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Meeting Abstracts

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Keynote Abstracts

"Dopamine Resistance" in Brain Reward Circuitry as a Function of Genetic Addiction Risk Score (GARSPDX) Polymorphisms in RDS: Synaptamine Complex Variant (KB220Z) Induced "Dopamine Sensitivity" as a Pro-Recovery Agent

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Abstract

Explorations of brain function in terms of both physiology and behavioral traits have resulted in a plethora of studies linking these activities to neurotransmitter functions having a genetic basis. We address the age-old question of "Nature vs. Nurture" as it relates to the question of happiness and to the larger question relating to human nature as an emerging science. Attempts to identify key "vector influences" that link genes, the brain, and social behaviors to a so-called state of "happiness" are important areas for developing a new science of human nature. It is well established that in both food and drug addicted individuals there is "dopamine resistance" due to an association with the DRD2 gene A1 allele. Based on newer current research a restrictive panel of at least ten reward gene risk polymorphisms called Genetic Addiction Risk Score (PDX)" has been shown to significantly associate with the Alcohol ($p<0.004$) and Drug ($P<0.05$) Addiction Severity Index–Media Version. Following age adjustments, the alcohol prediction of severity remained significant ($p<0.012$). Unlike other genetic tests GARSPDX predicts severity utilizing a mandated clinical outcome. Switching one gene risk allele for another one resulted in non-significance. Similarly, weighting each gene instead of just counting risk alleles also resulted in non-significance. These findings suggest that a "gene cluster or network" loads onto alcohol and drug severity risk. Evidence is emerging whereby the potential of utilizing an amino-acid non-addicting, safe putative D2 agonist may find its place in recovery of Reward Deficiency Syndrome (RDS).Utilizing qEEG and fMRI as imaging tools our work will show the impact of Synaptamine Complex Variant [KB220Z]™ as an activator of the meso-limbic system and administration significantly reduces or "normalizes" aberrant electrophysiological parameters of the reward circuitry site in abstinent psychostimulant abusers. rsfMRI in abstinent Heroin addicts reveal restoration of a reduced functional connectivity. In addition, it was found that administration of KB220Z in rat studies showed a significant enhancement in rsfMRI compared to placebo. Based on our neuroimaging studies presented herein we cautiously suggest that long-term activation of dopaminergic receptors (i.e., DRD2 receptors) will result in proliferation of D2 receptors leading to enhanced "dopamine sensitivity" and an increased sense of happiness in recovery.

Process Addictions and Addiction Transfer

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Abstract

Understanding Reward Deficiency Syndrome (RDS) has become a key principle in addiction treatment programs dealing with dual diagnosis patients whose clinical picture is complicated by the process addictions. The definition of addiction developed by the American Society of Addiction Medicine (ASAM) will be applied to process addictions. The core principles of RDS will be outlined, specific process addictions will be described as they occur and as they're managed in a clinical setting. The

concept of addiction transfer describes the substitution of a process addiction for substance abuse, e.g. stopping smoking and then increasing food intake. Addiction transfer is a difficult issue to deal with in addiction treatment and recovery and specific clinical techniques for its management will be outlined. Case examples will be provided.

Reward Deficiency Syndrome in Sports Psychiatry

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Abstract

RDS offers a novel approach to understanding a potential etiology and treatment of substance use disorders. Blum and colleagues have provided intriguing preclinical data and thoughtful analysis of a translational approach to creating clinical interventions utilizing the information generated from their ongoing research. In addition to drug abuse, Reward Deficiency likely plays an important role in other forms of psychopathology, particularly Mood Disorders and Eating Disorders.

The field of Sports Psychiatry is relatively new and focuses on psychopathology presenting in athletes (along with other areas, such as the role of exercise as a treatment modality, long-term psychiatric effects of concussion and use of performance-enhancing drugs). Many of the core psychiatric symptoms presented by athletes could be related to reward deficiency, especially in the mood spectrum area. Athletes are subject to ongoing drug testing, with pharmacotherapy often being viewed as problematic. Treatment interventions not involving the use of banned medications offer a significant advantage. In this presentation the presenter will provide an overview of sports psychiatry, and the role of RDS in understanding etiology, and possible treatment interventions.

Dopamine D2, Obesity and Reward Deficiency Syndrome

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Abstract

Studies have demonstrated that obese individuals present with reduced dopaminergic signaling, which may be a potential cause of pathological food consumption compensating for dopaminergic deficiency also known as reward deficiency syndrome (RDS). Dopamine (DA) deficiency in obese individuals may give rise to pathological eating as a way to compensate for the deficiency. DA interaction with D2R levels is also critical, particularly since chronic use of antipsychotics (e.g., D2 antagonists) are linked to metabolic syndrome comorbidities. Positron emission tomography (PET) brain scans have demonstrated a decrease of brain D2R availability in obese humans; and that this decrease in D2R availability was inversely proportional to body mass index (BMI). Food intake behavior has been directly associated with the D2R levels with studies concluding that low D2R levels were linked to overeating and that food restriction attenuated this effect. In addition, studies in healthy individuals have shown that eating behavior patterns were modulated by striatal D2R; and that palatable food intake decreased striatal D2R protein expression in obese rats with a change in their feeding behavior.

Recent PET studies have revealed that opportunistic eating behavior and BMI are both positively associated with D2R binding potential in the dorsal and lateral striatum, whereas BMI is negatively associated with D2R binding potential in the ventromedial striatum, suggesting that obese subjects have modifications in DA neurocircuitry that may increase their susceptibility to opportunistic overeating while at the same time making food intake less rewarding, less goal directed, and more habitual. Recent research has looked at the gene (variable D2R levels among a population) x environment (a diet high in fat and calories) interaction and how this may contribute to metabolic syndrome vulnerability as it relates to obesity and pathological eating.

