



*M*ental
Health



MENTAL HEALTH

Articles in the *Mental Health* Category

1. Alcoholics Have Blunted Responses to Psychological Stressors Such as Public Speaking
2. Alcoholics With Antisocial Personality Disorder Have Blunted Emotional Reactivity
3. Childhood Abuse May Predict Social Phobia, Agoraphobia and Post Traumatic Stress Disorder Among Adult Alcoholics
4. Searching for Anxiety Relief in Alcohol Can Be Dangerous
5. Suicidal Behavior Among Alcoholics
6. Adult Alcoholism and Attention Deficit Hyperactivity Disorder Are Connected
7. Alcohol Impairs Executive Cognitive Functioning Much Longer Than Expected
8. Alcohol Damages Day-to-Day Memory Function



ALCOHOLICS HAVE BLUNTED RESPONSES TO PSYCHOLOGICAL STRESSORS SUCH AS PUBLIC SPEAKING

- *Researchers measured the cardiovascular responses of alcoholics and nonalcoholics to the psychologically stressful act of public speaking.*
- *Alcoholics had blunted heart-rate responses to public speaking even though they reported similar anxiety responses to the nonalcoholics.*
- *This suggests a disconnection between perception of threat and the resulting physiological responses among the alcoholics.*

Secretion of a stress hormone called cortisol and activation of the sympathetic nervous system are components of the classic “fight or flight” response to danger. A common source of cortisol release and increased cardiovascular activity is public speaking. A study in the June issue of *Alcoholism: Clinical and Experimental Research (ACER)* builds upon previous work by comparing the cardiovascular responses of alcoholics and nonalcoholics to the psychological challenge of public speaking in relation to the physical challenge of standing (orthostasis).

“Since cortisol is central to our ability to handle stress,” said William R. Lovallo, director of the Behavioral Sciences Laboratories at the Veterans Affairs Medical Center in Oklahoma City and corresponding author for the study, “we were surprised several years ago when we found that patients with alcohol dependence had cortisol responses that were absent or greatly attenuated. It didn’t matter if the patient was asked to hold a hand in ice water, squeeze a hand-exercise device until it hurt, do mental arithmetic problems, or perform in a public-speaking simulation. Due to this cortisol response deficit, we suspected that these patients might also have a reduced fight or flight response. Most persons see public speaking as socially threatening, and they respond with the primitive fight or flight mechanism.”

Before testing alcoholics for their responses to a public-speaking task, researchers first needed to establish if their sympathetic nervous system was able to respond at all. “This would tell us if their blunting was specific to psychological stressors like public speaking,” said Lovallo, “or due to a generalized autonomic deficit.”

He and his colleagues examined 20 alcohol-dependent subjects, abstinent for 21 to 28 days, and 10 age-matched nonalcoholics. All subjects were males between the ages of 22 and 55 years. The researchers used impedance cardiography and dynamap blood pressure monitoring to assess the participants’ heart rate, stroke volume, cardiac output, total peripheral resistance, mean arterial pressure, systolic blood pressure and diastolic blood pressure during orthostasis and public speaking. Self-reported mood was also assessed during these two tasks.

Cardiovascular responses to orthostasis were similar for the two groups. However, the alcoholics had blunted heart-rate responses to public speaking even though they reported similar

continued ~

ALCOHOLICS HAVE BLUNTED RESPONSES TO PSYCHOLOGICAL STRESSORS SUCH AS PUBLIC SPEAKING

anxiety responses to the nonalcoholics. This suggests a disconnection between perception of threat and resulting physiological responses among the alcoholics.

“The similar cardiovascular responses to orthostasis among the alcohol-dependent patients indicate that their autonomic nervous systems were working normally,” said Lovallo. “Yet when we asked them to prepare and memorize a short speech and then deliver the speech to a video camera, the patients reacted with little or no change in heart rate, and of course, they failed to have a cortisol response. The patients reacted as if the social challenge of public speaking had no special meaning for them. So, the sympathetic nervous system in the patients looked normal, but their response to a psychological stressor was almost absent. When faced with a socially meaningful stressor, neither part of their fight-flight mechanism was working.”


“Emotion is the product of cognitive and physiological processes,” observed Ralph E. Tarter, professor of pharmaceutical sciences and psychiatry at the University of Pittsburgh. “Although speculative, the results of this study point to a physiologic-cognitive disconnection as a potential mechanism underlying the disturbed emotional experience of alcoholics. For example, although speculative, it could perhaps help explain why alcoholics appear outwardly unconcerned about their alcoholism when in fact their life is chaotic. This is commonly referred to as ‘denial.’ However, we need further research to delineate the extent to which deficient interpretation of cognitive and physiological processes is responsible for certain of the emotional tendencies of alcoholics.”

“Psychological stressors are usually events in our environment that have no ability to hurt us directly, in the way that cold, hunger or a predator can hurt us. So, why do we react as if we were in real danger when we are only giving a talk to an audience, and a fake audience at that? We process these kinds of events in our frontal cortex, the part of the brain that allows us to imagine things and to project ourselves into the future. This brain region has extensive connections with our limbic system, the primitive brain areas responsible for emotions and stress responses. Our results suggest that some aspect of this frontal-limbic connection has been altered in patients recovering from severe alcohol dependence, which has implications for their social functioning and comprehension,” said Lovallo.



