The 1st Congress of
APSAAR

"Together, Asia- Pacific Addiction Researchers"

Date   November 12(Thu) – 14(Sat), 2009

Venue   COEX Grand Conference 4fl.

Organized by

Asia-Pacific Society for Alcohol and Addiction Research
Korean Academy of Addiction Psychiatry
Korea Centers for Disease Control and Prevention
Korean Research Foundation for Addiction

Room 401

12 November (Thu) 2009

09:00-09:30	**Opening**		
	Plenary Lecture I	**Chair: Toshikazu Saito**	
09:30-10:20	Perspectives on Alcohol Research: Past, Present and Future	Ting-Kai Li	USA
	Bridging Structure and Function of Alcoholic Brain	**Chair: Ihn-Geun Choi/ Edie Sullivan**	
10:30-12:00	Mammillothalamic functional connectivity strength and memory impairment in alcoholic patients recovering from Wernicke-Korsakoff syndrome	Young-Chul Jung	Korea
	A Serial Study on Combination Use of Buprenorphine with Scopolamine and Promethazine (BSP) in China	Wei Hao	China
	Understanding Alcohol Induced Brain Injury Through Neuroimaging	Peter R. Martin	USA
	Alcoholism's Effect on the Brain: Insights from Human and Animal Neuroimaging Studies	Adolf Pfefferbaum	USA
12:00-13:00	**Lunch**		
	Alcoholism and Depression: Clinical and epidemiological studies sponsored by JSPRA	**Chair: Michie Hesselbrock/ Lu Ru-Band**	
13:00-14:30	Genetic Validation in Anxiety-depressive alcoholism	Lu Ru-Band	Taiwan
	Depression in alcoholic inpatients and outpatients	Ung Gu Gang	Korea
	Depression, suicidal ideation, and suicide attempts among Japanese patients with alcohol dependence and their effects on treatment outcome	Sachio Matsushita	Japan
	Affective disorder and persistence of alcohol dependence	Michie Hesselbrock	USA
	Underage Drinking: Old problem in the new era	**Chair: Sawitri Assanangkornchai/ Yoneatsu Osaki**	
14:30-16:00	Underage drinking problems in Japan	Yoneatsu Osaki	Japan
	Pattern of Alcohol Consumption in Underage Population in Indian City	Dipesh Bhagabi	India
	Social and school environmental influences on alcohol consumption among high school students in Thailand	Anocha Muekthong	Thailand
	Underage Drinking: A Developmental Perspective	Sandra A. Brown	USA
	Rehabilitation of Substance Use Disorders in Asia-Pacific Regions	**Chair: Susumu Higuchi/ Sawitri Assanangkornchai**	
16:20-17:50	Patient's characteristics in substance abuse treatment and rehabilitation system in Thailand	Sawitri Assanangkornchai	Thailand
	Fact and vision: Rehabilitation of alcohol use disorders in Korea	Seon Wan Ki	Korea
	Surveillance and rehabilitation of drug abuse in China	Jian-hui Liang	China
	Substance misuse treatment for Indigenous Australians	Richard Chenhall	Australia

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	Plenary Lecture II	**Chair: Ihn-Geun Choi**	
08:30-09:20	Update on Collaborative Studies on Genetics of Alcoholism (COGA)	Victor M. Hesselbrock	USA
	FASD, epidemiology and basic research	**Chair: Dongyul Oh/ Edward P. Riley**	
09:30-11:00	Alcohol Use during Pregnancy and Related Risk Factors in Korea	So Hee Lee	Korea
	Researching the Prevalence of FASD in South Africa, Italy, and the United States: Implications for Other Countries	Philip A. May	USA
	Brain and Behavior in FASD	Edward P. Riley	USA
	Over-expression of GSK3 beta Sensitizes Neuronal Cells to Ethanol Toxicity	Luo Jia	USA
	Genetics of Alcoholism	**Chair: Sung-Gon Kim**	
11:10-12:30	NrCAM and addiction	Hiroki Ishiguro	Japan
	Role of Dopaminergic Genes in Alcohol Dependence: First study from India	Meera Vaswani	India
	Dopamine receptor polymorphisms and alcoholism in Korean Drinkers	Keun Ho Joe	Korea
12:30-13:30	**Lunch**		
	Alcoholism and Depression: Possible common pathophysiology sponsored by JSPRA	**Chair: Toshikazu Saito**	
13:30-15:00	The Genetics and Physiology of Co-morbid Depression and Alcoholism	Boris Tabakoff	USA
	Cognitive Impairment in Alcoholism and Depression	Dai-jin Kim	Korea
	Genetic Aspects of Alcoholism and Depression	Hiroki Ishiguro	Japan
	Dysregualtion of Neurogenesis in Alcoholism and Depression	Eri Hashimoto	Japan
	Epidemiology	**Chair: Seon Wan Ki**	
15:00-16:20	The prevalence and correlates of alcohol use disorders in the United States and Korea-A cross national comparative study	Hae Kook Lee	Korea
	Alcohol Dependence in the United States: Correlates, Incidence and Predictors of 3-Year Course in NESARC	Tamara Wall	USA
	Changes in alcohol consumption and related harm including drink driving in Japan	Kimura Mitsuru	Japan
	Reducing Alcohol Consumption: Possible treatment goal of alcohol dependence	**Chair: Susumu Higuchi/ Toshikazu Saito**	
16:40-18:00	Introduction and overview: reducing alcohol consumption in the treatment of alcohol dependence	Susumu Higuchi	Japan
	Evidence-based Pharmacotherapy of Alcohol Abuse and Dependence	Hannu Alho	Finland
	Challenges in Designing Alcoholism Clinical Trials and Analyzing Outcomes	Robert Swift	USA