Marijuana Reform: The Evolving Landscape of International Drug Policy Reforms and Cannabis Legalization in California

Peter Banys

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Abstract

There is international fatigue with the War on Drugs and a growing trend away from criminal justice models (interdiction, incarceration) in favor of public health models (non-criminal sanctions, community-based treatments). Cannabis policy has become the stalking horse for many of these changes, including defining of "soft" drugs and personal use amounts of illicit drugs, and relying on non-criminal sanctions. Despite US incarceration on an unprecedented scale, the economics of drug production and drug demand remain unvanquishable either through international interdiction or domestic incarceration. Internationally, cannabis has been the basis for defections from decades of international conventions, the War on Drugs, and for "outlaw" international and domestic drug policy reforms. Medical Marijuana laws in 22 US states have prepared the way for recreational marijuana legalization in CO, WA, and OR. California voters will have a marijuana legalization initiative on the 2016 ballot and, it is likely that minors will be the only subgroup for whom marijuana remains illegal. Teenagers see marijuana as safer than cigarettes and are more likely to smoke marijuana. In public discourse, the risks of psychosis and addiction have been exaggerated; and, the risks to cognition, education and school retention have been minimized. This presentation will review cannabis-related risks for adolescents, including the impact on cognition, learning, and school retention. Recommendations for an evidence-based California public policy will emphasize the need for stably funded Student Assistance Programs (SAPs) within the secondary school system, ongoing outcomes research, and publicly-funded community treatment resources for juveniles.

Comprehensive Holistic Approaches in Addiction Medicine

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Abstract

We are cognizant that addictive behaviors including alcohol and drugs present at a rather high rate of relapse following treatment. To enhance treatment outcomes we developed a very comprehensive evidence-based neuroscience approach using many holistic modalities. These include but are not limited to nutrient induced reward circuitry rebalancing leading to dopaminergic homeostasis. Our program also includes cognitive behavioral therapy, mild hyperbaric oxygen therapy (HBOT), heavy metal toxicity monitoring, trauma release therapy, NLP, acupuncture, hypnotherapy, drumming, yoga, diet, exercise, music therapy, guided imagery, urine analysis monitoring, encouragement of 12 step program, fellowship attendance, family therapy and a strong aftercare program. Unlike other chemical treatment centers the neuro-adaptagen supplements are treated like other medications and compliance monitoring is a key. One example of our continued interest in clinical outcome measures involved comparing patient demographics and relapse rates in our chemical dependence track. Increased risk for relapse and lower academic achievement were found to have a significant association in recent outcome data from a holistic treatment center (HTC) located in North Miami Beach, FL. Relapse outcomes from the Drug Addiction Treatment Outcome Study (DATOS) (n=1738) and HTC (n=224) were compared for a 12-month period. Post-discharge relapse was reported by 26% of HTC patients and 58% of patients in DATOS. Also found was a correlation between relapse and education level where the lower the academic performers showed the highest relapse rates. Our results implicate the use of vitamin and mineral supplements coupled with a well-researched natural dopamine agonist nutrient therapy; both have been shown to improve cognition and behavior, and thus academic achievement.

Dopamine Neurotransmission in Reward Deficiency Syndrome

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Abstract

Indirect evidence indicates that dopamine neurotransmission is dysregulated in the conditions that are associated with reward deficiency syndrome (RDS). These conditions include addiction, attention deficit hyperactivity disorder, (ADHD), post-traumatic stress disorder (PTSD), clinical depression Tourette's syndrome and schizophrenia. The nature of dysregulation in these conditions however remains unclear because of difficulties associated with measurement of dopamine release in the healthy human brain. With recent development of single scan dynamic molecular imaging technique, it is now possible to detect, map and measure dopamine released at rest (tonic release) and that released acutely during a task performance (phasic release) in healthy volunteers and patients with RDS. These studies have allowed us to characterize the nature of dysregulated dopamine neurotransmission in RDS. Analysis of the data acquired in some of these conditions reveals that dopamine neurotransmission

is indeed dysregulated in all of the RDS conditions studied. The nature of dysregulation however does not appear to be the same. Thus the location and kind of dysregulation observed were different in each RDS condition. It appears that the reward deficiency is elicited when dopamine release deviates from the 'normal' level. Thus both abnormally high and abnormally low levels of dopamine lead to the syndrome of reward deficiency.

Are Eating Disorders Reward Deficiency Syndromes?

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Abstract

It has been postulated that specific genetic variations in individuals carrying the D2A1 allele may be at high risk for a reward deficiency syndrome (RDS) such that those individuals carrying the A1 allele would tend to have insufficient numbers of CNS D2 receptors thereby resulting in decreased reward and pleasure from activities that normally would provide others with pleasure. This has been postulated to result in addictions, mood disorders, compulsions, impulsivity, and other related disorders on the addictive-compulsive-impulsive spectrum. This presentation will review evidence for and against the hypothesis that eating disorders, including anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED), are examples of a reward deficiency syndrome (RDS). Eating disorders are characterized by reward seeking behaviors and are associated with substance and behavioral addictions, as well as obsessive compulsive disorder, obsessive compulsive personality disorder, anxiety disorders and PTSD. In addition, it has been argued that the primary behaviors associated with eating disorders, i.e., restricting, binge eating, purging, and excessive exercise, all have addictive properties and involve alterations in brain reward mechanisms. Since RDS has been postulated to involve specific variations in D2 dopamine gene expression, the available evidence that eating disorders and eating disordered behaviors involve disturbances in dopamine neurotransmission and D2 dopamine gene expression will be examined and discussed. Taken together, available findings suggest that genes acting within the dopamine system may contribute, either directly or indirectly via interactions with traumatic experiences, to differences in the presentation of eating disordered symptoms and associated comorbid traits.