Article is based on the following published research:

Panknin, T.L.,
Dickensheets, S.L.,
Nixon, S.J.,
Lovallo, W.R.
(June 2002).
Attenuated heart rate
responses to public
speaking in individuals
with alcohol
dependence.
*Alcoholism: Clinical
and Experimental
Research*,
26(6), 841-847.



ALCHOLICS WITH ANTISOCIAL PERSONALITY DISORDER HAVE BLUNTED EMOTIONAL REACTIVITY

- *Emotional reactivity refers to how people respond to pleasant and unpleasant events.*
- *New research has found that adult male alcoholics with antisocial personality disorder (ASPD) have abnormally low emotional responsiveness.*
- *Researchers speculate that the blunted responses found in this subgroup of alcoholics may be related to poor inhibitory abilities, which may, in turn, facilitate the development of alcoholism.*

Emotional reactivity refers to how people respond to both pleasant and unpleasant events, including ones that cause physical and mental stress. A study in the December issue of *Alcoholism: Clinical and Experimental Research (ACER)* has found abnormally low emotional responsiveness among adult male alcoholics with antisocial personality disorder (ASPD). Study authors say these findings may reflect dysfunction in brain regions that govern how humans relate to their environment and make adaptive decisions, which may in turn facilitate the development of alcoholism through maladaptive, disinhibited behavior.

“Despite their often subtle nature, emotional reactions hold a central position in determining how the brain regulates behavior,” said Robert Miranda, Jr., a National Institute on Alcohol Abuse and Alcoholism Postdoctoral Fellow at Brown University and first author of the study. “Through integration with cognitive processes, emotional reactions play an important role in learning and memory, evaluating variable environmental contingencies, and motivating adaptive behavior. There is considerable variability among individuals in terms of how emotionally reactive we are to different types of situations and events. These differences may indicate vulnerability to certain psychiatric conditions, such as mood and anxiety disorders and addictions. In the case of antisocial behavior and addictions, there may be diminished reactions to cues that signal aversive events, including punishment.”

Individuals who do not experience the appropriate amount of anxiety or negative emotion when threatened are unlikely to alter their behavior in response to the threat, said Peter R. Finn, professor of psychology at Indiana University in Bloomington. “Psychopaths, for example, are a subset of people with ASPD who show hyporesponsiveness to aversive stimuli. This study looks at reduced or hyporeactivity to aversive stimuli as evidence for poor inhibition, which may result in increased vulnerability to a wide range of problems including criminal, alcohol and/or drug problems. In other words, this hyporesponsivity may be manifesting itself in the antisocial behavior as well as the excessive use of alcohol.”

Researchers examined 62 males, divided into three groups: 24 were alcohol dependent; 17 were alcohol dependent and had ASPD; and 21 “controls” were neither alcohol dependent nor had ASPD. All of the participants completed self-report questionnaires, clinical interviews,

continued ~

A

LCOHOLICS WITH ANTISOCIAL PERSONALITY DISORDER HAVE BLUNTED EMOTIONAL REACTIVITY

and had their eye-blink electromyograms measured to acoustic startle probes while viewing color photographs rated as pleasant, neutral and unpleasant. (The startle response is a defensive reflex that is evoked when a person is presented with an abrupt event, such as a loud, unexpected noise. The reflex – in this case, the eye blink – is influenced by emotional states. It is “normally” larger when an individual is presented with unpleasant pictures, sounds or odors, and smaller when presented with pleasant stimuli.)

“We found that persons with co-existing alcoholism and ASPD are different from alcoholics without ASPD and non-ASPD, non-alcoholic controls in their responsiveness to emotional cues,” said Miranda. “The control and non-ASPD alcohol-dependent groups showed the normal linear increase in the eye-blink component of the startle reflex from pleasant to neutral to unpleasant stimuli. In contrast, alcoholics with ASPD did not show the typical increase of startle in response to the unpleasant stimuli or the decrease in response to pleasant stimuli. In short, their emotional responses appeared to be blunted. Importantly, all three groups rated the photographs similarly, ruling out the likelihood that response differences were due to altered subjective experiences of the photographs.”

Finn said these findings have both immediate and future applications. “Alcoholics tend to get into trouble a lot,” he said. “Yet these individuals simply may not be as affected by the prospects of negative outcomes, and may, in fact, have problems inhibiting their behavior to avoid such outcomes.”

Miranda agrees. “Conduct disorder (CD), the childhood predecessor to ASPD, is the most robust psychiatric risk factor for adolescent alcohol and drug use,” he said. “Numerous studies point to a consistent relationship between conduct problems in early and middle childhood and later drug use. Furthermore, the behavioral patterns exhibited by children and adolescents with CD may be a marker for underlying deficits in emotional reactivity and related impairment in frontal-limbic processes.”

