

Abstracts

ADDICTION: CURRENT
AND FUTURE TREATMENTS

Given space limitations and varying reprint permission policies, not all of the influential publications the editors considered reprinting in this issue could be included. This section contains abstracts from additional articles the editors deemed well worth reviewing.

Onset and Course of Alcoholism over 25 Years in Middle Class Men

Schuckit MA, Smith TL

Drug Alcohol Depend. 2011 Jan 1;113(1):21–8. Epub 2010 Aug 19

Background: Patterns of drinking and alcohol problems change with age. However, few studies use multiple data points and detailed history spanning early adulthood to middle age. This study reports such data from 373 men in the San Diego Prospective Study. **Methods:** Data were generated at baseline (T1) at ~age 20, and through face-to-face follow up interviews ~every 5 years in >90% of these eligible Caucasian and relatively higher educated men. Subjects were placed into 4 groups regarding their course: 62.5% with no alcohol use disorder (AUD); 17.2% with AUD onset <age 30 and a chronic course; 6.7% with onset ≥age 30 and no recovery; and 13.7% with AUD onset <age 30 and maintained remission for >5 years before the 25-year followup. **Results:** One a univariate level, low level of response (LR) to alcohol, family history of AUDs, and higher Novelty Seeking at ~age 20 predicted AUDs with onset before age 30 (mean age ~25), but among these only LR predicted later onset (mean age 38) as well. Additional predictors of AUDs included demography (lower education), and greater involvement with alcohol, drugs, and nicotine prior to T1. Sustained remission from AUDs among alcoholics was predicted by lower T1 and T10 drinking frequencies, and being separated or divorced at T10, along with a trend for higher Reward Dependence. **Conclusion:** These data indicate that information available in ages of the late teens to early twenties can help predict the future onset and course of AUDs, and underscore the importance of longitudinal studies in substance use disorders.

The Role of a Prescription in Anxiety Medication Use, Abuse, and Dependence

Fenton MC, Keyes KM, Martins SS, Hasin DS

Am J Psychiatry. 2010 Oct;167(10):1247–53. Epub 2010 Jul 1

Objective: Prescriptions for anxiety medications have increased substantially in recent years. Individuals with anxiety disorders are at risk of nonmedical use of these medications, but information about whether this risk is elevated among patients with a prescription for such medications is lacking. The authors compared risk of nonmedical use in individuals in a national sample with and without a prescription for anxiety medication and identified characteristics associated with nonmedical use. **Method:** Data were drawn from face-to-face surveys of 34,653 adult participants in the National Epidemiologic Survey on Alcohol and Related Conditions. The risk of nonmedical use of prescription anxiety medication and associated drug use disorders was computed for individuals who had or had not ever received a prescription for anxiety medication; among those who had received a prescription, characteristics associated with nonmedical use were analyzed. **Results:** Prescription of anxiety medication was associated with lifetime and past-year nonmedical use (odds ratios, 1.6 and 1.9, respectively) and lifetime DSM-IV abuse or dependence (odds ratio, 2.6). Among respondents who received a prescription (N = 4,294), nonmedical use was associated with male sex, younger age, white race, history of use of illicit drugs, history of other drug use disorders, and history of illegal behaviors. **Conclusions:** These results indicate that prescription for anxiety medications is associated with nonmedical use of these medications, although the direction of causality cannot be determined in this study. Although anxiety medications have clinical utility, greater clinical attention should be given to the potential for their abuse among patients at particular risk.

Therapeutic Use, Abuse, and Nonmedical Use of Opioids: A Ten-Year Perspective

Manchikanti L, Fellows B, Ailinani H, Pampati V
Pain Physician. 2010 Sep–Oct;13(5):401–35

The treatment of chronic pain, therapeutic opioid use and abuse, and the nonmedical use of prescription drugs have been topics of intense focus and debate. After the liberalization of laws governing opioid prescribing for the treatment of chronic non-cancer pain by state medical boards in the late 1990s, and with the introduction of new pain management standards implemented by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in 2000, opioids, in general, and the most potent forms of opioids including Schedule II drugs, in particular, have dramatically increased. Despite the escalating use and abuse of therapeutic opioids, nearly 15 to 20 years later the scientific evidence for the effectiveness of opioids for chronic non-cancer pain remains unclear. Concerns continue regarding efficacy; problematic physiologic effects such as hyperalgesia, hypogonadism and sexual dysfunction; and adverse side effects—especially the potential for misuse and abuse - and the increase in opioid-related deaths. Americans, constituting only 4.6% of the world's population, have been consuming 80% of the global opioid supply, and 99% of the global hydrocodone supply, as well as two-thirds of the world's illegal drugs. Retail sales of commonly used opioid medications (including methadone, oxycodone, fentanyl base, hydromorphone, hydrocodone, morphine, meperidine, and codeine) have increased from a total of 50.7 million grams in 1997 to 126.5 million grams in 2007. This is an overall increase of 149% with increases ranging from 222% for morphine, 280% for hydrocodone, 319% for hydromorphone, 525% for fentanyl base, 866% for oxycodone, to 1,293% for methadone. Average sales of opioids per person have increased from 74 milligrams in 1997 to 369 milligrams in 2007, a 402% increase. Surveys of nonprescription drug abuse, emergency department visits for prescription controlled drugs, unintentional deaths due to prescription controlled substances, therapeutic use of opioids, and opioid abuse have been steadily rising. This manuscript provides an updated 10-year perspective on therapeutic use, abuse, and non-medical use of opioids and their consequences.

