrepTrode (Pharmaceutical Innovations, Newark, NJ). Electrode impedance was held to $\leq$ 10 Kohms as measured with an electrode impedance meter (Grass, Quincy, MA). Raw signals were amplified $\times$ 10,000 using a Coulbourn V75-05 Bioamplifier with an 8-150 Hz bandpass, full-wave rectified, and integrated using a Coulbourn V76-23 contour-following integrator with a 10 ms time constant.

Integrated EMG activity to each probe was computer scored and then reviewed. Eye blink reflex magnitudes were calculated as the difference between the integrated EMG during the 20 ms before probe onset (baseline) and the maximum integrated EMG response between 21 and 120 ms following the acoustic probe. Trials were rejected if: a) onset of the startle reflex did not occur in the 21 to 120 ms poststartle period, b) EMG activity within the 20 ms baseline period was $\geq$ 12 μV (excessive noise), or c) the change from baseline to peak of activity during the 21 to 120 ms following probe onset was < 2 μV (adapted from Grillon, Ameli, Merkangas, Woods, & Davis, 1993). Based on these criteria, a percentage (19.4%) of reflexive eye blinks across participants was excluded.

Because of large individual differences in this measure, EMG blink magnitudes are expressed in the standardized *T*-score metric ($M = 50$, $SD = 10$) using the individual mean and standard deviation from each participant across all three slide valences. The data were then sorted by slide valence category. Importantly, each participant's response pattern was not altered by this standardization (*T*-score) procedure, in that the relative magnitude of each participant's response to the three slide valence categories was maintained. This standardization established a common metric across all participants and ensured that each individual contributed equally to their overall respective group pattern. Use of this transformation is consistent with previous investigations using the emotion-modulated startle paradigm (Herpertz, Kumert, Schwengter, & Sass, 1999; Patrick et al., 1993). Analyses were conducted using both raw and standardized scores for affective modulation of startle. Tests of homogeneity of variance among the dependent measures within the 9 cells of the 3 × 3 MANOVA indicated that this assumption was violated using the raw scores, Box's M, $F(12, 13955) = 6.53$, $p = .000000000009$, but *not* violated when using standardized scores, Box's M, $F(12, 13955) = 1.18$, $p = .29$. Because of

unequal sample sizes and the lack of homogeneity of variance-covariance matrices when raw EMG data were used, all analyses were conducted using the standardized scores unless otherwise specified (Tabachnick & Fidell, 1983).

Data Analysis

The main analyses focused on differences in startle magnitude between groups across slide valence conditions. Hypotheses involving the startle reflex were tested using a 3 Group (AD, AD-ASPD, control) × 3 Slide Valence (pleasant, neutral, unpleasant) repeated measure multivariate analysis of variance (MANOVA), where group was the between subjects factor and slide valence category was the repeated measure. This approach avoids the sphericity assumption (Maxwell & Delaney, 1990) and avoids inflation of Type I error rates when the sphericity assumption is not met (Vasey & Thayer, 1987). In line with other research (Patrick et al., 1993), polynomial trend analyses were used to examine the startle reflex across the three affective categories. Of particular interest was whether groups had the normal significant linear trend (unpleasant > neutral > pleasant). Exploratory analyses to evaluate the influence of concomitant variables on observed group differences in affect-modulation of startle reactivity were conducted using multivariate analysis of covariance (MANCOVA). Because group membership was determined nonrandomly and observed differences between groups may reflect inherent differences among the pathologies studied, these analyses were performed for heuristic value only and results are considered highly tentative and difficult to interpret meaningfully (Miller & Chapman, 2001; Maxwell & Delaney, 1990; Overall & Woodward, 1977). An alpha level of .05 was used for all statistical tests. When testing pairwise comparisons, the Scheffé approach for maintaining familywise alpha level at the desired level of .05 was used. This approach was adopted because it is the

most straightforward method for protecting against Type I error and places no limit on the number of contrasts to be tested (Keppel, 1991; Tabachnick & Fidell, 1983). All analyses were carried out using SPSS Version 10.0 for Windows (SPSS Inc., Chicago, IL).

Chapter Four: RESULTS

Continuously distributed variables were tested for skewness and checked for outliers. Variables diverging from normality were transformed, resulting in final distributions that were approximately normal. As suggested by Rummel (1970), the transformation that best normalized the distribution of each skewed variable was selected (see Table 5). Unless otherwise indicated, transformed values were used in all analyses and untransformed data were used for presentation.

Demographic characteristics. Comparisons of demographic characteristics across groups are presented in Table 6. Groups significantly differed on age and years of education. No other significant group differences in demographic characteristics were present.

Psychological and cognitive functioning variables. Table 7 contains group means and standard deviations for psychological and other measures. Results of a one-way MANOVA indicated a significant overall multivariate group difference, $F(10, 110) = 4.17, p < .0001, \lambda = .53$. Univariate analyses with post hoc comparisons indicated that the control group endorsed significantly fewer depressive symptoms relative to AD and AD-ASPD, $F(2, 61) = 15.42, p < .0001$, and controls reported lower levels of anxiety as compared to the AD group, $F(2, 61) = 6.99, p = .002$. In addition, control participants reported lower levels of psychopathy relative to AD-ASPD, $F(2, 61) = 4.84, p = .01$. No significant between group differences in verbal and abstract cognitive functioning were found.

Alcohol-related variables and nicotine use. Table 8 contains group means and standard deviations for alcohol-related variables and nicotine use. Results of a one-way MANOVA indicated a significant overall multivariate group difference, $F(12, 108) =$

18.62, $p < .001$, $\lambda = .11$. As expected, univariate analyses with post hoc comparisons indicated that participants in the AD and AD-ASPD groups were treated significantly more times for alcohol problems, $F(2, 61) = 165.36$, $p < .001$, began drinking at a younger age, $F(2, 61) = 15.91$, $p < .001$, and had consumed significantly more alcoholic beverages during their period of heaviest use relative to individuals in the control group, $F(2, 61) = 23.77$, $p < .001$. In addition, persons in AD groups reported regular alcohol use beginning at a significantly younger age than controls, $F(2, 61) = 10.39$, $p < .001$. Because AD groups were abstinent from alcohol during the 30-day period prior to participation, control participants reported consuming more alcohol during this timeframe, $F(2, 61) = 22.95$, $p < .001$. Similarly, controls reported that their last alcohol use was more recent than both AD and AD-ASPD participants, $F(2, 61) = 8.01$, $p = .001$. Notably, AD and AD-ASPD groups did not significantly differ on any of the alcohol-related measures ($ps > .12$), including the proportion of individuals in the AD (22/24) and AD-ASPD (16/17) groups with physiological dependence (i.e., tolerance and/or withdrawal) on alcohol, $\chi^2(1, 41) = .09$, $p = .77$.

Among groups, 88% of AD and 88% of AD-ASPD participants smoked cigarettes, whereas only 10% of control subjects smoked. Analysis of variance with nicotine dependence as the dependent measure indicated an overall effect of group, $F(2, 61) = 38.86$, $p < .001$. Post hoc analyses indicated that control participants had significantly lower levels of nicotine dependence than either the AD or AD-ASPD groups ($ps < .001$). No difference between AD groups emerged ($p = .97$).

Criminal history. Comparisons of criminal behavior across groups are presented in Table 9. AD-ASPD individuals had significantly greater number of arrests and more months of lifetime incarceration. They were also significantly more likely to be on

probation or parole at the time of participation. AD-ASPD reported a greater number of charges for a variety of illegal behaviors. Interestingly, the AD group reported significantly more alcohol and drug-related charges.

Eye blink reflex magnitudes. Subjective affect ratings collected just prior to the emotion modulation procedure were not significantly different between groups, $F(4, 116) = .86$, $p = .49$. Overall, participants were in pleasant mood states. A repeated measures MANOVA of EMG data revealed the expected overall main effect for valence, $F(2, 58) = 18.70$, $p < .001$, $\lambda = .61$, with blink magnitude being largest as participants viewed the unpleasant slides, intermediate during the neutral slides, and smallest while viewing pleasant slides, resulting in an overall significant linear trend effect, $F(1, 59) = 37.82$, $p < .001$, and a nonsignificant quadratic trend, $F(1, 59) = .01$, $p = .91$. The Group × Valence interaction was significant, multivariate $F(4, 116) = 3.34$, $p = .01$, $\lambda = .80$, $\eta^2 = .103$, with a medium effect size ($f = .33$). Cohen's f was used for effect size, as it is appropriate for analyses of variance (Cohen, 1988).