Resting State Functional Connectivity in Rat Brain during Extended Daily Access to Cocaine and Abstinence

Marcelo Febo[1,2], **Caitlin Orsini**[2], **Luis M. Colon-Perez**[2], **Sara C. Heshmati**[2], **Lori A. Knackstedt**[2] **and Barry Setlow**[2]

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Abstract

We used functional magnetic resonance imaging (fMRI) in a rat model to evaluate brain functional connectivity across stages of cocaine self-administration and abstinence. Adult male Long-Evans rats (n=8) were trained to self-administer cocaine (1.0 mg/kg/infusion) in 6 h sessions for 14 consecutive days. The remaining rats (n=5, control group) performed the same behavioral response to obtain oral access to a sucrose solution. Rats were imaged at three time points: prior to surgery, after 2 days of abstinence, and after 14 days of abstinence. Rats were scanned on a 4.7 Tesla MRI. Rats escalated cocaine intake over the course of the 14 self-administration sessions. At 2 days after self-administration, cocaine rats showed increased functional connectivity across a number of brain regions in the 'Salience Networks', including the Anterior Cingulate (ACg), Prelimbic Cortex, Insular Cortex (Ins), Dorsal Striatum (DS), and Amygdala. Of note was an increase in Insula-to-Dorsal Striatum connectivity that was observed only in cocaine but not in control (sucrose) rats. This was also observed for the Anterior Cingulate and Dorsomedial Striatum seeds. ACg-to-Lateral Hypothalamus connectivity and DS-to-Ins connectivity were also observed to be significant in cocaine but not control rats ($p<0.05$, cluster size corrected). Here we show that, using a longitudinal design, 14 days of long access cocaine self-administration produces an increase in functional connectivity in neural networks involving insula, anterior cingulate, and dorsal striatum. The cocaine-induced changes in functional connectivity reported here may contribute to the well-described deficits in these cognitive domains in chronic cocaine users.

Speaker Abstracts

Polysubstance Use and Brain Function. Why Bother?

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Abstract

The vast majority of substance abusers today use more than one or two substances concurrently; they are polysubstance users (PSU). Most research, however, on the effects of substances on the brain have studied groups that are ostensibly dependent only on one substance, such as alcohol, cocaine, or methamphetamines; other substance use has been either treated as a nuisance or ignored altogether (e.g., tobacco). It is questionable if information derived from such studies can properly inform the treatment of the majority of substance users today. We have examined how alcohol dependent individuals in treatment with and without comorbid stimulant dependence differ in the structure and function of the brain reward/executive oversight system (by magnetic resonance based morphometry, metabolism, and blood flow) and in cognition and self-regulatory behavior (risk-taking, decision-making, impulsivity). We demonstrate that the brain injury and cognitive/behavioral deficits detected in PSU differ from those in "pure" alcohol dependent individuals, and we propose that these differences have implications for designing better and better targeted treatment for different substance abusing groups. We also will present data that indicate significant functional recovery from brain abnormalities in PSU, the knowledge of which can reduce stigma for the individual, open windows onto actively facilitating neuroplasticity, and change public perception of drug addicts.

Interactions between Methamphetamine and Stress: A Dangerous Combination

Bryan K. Yamamoto

Indiana University School of Medicine, USA

Abstract

Substance abuse and stress are typically co-morbid conditions but little is known about how the two combined conditions may affect the neurochemistry of the brain. More specifically, our past and current animal studies have shown that chronic stress augments the acute effects of methamphetamine, not only on dopamine and glutamate neurotransmission but also exacerbates the long-term depletions of dopamine and serotonin produced by the drug. We have used a chronic unpredictable stress paradigm that varies the type and time of stress exposures to rats to approximate the pattern that humans might encounter with unexpected stressful life events. Moreover, the paradigm is not confounded with learning and adaptation but chronically elevates plasma corticosterone. Using this model, recent findings will be presented that the serial exposure to chronic unpredictable stress and a binge dosing regimen of methamphetamine also compromises the blood-brain barrier. In addition, animal studies will be described which support the role of corticosterone synthesis and inflammation in mediating the combined effects of chronic stress and methamphetamine on neurotransmitters and blood-brain barrier structure and function. These findings support that importance of considering co-morbid conditions when evaluating and translating the neuropharmacological effects of methamphetamine to human methamphetamine abusers.

Mental Health and Substance Use Correlates in a Population Sample of Canadian Adults with and without a History of Traumatic Brain Injuries

Gabriela Ilie[1], Edward M. Adlaf[2], Robert E. Mann[2], Anca Ialomiteanu[2], Hayley Hamilton[2], Jurgen Rehm[2], Mark Asbridge[3] and Michael D. Cusimano[1]

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Abstract

This presentation will focus on the prevalence of lifetime traumatic brain injuries (TBI) and the association between TBI and mental health and substance use among Canadian adults. Data presented will be discussed in the context of similar data

obtained from adolescent's surveyed the same year and geographic area. Data was obtained from a cross-sectional sample of 1,999 Ontario adults aged 18 to 93, which were surveyed by telephone in 2011 as part of Centre for Addiction and Mental Health's ongoing representative survey of adult mental health and substance use in Canada. Minimum criteria for brain injury constituted a loss of consciousness, for at least five minutes, or at least one overnight hospitalization due to symptoms associated with it. An estimated 16.8% (95% CI: 14.8, 19.0) of adults reported a TBI in their lifetime. Men had higher prevalence of TBI than women. Adults with lifetime TBI had higher odds of past year daily smoking (AOR=2.15), using cannabis (AOR=2.80) and nonmedical opioids (AOR=2.90), as well as reporting elevated psychological distress (AOR=1.97) in the past few weeks, than adults without TBI. The presentation will place the current results in the context of reports that examined this association in a population of adolescents, as well as smaller scale studies, and discuss clinical implications. The co-occurrence of lifetime TBI with reports of elevated psychological distress and substance use warrants vigilance among medical practitioners to assess the possibility of past TBI during reviews of the history leading to the occurrence of these conditions.