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	Plenary Lecture III	**Chair: Edward P. Riley**	
09:00-09:50	Genetics of Addictive Disorders in Korean Population: Does Ethnicity really matter?	Ihn-Geun Choi	Korea
	Advanced Research in Addictive Disorder	**Chair: JeongTae Lee/ M Haniki N. Mohamed**	
10:00-11:30	Morphine withdrawal syndrome and its amelioration	Seikwan Oh	Korea
	Methadone Maintenance treatment for treating heroin addicts in Malaysia	Noor Zurani Robson	Malaysia
	Effectiveness of VIVA QS® for Nicotine Addiction	M Haniki N. Mohamed	Malaysia
	Casino Employees and Gambling problems	Tae Kyung Lee	Korea
	Special Lecture	**Chair: Dongyul Oh**	
11:30-12:00	Joint Researches and Funding from NIAAA	Peggy Murray	USA

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	Cultural Differences in Patterns of Alcohol Consumption in Asia-Pacific Countries	Chair: Ian Newman/ Sawitri Assanangkornchai	
10:30-12:00	Cultural differences and the minimum legal drinking age	Ian Newman	USA
	Gender and age differences on alcohol beverage preferences in Thailand	Daranee Kamchansuwan	Thailand
	Culturally specific drinking patterns and per capita consumption data: using different types of data in the development of policies to reduce alcohol related harms	Qian Ling	China
	Alcohol consumption among Indigenous Australians: opportunities for brief intervention	Katherine Conigrave	Australia
12:00-13:00	Lunch		
	Pharmacotherapies in Alcohol Dependence (Korean Session)	Chair: Seong Nam Cho	
	Detoxification and management of alcohol withdrawal syndrome	Young-Hoon Chen	Korea
13:00-14:30	Pharmacotherapy in alcohol dependence: anti-craving agents	Sam-Wook Choi	Korea
	Pharmacotherapy of Co-morbid psychiatric disorders in Alcohol dependence	Hong Seok Oh	Korea
	Co-morbid physical conditions	Jeong Wook Kim	Korea
	Clinical Perspectives on Genetic Polymorphism of Alcohol-Metabolism Genes and Alcoholism	Chair: Shih-JiunYin/ Sung-Gon Kim	
14:30-16:00	Gender differences in the genotype frequencies of the ADH2 and ALDH2 gene in Korean alcohol-dependent patients	Sung-Gon Kim	Korea
	Pharmacokinetics and pharmacodynamics of acetaldehyde in Han Chinese carrying the ALDH2*2 variant gene allele	Gila-Sheun Peng	Taiwan
	Physiological basis for overcoming acetaldehyde-induced adverse reaction in ALDH2*1/*2 alcoholics.	Vi-Chyan Chen	Taiwan
	Clinical implications on the alcohol metabolic gene	Ru-Band Lu	Taiwan

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	Organ Damage	Chair: Sang ick Park/ B.J. Song	
09:30-11:00	A new anti-fibrotic mechanism of TRAIL through regulations of apoptosis and collagen production in hepatic stellate cells	Sang ick Park	Korea
	Molecular Mechanisms of Organ Damage by Alcohol and Other Toxic Compounds	B.J. Song	USA
	Hepatic stellate cells mediate alcoholic fatty liver through the activation of hepatic CB1 receptors by endocannabinoids	Won-Il Jeong	Korea
	Alcoholic Liver Disease in Korea, Present and Future	Dong Joon Kim	Korea
	Family Intervention for Addiction (Korean Session)	Chair: Seongho Min	
11:10-12:30	Family Problems and Family Treatment Model to Addiction	Suk Hi Chai	Korea
	The Intervention for the Family of an Addict	Hae Ryun Kim	Korea
	Communication Skills Training Program (CSTP) for Alcoholism Families	Yong Jin Kim	Korea
12:30-13:30	Lunch		
	Case Management for Alcoholics (Korean Session)	Chair: Jongho Shin	
13:30-15:00	Case Management in Mental Hospital	In-Bok Hwang	Korea
	Case Management in Alcohol Counseling center	Lee Yu Mi	Korea
	Case Management in The Korean Alcohol Research Foundation	Park Ae Ran	Korea
	Virtual Reality Therapy and Future	Chair: Chanjong Park/ Sanghoon Lee/ Doughyun Ham	
15:00-16:20	The here and the hereafter of virtual reality based on computer technology	Chanjong Park	Korea
	What's the virtual reality aversive therapy for alcohol-dependent patients	Sanghoon Lee	Korea
	The comparisons between alcohol-dependent patients and healthy subjects in virtual cue exposure	Doughyun Han	Korea
	Recent Issues of Addiction in Korea	Chair: Jin Hee Han/ Young Cheol Shin	
16:40-18:00	Alcohol Consumption and Carotid Atherosclerosis According to Cardiovascular Risk Factors	Belong Cho	Korea
	Implications of executive dysfunction of frontal lobe among alcoholics : A Neuropsychological approach	Kye-Seong Lee	Korea
	The Alcohol and Substance problems of Male North Korean Defectors in South Korea	Jin-Yong Jun	Korea
	Groping for the Addictions Policy in Korea, Separated vs. Unified	Kyung-Sung Kim	Korea
	Internet Addiction and its Treatment	Donghyun Ahn	Korea