Polynomial trend analyses were used to examine the startle reflex across the three affective categories. Of particular interest was whether groups had the normal significant linear trend (unpleasant > neutral > pleasant). Polynomial contrasts revealed a significant Group × Valence linear trend interaction, $F(2, 59) = 6.67$, $p = .002$, $\eta^2 = .184$, with a large effect size ($f = .42$); the quadratic trend interaction was not significant, $F(2, 59) = .34$, $p = .72$. Within group analyses indicated that startle blink magnitudes were larger during unpleasant as compared with pleasant slides for both the control and AD groups, resulting in significant linear trend effects, Fs(1, 20 and 1, 23) = 19.59 and 48.97 respectively, ps < .001, and nonsignificant quadratic trends Fs(1, 20 and 1, 23) = .41 and .17 respectively, ps > .53. In contrast, AD-ASPD did not show a significant difference in

blink magnitude during unpleasant and pleasant slides, and did not show a linear valence trend, $F(1, 16) = .29$,

$p = .60$. The quadratic trend effect was also nonsignificant, $F(1, 16) = .02, p = .89$.

Groups differed in raw startle magnitude, $F(1, 59) = 4.95, p = .01$; control participants had overall larger blink magnitudes than both AD and AD-ASPD participants ($ps < .05$). No differences in blink magnitude were found between the AD and AD-ASPD groups ($p = .85$). Groups did not show differential habituation of EMG magnitude across the three blocks of slides. Results of a 3 Group × 3 Block repeated measures MANOVA, with raw EMG data as the dependent measure, indicated the expected significant decline in response across blocks $F(2, 58) = 5.02, p = .01, \lambda = .85$, but no interactions were found with blocks for Group, $F(4, 116) = .53, p = .71, \lambda = .96$. Raw EMG data were used in these analyses of differences in overall blink magnitude and habituation because using standardized blink scores, where each participant has a mean of 50 and standard deviation of 10 regardless of response magnitude, would have been inappropriate (Allen et al., 1999).

Exploratory analyses: Covariates and emotion modulated startle. For exploratory purposes, five one-way repeated measure MANCOVAs were conducted to assess the influence of: 1) psychopathy, 2) age of onset of regular alcohol use, 3) density of familial substance use disorders, as well as 4) subclinical depressive and 5) anxious symptoms on group differences in startle response modulation across slide valence categories. Intercorrelations for personality and alcohol-related variables and startle responsivity across affective categories are presented in Table 10. When each variable was used to adjust the Group × Slide Valence linear trend interaction all results remained significant ($ps < .008$) and no significant quadratic trends emerged ($p > .35$). That is, no covariate

significantly changed the effect of Group on the affective modulation of startle responsivity across valence categories. As previously stated, the lack of random assignment of participants to groups rendered this analysis extremely tentative and results should be interpreted with caution.

Slide affect ratings. Overall, subjective arousal ratings were higher for slides classified as pleasant and unpleasant relative to neutral slides, multivariate $F(2, 58) = 76.1$, $p < .001$, $\lambda = .28$, producing a significant quadratic trend effect, $F(1, 59) = 146.22$, $p < .001$ (see Figure 3). A significant Group × Valence interaction, multivariate $F(4, 116) = 2.73$, $p = .03$, $\lambda = .84$, emerged and indicated that, although each group rated the unpleasant and pleasant slides as more arousing than the neutral set, control participants rated the unpleasant slides as more arousing relative to the other groups, univariate $F(2, 61) = 7.49$, $p = .001$. There were no group differences in arousal ratings for pleasant and neutral slides, Fs$(2, 61) < 1.38$, ps $> .26$. Separate polynomial contrasts by group indicated that both the AD and AD-ASPD groups demonstrated significant quadratic trend effects, Fs$(1, 23$ and $1, 16) = 54.68$ and 26.61 respectively, ps $< .001$, and nonsignificant linear trend effects, Fs$(1, 23$ and $1, 16) = .03$ and 2.29 respectively, ps $> .15$. Control participants, however, demonstrated both significant quadratic trend, $F(1, 20) = 72.30$, $p < .001$, and linear effects $F(1, 20) = 6.23$, $p = .02$. Since both AD groups differed from controls in arousal ratings and not from each other, this is unlikely to account for the primary group differences in affective modulation of the startle reflex.

Pleasantness ratings were greatest for pleasant slides, intermediate for neutral slides, and lowest for unpleasant slides, multivariate $F(2, 58) = 348.55$, $p = .000$, $\lambda = .077$, producing a significant linear trend effect, $F(1, 59) = 705.98$, $p < .000$ and a significant quadratic trend effect, $F(1, 59) = 13.55$, $p < .001$ (see Figure 4). Separate

polynomial contrasts by group indicated that both the AD and AD-ASPD groups demonstrated significant linear trend effects, Fs(1, 23 and 1, 16) = 197.62 and 182.62 respectively, ps < .001, and nonsignificant quadratic trend effects, Fs(1, 23 and 1, 16) = 2.02 and 1.17 respectively, ps > .17. Control participants, however, demonstrated both significant linear, $F(1, 20) = 385.58$, $p < .001$, and quadratic trend effects $F(1, 20) = 14.42$, $p = .001$. The quadratic trend effect was a function of a nonsignificant lower rating of pleasantness for the neutral slides relative to the other groups.

Chapter Five: DISCUSSION

The results indicated differences in the emotion modulation of the startle reflex in adult male alcoholics with antisocial personality disorder (ASPD) relative to alcoholics without ASPD, and controls. The non-ASPD groups showed the normal linear increase in the eye blink EMG component of the startle reflex, with response strength increasing from pleasant to neutral to unpleasant stimuli. In contrast, alcoholics with ASPD did not show the typical potentiation of startle EMG to the unpleasant stimuli or diminution of EMG to pleasant stimuli. Importantly, the groups did not differ in their pattern of subjective ratings for slide pleasantness or activation, ruling-out the likelihood that these differences were due to altered experience of the slides among the groups. Further, the restriction or direct examination of additional psychopathology in the present study significantly limited the possibility that observed group differences in emotional reactivity were due to other psychiatric conditions. These findings suggest altered bodily outputs related to central emotional states in persons with comorbid alcohol dependence and ASPD.

The present study is the first to examine emotion-modulated startle in alcohol dependent individuals, although others have examined startle responses in alcoholics or in those at high risk. Early-onset alcoholics, abstinent for 12 to 26 days, have increased EMG responses to auditory startle stimuli, and do not show the expected attenuation of startle with pharmacologic probes (Krystal et al., 1997). Nonabusing individuals with a family history of alcoholism (FH+) show a lack of startle habituation and also fail to show the usual prepulse inhibition effect (Grillon, Dierker, & Merikangas, 1997). Using the emotion-modulated startle paradigm, Miranda, Meyerson, Buchanan, et al. (2002) found that FH- show the normal linear increase in the eye blink EMG component of the

startle reflex, whereas FH+ lacked the typical potentiation of EMG to the unpleasant stimuli. Notably, FH+ reported significantly more antisocial traits relative to controls, a finding consistent with much previous work (Sher et al., 1991; Shedler & Block, 1990). Collectively, these findings implicate disruption of startle EMG regulation in relation to alcoholism and risk for the disorder, and suggest that such disruption may be closely associated with antisocial traits.

Although this study did not assess brain mechanisms directly, the results are consistent with a model implicating altered frontolimbic processing in ASPD and addiction. Modulation of the startle EMG provides an accessible peripheral measure of central nervous system states associated with variations in the experience of pleasantness (Bradley & Lang, 2000). Studies of fear conditioning in animals indicate that such modulation of the startle EMG is controlled by outputs from the central nucleus of the amygdala to brainstem motor areas (Davis, 1992). Amygdala stimulation enhances acoustic startle in rats and rabbits (LeDoux, Iwata, Cicchetti, & Reis, 1988; Rosen & Davis, 1988), and lesions of the central nucleus block the acquisition or expression of fear potentiated startle (Davis, 1992; Hitchcock & Davis, 1986). Affective modulation of startle may be more effective when right hemisphere structures are involved, suggesting differential engagement of the right amygdala in this process. Study of a rare individual with a well-characterized right amygdala lesion showed that the startle reflex on the left side, opposite the lesion, was diminished. Furthermore, the patient failed to show startle enhancement during presentation of aversive slides (Angrilli et al., 1996), suggesting that the right amygdala is necessary for startle enhancement during negative emotions. Further evidence is seen during lateralized presentation of acoustic startle probes to normal subjects viewing pleasant, neutral, and unpleasant slides (Bradley, Cuthbert, &

Lang, 1991b, 1996). Startle probes presented to the left ear, and processed primarily by the right hemisphere, produced smaller blinks when slides were pleasant and larger blinks when they were unpleasant. Startle probes to the right ear, processed in the left hemisphere, had no systematic effect.