Role of α5 Subunit Containing Nicotinic Receptors in Key Circuits Involved in Nicotinic Addiction and Beyond

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Abstract

Polymorphisms in the gene for the α5 nicotinic acetylcholine receptor (nAChR) subunit are associated with vulnerability to nicotine addiction. Previous work has shown that the α5 subunits in the habenula-interpeduncular nucleus (IPN) pathway are potent modulators of nicotine consumption. Emerging data suggest that the role of α5 control of drug seeking extends beyond nicotine intake to other drugs of abuse (e.g. alcohol, Giorgio et al., 2014). α5 is expressed throughout the mesolimbic system, including presynaptically on DA terminals in the ventral striatum where it is poised to contribute DA transmission that is critical to the acquisition and maintenance of drug addiction. Data will be presented in support of α5 nAChR playing a role in modulating ventral-striatal DA release, and behaviors controlled by this circuitry, such as motivation and reward processes. Through these effects, aberrant a5 subunit signaling could contribute to pathological drug seeking behavior via actions in brain regions outside the habenula and IPN.

Quality of Life of Users of Psychoactive Substances, Relatives, and Non-Users

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Abstract

Quality of life is related to one of the basic human desires, which is to live and feel well. We evaluated the quality of life of psychoactive substance users and relatives, compared to non-users, analyzed with socioeconomic strata. A cross-sectional study with users of psychoactive substances, relatives, and other individuals who called the Information and Orientation Service regarding drug abuse in Brazil (Ligue 132). Data was collected from users, relatives, and non-users, including socioeconomic characteristics and data regarding substance consumption when appropriate. In addition, the abbreviated version of the World Health Organization Quality of Life (WHOQOL-BREF) questionnaire was given to 347 individuals. From this sample, 138 (70%) used alcohol, 111 (57%) tobacco, 78 (40%) cocaine, 76 (39%) marijuana and 70 (36%) crack. The control group had higher scores than the relatives of users and users in all areas of the questionnaire ($p<0.05$). As expected, users of psychoactive substances had lower scores in almost all domains and in the overall score on the WHOQOL-BREF, in comparison to the sample of non-drug users. Interestingly, the relatives of users showed the lowest levels of quality of life, with differences in all domains. These findings reflect the poor quality of life of users and their relatives. It was possible to confirm that chemical dependence affects not only the users but also relatives who live with them, in terms of psychological pathology, which is strongly reflected in quality of life.

The Concerning State of Opioid Addiction Trials and Guidelines: To Whom Does this Evidence Apply

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Abstract

Background: Trials evaluating opioid substitution and antagonist therapies (OSATs) suffer from serious limitations. From the use of strict inclusion criteria to the lack of consensus over patient important outcomes we are left questioning the major findings from trials in the field of addiction.

Objectives: To establish 1) the measures of effectiveness in OSAT trials, 2) the trials' eligibility criteria and determine how international clinical practice guidelines incorporate evidence from these trials.

Methods: A systematic review to identify trials evaluating OSATs for the management of OA. To quantify the effect of trials' eligibility criteria on generalizability, we applied these criteria to data from an observational study of OA patients (n=394). We then accessed the Canadian, American, British (NICE), and World Health Organization (WHO) OSAT guidelines to evaluate how evidence is used in the recommendations.

Findings: Sixty trials identified with 77 outcomes. Retention was the only outcome consistently measured across trials. More than half of trials excluded patients with psychiatric and physical comorbidity. Additionally, 31.7% of trials excluded patients with current alcohol/substance-use problems and 48.3% exclude patients taking psychotropic medications. These criteria rendered 70% of the observational sample ineligible. North American guidelines made strong recommendations supported by poor evidence. NICE and WHO guidelines provide a critical assessment of the literature used to inform their recommendations.

Conclusion: There is a lack of consensus over OA outcomes, which led to an accumulation of a large yet very weak body of evidence with limited external validity. Guidelines should consider these limitations when drafting clinical recommendations.

Medication Abuse in Europe: Which Pharmacoepidemiological Resources?

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Abstract

At the European level, monitoring the potential for abuse and dependence of psychoactive substances falls within the scope of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) for substance abuse in general and of the European Medicine Agency (EMA) for marketed drugs. As a single source of information is not generally sufficient to measure a phenomenon as difficult to apprehend as medication-related addiction, different sources are needed to identify early signals of diversion, abuse and dependence, and to investigate the magnitude of the phenomenon. If France has set up in the early 1990s an original system to assess potential for abuse of psychoactive substances, with specific tools combining both the evaluation of the use of these substances (illicit substances or diverted drugs), and the consequences of that use in terms of morbidity and mortality, there is no equivalent in other European countries. Indeed, unlike the United States, who, for several decades, organized this type of surveillance, with a multi source approach (sentinel systems, databases, medical and administrative data, databases for seeking care in relation abuse), there is no integrated system in European countries for identifying a signal of drug abuse, or to assess the impact of measures for minimizing the risk of abuse. However, some recent examples show a growing concern about drug addiction, based on a pharmaco epidemiological approach using pharmacovigilance or medical administrative databases. These examples illustrate the interest of these approaches in the field of drug of abuse.