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	Psychomotor Stimulant Addiction, basic to practice	Chair: Seong Nam Cho / Tong H. Lee	
10:00-11:30	Human Study for Methamphetamine Abusers in Korea	DH Kwon	Korea
	Preclinical and Translational Identification of Novel Pharmacotherapeutic Strategies for Psycho stimulant Abuse Treatment	Tong H. Lee	USA
	The role of ERM proteins in psychomotor stimulant addiction	Jeong-Hoon Kim	Korea
	Epidemiological trends of drug abuse in Korea and drug hair testing.	Hwakyung Choi	Korea

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Welcoming Address

Welcome Message from the President of APSAAR

On behalf of the Asian Pacific Society for Alcohol and Addiction Research (APSAAR), It is my great pleasure to warmly welcome you to the First Congress of Asian Pacific Society for Alcohol and Addiction Research held in Seoul, Korea from November 12 to 14, 2009.

APSAAR, which was established in January 2008 with just a few Asian Pacific neighborhoods such as Australia, China, India, Japan, Korea, Taiwan, and Thailand has become a host to an international conference. This conference would not have happened without the tremendous support from APSAAR members, KAAP, KCDC, KRFA, NIAAA, ISBRA, and the Seoul local organizing committee. Furthermore, I would like to especially thank Dr. TK Li for his continuous contributions to APSAAR.

This year's theme is "Together, Asia Pacific Addiction Researchers" for three main reasons:

First, APSAAR hopes to bring the international attention on alcohol addiction research from North Americas and Europe to Asia Pacific within the next 10 years.

Second, APSAAR will serve as a meeting ground for enthusiastic and interested researchers to collaborate their efforts to share knowledge and experience.

Third, considering Asia Pacific regional culture, APSAAR will mainly focus on alcohol addiction but hopes to extend its research areas to drug, gambling, and IT addictions.

As the theme suggests, the goal of this Congress is to provide opportunities for participants to exchange knowledge and ideas of the latest information and clinical experiences related to addiction. We look forward to showcasing oral presentations, social programs, and innovated research projects conducted by esteemed colleagues from every corner of the globe.

The conference brings together about 200 leading experts and researchers from all over the world. Symposium addresses topics with broad, interdisciplinary interest and is balanced with plenary lectures and poster sessions. Researchers from around the world share their latest findings, technical expertise, and experience making this a much-anticipated international event. Our aim is to offer you a conference that is conducive to the vital work of interdisciplinary collaboration so crucial to APSAAR's mission—and also to provide opportunities where you will enjoy catching up with old friends and colleagues, as well as making new ones.

We also hope our guests enjoy their visits to Seoul, the capital city of South Korea. Seoul presents a coexistence of a long, proud history and technological innovation along with its natural beauty. Please take time to enjoy the history, leisure, dining, natural beauty, and recreation that our city has to offer.

Best wishes and welcome!

Dongyul Oh
President, APSAAR

Welcome Message from the President of KAAP

On behalf of the Korean Academy of Addiction Psychiatry (KAAP), I would like to express my warm welcome to all participants in the first Congress of Asian Pacific Society for Alcohol and Addiction Research (APSAAR) and 28th Meeting of KAAP convened from November 12 to 14, 2009 at COEX in Seoul, Korea. KAAP was formed in April 1996 by Korean psychiatrists who had interest in addiction psychiatry. KAAP has over 150 lifetime members now, and each meeting of KAAP has had over 150 participants including psychiatrists, nurses, social workers and clinical psychologists.

The joint meeting of APSAAR and KAAP is a quite an attractive academic event that will deliver many outstanding lectures in 3 plenary sessions, one special lecture, 19 symposia and many poster presentations. The scientific sessions will cover all current topics of basic and clinical aspects of addiction. From epidemiology to genetic and neuroimaging studies are the examples of basic research in addiction. Cultural differences, organ damage, pharmacotherapy, rehabilitation and virtual reality therapy are the topics for clinical aspects of addiction.

I sincerely hope that you can join the joint meeting of APSAAR and KAAP and have a special opportunity to develop your study further and broaden your clinical experience with many delegates from not only Asia Pacific region but also the United States and Europe, simultaneously enjoying Korean traditional cultures as well as brisk air of Seoul in November. I cordially invite you to the joint meeting of APSAAR and KAAP, Seoul, Korea.

Ihn-Geun Choi
Congress President, The Joint Meeting of APSAAR and KAAP

Welcome Message from Chair of the Local Organizing Committee

Dear Friends,

We are delighted to welcome you to attend the First Congress of Asian Pacific Society for Alcohol and Addiction Research (APSAAR) held in Seoul, Korea from November 12 to 14, 2009.

The 1st Congress of APSAAR will be a resounding success. It will bring a wealth of research on Asian-Pacific addiction psychiatry and the opportunity for the gathering of leaders in Asian-Pacific psychiatry to discuss common issues, especially in the rapidly advancing region of this area. This Congress will be promising to be an exciting opportunity to present the latest research in addiction psychiatry and innovations that can bring changes not only to the Asia-Pacific area but also to other parts of the world. The 1st Congress of APSAAR is a forum on the rapidly developing field of addiction psychiatry, not only for psychiatrists but all experts with interest in research, teaching and services in Asia-Pacific area.

I am pleased that Korea is honored to be the host of the 1st Congress of APSAAR, and I want to assure you that Korea will continue to improve its psychiatry healthcare system and is ready to learn about the latest treatment and prospective on psychiatry from all over the world.

Seoul is the traditional capital of Korea and an attractive city with a lot of historical and modern features. November is a good month of the year for visitors and there are many scenic landscapes and shops nearby. Please enjoy the fall of beautiful Seoul.