Although a number of studies have identified a strong relationship between child and adolescent conduct problems and drug use, Miranda added, little research has targeted the underlying mechanisms that might explain this association. He said future research would attempt to do just that.

Article is based on the following published research:

Miranda Jr., R.,
Meyerson, L.A.,
Myers, R.R.,
Lovallo, W.R.
(December 2003).
Altered affective
modulation of the
startle reflex in
alcoholics with
antisocial personality
disorder.
*Alcoholism: Clinical
and Experimental
Research*,
27(12), 1901-1012.



CHILDHOOD ABUSE MAY PREDICT SOCIAL PHOBIA, AGORAPHOBIA AND POST TRAUMATIC STRESS DISORDER AMONG ADULT ALCOHOLICS

- *Many alcoholics report coexisting psychiatric disorders such as social phobia, agoraphobia, and post traumatic stress disorder.*
- *New research indicates that childhood abuse – sexual, physical or both – may play a role in the later development of coexisting psychopathologies among alcoholics.*

Findings published in the March issue of *Alcoholism: Clinical and Experimental Research (ACER)* have uncovered the important role that an environment of childhood abuse – sexual, physical or both – appears to play in the development of psychiatric comorbidity among alcoholic patients.

“Our findings clearly indicate that childhood abuse – more specifically, sexual abuse and combinations of sexual and physical abuse – is an important factor for the presence of comorbid anxiety disorders in treated alcoholics, particularly regarding social phobia, agoraphobia and post traumatic stress disorder,” said Willemien Langeland, a freelance trauma researcher at the University of Amsterdam and the Vrije Universiteit in Amsterdam, as well as first author of the study.

Langeland added that compared with other environmental risk factors, childhood sexual and “dual” abuse contribute independently to a more severe clinical profile, that is, more comorbid diagnoses in abused versus non-abused alcoholic patients. “This has not been previously demonstrated in treated alcoholics,” she said. “In addition, more severe and intrusive forms of early sexual abuse as well as early multiple traumas are associated with a more complex symptom constellation that includes dysthymia (a chronic mood disorder) and suicidality.”

“This study and a few others clearly show that seeing alcoholics only as people having an alcohol problem should be a thing of the past,” said Onno van der Hart, professor of psychopathology of chronic traumatization in the department of clinical psychology at Utrecht University in the Netherlands. “Very often the alcohol dependency or abuse is an indissoluble part of a history of childhood maltreatment or other adverse life events or conditions, as well as a range of other mental health problems. Insight into such complex patterns will lead to the realization that the simple treatment goal of ‘stopping drinking’ makes sense only when the overall treatment is geared toward this more complex system of problems.”

Researchers collected data during eight months (September 1994 - May 1995) from 155 alcoholics (122 males, 33 females) applying for treatment in a center for substance-use disorders. All study participants were assessed for demographics and treatment history through use of the European Addiction Severity Index. Numerous childhood stressors were indexed by the Structured Trauma Interview, and lifetime diagnoses of major depression, dysthymia, panic

continued ~

CHILDHOOD ABUSE MAY PREDICT SOCIAL PHOBIA, AGORAPHOBIA AND POST TRAUMATIC STRESS DISORDER AMONG ADULT ALCOHOLICS

disorder, social phobia, agoraphobia, generalized anxiety disorder and post traumatic stress disorder (PTSD) were assessed with the Composite International Diagnostic Interview. Participants were also asked about lifetime suicide attempts.

Alcoholic patients who reported childhood abuse – sexual, or sexual and physical – also reported social phobia, agoraphobia and PTSD more often than patients with no history of abuse. “Our study suggests a distinct pattern of psychiatric comorbidity associated with childhood abuse in treatment-seeking alcoholics,” said Langeland. “These findings point to the need for greater clinical attention to the role of childhood stressors in the evaluation and treatment of alcoholic patients. They also underline the importance of routine assessment of childhood trauma and possible trauma-related disorders in individuals presenting to alcohol-treatment services. Usually, standard or routine screening procedures do not include possible trauma-related symptoms such as PTSD, leading to underdiagnosis of this disorder.”

Although this study’s sample size of men was much greater than the sample size of women, Langeland said it is likely that gender may influence the way that alcohol problems and a co-occurring psychiatric disorder are related. “For example,” she said, “there is some evidence that women may be at higher risk than men to [develop] the form of comorbidity in which PTSD develops first.”

In addition, said Van der Hart, “it may well be that many female patients with alcohol dependence or abuse seek treatment in, or are referred to, more general mental-health centers. Perhaps their comorbid disorders, such as depression and anxiety disorders, as well as their trauma history (females report higher degrees of sexual abuse history), are more in the foreground, with the alcohol problems regarded as part of this overall clinical picture.”

“Given the fact that a considerable proportion of alcoholics report a history of childhood trauma and adverse events that include childhood physical and/or sexual abuse, as well as maternal dysfunction, which may point to neglect,” added Van der Hart, “studies should investigate whether the use of substances may be a form of coping or self-soothing. In addition, future studies, like the current one, should not only focus on one type of trauma, such as childhood sexual abuse, but should take the whole range of adverse life events and conditions into account.”