Breaking Barriers in the Genomics and Pharmacogenetics of Drug Addiction

Ho MK, Goldman D, Heinz A, Kaprio J, Kreek MJ, Li MD, Munafò MR, Tyndale RF
Clin Pharmacol Ther. 2010 Dec;88(6):779–91. Epub 2010 Oct 27

Drug addiction remains a substantial health issue with limited treatment options currently available. Despite considerable advances in the understanding of human genetic architecture, the genetic underpinning of complex disorders remains elusive. On the basis of our current understanding of neurobiology, numerous candidate genes have been implicated in the etiology and response to treatment for different addictions. Genome-wide association (GWA) studies have also identified novel targets. However, replication of these studies is often lacking, and this complicates interpretation. The situation is expected to improve as issues such as phenotypic characterization, the apparent “missing heritability,” the identification of functional variants, and possible gene-environment ($G \times E$) interactions are addressed. In addition, there is growing evidence that genetic information can be useful in refining the choice of addiction treatment. As genetic testing becomes more common in the practice of medicine, a variety of ethical and practical challenges, some of which are unique to drug addiction, will also need to be considered.

An Approach to the Patient with Substance Use and Abuse

Maldonado JR
Med Clin North Am. 2010 Nov;94(6):1169–205, x-i

Substance use is ubiquitous among medically ill patients. The 2008 National Survey on Drug Abuse and Health survey estimated that 20.1 million Americans aged 12 years or older (8% of the US population) had used an illicit drug during the preceding month. Some licit substances also create havoc. The survey found that slightly more than half (56%) of Americans reported being current drinkers of alcohol. A total of 6.2 million (2.5%) Americans used prescription-type psychotherapeutic drugs for nonmedical purposes and 70.9 million Americans (or 28.4%) used tobacco during the survey period. Substance abuse

problems were diagnosed in up to 36% of medically hospitalized patients for whom a psychiatric consultation was requested. Given how prevalent the use of substances is among the medically ill and their potential effect on comorbid medical conditions, it is important for physicians to be mindful of their prevalence and presentation. This article covers the presenting symptoms of intoxication and withdrawal states, addresses the acute management of the most commonly encountered substances, and summarizes all others in a table.

Mental Disorders as Risk Factors for Substance Use, Abuse and Dependence: Results From the 10-Year Follow-up of the National Comorbidity Survey

Swendsen J, Conway KP, Degenhardt L, Glantz M, Jin R, Merikangas KR, Sampson N, Kessler RC
Addiction. 2010 Jun;105(6):1117–28. Epub 2010 Mar 10

Aims: The comorbidity of mental disorders and substance dependence is well documented, but prospective investigations in community samples are rare. This investigation examines the role of primary mental disorders as risk factors for the later onset of nicotine, alcohol and illicit drug use, abuse and dependence with abuse. **Design:** The National Comorbidity Survey (NCS) was a nationally representative survey of mental and substance disorders in the United States carried out in 1990–92. The NCS-2 re-interviewed a probability subsample of NCS respondents in 2001–03, a decade after the baseline survey. **Participants:** A total of 5001 NCS respondents were re-interviewed in the NCS-2 (87.6% of baseline sample). **Results:** Aggregate analyses demonstrated significant prospective risks posed by baseline mental disorders for the onset of nicotine, alcohol and illicit drug dependence with abuse over the follow-up period. Particularly strong and consistent associations were observed for behavioral disorders and previous substance use conditions, as well as for certain mood and anxiety disorders. Conditional analyses demonstrated that many observed associations were limited to specific categories of use, abuse or dependence, including several mental disorders that were non-significant predictors in the aggregate analyses. **Conclusions:** Many mental disorders are associated with an increased risk of later substance use conditions, but important differences in these associations are observed across the categories of use, abuse and dependence with abuse. These prospective findings have implications for the precision of prevention and treatment strategies targeting substance use disorders.