The experience of a stimulus as more or less pleasant involves activity of specific frontal lobe systems acting in concert with amygdaloid circuits (Damasio, 1994). The orbitofrontal cortex comprises the most ventral regions of the prefrontal cortex and, in both anatomy and function, is critically intertwined with the amygdala. It is through its close connection with the amygdala that this brain region integrates the sensory characteristics of biologically significant stimuli (Zald & Kim, 2001). Through connections with memory-related regions, these brain regions evaluate the characteristics of a stimulus against previous experience and modify approach and avoidance behaviors. Of particular relevance here and as described above, function of this circuitry is peripherally indexed through the emotion modulated startle paradigm. As such, abnormalities in affective modulation of startle are assumed to reflect functional alterations in these central nervous system processes.

Behaviorally, the amygdaloid-septal-frontal circuit has been implicated as a mediator of empathic, civil, and socially appropriate behavior (Chow & Cummings, 1999). In normal individuals, activation in these brain regions constrains impulsive and emotion-driven behavior. Dysfunction of this circuit results in social impairment and is associated with impulsive and undercontrolled behavior, as well as irreverence and antisocial tendencies. Functional neuroimaging studies have provided further evidence that decision-making impairments are linked to dysfunction of this brain circuitry, including the ventromedial prefrontal cortex, amygdala, and the insular/somatosensory

cortices. Patients with damage to pathways linking the amygdala to the ventromedial prefrontal cortex lack the usual modification of behavior associated with rewards and punishments on a decision-making gambling task sensitive to the specific functional role of these brain regions (Bechara et al., 1994; Bechara et al., 1999).

Studies indicate that cocaine, opiate, and alcohol abusers show impairments on the gambling task, such that these individuals play cards from decks with larger immediate rewards but larger delayed losses (Rogers et al., 1999; Mazas, Finn, & Steinmetz, 2000). A disadvantageous decision bias was associated with drinking greater quantities of alcohol. Interestingly, individuals with comorbid alcohol dependence and ASPD perform less efficiently than non-ASPD alcohol dependent individuals (Mazas et al., 2000). Performance patterns among this population are similar to those found among patients with ventromedial lesions (Bechara et al., 1999). Mazas and colleagues (2000) has suggested that "prefrontal dysfunction may predispose an individual to make disadvantageous personal choices that possibly lead to socially inappropriate or socially deviant behavior (Bechara et al., 1994; Bechara, Damasio, Tranel, & Damasio, 1997) and to drink excessively even when it leads to significant problems" (p. 1037). Interestingly, though not part of the present study, all volunteers included in the study reviewed herein participated in an additional investigation using the gambling task. Results replicated findings from the study by Mazas and colleagues (2000), showing that alcoholics with ASPD made less advantageous choices than non-ASPD alcoholics and controls had the best performance (Miranda, Meyerson, Myers, & Lovallo, 2002). Collectively, these findings coincide with studies that have used a variety of tasks and paradigms and found that persons with ASPD make less advantageous behavioral choices. The ecological

validity of these findings is evident in the pervasive disinhibited and sensation seeking behavior which defines the disorder.

As a whole, findings of the present study coincide with previous work showing abnormalities in emotional responsiveness in persons with ASPD. As reviewed above, electrophysiological and linguistic studies, as well as mounting brain-imaging evidence has specifically pointed to deficient reactivity to punishing and unpleasant stimuli among individuals with ASPD. The current findings extended previous work by demonstrating deficits in reactivity to pleasant stimuli among male alcoholics with ASPD as well. Though findings from the present study could indicate that abnormalities in emotional reactivity are associated with ASPD and not related to alcoholism per se, previous work more strongly supports the thesis that affect dysregulation plays a meaningful role in alcohol use disorders for a distinct subset of alcoholics.

Antisocial Personality Disorder and Emotional Dysregulation: Implications for Addiction

Several lines of empirical work support the contention that abnormalities in emotional regulation are related to alcohol and other substance use disorders among individuals with ASPD. First, neural circuits that govern emotion are the primary cites of action for all drugs of abuse, including alcohol (Kandel, Schwartz, & Jessell, 2000). This circuitry involves limbic structures and includes the central nucleus of the amygdala, bed nucleus of the stria terminalis, nucleus accumbens, and cingulate gyrus, all of which are modulated by ascending dopaminergic projections (Lamont & Kokkinidies, 1998). It has been also well-documented that serotonin (5-HT) is important for normal functioning of this brain region and the regulation of affect and motivation.

Neurobiological models of addiction have shown that increased activity of the mesolimbic dopaminergic pathway within the limbic system, particularly in the nucleus accumbens and hippocampal formation, plays a pivotal role in the rewarding properties of substance use (Koob & Bloom, 1988; Koob & Le Moal, 1997). Importantly, the mesolimbic dopaminergic pathway mediates basic biological drives and motivational states by gating activation of these various limbic structures. Effective limbic functioning is necessary for the evaluation of events in the environment, affective responses associated with these events, motivation of behavior, and the generation of bodily responses via the hypothalamus and brainstem.

Deficient dopaminergic (DA) activity at the nucleus accumbens may contribute to drug abuse vulnerability, in part, by rendering persons susceptible to the hedonic effects of alcohol and other drugs (Koob & Bloom, 1988). Human and animal work have both shown that deficient DA inhibits emotional responsiveness to environmental cues and is associated with indifference and dysphoria (Farde, Gustavsson, & Jonsson, 1997). Similarly, deficiencies in central 5-HT are often accompanied by negative affect, and drugs that increase its synaptic availability can therapeutically regulate dysphoric moods such as those associated with drug withdrawal. One hypothesis concerning vulnerability to abused drugs states that persons with deficient DA and 5-HT activity in orbitofrontal-limbic brain regions are particularly susceptible to the capability of alcohol and other substances to restore and potentiate DA and 5-HT to homeostatic and hedonic levels at initiation of alcohol use (Koob & Le Moal, 1997).

Animal and human studies have shown a consistent relationship between deficient central serotonergic function and antisocial and aggressive tendencies. A variety of studies have found low cerebral spinal fluid concentration of 5-hydroxyindoleacetic acid,

the major metabolite of 5-HT, in individuals with ASPD and early-onset alcoholism (Fils-Aime et al, 1996) and alcoholics with a history of impulsive criminal behavior (Linnoila, DeJong, & Virkkunen, 1989; Linnoila et al., 1983; Virkkunen, Nuutila, Goodwin, & Linnoila, 1987; Virkkunen et al., 1994). Further, a large study of Finnish twins found a link between alcoholics with ASPD and the 5-HT autoreceptor *HTR1B G861C* polymorphism on chromosome 6*q*13-15, suggesting a genetic predisposition to altered 5-HT activity that underlies comorbid ASPD and alcoholism. There also is emerging evidence indicating deficient neuronal dopamine activity among antisocial individuals. Gabel and colleagues found low levels of cerebrospinal fluid dopamine-β-hydroxlase, the enzyme facilitating the conversion of DA to norepinephrine, among antisocial youth with a paternal history of incarceration (Gabel, Stadler, Bjorn, & Shindledecker, 1995). In another study, alterations in DA functioning among a sample of alcoholics was positively correlated with novelty seeking and antisocial traits (Laine, Ahonen, Raesaenan, & Tiihonen, 2001). Though studies have not uniformly found an association between DA and 5-HT hypoactivity and antisocial behavior and alcoholism, this work highlights the need to further study these relationships.

Dysfunction in neuronal regulation of 5-HT and DA among persons with ASPD is in accord with a prominent psychological theory of the disorder and a neurobiological thesis regarding addiction. The stimulation seeking theory has been widely adopted to explain the relationship between poor emotional and physiologic responsiveness and antisocial behavior (Eysenck, 1964; Quay, 1965; Raine, 1993, 1996). Within this model, emotional under-responsiveness is experienced as an aversive physiological state. Accordingly, individuals with poor emotional reactivity engage in impulsive, sensation seeking behaviors in order to increase arousal to a "normal" or optimal level. This

perspective mirrors the hedonic-homeostatic model of addiction proposed by Koob and Le Moal (2001), in which addiction and risk for substance use disorders is associated with alterations in the neural circuitry of reward and reinforcement. In brief, according to this model, individuals enter and persist in the addiction cycle because of the negatively reinforcing function of their drinking behavior. Within this framework, drug use and other highly stimulating behaviors (i.e., antisocial acts) restore an otherwise dysregulated internal state for individuals who are devoid of emotional experience.