I look forward to meeting all of you in Seoul in 2009 !

Sung-Gon Kim
Chair of the Local Organizing Committee

Symposium Session

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Perspective on Alcohol Research: Past, Present and Future.

Li, Ting-Kai
Duke-National University of Singapore Graduate Medical School, Durham, NC,
USA and Singapore

The age old questions about alcohol use and misuse/addiction are:

1   Why do people drink?
2   Why some drink more than others?
3   Why some drink despite negative consequences?

The use and misuse of alcoholic beverages date back more than eight thousand years, and Grecian scholars as far as 2500 years ago had issued warnings about the dangers of excessive consumption (drinking too much, too fast and drinking too much too often) and provided moderate drinking guidelines. In China, the use of herbal medicines containing extracts of Radix pueraria (Kudzu) to treat acute and chronic inebriation was recommended more than 2000 years ago. In the absence of physiological, biochemical and genetic evidence to the contrary, aberration of drinking behavior was attributed to moral weakness. With the advent of modern biomedical research technologies in the last several decades, this notion has been dispelled. It is now being acknowledged, and should be widely disseminated to the public at large, that alcoholism/addiction is a "complex" behavioral disorder, similar to diabetes, hypertension and other common diseases. Complexity means that there are multiple genetic and environmental risk factors influencing the onset, course and severity of the disorder over the lifespan of the affected individual. For alcoholism/alcohol addiction, it has been firmly established that the functional polymorphisms of ADH and ALDH2 lead to genetic variations in alcohol metabolism (pharmacokinetics) and responses to alcohol (pharmacodynamics). Hence alcoholism/alcohol addiction qualifies as a pharmacogenetic disorder of alcohol self-administration with genetic variation being a major reason for individual differences in drinking behavior. The other major contributor to variation is differences in environmental exposure to the causative agent ethanol, and the age and circumstances of exposure. Studies in outbred and genetically modified animal models exposed to different conditions under which they **self–administer alcohol**, have identified brain pathways and neurotransmitter systems that mediate acute and chronic alcohol self-administration, both for its positive and its negative reinforcing effects. The latter, occurring as result of neurodaptive responses to chronic ethanol exposure, can lead to anxiety and other distressful negative states that promote continuation and resumption of alcohol self-administration. Identification of the neurotransmitter systems involved in the actions of alcohol provides targets for medication development that will be effective in alleviating negative reinforcement as well as curbing the

excessive appetite for alcohol present in some animals and humans. Promising new directions might explore the CNS effects of ethanol's metabolites, acetaldehyde and acetate, especially since acetate can serve as a source of energy for the brain.

Mammillothalamic functional connectivity strength and memory impairment in alcoholic patients recovering from Wernicke-Korsakoff syndrome

Young-Chul Jung, MD, PhD
Department of Psychiatry,
Yonsei University College of Medicine, Seoul, Korea

<ABSTRACT>

Wernicke's encephalopathy is an acute disorder characterized by ataxia, opthalmoplegia and confusion, while Korsakoff's syndrome is defined as a disproportionate impairment in memory, relative to other features of cognitive function. Because of the pathophysiological connection (deficiency of vitamin B1), it is often coupled as the Wernicke-Korsakoff syndrome, as if a single entity. However, recent studies have reported that Korsakoff's syndrome is not inevitable in patients with Wernicke encephalopathy. By far the most common cause of vitamin B1 deficiency throughout the world is alcoholism. Prompt treatment of Wernicke's encephalopathy with adequate dose of parenteral thiamine in alcoholic patients might prevent the development of Korsakoff's syndrome. Thus, for the clinical purpose, monitoring treatment response and detecting the changes of the function in the responsible brain regions are becoming more necessary.

There are still debates about the neural mechanisms underlying pathogenic or even recovering processes of Wernicke encephalopathy. Therefore, we aimed to validate the usefulness of resting-state functional connectivity analysis in assessing the memory function and its neural correlation with the mammillothalamic tract in patients recovering from Wernicke's encephalopathy.

Seven alcoholic patients recovering from Wernicke's encephalopathy (WE), 14 alcoholic comparisons without Wernicke's encephalopathy (AC), and 14 healthy comparisons (HC) underwent resting state functional connectivity magnetic resonance image analysis, as well as verabl and nonverbal memory tests after at least 1 month-duration of abstinence (30~93 days). The resting-state functional connectivity strength between the anterior thalamus and the mammillary bodies was investigated by calculating temporal correlations in magnetic resonance signal levels between the two regions during a 5-minute passive viewing task. The mean values of the functional connectivity strength between the left anterior thalamus and ipsilateral mammillary body differed significantly between the WE group and the HC group (P = 0.014). This connectivity strength of the AC group fell between those of the former two groups. In addition, the strength of this left-sided functional connectivity significantly correlated with delayed verbal recall scores (r = 0.771, P = 0.042) and verbal recognition score (r = 0.825, P = 0.022) in the WE group.

Our findings indicate that the memory function in patients recovering from Wernicke's encephalopathy parallels with the level of the mammillothalamic functional connectivity, supporting

the usefulness of the resting-state functional connectivity analysis as a practical alternative to pathological examination of the mammillothalamic tract in 'living' patients with Wernicke's encephalopathy.