Article is based on the following published research:

Langeland, W.,
Draijer, N.,
& van den Brink, W.
(March 2004).
Psychiatric comorbidity
in treatment-seeking
alcoholics: The role of
childhood trauma and
perceived parental
dysfunction.
*Alcoholism: Clinical
and Experimental
Research*,
28(3), 441-447.



SEARCHING FOR ANXIETY RELIEF IN ALCOHOL CAN BE DANGEROUS

- *Practically everyone experiences some degree of anxiety in his or her life.*
- *Anxiety sensitive (AS) individuals have a fear of anxiety symptoms.*
- *Many people with alcohol problems have higher AS levels than “normal” drinkers.*
- *High AS individuals appear to be more “soothed” by alcohol than low AS individuals.*

People with high anxiety sensitivity (AS) have a fear of anxiety symptoms. Feeling common anxiety symptoms such as “butterflies in your stomach,” rapid breathing or an increased heart rate in the face of a stressful situation tends to amplify their anxious response. A study in the November issue of *Alcoholism: Clinical and Experimental Research (ACER)* investigated if high AS individuals are more soothed by alcohol than low AS individuals after being exposed to a stressful situation.

“People diagnosed with alcohol problems exhibit significantly higher levels of anxiety sensitivity than non-clinical populations,” said Alan B. MacDonald, a doctoral candidate in psychology at Dalhousie University and one of two first authors of the study. “Just as everyone experiences some degree of anxiety in their lives, almost everyone has some degree of anxiety sensitivity. However, people who have high anxiety sensitivity are people on the upper end of the continuum.” MacDonald estimates that approximately 16 percent of the population has high AS.

“Anxiety sensitive individuals are people who have a fear of anxiety, basically,” said Robert O. Pihl, professor of psychology and psychiatry at McGill University. “It’s kind of an anticipatory type response. This study helps us understand why these individuals are highly likely to become alcohol abusers.”

Although prior research has clearly demonstrated a link between alcohol problems and high AS, it has not established causality. This is, does high AS contribute to alcohol abuse or is it the other way around? This study examined volunteer undergraduate students with high or low AS who did not have, or were not yet diagnosed with, an alcohol problem. Participants were asked to hyperventilate for three minutes to induce anxiety-like symptoms. Following hyperventilation, participants were asked to report on three aspects of their experience: fearful thoughts, such as losing control; negative feelings, such as nervousness; and body sensations, such as an increased heart rate. Two doses of alcohol (high and low) were then administered.

Following the hyperventilation exercise and while completely sober, high AS participants reported significantly more fearful thoughts and negative feelings than the low AS participants. They also reported experiencing these negative thoughts and feelings more intensely than their low AS counterparts. After ingesting alcohol (both the high and low doses), high AS individuals showed much greater reductions in their fearful thoughts and negative feelings than the low AS participants. The high AS individuals not only found the alcohol more “soothing” (in that they experienced a greater reduction in their worries and concerns) than did their low AS counterparts, but this soothing effect became more pronounced the more they drank.

continued ~

SEARCHING FOR ANXIETY RELIEF IN ALCOHOL CAN BE DANGEROUS

MacDonald said that “coping” as a reason for drinking is a well-known marker for future alcohol abuse. “Our findings support the idea that high AS individuals may drink to cope with unpleasant sensations associated with anxiety, which could in turn lead to alcohol abuse,” said MacDonald. “Moreover, the more they drink, the greater the benefit they experience in terms of avoiding these unpleasant sensations. This may explain why high AS individuals report drinking to excess more frequently than the regular population.”

Although it might be said that people with high AS experience more benefits or positive effects from the stress-response dampening properties of alcohol, developing a dependency on alcohol is a potential downside. High AS individuals could become highly motivated to drink as a means of avoiding or reducing the anxiety sensations that they find so uncomfortable.

“Our findings have opened a small window into why some people may learn to abuse alcohol,” said MacDonald. “Knowing why leads to knowing what to do about it. We know that about one in seven readers of this article may have a high degree of AS. We are not saying that all people with high AS will necessarily go on to abuse alcohol, but it does appear that they are a high-risk group. If a reader recognizes that they may have high AS, perhaps they should think twice about using alcohol to feel better about their anxiety symptoms.”

MacDonald believes the study’s findings have implications for both prevention and treatment programs. “There is something unique about anxiety sensitivity, rather than anxiety per se, which may lead to future alcohol problems. Also, we need to study how well people are able to stay abstinent with or without treatment of anxiety sensitivity.” He suspects that treatment of high AS may enhance this population’s ability to stay abstinent from alcohol.

Indeed, Pihl believes it is imperative to be as specific as possible when looking for the different reasons why people abuse alcohol and other drugs. “We can’t look at these individuals as one kind of ubiquitous mass,” he said. “When someone talks about alcoholism, that doesn’t really explain anything. That doesn’t tell you ‘why.’ There are multiple reasons why things happen, and it’s important to understand these reasons before you get into any kind of treatment. Treatment should be specific to the ‘why.’”