In a similar vein, Blum, Cull, Braverman, & Comings (1996) have postulated that a genetic anomaly associated with biologic emotion systems confers shared vulnerability for both addiction and ASPD. They propose that this characteristic is manifested as a mutation in the biological substrata associated with obtaining rewarding experiences from the environment. Specifically, a variant form of the gene for the dopamine D_2 receptor, labeled the A_1 allele, is hypothesized to result in alterations in intercellular functioning of the complex reward and reinforcement system of the brain referred to as the limbic system (i.e., nucleus accumbens, amygdala, hippocampus). Within this model, biochemical alterations of the limbic system and related neural structures associated with deficient emotional responsiveness to reward and reinforcement result in a deficiency of positive experiences, thereby leaving these individuals vulnerable to dysphoric mood states and boredom. This gene-driven abnormality in brain pleasure centers is referred to as "reward deficiency syndrome." Empirical support for this theory has come from more than 14 independent laboratories that have reported a significantly higher percentage of the allele (A_1) among "severe" alcohol dependent individuals as compared to their nonalcoholic counterparts (for review see Blum & Noble, 1994). Further support for the role of DA receptor variants comes from Hutchison and colleagues, who in a series of

behavioral genetic studies, found that a polymorphism of the DA D_4 receptor moderates craving for alcohol after an acute priming dose (Hutchison, McGeary, Smolen, Bryan, & Swift, in press), and that olanzapine, a prominent D_4 receptor antagonist, attenuates craving among persons with a certain D_4 polymorphism (Hutchison, Swift, Rohsenow, Monti, Davidson, & Almeida, 2001). Though others have failed to show a link between ASPD and alterations in the DA receptors, disparate findings may be due to differences in sampling and the heterogeneity and multigenicity of alcoholism (Cloninger et al., 1981). Although selection of a single gene alteration as solely responsible for behaviors that predispose toward alcoholism seems overly simplistic, the formulation is noteworthy in that the neural pathways postulated to be affected by ethanol are the same as those involved with reward and reinforcement.

Another way abnormalities in emotion systems may be linked with addiction is through deviations in temperament. Temperament encompasses inherited individual differences in behavioral tendencies and self-regulation (Thomas and Chess, 1977), and reflects phenotypic variations of genetic-environmental interactions (Tarter et al., 1999). It has been postulated that deviations in temperament are related to variations in emotional regulation and affective responsivity to environmental cues (Bates, 2000; Strelau, 1983, 1994). Within this conceptual framework, alterations in affective responsiveness impede central inhibitory processes and lead to poor behavioral control (Finn et al., 1994; Gorenstein and Newman, 1980; Gray, 1991). A variety of evidence has shown that individuals at genetic risk for developing alcoholism exhibit poor impulse control, antisocial tendencies, and sensation seeking (Finn et al., 1997; Sher et al., 1991), and these, in part, mediate the relationship between risk and the development of alcohol use disorders (Chassin et al., 1999; Finn et al., 2000). To this end, emotion dysregulation

underlies deviations in temperament and serves as a catalyst for alcohol misuse via fearlessness and self-regulatory deficits. These deficits result in difficulties learning to drink responsibly because of fundamental neurologic abnormalities in their ability to respond to aversive experiences and adaptively regulate their behavior (Finn et al., 1994; Finn et al., 2000). Taken together, theory and research from neurobiological, psychological, and temperament perspectives converge on each other and suggest that abnormalities in brain systems that modulate emotional reactivity may confer liability for alcoholism and other substance use disorders, and plan a role in the maintenance of these conditions.

Empirical and epidemiological support for the role of emotional dysfunction in addiction via altered temperament comes, in part, from work examining disinhibited youth. Emerging evidence suggests that abnormal neurophysiologic functioning of emotion systems is more prevalent among conduct disordered youth and may contribute to AUD liability. Conduct disorder (CD), a necessary precursor for ASPD, is one of the most robust risk factors for adolescent alcohol use. Characterized by a persistent pattern of aggressive and antisocial behavior, and failure to learn from aversive experiences, epidemiological studies have estimated the incidence of CD in the general population to be between 1 and nearly 10% (Zoccolillo, 1993). Using an array of instruments and paradigms, studies have indicated that adolescents with CD are hyporeactive to emotionally-relevant stimuli. For example, studies repeatedly show that youth with CD display decrements in P300 reactivity in the frontal and parietotemporal regions (Bauer & Hesselbrock, 1999; Bauer, Hesselbrock, O'Connor, & Roberts, 1994; Bauer, O'Connor, & Hesselbrock, 1994; O'Connor, Bauer, Tasman, & Hesselbrock, 1994). Others have observed a stress cortisol hyporesponsiveness in preadolescent boys with a family history

of substance abuse relative to family-history-negative peers (Moss et al., 1995). Analyses indicated this difference was fully accounted for by conduct problems. Related work has used standard neuropsychological batteries to examine frontal lobe function among delinquent youth. Common deficits associated with CD include problems with cognitive flexibility, shifting cognitive sets, sustained attention, and free recall of verbal material (for review see Teichner & Golden, 2000).

Efforts to delineate risk factors associated with alcohol misuse have consistently shown that adolescents with CD are at the highest risk for drinking alcohol and developing alcohol use disorders (Gittleman et al., 1985; Clark et al., 1997). Previous studies have found that adolescents with CD have an earlier onset of alcohol use, experience more alcohol related problems, and have a greater severity of dependence (Babor et al., 1992; Cloninger, 1987; Lynskey & Fergusson, 1995; Shedler & Block, 1990; Windle, 1990). Prevalence rates of CD among adolescents in substance abuse treatment have ranged from 35 to 40% (Henggeler, Pickrel, Brondino, & Crouch 1996; Monopolis, Brooner, Jadwisiak, Marsh, & Schmidt, 1990) and 42 to 70% (Kaminer, Tarter, Bukstein, & Kabene, 1992; Bukstein, Brent, & Kaminer, 1989) in outpatient and inpatient programs, respectively. Clinically, CD youth are more likely to drop out of substance abuse treatment and show a poorer clinical course following completion of alcohol and drug intervention (Brown et al., 1996; Kaminer et al., 1992). Moreover, 53% of adolescent males and 39% of adolescent females with an alcohol use disorder still meet diagnostic criteria for CD when deviant behaviors related to alcohol and drug involvement are excluded (Brown et al., 1996). This is consistent with prospective data documenting that CD is usually antecedent to alcohol and other substance use (Clark et al., 1997; Loeber, 1990).

Researchers have proposed putative explanations for the relationship between temperament, antisocial behavior, and addiction, which have emphasized the relevance of abnormalities in emotional responsiveness. Raine (1993, 1996) has proposed a *fearlessness theory* that states there must be a diminution in fear or anxiety in order to execute antisocial behavior. This theory is in accordance with temperament research, which indicates that high levels of emotional arousal and reactivity are positively correlated with fear, anxiety and behavioral inhibition (Strelau, 1994). Elevated levels of arousal function as a suppressant of impulsive, antisocial behavior. Conversely, low arousal levels are theorized to be related to reduced anxiety and fear. Emotional underresponsiveness to fearful stimuli may also be manifested in poor conditioning under contingencies of punishment. Specifically, referring to the work of Eysenck and Gudjonsson (1989), Raine, Venables, and Williams (1996) state that, "the ability to form associations between a signal of punishment (conditional stimulus) and the punishment itself (unconditional stimulus) [is] essential to the development of anticipatory fear. It is this conditioned anticipatory fear that, it is argued, provides the incentive for individuals to avoid antisocial stimuli that are associated with punishment...the greater the individual's ability to develop classically conditioned emotional responses...the lower the probability of becoming antisocial" (p. 624). Notably, antisocial individuals show diminished arousal and emotional responsiveness, as well as deficits in learning the potential aversive consequences of their behavior (Raine et al., 1996). In point of fact, deficient learning from aversive consequences is presumably due to a lack of neural responsiveness at the amygdala – which is known to be essential for classical conditioning. This impaired ability to develop conditioned anticipatory fear may

obstruct the incentive for persons with ASPD to modify their drinking patterns in the face of alcohol-related problems.

Interestingly, decreased electrodermal responses to conditioned cues signaling punishment also have been shown to predict alcohol-related problems in young adults at genetic risk for developing alcoholism (Finn et al., 1994). It has been postulated that failure to experience appreciable negative consequences associated with alcohol use results in an inability to adaptively regulate drinking in response to social cues and failure to take precautions to avoid alcohol-related problems (i.e., avoid interference with responsibilities; Finn et al., 2000). Support for this contention has come from studies showing that persons genetically prone to alcoholism, who show high levels of social deviancy, consume similar quantities of alcohol per week but experience significantly more problems associated with their use (Finn et al., 1994, 1997).

Conclusions and Significance

The most salient finding of the present study is that adult male alcoholics with ASPD have abnormal emotional responsiveness to both pleasant and unpleasant stimuli relative to alcoholics without ASPD, and controls. Though findings from the present study could indicate that abnormalities in emotional reactivity are associated with ASPD and not related to alcoholism per se, previous work more strongly supports the thesis that affect dysregulation plays a meaningful role in alcohol use disorders for a distinct subset of alcoholics.