A Serial Study on Combination Use of Buprenorphine with Scopolamine and Promethazine (BSP) in China

Wei Hao, Xuhui Zhou, Xuyi Wang
Mental Health Institute, WHO Collaborating Center in Drug Abuse and Health,
Second Xinagya Hospital, Central South University
China

Buprenorphine is considered to be an alternative to methadone in the maintenance and detoxification of heroin addicts. However, Sublingual buprenorphine table was abused by injection among drug users (IDUs) in some countries, such as Ireland, France, Australia and Finland.

In China, preliminary study showed that the combination use of buprenorphine with scopolamine and promethazine (BSP abuse) were popularly used in heroin addicts in street in some areas in China and caused a lot problems

The authors conducted a series study on BSP including:

1. Survey for clinical characteristics and cognitive damages in patients with BSP and heroin abuse in two drug treatment facilities in Changsha city, Hunan Province.

2. Brain imaging study on BSP-dependent and heroin dependent patients in 3 days, one month and two months after withdrawal.

3. Animal study on changes in CPP, spatial memory and D2R and CHAT mRNA expressions in rats treated with BSP

The results showed:

1. The combination use of buprenorphine, scopolamine and promethazine (BSP use) in street is an emerging problem in China;

2. BSP is well accepted by heroin users, not only because of less expenditure, and its good availability, but also good efficacy on releasing withdrawal symptom and insomnia. However, BSP use causes more damages in cognition and problems showing brain image study;

3. Scopolamine and promethazine may act synergistically to enhance effects of buprenorphine, and the most likely mechanism is by means of increasing the release of dopamine in the meso-limbic dopamine system.

The author propose a new approach for the acute drug treatment based on following assumption:

1. Buprenorphine, scopolamine and promethazine may act synergistically in acute withdrawal symptoms if the side effects, such as cognitive damage and delirium can be controlled

2. Targeting multiple receptors, such as opioid, dopamine, histamine and acetylcholine receptors by "cocktail treatment" may be one of good solutions for opiate acute withdrawal.

The authors will report the results of a pilot study of "cocktail treatment" for 15 cases of heroin addicts.

Understanding Alcohol Induced Brain Injury Through Neuroimaging

Peter R. Martin
Vanderbilt University School of Medicine
USA

Chronic alcohol consumption is toxic to many tissues of the body, especially the nervous system. Consequently, it may be challenging to disentangle the adverse effects on brain functioning of alcohol per se from those attributable to the protean complications of alcohol dependence. Neurocognitive impairments may be due to adverse effects of alcohol consumption on brain functioning. In addition, some alcoholism-associated neurocognitive defi- cits may recover with abstinence, whereas others seem to persist for months or years beyond cessation of drinking. However, the high prevalence and limited improvement with abstinence of certain neurocognitive deficits in chronic alcoholics suggest another alternative ?that such 器 rreversible?brain abnormalities may pre-date pathological alcohol consumption and actually may have contributed to, or have facilitated the development and progression of out-of-control drinking. Accordingly, neurocognitive deficits may represent predisposing or risk factors for development of alcohol dependence and also may contribute to the neuroadaptive changes accompanying the accelerating progression of this disorder. Therefore, impaired neurocognitive functions should be considered in treatment planning. Data to be presented, derived primarily from proton magnetic resonance spectroscopy (MRS) studies and relevant other research, support the hypothesis that not all neurocognitive deficits in alcoholics can clearly be attributed to alcohol consumption per se or the complications of alcohol dependence. Mechanistic interpretation of MRS findings and implications for treatment are discussed.

Alcoholism's Effect on the Brain: Insights from Human and Animal Neuroimaging Studies

[1,2]Adolf Pfefferbaum, M.D. and [2]Edith V. Sullivan, Ph.D.
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[2]Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine,
Stanford, California, U.S.A.

Men and women who chronically drink excessive amounts of alcohol are at risk for sustaining brain injury affecting the macrostructure, microstructure, and function of the brain, detectable in vivo with magnetic resonance imaging (MRI) and spectroscopy (MRS). Alcoholism is often associated with impoverished diet and poor nutritional status, which can contribute to the observed brain abnormalities and to the neuropathology of several alcoholism-related clinical syndromes, such as Marchiafava-Bignami disease, central pontine myelinolysis, and the Wernicke-Korsakoff Syndrome. Hematological indices reflective of nutritional, liver, and kidney function have been associated with MRI measures of alcoholism-related brain abnormalities. In particular, we have related interstitial fluid accumulation in the pons to red blood cell count, mean cell volume, and serum albumin concentration, and enlarged ventricular volumes to low red blood count, hemoglobin, and hematocrit. Longitudinal study of treatment-seeking alcoholic men found that low hemoglobin values correlated with enlarged ventricular volumes and smaller white matter volumes; change in these measures was related to reduction in ventricular volume with treatment. MR diffusion tensor imaging (DTI) has revealed degradation of white matter microstructure, notably in indices of myelin integrity, which, in alcoholic women, were below the detection of conventional MRI. The extent of regional fiber disrepair is predictive of poor performance on tests of visuospatial function, working memory, and gait and balance in sober alcoholics. Translational neuroimaging studies of alcoholism using animal models have extended human investigations because of the ability to control over factors not possible in naturalistic human study. Using MRI in a rat model of Wernicke's Encephalopathy, alcohol-preferring rats were scanned before and after receiving a thiamine deficient diet for 2 weeks. Compared with thiamine-treated rats, thiamine deficient rats had significantly enlarged ventricles and signs of interstitial fluid accumulation in the thalamus and inferior colliculus; each abnormality showed a different pattern of recovery with thiamine repletion. This model of Wernicke's Encephalopathy was invaluable for identifying the separate contribution of nutritional deficiency and direct alcohol neurotoxicity in the production of alcoholism-related brain damage. Other animal studies using MRS measured the kinetics of acute alcohol metabolism in the brain at a 4-minute resolution. Use of MR structural and spectroscopic imaging has enabled tracking of the chronic effects on selective brain metabolites of high doses of alcohol maintained over days and recovery following days of alcohol abstinence. The resulting patterns of regional

brain structural, functional, or biochemical insult associated with chronic alcoholism provide insight into the scope and limits of recovery and neural mechanisms responsible for alcoholism's dynamic course on brain structure and function. **Support:** National Institute on Alcohol Abuse and Alcoholism (AA005965, AA012388, AA017347, AA013521-INIA, AA010723, AA017168)