Article is based on the following published research:

MacDonald, A.B.,
Baker, J.M.,
Stewart, S.H.,
& Skinner, M.
(November 2000).
Effects of alcohol on
the response to
hyperventilation of
participants high and
low in anxiety sensitivity.
*Alcoholism: Clinical
and Experimental
Research*,
24(10), 1656-1665.

SUICIDAL BEHAVIOR AMONG ALCOHOLICS

- *Alcoholics have a much higher rate of death by suicide than do members of the general population.*
- *Those alcoholics with a history of suicide attempts appear to have a significantly more severe course of alcohol dependence than other alcoholics.*
- *The fathers, mothers and siblings of alcoholics who had attempted suicide also showed a significantly higher prevalence of suicide attempts.*

Contemplating suicide is very common, according to a 1997 article in the *New England Journal of Medicine*. In fact, up to one third of the general population has thought about suicide at some point in their lives. The strongest predictor of suicide is psychiatric illness; more than 90 percent of people who commit suicide have diagnosable psychiatric illnesses at the time of death – usually depression, alcohol abuse or both. The lifetime risk for suicide completion among alcohol-dependent individuals has been reported to be almost 10 percent, which is five to 10 times greater than that found among the general population. A study in the April issue of *Alcoholism: Clinical and Experimental Research (ACER)* seeks to identify risk factors for suicide attempts among a large family-based sample of alcoholics from the Collaborative Study on the Genetics of Alcoholism (COGA).

“We found that alcohol-dependent individuals with a history of suicide attempts had a significantly more severe course of alcohol dependence,” said Marc A. Schuckit, principal COGA investigator at the University of California-San Diego site, also of the Veterans Affairs Medical Center and corresponding author for the study. “They also had a higher prevalence of both independent and substance-induced psychiatric disorders, as well as other substance dependence.” Schuckit speculated that increased alcohol intake by this subgroup of alcoholics may have led to more severe problems, which may have then resulted in brain dysfunction, neuropsychological changes and subsequent judgment impairment, an increased likelihood of mood swings and alcohol-related violent behavior. All of these factors could have contributed to life problems, as well as suicide attempts.

For this COGA investigation, 3,190 alcoholic men and women were given semi-structured, detailed interviews. Information about suicidal behavior, socioeconomic characteristics, psychiatric comorbidity, substance-use disorders and characteristics of alcohol dependence were obtained from the alcohol-dependent probands (original subjects of the study), their relatives, and controls (families without a history of alcohol dependence).

Of the total number of alcoholics, 522 (more than 16 percent), had a history of ever having attempted suicide; whereas 2,668 (close to 84 percent), did not. First-degree relatives (fathers, mothers and siblings) of individuals who had attempted suicide also showed a significantly higher prevalence of suicide attempts than other alcoholics, but – according to previous research – no enhanced rate of alcohol dependence, psychiatric comorbidity or other sub-

continued ~

SUICIDAL BEHAVIOR AMONG ALCOHOLICS

stance-use disorder. This suggests that suicidal behavior may be transmitted in families independent of alcohol dependence, psychiatric disorders or other substance-use disorders.

“Is there a suicide gene? Probably not,” said Robert M. Anthenelli, associate professor of psychiatry in the College of Medicine at the University of Cincinnati and director of substance dependence programs at the Cincinnati Veterans Affairs Medical Center. “But that’s beyond the scope of this paper’s findings. What this finding does is give some support for the idea that ‘suicidality’ or suicide attempts seem to run in families. However, family studies rarely do a good job of teasing out nature versus nurture, or genetics versus environment. What this study does nicely is show that a suicidal trait seems to exist independent of substance abuse disorders as well as other psychiatric disorders.”

Anthenelli added that the size of the study makes the associations found between suicidality and alcohol dependence more meaningful and believable than similar findings in previous, smaller studies. “Another strength is the percentage of women included, almost 40 percent,” he said, “which a lot of other studies are not always able to achieve.” In fact, he said, some of the gender differences in the findings were notable.

“The odds ratio of alcoholic women making a suicidal attempt was 2.86,” he said. “This means that an alcoholic woman has almost a three-fold greater likelihood of attempting suicide than a male alcoholic. That’s powerful. It also fits well with the knowledge that women in the general population make more suicide attempts than men, even though men have a higher completion rate.”

Schuckit plans to continue with the investigation of suicidality among alcoholics in order to better understand and prevent suicide attempts and completions among this subgroup. “The underlying theme of this paper,” said Schuckit, “and of the COGA studies in general, is that alcohol-dependent individuals who drink will likely have mood problems. Those that drink a lot will have major problems.”



Article is based on the following published research:

Preuss, U.W.,
Schuckit, M.A.,
Smith, T.L., Danko, G.P.,
Buckman, K.,
Bierut, L., Bucholz, M.N.,
Hesselbrock, M.N.,
Gesselbrock, V.M.,
& Reich, T.
(April 2002).
Comparison of 3,190
alcohol-dependent
individuals with
and without suicide
attempts.
*Alcoholism: Clinical
and Experimental
Research*,
26(4), 471.