Alcohol addiction is a maladaptive behavioral pattern that evolves from complex interactions between biogenetic factors and environmental contingencies. An observant review of the literature indicates that the majority of researchers approach alcoholism as a homogeneous disorder despite developmental and typological research clearly indicating

that alcoholics constitute a variegated population with differing etiological pathways and maintaining factors. The findings reported here implicate alterations in brain systems that govern emotional processing among this subgroup of alcoholics. Abnormal affective modulation of startle in ASPD is consistent with models of addiction risk that focus on alterations of the mesolimbic dopaminergic reward system. Deficient DA activity at the nucleus accumbens among persons with ASPD may contribute to abuse vulnerability by rendering persons susceptible to the hedonic effects of alcohol and other drugs (Koob and Bloom, 1988; Koob and Le Moal, 1997).

Advancing our understanding of alcoholism among individuals with ASPD is of particular societal importance. A significant proportion of violent crime in the U. S. occurs while the perpetrator is under the influence of alcohol. A recent report indicated that alcohol use was involved in approximately 4 of 10 victimizations, including an annual average of 183,000 rapes and sexual assaults, 197,000 robberies, 661,000 aggravated assaults, and nearly 1.7 million simple assaults (Greenfeld, 1998). In accordance with this robust association between alcohol and crime, studies have shown that approximately 70% of individuals diagnosed with ASPD met diagnostic criteria for lifetime alcohol abuse or dependence (Reiger et al., 1990). Clinically, individuals with ASPD have a poorer prognosis for alcohol use disorders (Rounsaville et al., 1987; Woody, McLellan, Luborsky, & O'Brien, 1985). Despite efforts, no efficacious treatment has been clearly identified for treating alcohol dependence among persons with ASPD (Kadden, Cooney, Getter, & Litt, 1989; Longabaugh, Rubin, Malloy, Beattie, Clifford, & Noel, 1994; Project MATCH, 1997; Rounsaville et al., 1987). This of particular concern given the high prevalence of comorbid alcohol dependence and ASPD among prison populations (Chiles, Von Cleve, Jemelka, & Trupin, 1990).

Strengths and Limitations of the Present Study

Several limitations should be considered when interpreting the current findings. First, this study used differential selection criteria across groups with regard to knowledge of biological family members. Specifically, control participants were required to have specific knowledge of substance misuse among biological parents and grandparents. In contrast, the alcohol dependent groups were not required to possess such knowledge, with the exception of maternal alcohol use during pregnancy. Though such selection criteria could have resulted in a sampling bias, this procedure was used to maximize the probability of obtaining normal startle modulated effect among control participants. Previous work has indicated that non-alcohol dependent FH+ show abnormalities in affective modulation of the startle reflex (Miranda, Meyerson, Buchanan, et al., 2002). Failure to find normal affective modulation of startle among control participants would have called into question adequate functioning of the equipment and precluded interpretation of the results. In addition, this study relied on participants' self-reports of familial substance use disorders. Though family history of substance use disorders was examined using the FH-RDC, a sensitive and specific index of parental alcoholism when offspring are the informants, reliability of this measure would have been maximized by contacting collateral family members. Related, this study did not assess for alcoholism or drug abuse among participants' siblings and, as stated in the methods, calculation of family density was done on a continuous scale with conservative criteria. As such, the estimation of FH density used in this study may have resulted in an inadequate test of FH status on emotional reactivity among alcoholics.

Second, relatively homogeneous groups of alcohol dependent males were examined in this study. While the strict inclusion criteria employed in this study

attenuated threats to internal validity and afforded a less confounded interpretation of results, this may have resulted in a non-representative sample of alcoholics. Alcohol dependent individuals commonly present with complex psychiatric and medical histories that include significant comorbid psychopathology. In a similar manner, this study selectively studied men thereby precluding the generalizability of these findings to women with alcoholism and ASPD. Given that FH+ women showed greater alterations in affective modulation of the startle response as compared to FH+ men suggests the need for further work (Miranda, Meyerson, Buchanan, et al., 2002). Similarly, the ethnic homogeneity of the sample also precludes the extension of the current findings to non-Caucasian individuals.

Third, studies of amygdaloid function in humans occasionally demonstrate a laterality of function, suggesting greater negative affective associations with right amygdala activity (see Angrilli et al., 1996). The present study recorded from only the left eye, and the left *orbicularis* muscle is controlled from the right side of the brain. Recording from both eyes in future studies would provide information about possible lateralized function in relation to alcoholism and ASPD.

Fourth, despite the use of a technique associated with well-delineated neuroanatomy, this study used a peripheral indicator of neurological functioning in response to affect-laden stimuli and did not directly measure brain function. This limitation precludes certainty about the precise underlying mechanisms involved. Future work using brain imaging techniques would allow for a clearer assessment of brain activity in response to emotionally relevant stimuli.

Fifth, many of the participant selection criteria relied on retrospective self-report among a sample of men with pathological antisocial tendencies. Because of this, the

veracity of the subjective data could be questioned. Hare (1998b) has suggested the use of collateral informants and objective historical data (i.e., legal records) when studying individuals with ASPD. The reliance on self-report data could have contributed to certain null findings, such as the nonsignificant relationship between psychopathy and affective modulation of startle during unpleasant stimuli. Similarly, participants' histories of brain injury, previous alcohol and other substance use, and age onset of drinking were all collected via self-report, calling into question the relative accuracy of analyses involving these measures.

Sixth, though current and lifetime psychiatric disorders were evaluated in the present study, certain childhood disorders were not assessed. Most notably, the presence of attention-deficit/hyperactivity disorder (ADHD), as a child or adult, among participants was not known. Studies have shown that ADHD is a commonly comorbid condition with CD, as well as adult ASPD, and persons with ADHD have an earlier onset of alcohol use disorders and heavier drinking patterns more generally (Hesselbrock et al., 1984).

Finally, though great lengths were taken to assess alcohol and other substance use among participants, the impact of these variables on the dependent measures is not entirely known. Results indicated that alcoholics with ASPD had a higher prevalence of some substance use disorders relative to the other groups. In addition, the age of onset for each drug was not examined. Because various investigators have reported distinct results depending on the quantification method used, it is possible that other ways to quantify variables of interest may have rendered different results.

Despite these limitations, this study delineated the importance of ASPD while examining emotional responsiveness among alcoholics. This fills a notable gap in the

literature, where studies have examined alcohol dependent individuals as a homogenous diagnostic group and neglected a large body of work indicating emotional dysfunction among individuals with ASPD. In addition, this investigation studied clearly defined groups using structured clinician administered interviews, with observed reliability of diagnostic decisions. This is a substantial improvement over previous work in which the taxonomy used to categorize participants is oftentimes vague or absent, and when described, reliability information regarding diagnostic decisions is infrequently provided. Along these lines, this study employed explicit criteria for participation that restricted threats to internal validity and afforded a less confounded interpretation of results. In addition, this study used an objective and well-established measure of emotional reactivity. Finally, within the subspecialty of psychophysiology, this study examined a relatively large sample. This, combined with the relative homogeneity within groups studied here, provided a robust test of the hypotheses.

Future Directions

One avenue for future work is to examine responsiveness of alcohol dependent individuals with ASPD to alcohol and other drug-related cues. The abnormalities in emotional responsiveness across valence found in this study suggest that alcoholics with ASPD could have altered reactivity to substance-related cues as well. Consistent with conditioning theories of addiction, alcohol and other substance-related stimuli (e.g., sight and smell of customary alcoholic beverage) have been repeatedly shown to evoke physiological changes and drug craving among individuals with substance use disorders (Monti et al., 1987; Rohsenow et al., 1994). Although the roles of craving and cue reactivity in addiction and relapse have been studied extensively, efforts to identify the neurobiological basis of this phenomenon have only recently begun. Animal models

have shown that drug-related cues induce responses in brain regions associated with emotion and decision making (Schroeder, Holahan, Landry, & Kelley, 2000). In humans, functional neuroimaging methods have revealed atypical activation in a variety of brain regions, including the orbitofrontal cortex, in response to drug-related cues among substance abusers (Childress et al., 1999; Garavan et al., 2000; Grant et al., 1996; Sell et al., 2000; Volkow et al., 1999; Wang et al., 1996). Notably, activation of this brain region has been correlated with urge to use (Volkow et al., 1999). Using fMRI, Tapert and colleagues (2001) found that greater cue-induced alcohol craving was correlated with more extensive blood oxygen level dependent responses within the orbitofrontal region among alcohol dependent women relative to non-dependent women. Although it remains undetermined whether activation of the orbitofrontal cortex is responsible for the subjective experience of craving, the identified functions of this region and its interconnected regions strongly support such an interpretation (London, Ernst, Grant, Bonson, & Weinstein, 2000).