A Genome-Wide Association Study of Alcohol Dependence

Bierut LJ, Agrawal A, Bucholz KK, Doheny KF, Laurie C, Pugh E, Fisher S, Fox L, Howells W, Bertelsen S, Hinrichs AL, Almasy L, Breslau N, Culverhouse RC, Dick DM, Edenberg HJ, Foroud T, Gruzca RA, Hatsukami D, Hesselbrock V, Johnson EO, Kramer J, Krueger RF, Kuperman S, Lynskey M, Mann K, Neuman RJ, Nöthen MM, Nurnberger JI Jr, Porjesz B, Ridinger M, Saccone NL, Saccone SF, Schuckit MA, Tischfield JA, Wang JC, Rietschel M, Goate AM, Rice JP; Gene, Environment Association Studies Consortium
Proc Natl Acad Sci U S A. 2010 Mar 16;107(11):5082–7. Epub 2010 Mar 2

Excessive alcohol consumption is one of the leading causes of preventable death in the United States. Approximately 14% of those who use alcohol meet criteria during their lifetime for alcohol dependence, which is characterized by tolerance, withdrawal, inability to stop drinking, and continued drinking despite serious psychological or physiological problems. We explored genetic influences on alcohol dependence among 1,897 European-American and African-American subjects with alcohol dependence compared with 1,932 unrelated, alcohol-exposed, nondependent controls. Constitutional DNA of each subject was genotyped using the Illumina 1M beadchip. Fifteen SNPs yielded $P < 10^{-5}$, but in two independent replication series, no SNP passed a replication threshold of $P < 0.05$. Candidate gene GABRA2, which encodes the GABA receptor alpha2 subunit, was evaluated independently. Five SNPs at GABRA2 yielded nominal (uncorrected) $P < 0.05$, with odds ratios between 1.11 and 1.16. Further dissection of the alcoholism phenotype, to disentangle the influence of comorbid substance-use disorders, will be a next step in identifying genetic variants associated with alcohol dependence.

Treatment Challenges Associated With Comorbid Substance Use and Posttraumatic Stress Disorder: Clinicians' Perspectives

Back SE, Waldrop AE, Brady KT
Am J Addict. 2009 Jan-Feb;18(1):15–20

A significant proportion of individuals with substance use disorders (SUDs) meet criteria for comorbid posttraumatic stress disorder (PTSD). This comorbidity confers a more complicated clinical presentation that carries with it formidable treatment challenges for practitioners. The current study examined sources of difficulty and gratification among clinicians ($N = 423$) from four national organizations who completed an anonymous questionnaire. As expected, the findings revealed that comorbid SUD/PTSD was rated as significantly more difficult to treat than either disorder alone. The most common challenges associated with treating SUD/PTSD patients included knowing how to best prioritize and integrate treatment components, patient self-destructiveness and severe symptomatology, and helping patients abstain from substance use. The findings increase understanding of SUD/PTSD treatment challenges, and may be useful for enhancing therapist training programs, supervision effectiveness, and designing optimal SUD/PTSD interventions.

Effectiveness of Current Treatment Approaches for Benzodiazepine Discontinuation: A Meta-analysis

Parr JM, Kavanagh DJ, Cahill L, Mitchell G, McD Young R
Addiction. 2009 Jan;104(1):13–24. Epub 2008 Oct 31

AIMS: To assess the effectiveness of current treatment approaches to assist benzodiazepine discontinuation. **Methods:** A systematic review of approaches to benzodiazepine discontinuation in general practice and outpatient settings was undertaken. Routine care was compared with three treatment approaches: brief interventions, gradual dose reduction (GDR) and psychological interventions. GDR was compared with GDR plus psychological interventions or substitutive pharmacotherapies. **Results:** Inclusion criteria were met by 24 studies, and a further eight were identified by future search. GDR [odds ratio (OR) = 5.96, confidence interval (CI) = 2.08–17.11] and brief interventions (OR = 4.37, CI = 2.28–8.40) provided superior cessation rates at post-treatment to routine care. Psychological treatment plus GDR were superior to both routine care (OR = 3.38, CI = 1.86–6.12) and GDR alone (OR = 1.82, CI = 1.25–2.67). However, substitutive pharmacotherapies did not add to the impact of GDR (OR = 1.30, CI = 0.97–1.73), and abrupt substitution of benzodiazepines by other pharmacotherapy was less effective than GDR alone (OR = 0.30, CI = 0.14–0.64). Few studies on any technique had significantly greater benzodiazepine discontinuation than controls at follow-up. **Conclusions:** Providing an intervention is more effective than routine care. Psychological interventions may improve discontinuation above GDR alone. While some substitutive pharmacotherapies may have promise, current evidence is insufficient to support their use.

Drug Addiction: The Neurobiology of Disrupted Self-Control

Baler RD, Volkow ND
Trends Mol Med. 2006 Dec;12(12):559–66. Epub 2006 Oct 27

The nature of addiction is often debated along moral versus biological lines. However, recent advances in neuroscience offer insights that might help bridge the gap between these opposing views. Current evidence shows that most drugs of abuse exert their initial reinforcing effects by inducing dopamine surges in limbic regions, affecting other neurotransmitter systems and leading to characteristic plastic adaptations. Importantly, there seem to be intimate relationships between the circuits disrupted by abused drugs and those that underlie self-control. Significant changes can be detected in circuits implicated in reward, motivation and/or drive, salience attribution, inhibitory control and memory consolidation. Therefore, addiction treatments should attempt to reduce the rewarding properties of drugs while enhancing those of alternative reinforcers, inhibit conditioned memories and strengthen cognitive control. We posit that the time has come to recognize that the process of addiction erodes the same neural scaffolds that enable self-control and appropriate decision making.