"This is Your Brain on Drugs": Adolescent Substance Use Prevention through Neuroscience Education

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Abstract

Interest in the brain has risen dramatically in recent decades, suggesting that neuroscience-based information about substance use risks could be a compelling addition to prevention efforts. However, no studies have tested this approach among adolescents. We pilot-tested the effects of a high school science curriculum called "The Brain: Understanding Neurobiology through the Study of Addiction" developed by the U.S. National Institutes of Health (NIH) to teach students about how alcohol and drugs affect the brain. We examined students' knowledge, attitudes, and use of tobacco, alcohol, and drugs. Participants were 9th-11th graders attending 2 urban high schools whose parents consented (222/282=79%). We standardized the 5-lesson curriculum and trained 5 science teachers; 8 intervention classes (n=133), 5 matched-grade comparison classes (n=89). We used a self-administered survey to assess demographics, knowledge and perceived risk of harm from substance use, substance use, peer/family substance use, and prior health education. We collected data 1-2 weeks' pre-intervention (T1), immediately post-intervention (T2; 1 month after T1), and 6-8 months later (T3). We used multiple logistic regression with GEE for posttest comparisons, adjusting for T1 differences and within-class correlation. 180/222 (81%) students completed all measurements; group completion rates were similar. Compared to control, intervention students had lower past-30-day cigarette use at T2 (7% vs. 21%, adjusted odds ratio [OR]=0.20, 95%CI 0.08-0.49, p=.01), and a marginal trend toward lower alcohol initiation between T1 and T2 (3% vs. 20%; OR=0.09 95%CI 0.01-1.03, p=.052). Among low-frequency marijuana users (1-5 times lifetime at baseline), fewer intervention students had past-30-day marijuana use at T2 (5% vs. 35%, OR=0.01, 95%CI 0.00-0.30, p=0.03). All between-groups differences were extinguished by T3. Neuroscience education is a promising supplemental strategy for adolescent substance use prevention; however, ongoing reinforcement is needed.

Family Members Effected by a Relative's Substance Misuse Looking for Social Support: who are they?

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Abstract

Background: This study proposes to describe family members in the city of Sao Paulo that are currently seeking support in mutual self-help groups to deal with a substance misuse relative. Method: Five hundred participants (one participant by family) completed a structured questionnaire containing socio-demographic information, length of time took for seeking help, and where they search help. Participants were recruited in the mutual self-help group 'Amor Exigente' in the city of Sao Paulo, Brazil.

Results: Parents of substance misusers counted as the largest group of family members. It took an average time of 3.7 years for the family members to discover their relatives' substance misuse 42% had then sought help immediately; it took an average of 2.6 years for the remaining 58% of the sample to seek some form of support. Physical and psychological forms of distress reported by the families that led to conflicts are the ones associated to the unreliable characteristics of the substance misusers, difficulty to communicate, problems related to money, the provocative attitudes and physical fights.

Discussion: A belief that the substance use of their relatives was just a transient problem or that they could cope with the situation by themselves were among the most indicated reasons for delaying seeking help.

Conclusion: Findings stress the importance of implementing services that take into account the different difficulties that families have in finding help to deal with the substance misuse relative.

ADAR2-Dependent GluA2 Editing Regulates Cocaine Seeking

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Abstract

Activation of AMPA receptors in the nucleus accumbens is necessary for the reinstatement of cocaine-seeking. AMPA receptors are tetrameric protein complexes that consist of GluA1-GluA4 subunits, of which GluA2 imparts calcium permeability. Adenosine deaminase acting on RNA (ADAR2) is a nuclear enzyme that is essential for editing GluA2 pre-mRNA at Q/R site-607. Unedited GluA2(Q) subunits form calcium permeable AMPA receptors (CP-AMPARs), whereas edited GluA2(R) subunits form calcium impermeable channels (CI-AMPARs). Emerging evidence suggests that the reinstatement of cocaine seeking is associated with increased synaptic expression of CP-AMPARs in the nucleus accumbens. However, the role of GluA2 Q/R site editing and ADAR2 in cocaine seeking is unclear. In the present study, we investigated the effects of forced cocaine abstinence on GluA2 Q/R site editing and ADAR2 expression in the nucleus accumbens. Our results demonstrate that 7 days of cocaine abstinence is associated with decreased GluA2 Q/R site editing and reduced ADAR2 expression in the accumbens shell of cocaine-experienced rats compared to saline controls. ADAR2b over expression in the shell attenuated cocaine priming-induced reinstatement of drug seeking and increased GluA2 Q/R site editing and surface expression of GluA2-containing AMPARs. Together, these findings support the novel hypothesis that an increased contribution of accumbens shell CP-AMPARs containing unedited GluA2(Q) promotes cocaine seeking. Therefore, CP-AMPARs containing unedited GluA2(Q) represent a novel target for cocaine addiction pharmacotherapies.

Opioid Medications: Efficacy and Risks

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Abstract

Why are opioid medications prescribed in large quantities and high frequency when there is little or no proven efficacy for their therapeutic value? Why are opioids the most commonly prescribed medication in the United States for the past decades when the adverse consequences continue to grow and mount? Why does the medical profession continue to prescribe opioid medications that result in increased pain and increased disability?