Another potential direction for future work is to examine the relevance of putative abnormalities in central nervous system processes that regulate emotion to treatment outcome of addictive disorders. While research has indicated that alcoholics with ASPD are poor responders to psychological intervention, limited evidence suggests these individuals show better outcomes to certain pharmacotherapeutic agents. In several studies, early onset alcoholism, a condition associated with antisocial behavior and a familial history of alcoholism, has been shown to moderate response to Ondansetron, a 5-HT_3 antagonist (Johnson et al., 2000; Johnson, Ait-Dauod, & Prihoda, 2000). In one example, early-onset alcoholics reported fewer drinks per day and a greater percentage of abstinent days following an 11-week administration of Ondansetron as compared to late-

onset alcoholics. Importantly, medication compliance did not differ between groups (Johnson et al., 2000). Similar findings have been noted in studies using Naltrexone, a mu-opiate receptor antagonist (Monterosso et al., 2001). Given the putative relationship between certain neurotransmitter systems and alcoholism and ASPD, these findings are intriguing and suggest the need for further work on individual differences in pharmacological studies.

Lastly, though results from this study are clear and compliment other work using different methods, the role of altered emotional responsiveness in the development of alcoholism and other substance use disorders remains unknown. Because this study examined recovering alcoholics, it is unclear whether the detected abnormalities are genetically based, due to environmental insult, or are a function of excessive stress and disruption of the hypothalamic-pituitary-adrenal axis early in life. The fact that non-ASPD alcoholics in this study showed normal affective modulation of the startle reflex, and that previous work has found abnormalities in emotional responsiveness and hypothalamic-pituitary-adrenal axis functioning among non-alcoholic FH+, a neurotoxic explanation for the current results seems unlikely. However, because of limitations of the current study and other previous work, all of the aforementioned explanations are plausible. Future work needs to better delineate the effects of such variables and prospectively examine the role of altered emotional reactivity in the development of alcohol misuse and alcoholism. While much work in alcoholism has concentrated appropriately on withdrawal, treatment, and relapse, understanding individual differences that predate and are associated with development and/or maintenance of the disorder, would allow for improved identification of those at greatest risk and point the way toward better prevention and early intervention.

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Table 1

Percentage of Current and Lifetime Additional DSM-IV Axis I Diagnoses by Group

Axis I Disorder	AD	AD-ASPD	Control	χ^2	*p*
Current					
Social Phobia	8.3	5.9	0.0	1.75	.42
Lifetime					
MDD	25.0	18.0	0.0	5.83	.05
Panic Disorder	4.2	5.9	0.0	1.15	.56
Social Phobia	8.3	11.8	0.0	2.38	.30
Specific Phobia	0.0	5.9	0.0	2.69	.26
MD-Substance	12.5	29.4	0.0	7.24	.03[a]
Anxiety-Substance	0.0	5.9	0.0	2.69	.26

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder; MDD = Major Depressive Disorder; MD-Substance = Substance-Induced Mood Disorder; Anxiety-Substance = Substance-Induced Anxiety Disorder. Because the minimum expected cell count when all groups were included was low (.27 - 2.74), and for all analyses three cells (50%) had expected counts less than 5, chi-square analyses were repeated for AD groups only. No significant differences between AD groups emerged (*p*s > .23).

[a]Follow-up chi-square analysis indicated that Control < ASPD, $\chi^2 = 7.11$, $p = .008$.

Table 2

Percentage of Current Additional DSM-IV Axis II Diagnoses by Group

Axis II Disorder	AD	AD-ASPD	Control	χ^2	*p*
Avoidant	8.3	11.8	0.0	2.52	.28
OCPD	16.7	11.8	0.0	3.68	.16
Paranoid	0.0	11.8	0.0	5.47	.07
Schizoid	4.2	0.0	0.0	1.61	.45
Narcissistic	0.0	5.9	0.0	2.69	.26

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder; OCPD = Obsessive-Compulsive Personality Disorder. Because the minimum expected cell count when all groups were included was low (.27 - 1.65), and for all analyses three cells (50%) had expected counts less than 5, chi-square analyses were repeated for AD groups only. No significant differences emerged (*p*s > .09).

Table 3

Percentage of Additional Substance Use Disorder Diagnoses among Alcohol Dependent Groups

Substance Use Disorder	AD ($n = 24$)	AD-ASPD ($n = 17$)	χ^2	p
Cannabis Use Disorder	65	95	4.68	.03
Abuse	26	18		
Dependence	39	77		
Sedative/Hypnotic/Anxiolytic	26	65	5.97	.02
Abuse	17	24		
Dependence	09	41		
Cocaine Use Disorder	48	53	.10	.75
Abuse	22	06		
Dependence	26	47		
Stimulant Use Disorder	56	71	.83	.36
Abuse	04	00		
Dependence	52	71		
Opioid Use Disorder	17	36	1.67	.20
Abuse	13	18		
Dependence	04	18		
Hallucinogen Use Disorder	26	82	12.38	.00
Abuse	17	35		
Dependence	09	47		
Polysubstance Use Disorder	13	29	1.64	.20
Abuse	00	00		
Dependence	13	29		
Other[a]	22	24	.02	.89
Abuse	13	12		
Dependence	09	12		

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder.
[a]Other substances included inhalants (i.e., gas, glue, paint) and nitrous oxide.

Table 4

Percentage of Potential Participants Excluded during Screening by Exclusionary Criteria (n = 105)

Exclusion Criteria	%
Probable psychiatric condition	11
Health problems	17
CNS acting medication	16
TBI	12
Prenatal ethanol exposure	10
English illiterate	03
Hearing difficulties	03
Age (> 39)	02
Other substance abuse[a]	18
Alcohol abuse[a]	11
Never consumed alcohol[b]	05
FH+[b]	31
Lacked FH knowledge[b]	05

Note. TBI = Traumatic brain injury; FH+ = Family history of alcohol or other substance use disorder.

[a]Criteria for alcohol or other substance dependence never met precluding consideration for alcohol dependent groups or the control group.
[b]Precluded consideration for the control group.

Table 5

Transformations Used To Normalize Skewed Variables

Variable	Transformation	Skewness Ratio
Age	1/X	0.70 - 1.82
Age of first regular alcohol use	Log base 10	0.05 - 1.15
Alcohol treatment (No.)	1/X	0.74 - 2.46[a]
Beck Anxiety Inventory	Log base 10	0.37 - 1.98
Beck Depression Inventory-II	Log base 10	0.20 - 0.67
Family history density	Log base 10	1.23 - 1.92[a]
Length of longest fulltime employment	Log base 10	0.22 - 1.12
Last alcohol use (months)	Log base 10	0.87 - 1.54
Lifetime incarceration (months)	Log base 10	0.09 - 0.81[a]
Number standard drinks (past)	Log base 10	0.93 - 2.73
Number standard drinks (current)	Log base 10	0.14[b]
PANAS-negative	1/X	0.91 - 1.59
Shipley abstract subtest	X^2	0.15 - 1.74

Note. Skewness Ratio = Skewness statistic divided by its standard error as a test of normality. Scores indicate range of skewness across groups.

[a]All control participants had a value of 0 on this variable, as such the test of skewness was done for alcohol groups only.

[b]All participants in both alcohol dependent groups had a value of 0 on this variable, as such the test of skewness was done for the control group only.

Table 6

Demographic Characteristics of the Sample [mean (SD) or percent]

Variable	AD (a)	AD-ASPD (b)	Control (c)	Test Statistic	*p*	Post Hoc
N	24	17	21			
Age	29.3 (5.8)	26.7 (6.2)	22.6 (4.3)	$F = 8.4$	.001	a > c
Years of education	12.7 (2.5)	11.3 (1.4)	14.5 (1.4)	$F = 13.6$	.001	c > a and b
% HS diploma or GED	79.2	82.4	100.0	$\chi^2 = 4.8$	.09	---------
% Caucasian	95.8	82.4	85.7	$\chi^2 = 2.1$	.35	---------
% Married	20.8	23.5	28.6	$\chi^2 = .37$	.83	---------
% Never married	45.8	52.9	71.4	$\chi^2 = 3.1$	.21	---------
% Protestant	25.0	47.1	42.9	$\chi^2 = 2.5$	.28	---------
No. months of longest employment	48.4 (46.1)	39.8 (57.5)	35.2 (34.5)	$F = .39$	.68	---------
% Full-time employed	75.0	64.7	38.1	$\chi^2 = 6.6$	.04	c < a
% Part-time employed	16.7	17.6	61.9	$\chi^2 = 12.8$	.002	c > a and b

Table 6 (continued)

Variable	AD (a)	AD-ASPD (b)	Control (c)	Test Statistic	*p*	Post Hoc
Occupation						
% Clerical/professional	20.0	11.8	71.4	$\chi^2 = 20.1$	.001	c > a and b
% Skilled worker	54.2	58.8	19.0	$\chi^2 = 7.8$	.02	c > a and b
% Unskilled worker	29.2	29.4	9.5	$\chi^2 = 3.1$	.21	---------

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder. Occupational status was determined based on Hollingshead categories as outlined in the Addiction Severity Index.