Genetic Validation in Anxiety-depressive alcoholism

Ru-Band Lu M.D.
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Tainan, Taiwan, R.O.C.

Being a multi-factorial mental disorder, alcohol dependence (AD) is also influenced by heterogeneity and socio-cultural factors (Cloninger, 1987; Goldman, 1993; Merikangas, 1990). The typology of alcoholism to reduce heterogeneity is therefore important and critical in both the area of research and clinical practice. A lot of subtype of alcoholism have been reported, but no a demonstrated genetic validation. In our research team subdivided alcoholics into pure alcoholics (pure ALC), anxious ∕depressive alcoholics (ANX∕DEP ALC), and antisocial alcoholics. Pure ALC group members included subjects with a diagnosis of only AD in their past or current history included subjects with a diagnosis of only AD in their past or current history. ANX∕DEP ALC group members had a past or current history of major depression or anxiety disorder or both in addition to a diagnosis of AD. Finally, antisocial ALC group members had a history of AD and comorbid antisocial personality disorder.

Subjects carrying the *MAOA-uVNTR* (variable number of tandem repeat located upstream) *3-repeat* allele and genotype *A1∕A1* of the *DRD2* were 3.48 times more likely to be ANX∕DEP ALC than the subjects carrying the *MAOA-uVNTR 3-repeat* allele and *DRD2 A2∕A2* genotype (Huang et al., 2007). After stratification of the *MAOA-uVNTR* gene, significant association between *ALDH2* polymorphisms and ANX/DEP ALC were still noted in both *3-repeat* and *4-repeat* genotypes. However, subjects with *MAOA-uVNTR 3-repeat* (odds ratio=0.343) and *4-repeat* (odds ratio=0.117) were non-homogenous (p=0.035). The protective effects of the *ALDH2*2^{+}* allele seems to be significantly higher in the presence of the *MAOA-uVNTR 4-repeat* allele than those with *3-repeat* allele*. DRD2* gene was not associated with pure alcohol dependence, but was found to be associated with ANX/DEP ALC. Moreover, ANX/DEP ALC was associated with the *DRD2* gene under the stratification of *ALDH2*1/*1*, the *DRD2* gene might interact with the *ALDH2* gene in the development of ANX/DEP ALC.

We conclude that ANX/DEP ALC is a specific subtype of alcohol dependence.

Depression in alcoholic inpatients and outpatients

Jae Yeon Hwang, M.D. and Ung Gu Kang, M.D., Ph.D.
Sept. of Psychiatry and Behavioral Sciences,
Seoul National University College of Medicine
Republic of Korea

Treatment of alcoholism in Korea was mainly focused on the inpatient treatment. Inpatient treatment is usually composed of 8 or 12 weeks intensive program, which requires a great deal of resources including the time lost during the admission period. Recently, the number of patients seeking treatment without admission is increasing. However their characteristics are not well understood. In this study we compared some clinical characteristics between the inpatient and the outpatient alcoholics.

Thirty-three inpatients were compared with 44 outpatients. Patients were evaluated using K-MINI, AUDIT-K, BAI, BDI, and RTCQ-TV(Readiness to Change Questionnaire: Treatment Version)

Outpatients were more educated and had more stable marital status compared to the inpatients. The age of onset of usual drinking was not different, while the onset of problematic drinking was later in the outpatients. They had less prior admissions for alcoholism and experienced less withdrawal symptoms. The prevalence of psychiatric comorbidity including depression was not different. However the outpatients had less suicidal idea and lower degree of anxiety and depression. The outpatients were more motivated for the change.

In short, the outpatients had less severe psychopathology in general. However, we could not find a definite difference. The outpatients were also depressed and require treatments. We suggest that early interventions in the OPD may prevent the progression of alcohol use disorder and reduce the resources required for inpatient treatment.

Depression, suicidal ideation, and suicide attempts among Japanese patients with alcohol dependence and their effects on treatment outcomes

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Background: Depression is common among patients with alcohol dependence (AD) and is important not only because of comorbidity but also because it might be associated with poorer treatment outcomes of AD and with increased risk of suicidal behavior. However, most evidence showing an association between depression and AD has been obtained in Western countries and clinical evidence regarding psychiatric comorbidities of AD and their influence on the treatment outcome of AD is scant in Japan. Therefore, we established a study group named the Japan Collaborative Clinical Study on Alcohol Dependence (JCSA) Group and conducted several nationwide surveys on clinical characteristics of patients with AD and treatment outcomes. We also examined the prevalence of depression, suicidal ideation and suicide attempts in Japanese AD patients and their effects on treatment outcomes.

Aims: With that background, the present study aimed to clarify the prevalence rates of depression, suicidal ideation and suicide attempts in patients with AD in Japan and also aimed to elucidate the influence of depression, suicidal ideation and suicide attempts on the treatment outcomes of AD.