A **ADULT ALCOHOLISM AND ATTENTION DEFICIT HYPERACTIVITY DISORDER ARE CONNECTED**

- *Attention deficit hyperactivity disorder (ADHD) symptoms include inattention, motor hyperactivity and impulsiveness.*
- *ADHD is five to 10 times more frequent among adult alcoholics than among the normal population.*
- *Investigation of the serotonin transporter gene (5-HTT) and the 5-HT_{2c} receptor Cys23Ser polymorphism does not support a genetic commonality of ADHD and alcoholism.*

Attention deficit hyperactivity disorder (ADHD) symptoms include inattention, motor hyperactivity and impulsiveness. Roughly half of the adults who report ADHD symptoms also report a co-existing substance abuse disorder. New findings published in the October issue of *Alcoholism: Clinical and Experimental Research (ACER)* have identified a distinct phenotype or “profile” of individuals with co-existing ADHD and alcoholism. Although prior studies have suggested a genetic commonality of ADHD and alcoholism, the study found no significant contribution of two specific candidate genes, the promoter polymorphism of the serotonin transporter gene (5-HTT) and the 5-HT_{2c} receptor Cys23Ser polymorphism.

“Our results indicate that individuals with persisting ADHD symptoms in adulthood seem to be at high risk of developing an alcohol use disorder,” said Monika Johann, medical doctor and research associate at the University of Regensburg and first author of the study. “Moreover, there is evidence for a highly increased severity of alcohol dependence in subjects with ADHD.”

Researchers examined 314 adult alcoholics (262 males, 52 females) as well as 220 unrelated healthy control subjects, all of German descent. Each participant was assessed for psychiatric disorders, such as substance-use disorders (including alcoholism), ADHD and antisocial personality disorder (ASPD). Patients with a history of major psychiatric disorders, including depression and schizophrenia, and those with addictions to drugs other than alcohol and nicotine, were excluded from the investigation. Genotyping was performed without knowledge of diagnostic status, with a focus on the 5-HTT promoter and the 5-HT_{2c} Cys23Ser polymorphism.

“Prior neuroendocrine challenge studies with a drug called fenfluramine in subjects with ADHD or alcoholism revealed similar differences in the serotonergic neurotransmission when compared to normal subjects,” explained Johann. “The usual response to fenfluramine administration is a measurable increase in the circulating prolactin. This usual increase is blunted in subjects with ADHD or alcoholism. The main structures responsible for the fenfluramine-induced prolactin release are the 5-HTT and the 5-HT_{2c} receptors. Therefore, both seemed plausible as overlapping sources of genetic liability of ADHD and alcoholism.”

Neither of them, however, appear to be genetic risk factors in the sample examined. “Our data

continued ~

A DULT ALCOHOLISM AND ATTENTION DEFICIT HYPERACTIVITY DISORDER ARE CONNECTED

demonstrate that the 5-HTT promoter and the 5-HT_{2c} Cys23Ser polymorphism do not contribute to the putative common genetic predisposition for ADHD and alcohol dependence,” said Johann. “However, several other candidate genes have yet to be investigated.”

Nonetheless, the findings do indicate a distinct phenotype, a way to measure an observable trait or behavior. Adult alcoholics with ADHD had a significantly higher daily and record intake of alcohol per month, an earlier age of onset of alcohol dependence, a higher frequency of thoughts about suicide and a greater number of court proceedings .

Despite the lack of support for a common genetic predisposition, “the data show once again that to have ADHD means to be at high risk for developing alcohol dependence,” said Ema Loncarek, a medical doctor and clinician at the psychiatric clinic of the University of Regensburg. “Dr. Johann’s findings of a phenotype are very close to what we see in drug addicts with ADHD, and what has been described before by other authors. ”

Johann described in more detail the phenotypic variations she and her colleagues found. “Within this group of alcoholics, subjects with ADHD in adulthood are five to 10 times more frequent than in the normal population,” she said. “Compared to alcoholics without ADHD, alcoholics with ADHD in adulthood were at least four years younger at onset of alcoholism, drank about 50 grams pure alcohol more per day during the previous month, had a nearly twofold higher rate of first-degree positive family history of alcoholism, had a nearly three times higher frequency of antisocial personality disorder, had a nearly seven times higher frequency of court proceedings, and had a more than two times higher frequency of suicidal thoughts.”

Both Johann and Loncarek spoke of a need for the development and evaluation of specialized treatment programs that address “phenotypical specifics” as well as co-existing disorders such as alcoholism and ADHD. While pharmacological remedies, they noted, have been extensively evaluated for the treatment of ADHD in childhood, little attention has been given to substance abusing individuals with ADHD in adulthood.”

“ADHD seems to be highly underestimated in adulthood,” said Johann, “yet seems to be an important risk factor for the development of alcohol dependence.”