Table 7

Means and Standard Deviations of Psychological and Cognitive Variables

	AD ($n = 24$)		AD-ASPD ($n = 17$)		Control ($n = 21$)	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*
Depressive symptoms	12.0	9.7	12.1	7.9	3.7	4.1
Anxious symptoms	8.4	7.6	5.7	5.7	3.3	5.6
PANAS-negative	13.5	3.9	13.2	5.1	11.7	1.8
PANAS-positive	31.9	8.3	29.4	9.6	31.5	6.9
Shipley-verbal	44.4	8.2	42.4	14.1	50.8	10.4
Shipley-abstract	48.7	12.1	48.1	10.3	53.2	8.5
Psychopathy	377.7	35.2	403.1	28.0	371.0	34.1

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder.

Table 8

Means and Standard Deviations of Alcohol Related Variables

	AD (n = 24)		AD-ASPD (n = 17)		Control (n = 21)	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*
Alcohol consumption						
Current	0.0	0.0	0.0	0.0	19.7	29.3
Past	294.5	269.0	379.7	311.9	66.6	67.4
Age of first use	12.5	2.7	11.6	2.9	16.8	3.6
Age of first regular use	16.6	3.4	14.8	1.5	18.6	2.5
Alcohol treatment	1.9	1.3	1.9	1.6	0.0	0.0
Months since last alcohol use	17.5	30.0	13.6	21.7	10.2	19.8
Nicotine dependence	5.1	1.4	4.9	2.0	-	-

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder. Because only 2 of 21 control participants smoked, descriptive information for nicotine dependence among this group is not reported.

Table 9

Behavior Resulting in Arrest or Legal Charges by Study Group [mean (SD) or percent]

Variable	AD (a)	AD-ASPD (b)	Control (c)	Test Statistic	*p*	Post Hoc
N	24	17	21			
No. months incarcerated	9.7 (15.9)	23.5 (32)	0.0 (0.0)	$F = 27.1$	< .001	c < a and b
No. arrests	3.3 (1.6)	4.8 (2.3)	0.0 (0.0)	$F = 50.0$	< .001	b > a and c a > c
Current probation/parole	66.7	88.2	0.0	$\chi^2 = 38.5$	.000	c < a and b†
Shoplifting/vandalism	16.7	47.1	0.0	$\chi^2 = 13.5$	.001	c < a† and b† b > a†
Probation/parole violations	46.0	64.7	0.0	$\chi^2 = 19.0$	.001	c < a and b†
Forgery	4.5	11.8	0.0	$\chi^2 = 2.9$	.239	---------
Weapons offense	16.7	47.1	0.0	$\chi^2 = 13.5$	.001	c < a† and b† b > a†
Burglary, larceny, breaking and entering	16.7	53.0	0.0	$\chi^2 = 16.3$	.000	c < a† and b† b > a

Table 9 (continued)

Variable	AD (a)	AD-ASPD (b)	Control (c)	Test Statistic	*p*	Post Hoc
Robbery	8.3	17.6	0.0	$\chi^2 = 4.0$	.139	---------
Assault	16.7	41.2	0.0	$\chi^2 = 11.0$	.004	c < a† and b†
Rape	4.5	0.0	0.0	$\chi^2 = 1.6$	.447	---------
Prostitution	0.0	5.9	0.0	$\chi^2 = 2.7$	.260	---------
Contempt of court	4.5	11.8	0.0	$\chi^2 = 2.9$	.239	---------
Major driving violations	87.5	88.2	81.0	$\chi^2 = .53$	.767	---------
Drug charges	58.3	53.0	0.0	$\chi^2 = 18.9$	.000	c < a and b†
Driving under influence	75.0	53.0	0.0	$\chi^2 = 26.5$	.000	c < a and b†
Other violations	66.7	70.6	0.0	$\chi^2 = 26.2$	.000	c < a and b†

Note. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder. Other violations included disorderly conduct, public intoxication, and vagrancy. † Minimum expected cell count was low (> 1) and more than 20% of cells had counts less than 5. Because small expected values contribute disproportionately to the chi-square statistic, results of this analysis should be interpreted with caution

Table 10

Zero-Order Intercorrelations of Startle Responsivity across Valence Categories and Study Variables

Variable	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Pleasant	-.54**	-.41	.20	-	.11	-	-	-.18	.11	-.19	.23	-.22	.25
2. Neutral		-.49**	.16	-	-	-.10	-	-.17	-	.22	-	-.14	-
3. Unpleasant			-.35	-.13	-.19	.13	.20	-	-	-.11	-	.37	-.20
4. Shipley-verbal				-.33	-	-.36	-.13	-	-	.41	-	-	-
5. Shipley-abstract					-	-	-	-	-.32	.24	-.23	.16	-
6. Psychopathy						.18	.10	-	-.27	-.23	.10	-.37	.28
7. Depressive symptoms							.73**	-.26	-.14	-.53**	.26	-.37	.25
8. Anxious symptoms								-.22	-.10	-.45*	-	-.10	.30
9. PANAS-negative									-.11	-	-	-	-
10. PANAS-positive										.14	-	.15	-
11. Alcohol-current											-.38	.44*	-.33
12. Alcohol-past												-.33	.41
13. Age first regular use													-.27
14. Family density													-

Note. Pearson *r* correlations. Entries of $r \leq .10$ are not shown. Pleasant = startle magnitude to pleasant slides; Neutral = startle magnitude to neutral slides; Unpleasant = startle magnitude to unpleasant slides. Given the number of Pearson *r* correlations performed, the Bonferroni adjustment was used to maintain an alpha level of .05. * $p < .05$. ** $p < .01$

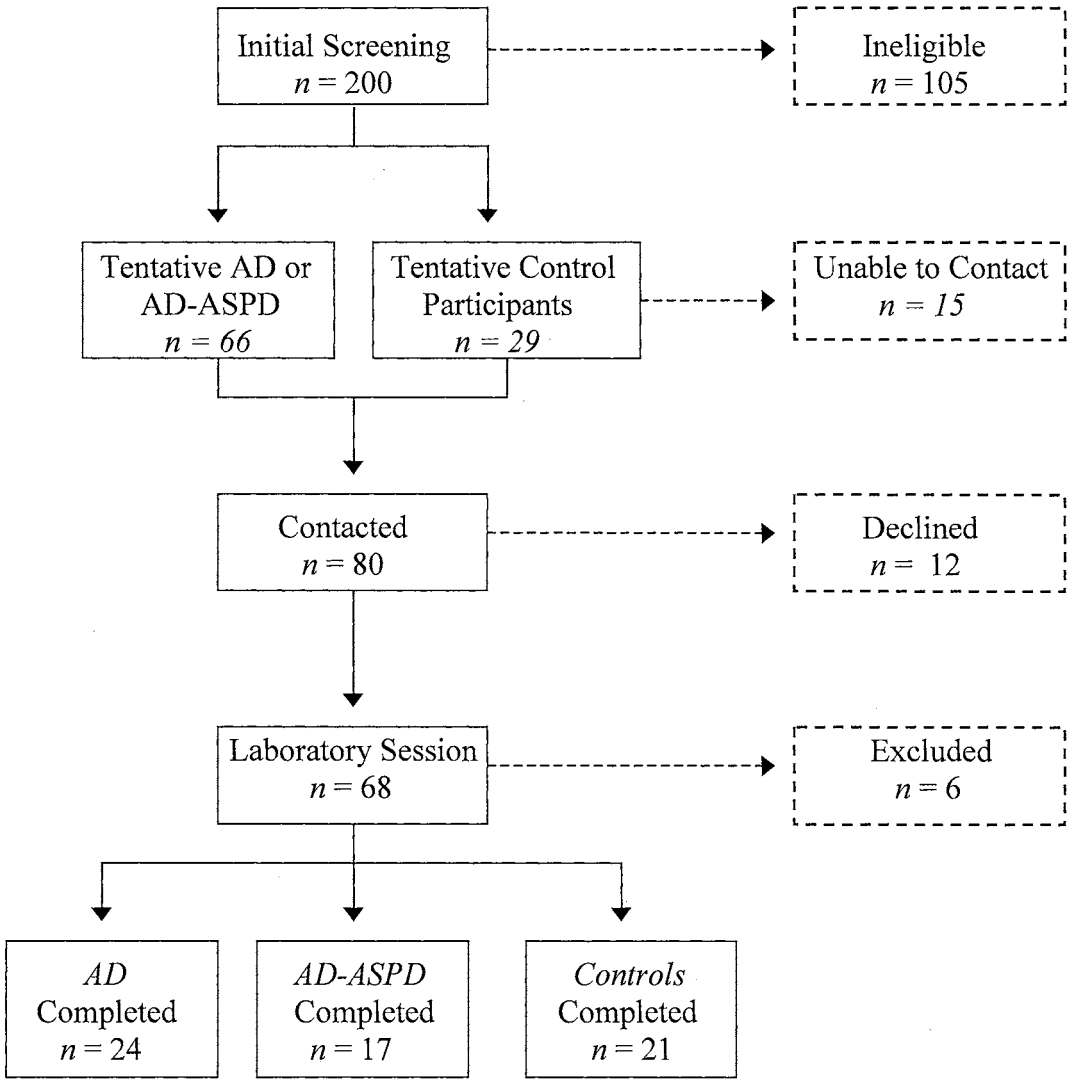

Figure 1. Diagram of participant screening and selection process. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder.