Epigenetic Networks: Biopsycho-Spiritual Approaches for Treating Prescription Opioid Addiction

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Abstract

A history of substance abuse disorder (SUD) is a strong risk factor for prescription opioid abuse among persons treated with opioids for persistent pain states, and relapse of SUD is not uncommon. Alarming rates of diversion, overdose and addictive disorders are unintended consequences of the previous twenty years of open- ended opioid prescribing practice without full appreciation of reward mechanisms and neural adaptive consequences for persons at risk of addictive disorders. Now that the science has advanced to an understanding of Reward Deficiency Syndrome and relevant epigenetic changes, a clinical challenge is created for applying these scientific findings to treating persons with coexisting pain states and SUD. System thinking has given rise to a new language to be applied to the highly complex and dynamic systems and processes involved in diseases of addiction and persistent pain states. Epigenetic modification and subsequent gene expression have been implicated in the highly orchestrated processes of habitual addictive behavior and persistent pain states when opioids are used. These changes in gene expression may contribute markedly to CNS plasticity. This presentation discusses networks of extrinsic and extrinsic epigenetic

factors implicated for treatment of opioid addiction and persistent pain states with biopsycho social-spiritual approaches addressing these factors used to treat prescription opioid addiction.

An Assessment of Outcomes Measure Implementation in the Addiction Treatment Space

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Abstract

The construction and widespread implementation of long-term, multimetric outcomes measures that incorporate leading addiction treatment methodologies could have significant effects on the addiction treatment space. Therefore, it is of the utmost importance that individuals involved in related fields have an understanding of the state of outcomes measurement systems and their implementation, and how this impacts the treatment space.

This project builds upon the presenters' and co-author previous research into the utilization of outcomes measures. Specifically, the poster will present the following: trends in the construction and implementation of existing outcomes measures, gaps in current measurement systems, the manner in which these gaps negatively impact the prospect for successful addiction treatment, and finally, recommendations for rectifying these gaps.

This project utilizes an extensive desk review and a mixed-methods analytical approach to systematically analyze existing outcomes measure instruments and the current state of related literature. Through these methods, the authors identify several key findings that have broad implications on the treatment space. The majority of existing outcomes measurement instruments are insufficient; they lack multidimensionality, a long term outlook, and/or robust measurements. There exist considerable measurement differences across systems depending on the institutional background of their creation. Numerous institutions, at various scales, have introduced reporting systems (e.g. NOMs) with enforcement mechanisms; however, compliance with these systems has been wholly inconsistent. This project has found the necessity of institutions, at various scales, rectifying shortcomings in existing systems and/or developing novel long-term, multimetric systems as a means to increase treatment effectiveness.

Modeling Recovery

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Abstract

Recovery from alcoholism has been subject to limited preclinical investigation, especially when alcohol remains accessible. Recently, we developed a preclinical model of recovery where providing rats the ability to respond for food without changing accessibility of alcohol reduces responding for ethanol. This model improves upon existing procedures in ways that allow investigations into the processes underlying successful recovery. In particular, we found that longer periods of this model recovery increased the persistence of responding for an alternative reward (food) when rats were re-exposed to stimuli that had previously occasioned alcohol use (and little alternative behavior). We did not observe any increase in alcohol seeking with longer periods of reduced alcohol use. These results are unlike those observed using other preclinical models, but are consistent with clinical findings. This outcome permits investigation into the behavioral processes that underlie the decreasing likelihood of relapse after increasing periods of recovery. Our studies indicate that recovery might decrease attention to stimuli that had previously resulted in ethanol responding, and instead result in greater control over behavior by the global environmental context. Further, our studies suggest that the common preclinical finding of enhanced reinstated responding for alcohol after longer periods of abstinence depend on how alcohol use is reduced. Ultimately, our procedure may prove useful in the development of therapies for maintaining recovery from alcoholism. Recently initiated studies will extend our model to oral oxycodone abuse, a rapidly growing substance abuse problem.

Getting in and Out Whole: Connecting with Patients' Emotional Pain in the Psychiatric Setting

Judith Van Sant

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Abstract

As a strong component in patient healing, interpersonal connection in the psychiatric/mental health setting threatens nurse's health. Issues of physical, emotional, and sexual abuse, neglect, horrific trauma, loss, addiction, and severe and isolating mental illness often provide much of the context for mental health nursing. Frequently, the nurse is confronted with a vast array of raw emotional pain from within a multiplicity of persons incapable of processing that pain on their own. For these persons the nurse remains a significant therapeutic tool. Psychiatric/mental health nurses are at risk for energy depletion or imbalance from the interactions among patients' raw emotional pain, poor boundaries, ineffective coping and possible enervating relational style and the nurse's requisite open, whole, and vulnerable self.

This session will present an evidence-based model of the process of connecting with patients' emotional pain in the psychiatric/mental health setting that delineates how the nurse, from within that nurse's personal world view, can connect and then disconnect with patients' emotional pain while still maintaining a separate and protected self. This process was discovered though participant observation on four behavioral health and addictions' units of a community hospital in the mid-Atlantic United States. Findings from 12 nurses highlighted connectedness as a process and personal decision that, with self-awareness and individualized self-protective/self-separating strategies, one can enhance patient healing as well as nurse satisfaction and growth. The evolved model may help nurses ease emotional labor, combat compassion fatigue, enhance performance, and preserve self in today's complex acute care setting.