Article is based on the following published research:

Johann, M., Bobbe, G.,
Putzhammer, A.,
Wodarz, N.
(October 2003).
Comorbidity of alcohol
dependence with
Attention deficit
hyperactivity disorder:
differences in phenotype
with increased
severity of the
substance disorder,
but not in genotype
(serotonin transporter
and
5-hydroxytryptamine-
2c receptor).
*Alcoholism: Clinical
and Experimental
Research*,
27(10), 1527-1535.

A

LCOHOL IMPAIRS EXECUTIVE COGNITIVE FUNCTIONING MUCH LONGER THAN EXPECTED

- *Executive cognitive functioning (ECF) includes cognitive abilities such as abstract reasoning, planning and the capacity to govern self-directed behavior.*
- *Researchers have found that ECF is more impaired during the descending limb of the blood alcohol concentration curve, when people no longer feel stimulated by alcohol.*
- *These findings indicate that intoxication effects last much longer than previously believed.*

Executive cognitive functioning (ECF) encompasses a number of higher order cognitive abilities, such as attention, abstract reasoning, organization, mental flexibility, planning, self-monitoring and the ability to use external feedback to moderate personal behavior. A study in the May issue of *Alcoholism: Clinical and Experimental Research (ACER)* has confirmed that not only does alcohol impair ECF but, surprisingly, this effect is more pronounced on the descending rather than the ascending trajectory (or limb) of the blood alcohol concentration (BAC) curve.

“Executive functioning is basically a metaphor for frontal lobe functioning,” explained Robert O. Pihl, professor of psychology and psychiatry at McGill University and first author of the study. “This area of the brain, the prefrontal cortex, arguably defines us as a species; it is roughly 120 percent larger in humans than in our closest primate relatives. In fact, some Russian neurophysiologists refer to it as the area of the brain that pulls the past, the present and the future together. In other words, it puts things in context.”

“Research on alcohol’s effects on ECF is important primarily because it sheds light on the relationship between intoxication and aggression,” added Jordan B. Peterson, associate professor of psychology at the University of Toronto. “Approximately 50 percent of murderers are intoxicated at the time of their crime. The same holds true of their victims.”

Study participants (n=41) were divided into two groups: 21 subjects were given 1.32 ml of 95 percent alcohol per kg of body weight mixed with orange juice; the remaining 20 were given a placebo. Participants were randomly assigned to either an ascending or descending limb group. (When people drink alcohol, stimulation is initially prominent, while blood alcohol levels are rising during the ‘ascending limb’ of the blood alcohol concentration [BAC] curve. During the ‘descending limb’ of the BAC curve, when blood alcohol levels are falling, sedation becomes the prominent experience.) All of the participants were given six tests of ECF when a breath measure of their BAC reached 0.08.

Intoxicated participants on both limbs demonstrated ECF impairment. However, the descending alcohol limb group showed greater ECF impairment than their ascending limb counterparts, particularly in spatial functioning.

“Our results were unexpected,” said Pihl. “Based on prior research, we had expected cognitive deficiencies to be greater on the ascending limb. Although ‘intoxication’ clearly lasts a long

continued ~

ALCOHOL IMPAIRS EXECUTIVE COGNITIVE FUNCTIONING MUCH LONGER THAN EXPECTED

time, you don't have the same feedback of feeling intoxicated on the descending limb. You have a different perception of what your decrements are when you 'feel' intoxicated and energized versus when you think, 'Hey, I'm getting sober.' Yet our findings show that even when you're at the same blood alcohol level on the downward limb, you have more pronounced deficits."

This finding has important ramifications for behaviors such as driving, Pihl added. "People who think they've waited their two hours before driving home may need to actually wait six hours. Or else, maybe at the time when you least expect it, you're the most vulnerable."

"The subjective effects that alcohol drinkers pursue are most likely experienced during the short, ascending limb," said Peterson. "Conversely, the descending limb lasts a very long time. This means that the drinker in the process of re-attaining sobriety is likely to be more dangerous, for example, than the drinker who is still imbibing. As the authors point out, this may also be relevant with regards to impaired driving: it could be that the drinker at a BAC of 0.08 is less qualified to drive while immediately recovering from a drinking episode than while actively drinking."

Peterson praised Pihl's lab for its investigation of relatively high-dose alcohol administration – research that has become increasingly difficult in recent years. "However, such high doses appear absolutely necessary to produce the kind of cognitive effects reported in this manuscript," he said. "Furthermore, they are clearly in keeping with the levels of intoxication that drinkers reach when drinking for pleasure in bars and at parties." He suggested that future research examine how long the detrimental descending-limb cognitive effects last. "Are drinkers back to baseline cognitive function once their BACs fall to 0.04, for example, or are they still substantively impaired? Have they returned to baseline the next day, after sleeping through the sobering-up process, even if they still feel some hangover effects?" he asked.



Article is based on the following published research:

Pihl, R.O.,
Paylan, S.S.,
Gentes-Hawn, A.,
Hoaken, P.N.S.
(May 2003).