Methods: Fifty-four hospitals throughout the country participated in the JCSA. In each hospital, an assessment of sociodemographic and alcohol-related data, psychiatric diagnosis and clinical symptoms on admission, as well as addiction severity index (ASI) of up to 25 patients who were consecutively hospitalized within the fixed study period was conducted. Six-month outcomes after discharge from the hospitals were also assessed.

Results: Eight hundred and fifty-three patients with AD (females 16%) were enrolled in the study. More than 18% of the subjects with AD had experienced depressive episodes before admission. Lifetime prevalence of suicidal ideation and suicide attempts exceeded 16% and 8% respectively. Female AD patients had significantly higher prevalences of depressive episodes and suicidal ideation than male patients, and female patients tended to have higher prevalence of suicide attempts than male counterparts. History of depression, suicidal ideation or suicide attempts did not have any influence on treatment outcomes of AD. In contrast, AD patients with depressive episodes after discharge had poorer treatment outcomes than those without depressive episodes.

Conclusion: The JCSA provided basic information on clinical characteristics and treatment outcomes of AD in patients admitted to specialized treatment facilities in Japan. This presentation

will focus on psychiatric comorbidities and their influence on treatment outcomes of AD based on results of the JCSA.

Affective disorder and persistence of alcohol dependence

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Purpose: Depressive disorder and depressive symptoms are common among individuals with alcohol dependence, particularly among females. However, depression's role in the longitudinal course of alcohol dependence remains somewhat controversial. This presentation will focus on n=1835 persons from the Collaborative Study on the Genetics of Alcoholism (COGA) with a DSM-IV diagnosis of alcohol dependence, with and without depression, at baseline who were then re-interviewed five years later.

METHODS: COGA, a large scale multi-site family study of alcohol dependence being conducted in the US, is designed to identify genetic susceptibility factors for alcohol dependence. All probands were recruited from treatment facilities; biological family members were invited to participate as well. The current sample of 15,000+ subjects represents over 1800 extended families. A sub-sample of N=1835 adult (18+years old) subjects with DSM3R alcohol dependence participating in COGA were interviewed at baseline and five years later using a standardized diagnostic interview (Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA)).

RESULTS: At baseline, 925 subjects had alcohol dependence only, 624 had an additional alcohol-related induced depression, and 279 had both alcohol dependence and a non-induced major depression. Subjects with either type of depression reported more lifetime alcohol symptoms, a higher maximum (lifetime) drinks/day and more suicide attempts. Five years later, 63.2% of the alcohol-only group persisted in their alcohol dependence while 69.2% of the non-induced depression group had persistent alcohol dependence. However, 77% of those subjects with an alcohol induced depression at baseline also had persistent alcohol dependence at follow-up. Of those 563 subjects whose alcohol dependence remitted over the five year interval, 59.68% reported no history of depression compared to only 15% with a history of non-induced major depressive disorder and 25.2% with an alcohol-induced depression.

Conclusions: Our findings indicate that among more severely affected individuals, alcohol dependence is quite persistent, with almost 69% diagnosed at baseline continuing to carry the diagnosis five years later. Among those subjects having a lifetime diagnosis of depression – whether induced or not induced by heavy drinking – 53.3% persisted in their alcohol dependence. These findings indicate a strong role for depression's contributions to persistent alcohol dependence and to its alcohol-related problems.

Underage drinking problems in Japan

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Trends in alcohol drinking prevalence were assessed among Japanese adolescents, and possible reasons for a decrease in drinking prevalence observed in recent surveys.

Cross-sectional nationwide surveys were conducted periodically. High schools were randomly sampled from throughout Japan in 1996, 2000, 2004, and 2008. All enrolled students in sampled schools. Self-reporting anonymous questionnaires were collected from 115,814 students in 1996, 106,297 in 2000, 102,451 in 2004, and 95,680 in 2008. Questions about drinking prevalence of students and family members, proportion of students who have no friends, sources of alcohol were included. Students who drunk at least one day of the 30 days preceding the survey were defined as the current drinkers.

The drinking prevalence in 2004 was decreased in comparison to that in 1996 and 2000 in both sexes and in all school grades. The current drinking rate (monthly drinker) among junior high school boys was 29.4% in 1996, 29.0% in 2000, and 20.5% in 2004, while that among senior high school boys was 49.7%, 48.7%, and 36.2%, respectively. The respective prevalence among junior and senior girls was 24.0%, 25.5%, and 20.0%, and 40.8%, 42.1%, and 34.1%. In 2008 survey, the decrease trend is continuing. The prevalent sources of alcohol beverages were searching in home, stores (convenience store, supermarket, or gas-stand), liquor shops, and bars. An analysis of the reasons for this decrease identified a decrease in drinking prevalence in students' families, especially by fathers and older brothers, and an increase in the proportion of students who had no friends.

A decrease in drinking prevalence of male family members and a limitation of sources of alcoholic beverages may contribute to the decrease in adolescent drinking prevalence.

 In Japan, there are still some problematic situations concerning minors drinking, such as the low price of alcohol beverages (less than 1 US$ for the cheapest beer or alcopop), the popularity of alcopop among both sexes, many TV commercials for alcoholic beverages. It is expected that the alcohol consumption among adolescents will increase with the reduction in the price of alcohol beverages. Periodical nationwide surveys on adolescent drinking and survey of environmental factors (TV CM, drinking scenes in TV drama, comics or movie, advertisements in magazines and sponsorship of many events by the alcohol industry) are necessary to deal with the social problems of adolescent drinking.