Integrating Substance Use and Eating Disorder Treatment: Adapting Evidence Based Treatments

Therese K. Killeen

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Abstract

Substance use commonly occurs in eating disorders and disordered eating has been reported in individuals receiving treatment for substance use disorders. Eating disorders are rarely addressed or even adequately assessed in substance abuse treatment programs. Identifying these comorbid disorders are essential to maximize treatment benefits. Addressing both disorders concurrently has several advantages, namely increased efficiency and cost effectiveness, reducing attrition that is more likely to occur with sequential treatment and avoiding inconsistencies between therapies and therapists. Both disorders share common features that have implications for integrated treatment approaches. Effective evidence-based treatments implemented in both eating and substance use disorders include cognitive behavioral therapy, motivational interviewing/motivational enhancement therapy and contingency management. Assessment tools used to identify ED and SUD comorbidity and treatment approaches that can be adapted to address both disorders concurrently will be discussed in this presentation.

Motivational Interviewing - Patient-Centered Communication in Brief Health Care Encounters

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[2]*University of Wisconsin Oshkosh, USA*
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Abstract

Motivational Interviewing (MI) has been defined as a patient-centered, goal-oriented style of communication focused on strengthening personal motivation for behavior change. In MI, five principles (rolling with resistance, expressing empathy, avoiding argumentation, developing discrepancy, and supporting self-efficacy), and a variety of strategies and micro skills are

used. The philosophy of MI is based on the collaboration, evocation, and supporting patient autonomy-the Spirit of MI.

With progressing changes in the focus towards patient-centeredness in the US healthcare system, health professions schools are increasingly focusing on communication skills, including MI, to help future providers engage in medication therapy management and comprehensive disease management. The following MI domains are vital in facilitating the change process when health care providers practice in settings that require brief encounters with patients: MI Philosophy, Health Interviewing, Motivation, MI Principles, and Interpersonal Process. The domains have been identified based on a research study focused on the development of a valid and reliable assessment tool that measures MI skills in health care encounters. The Health Interviewing and Interpersonal process domains are specifically applicable to the health care field. The Health Interviewing domain consists of skills used to addresses the patient's understands about the illness and treatment, the patient's awareness of risks if a health condition remains untreated, and the patient's desired health outcomes. The Interpersonal Process domain consists of skills that facilitate patient-centered communication and strengthen the therapeutic alliance. Mastering the skills in the MI domains requires consistent training in and accurate assessment of MI skills in health care providers.

Mechanisms of Pain and Opioid Pharmacology

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Abstract

Opioid-induced hyperalgesia (OIH) is a very common consequence of pain management with opioids. Characteristics of OIH are worsening pain over time despite an increased dose of the opioid. It is often recognized neither by the physician nor the patient, and it results in increasing doses of opioid medications and continued unsatisfying pain levels experienced by the patient. The increased use of narcotics has a negative impact on patient outcome, as patients suffer from increased pain levels and often develop depression. Patients with OIH require frequent assessment for aberrant behaviors as an indicator of addictive use. Opioid-seeking behavior may complicate the clinical picture of failed opioid therapy. The treatment of OIH is to discontinue the opioid medication and to treat the patient's withdrawal symptoms, if necessary, in an inpatient setting with medical monitoring.

Similarities and Differences in Neurocognitive and Neuroimaging Findings among Internet Gaming Disorder and Alcohol Use Disorder

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Abstract

Internet Gaming Disorder (IGD) causes significant public mental health problems worldwide, especially in Korea. It is important to compare characteristics of IGD with those of substance use disorder in order to elucidate the pathophysiology of IGD. In this study, we explored the neurocognitive and neuroimaging features among patients with IGD and those with Alcohol Use Disorder (AUD).First, we performed neurocognitive tasks in male patients with IGD (N=15; 20.80±5.09 years) and compared the results with those of male patients with AUD (N=15; 29.60±6.23 years), gambling disorder (GD; N=15; 27.53±5.21 years), and healthy controls (N=15; 25.33±5.30). Second, we performed resting state functional MRI study in male patients with IGD (N=16; 21.63±5.92 years), AUD (N=14; 28.64±5.92 years), and healthy controls (N=15; 25.40±5.92 years). Patients with IGD showed higher levels of impulsivity, which were comparable to those of the AUD group. In contrast, the GD group showed higher levels of compulsivity. In the resting state functional MRI, the IGD group showed a significant regional homogeneity (ReHo) decrease in the right superior temporal gyrus (STG) and increase in the posterior cingulate cortex (PCC) compared with healthy controls. The AUD group showed significant decrease in the anterior cingulate cortex (ACC) and increase in the PCC compared with healthy controls. These results showed neurobiological similarity and disparity of neurocognitive and resting state fMRI features among IGD, AUD and healthy controls. These findings may contribute to elucidate the pathogenesis and neurobiological underpinning of IGD.

Greater Mesolimbic Loss-Sensitivity in Young Adult Social Drinkers at Risk for Alcohol Dependence

Jane E. Joseph, Michelle DiBartolo, Xun Zhu, Joseph Schacht and Raymond Anton

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Abstract

Non-alcohol dependent individuals who report drinking problems have shown reduced mesolimbic fMRI response to high-magnitude incentives(reward and loss) on a monetary incentive delay task (MID; Joseph et al., 2015). The present study aimed to replicate that finding with social drinkers characterized as being of high- or low-risk for alcohol dependence, based on scores from the Alcohol Use Disorders Identification Test. The high- and low-risk groups were equated for recent alcohol use (11 v. 10 drinks per week, respectively, n.s.). The same MID task used by Joseph et al. was used for this study, but the number of trials was doubled. As a group, social drinkers showed reduced mesolimbic fMRI response to high relative to low magnitude sensitivity in the caudate nucleus after 45 trials (the same number of trials used by Joseph et al.) during the outcome stage of the MID. However, the high-risk drinkers converted to greater loss-sensitivity and low-risk drinkers converted to greater gain-sensitivity by the end of the experiment (after 90 trials). High-risk drinkers also showed greater loss-sensitivity in the caudate during cue anticipation over the course of the experiment. Finally, high-risk drinkers scored higher on personality measures of urgency, neuroticism, and sensitivity to punishment. Taken together, these findings suggest that one aspect of problem drinking might be characterized by a neurobehavioral profile of negative emotional valence. In particular, this profile is marked by a mesolimbic response that is not only reward deficient, but also hyper-sensitive to loss outcome and anticipation.