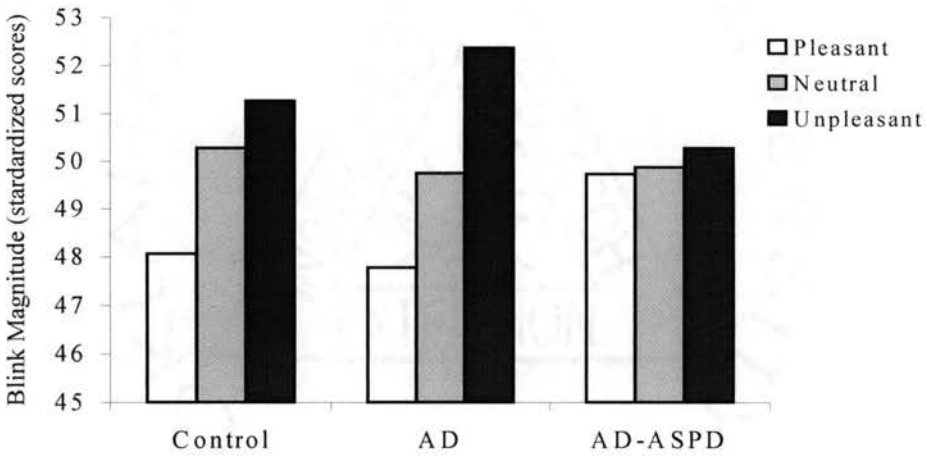

Figure 2. Mean eye blink reflex magnitudes to acoustic startle probes presented during emotionally positive, neutral, and negative photographic slides. Startle magnitudes are expressed in the standardized *T*-score metric (M = 50, SD = 10) using the individual mean and standard deviation from each participant across all three slide valences. AD = Alcohol Dependent; AD-ASPD = Alcohol Dependent with comorbid Antisocial Personality Disorder.

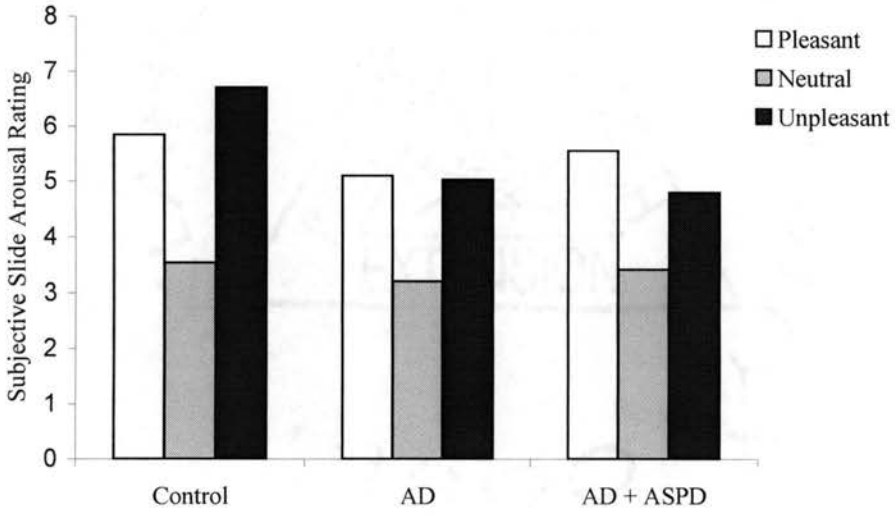

Figure 3. Subjective affective rating of the slide arousal dimension obtained using the self-assessment manikin and displayed by valence and study group. Each group rated the unpleasant and pleasant slides as more arousing than the neutral set and control participants rated the unpleasant slides as significantly more arousing relative to the other groups. There were no group differences in arousal ratings for pleasant and neutral slides.

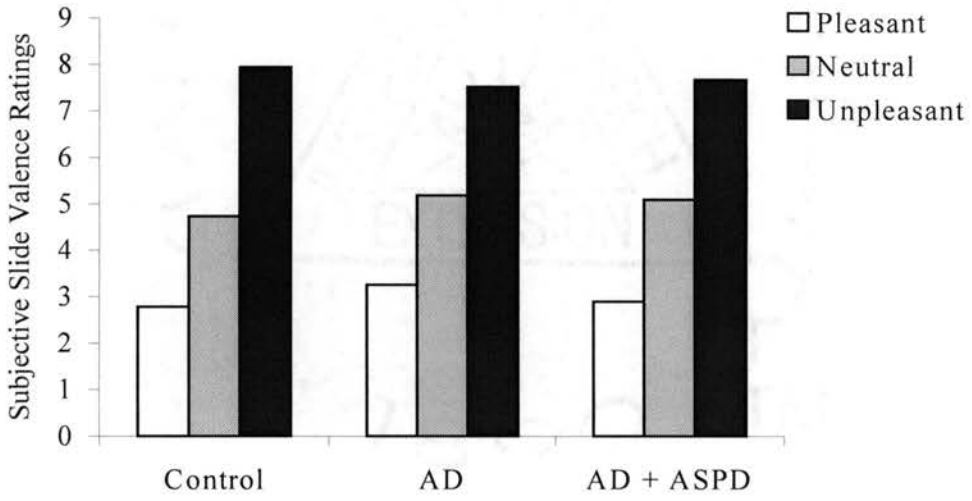

Figure 4. Subjective affective rating of the slide valence dimension obtained using the self-assessment manikin and displayed by valence and study group. For each group, pleasantness ratings were greatest for pleasant slides, intermediate for neutral slides, and lowest for unpleasant slides. Higher scores on the self-assessment manikin indicate greater unpleasantness ratings.

APPENDIX

OKLAHOMA STATE UNIVERSITY
INSTITUTIONAL REVIEW BOARD

Date: June 11, 1999 IRB #: AS-99-070

Proposal Title: "ALTERED PHYSIOLOGY OF EMOTIONS IN RISK FOR ALCOHOLISM"

Principal Investigator(s): Frank Collins
Robert Miranda
Brian Marx

Reviewed and Processed as: Expedited

Approval Status Recommended by Reviewer(s): Approved

Signature:

Carol Olson, Director of University Research Compliance

June 11, 1999
Date

Approvals are valid for one calendar year, after which time a request for continuation must be submitted. Any modification to the research project approved by the IRB must be submitted for approval. Approved projects are subject to monitoring by the IRB. Expedited and exempt projects may be reviewed by the full Institutional Review Board.

VITA 2

Robert Miranda, Jr.

Candidate for the Degree of

Doctor of Philosophy

Thesis: ABNORMAL EMOTIONAL REACTIVITY AMONG ALCOHOLICS: DELINEATING ANTISOCIAL PERSONALITY DISORDER

Major Field: Psychology

Biographical:

Personal Data: Born in New Bedford, Massachusetts on May 29, 1971, the son of Robert and Billie Miranda.

Education: Graduated from Apponoquet High School, Lakeville, Massachusetts in June 1989; received Bachelor of Arts degree in Psychology and Master of Education degree in Rehabilitation from the University of Georgia, Athens, Georgia in August 1994 and June 1996, respectively. Received the Master of Science degree with a major in Psychology at Oklahoma State University in December 1998. Respecialization in Biological Psychology completed at the University of Oklahoma Health Sciences Center in May 2002. Completed the requirements for the Doctor of Philosophy degree with a major in Clinical Psychology at Oklahoma State University in August 2002.

Experience: Internship in Clinical Psychology at Brown University, Providence, Rhode Island 2001-2002; Psychology Trainee at the Center on Child Abuse and Neglect, Oklahoma City, Oklahoma 1999-2001; Psychology Trainee at the Veterans Administration Medical Center in Oklahoma City, Oklahoma 1998-1999; Instructor for Introductory Psychology Course, Oklahoma State University, Stillwater, Oklahoma, 1997-1998; Psychology intern at Athens Regional Hospital's Psychiatric Unit, Athens, Georgia, 1995-1996.

Professional Memberships: American Psychological Association, Research Society on Alcoholism, Association for the Advancement of Behavior Therapy.