Alcohol affects executive
cognitive functioning
differentially on the
ascending versus
descending limb of
the blood alcohol
concentration curve.
*Alcoholism: Clinical
and Experimental
Research*,
27(5), 773-780.

A

LCOHOL DAMAGES DAY-TO-DAY MEMORY FUNCTION

- *Researchers know that heavy alcohol use damages retrospective memory.*
- *New research shows that heavy alcohol use also damages day-to-day memory, which includes prospective memory (remembering to do things at some future point in time) and everyday memory (remembering to complete daily activities).*
- *This damage occurred within drinking limits suggested by U.K. government guidelines.*

Research has shown that heavy alcohol use clearly damages retrospective memory, that is, the learning, retention and retrieval of previously presented materials. Less is known about the effects of alcohol on day-to-day memory function, specifically, prospective memory (remembering to do things at some future point in time) and everyday memory (remembering to complete daily activities). A study in the June issue of *Alcoholism: Clinical and Experimental Research (ACER)* uses Internet-based methodology to find that heavy alcohol consumption has a negative impact on day-to-day memory.

“Prospective memory impairments include things like forgetting to send someone a birthday card on time, or forgetting what you’re going to say in the middle of a sentence,” said Jonathan Ling, a senior lecturer in psychology at the University of Teesside in the United Kingdom and first author of the paper. “Everyday memory failures include telling someone a story that you’ve told them before, or forgetting where things are normally kept. Obviously we all forget things from time to time, however, heavy users of alcohol make noticeably more of these mistakes than either non- or low-users of alcohol.” Ling added that most of what is known about heavy drinkers’ retrospective memory function is based on laboratory research, and even less is known about alcohol’s effects on normal memory-related tasks that people perform from day-to-day.

For this study, researchers collected data from 763 participants (465 female, 298 males) using a specially created Web site on the University of Westminster Web server. Memory was assessed using two self-report questionnaires: the Prospective Memory Questionnaire (PMQ), and the Everyday Memory Questionnaire (EMQ). The PMQ has three sub-scales that measure short-term habitual PM, long-term episodic PM and internally-cued PM. Respondents also self-reported their level of use of alcohol and other drugs by responding to the UEL (University of East London) Recreational Drug Use Questionnaire.

The results indicate a dose-dependent effect of alcohol use on day-to-day memory function. “We found that heavy users of alcohol reported making consistently more errors than those who said that they consumed little or no alcohol,” said Ling. “A typical heavy user of alcohol reported over 30 percent more memory-related problems than someone who reportedly did not drink, and almost 25 percent more problems than those who stated they drank only small amounts of alcohol. More specifically, those participants who reported higher levels of alcohol consumption were more likely to miss appointments, forget birthdays and not pay bills on time. Deficits in everyday memory included problems with remembering whether they had done something like locking the door or switching off the lights, or forgetting where they put items like house keys.”

continued ~

A

LCOHOL DAMAGES DAY-TO-DAY MEMORY FUNCTION

Colin R. Martin, a lecturer in mental health in the Department of Health Sciences at the University of York and honorary consultant psychologist to the Addiction Service and National Monitoring and Evaluation Center of the Salvation Army, said these results “contribute to the increasing evidence that a diverse range of memory impairment is associated with excessive alcohol consumption. The underlying mechanisms responsible for memory deficits associated with excessive alcohol consumption are multi-factorial and, in many areas of specific deficit, continue to be currently poorly understood. This study is important because it extends our knowledge of alcohol-related memory impairment to everyday situations that most people can identify with, in contrast to laboratory-based memory tasks.”

“We also found a significant increase in reported memory problems by people who claimed to drink between 10 and 25 units each week in comparison to non-drinkers,” added Ling. One unit of alcohol is the equivalent of 10 ml of ethanol; roughly half a pint of beer or one small glass of wine. Current U.K. guidelines for maximum safe units per week are 21 units for women and 28 units for men. “This is an important finding, as it indicates that even if people are using alcohol within the limits suggested by U.K. government guidelines, these individuals still report experiencing memory problems.”

Martin concurred. “Interested readers may wish to reflect on the relevance of government recommended safe drinking limits, since decreased memory performance was observed even within what is generally acknowledged as safe drinking levels,” he said. “Recommended levels may be safe for the liver, but we can’t be sure that they represent safe limits for optimum brain function.”

Martin suggested that the role of deficits in day-to-day memory performance should be explored and extended to those individuals receiving treatment for alcohol-dependency problems. “Memory deficits are common in individuals who are receiving inpatient and community treatment for alcohol dependency,” he noted, “yet assessment of everyday memory performance in this group has yet to be established. This is particularly important because a number of the counseling and relapse prevention therapies and strategies used in this group are reliant on a fundamentally intact memory system.”



Article is based on the following published research:

Ling, J.,
Heffernan, T.M.,
Buchanan, T.,
Rodgers, J.,
Scholey, A.B.,
Parrott, A.C.
(June 2003).
Effects of alcohol
on subjective ratings
of prospective and
everyday memory
deficits.
*Alcoholism: Clinical
and Experimental
Research*,
27(6), 970-975.