Expression of Reward Deficiency Syndrome Depends on More than Dopamine

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Abstract

Although it is clear that DA (Dopamine) is the brain's primary reinforcement neurotransmitter, exclusively DA levels or turnover rates do not govern expression of Reward Deficiency Syndrome (RDS). Building on a published eight-element decision-making model (Nussbaum et al., 2011), this talk will present an expanded ten-element model that describes the symbiotic reinforcement/approach tendencies of DA, Testosterone, Endogenous Opioids, Glutamate, Cannabinoids and Acetylcholine, and the opposing inhibitory/avoidance tendencies of Serotonin (promoting a "Stop and Think" stance), Nor-Epinephrine and Cortisol (promoting anxiety/fear based termination of goal pursuit.) The bi-potential of GABA in this system, depending on whether it inhibits a reward or inhibition network completes the model. Implications for treatment will be discussed.

Fetal Alcohol Spectrum Disorder-Can Prenatal Nutrition Strategy Make a Difference for Brain Development

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University of Manitoba, Canada

Abstract

Fetal alcohol spectrum disorder (FASD) is a complex, multi-factorial and intriguing disorder. The consequences that can ensue from alcohol consumption vary on the spectrum from producing little to no effect to fetal mortality. As numerous metabolic derangements ensue as a result of alcohol consumption during pregnancy, it is critical to determine a means to resolve and reduce the physical and neurological malformations that develop in the fetus. It is well known that the quantity and quality of food intake play significant roles in maintaining optimal nutrition status during pregnancy and fetal development, thus maternal nutrition intervention may be a promising strategy to reduce the incidence of FASD. However, there is currently a lack of nutritional status information for pregnant women (including First Nations women in Manitoba), especially for those consuming alcohol prenatally. While robust information on the role of nutrients and intervention are scarce in FASD, some

potential nutrients are proposed, such as vitamin A, DHA, folic acid, zinc, choline, vitamin E and selenium. Our recent findings showed that DHA intake, an important component of brain membrane formation, was significantly low in pregnant drinking women. This paper will examine current evidence supporting the role of selected nutrients in mitigating brain damage associated with FASD in conjunction with our current human and animal studies. Overall, it is essential for the health professionals to offer support and education to vulnerable populations in order to reduce the prevalence rates and incidences of children born with FASD.

Reward Deficiency Syndrome: Attentional/Arousal Subtypes, Limitations of Current Diagnostic Nosology, and Future Research

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Abstract

We theorize that in some cases Attention Deficit Hyperactivity Disorder (ADHD) predisposes to narcolepsy and hypersomnia, and that there may be a shared pathophysiology with various addictions [Reward Deficiency Syndrome (RDS)]. Reticence to acknowledge such connections may be due to a narrow nosological framework. Additionally, we theorize that the development of narcolepsy on a baseline of ADHD/RDS leads to an additional assault on the dopaminergic reward system in such individuals. In this study, we propose to test these hypotheses by using a combination of broad genetic screening, and neuroimaging with and without pharmacological intervention, in those with pure ADHD, pure narcolepsy, and the combined ADHD-narcolepsy phenotype. Results of this proposed study may reveal a common pathophysiology of ADHD, narcolepsy and RDS, and perhaps an additional compromise to the reward system in those with combined ADHD-narcolepsy. If the evidence supports the hypothesis that indeed there is a shared pathophysiology for narcolepsy with RDS and thus its subtype ADHD, early intervention/prevention treatment amongst those with ADHD may be beneficial with the putative dopaminergic compound KB220Z™.

A Glutamatergic Reward Input from the Dorsal Raphe to the Ventral Tegmental Dopamine Neurons

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Abstract

For more than 40 years, it has been recognized that the Dorsal Raphe Nucleus (DR, classical serotonergic structure) and the Ventral Tegmental Area (VTA, classical dopaminergic structure) are two of the more relevant brain reward areas where electrical stimulation produces responding at the highest rates and lowest thresholds. Although multiple studies have examined the connectivity between DR and VTA and its contribution to reward, these studies have been focused on serotonergic effects on reward. As a result, these investigations have produced conflicting results, and the true role of DR to VTA circuitry in regulating motivated behaviors is still unknown. Contrary to the widespread idea that the major input from DR to the VTA is serotonergic, we found that DR neurons expressing the vesicular glutamate transporter-3 (VGluT3) are the major input from DR to VTA neurons. Within the VTA, these DR-VGluT3 neurons mostly make synapses on dopamine neurons; some of these dopamine neurons specifically innervate the nucleus accumbens. By genetic approaches to specifically express channel rhodopsin in DR-VGluT3 neurons, we found that intra-VTA light stimulation of the VGluT3-fibers elicits AMPA-mediated excitatory currents on dopamine-neurons that innervate the nucleus accumbens. Such stimulation causes dopamine release in the nucleus accumbens, reinforces instrumental behavior, and established conditioned place preference. Our discovery of a rewarding excitatory synaptic input to the mesoaccumbens dopamine neurons by a glutamatergic projection arising selectively from neurons of the dorsal raphe that contain VGluT3 opens new avenues to examine its participation in a variety of mental disorders related to motivation.

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