Pattern of Alcohol Consumption in Underage Population in an Indian City

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In India minimum legal age of Alcohol consumption varies from 18 to 25 years across the states. In a study by an NGO (Campaign Against Drunken Driving) it was found that 80% of bar and pub occupancy in Delhi was below age of 25 and 67% below 21 years. This study further showed that about 2000 youths die of motor vehicle accidents, other unintentional injuries, homicides, suicides that involve underage drinking every year. Drinking age came down from 28 yrs to 19 yrs in Delhi since 1990.(Study conducted December 2008 to January 2009)

Considering the fact that minimum legal age for consumption of Alcohol is 18yrs in Assam(A state in India) to 25 years in New Delhi(Capital of India) and the findings from the Delhi study, the present study was undertaken in Guwahati, the capital city of Assam . The study was conducted across schools from age groups 14 t0 18 years. The minimum age reported was in a group of 14 year old girls . Pattern of Alcohol consumption varied from drinking in pub, mixing colourless alcoholic drink with water carried in water bottle to school, drinking from father's liquor cabinet and get together with friends. Alcohol was linked to reckless driving, accident, brawls, and absenteeism.

It is evident that though there is a law against underage drinking, enforcement of the law is not adequate. Further parental supervision and Alcohol education could be useful in prevention of underage drinking.

Undertaking: There is no conflict of interest with any organization or Pharmaceutical Company

Social and School Environmental Influences on Alcohol Consumption among High-School Students in Thailand

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Background: Alcohol consumption is popular among teenagers and leads to several consequences. This presentation will examine the influences of perceptions regarding social environments, school rules, alcohol advertising, and positive attitudes toward alcohol on the students' drinking behaviour.

Methods: The 2007 national school survey was conducted from 201 schools in 40 provinces. All students in the selected classrooms were asked to complete a self-administered questionnaire. The total was 50,033, with 46% males. The mean age was 15.1 years.

Results: Overall, 25% and 14% of male and female students were current drinkers who had drunk alcohol in the past 12 months of the survey. Current drinkers were more likely to exhibit more frequent behavioural problems, such as physical fighting, alcohol and substance use, than were the non-drinking students. 40.6%, of students who drink perceived there were a higher number of students in their school drinking, and 25.4 % thought that drinking was permissible in school if it was within a safe limit. Among drinking students, 80.2% reported having seen or heard alcohol advertising in the mass media, while only 71.6% of non-drinkers had (AOR=1.51, 95% CI=1.40, 1.64). The students who drank were more likely to be able to memorize alcoholic beverage brands (AOR = 1.75, 95% CI=1.63, 1.89) and want to try out an alcoholic beverage than were the non-drinking students (AOR = 3.10, 95% CI=2.82, 3.42). Current drinkers had higher odds of perceiving that drinking alcohol was good in many ways, e.g. allowing people to have fun (AOR=3.11, 95% CI=2.87, 3.37), compared to non-drinkers.

Conclusion:
    Factors associated with alcohol consumption among Thai students included their perception of the school social environment, their exposure to alcohol advertisements and their positive attitudes toward drinking. Preventive measures for problems-related to underage drinking are discussed.

Underage Drinking: A Developmental Perspective

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ABSTRACT

Alcohol use disorders are developmentally related disorders with substantial health, social and intellectual consequences.   It is becoming increasingly clear that alcohol use of use begins in adolescence and is characterized by escalation in hazardous drinking and alcohol related problems in late adolescence, which is the period of greatest risk for the onset of an alcohol use disorder. Experimental research demonstrates that compared to adults, adolescents are more vulnerable to the adverse consequences of heavy drinking on both biological and social functioning.

Through longitudinal study of three cohorts of over 600 clinical and community based teens examined semi-annually from adolescence to adulthood we have determined the common outcomes for those who develop alcohol problems early in life, identified the ways adolescents succeed and fail following treatment, and determined the impact of alcohol and drug involvement on functioning in work, education and family domains.   In particular, neurocognitve impairments associated with both alcohol and other drug use, which are subtle in middle adolescence become more pronounced with continued alcohol use in young adulthood.   Using these research findings we have developed a model of early intervention which is tailored to the needs and concerns of youth.   The intervention has been tested in multiple schools settings, shown to increase youth efforts to reduce drinking and results in a reduction of alcohol related problems.

Patients' characteristics in substance abuse treatment and rehabilitation system in Thailand

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Despite of several attempts in the prevention and control of substance abuse problems as well as in the treatment of substance dependence in Thailand in recent years, the number of substance abusers was not decreased and several have relapsed to substance abuse. This presentation discusses substance abuse treatment and rehabilitation systems in Thailand and the characteristics of patients over the past five years. The number of patients in all treatment centres increased markedly from 35,215, 43,201, 49,796 and 59,660 in 2004-2007 to 78,093 in 2008. Amphetamine abuse patients accounted for the highest proportion (63-82%) of all patients each year and the number increased from 2004 to 2008 by three folds. The other four most commonly abused substances were cannabis and inhalants, which also increased and heroin and opium, which decreased in numbers by year. Most amphetamine patients aged 12-24 (50%) and 25-34 years (30%) while heroin patients aged 25-34 (45%) and 35-44 years (25%). The ratios of new-to-old patients were 4:1 for amphetamine, cannabis and inhalants, 1:2 and 1:1 for heroin and opium. About 57-59% of the patients were single and the percentages of female patients were 9.5-11.4% each year. The implementation of the substance abuse rehabilitation law in 2002 has brought about the new movement in the management of substance abuse problems, which is the co-operation of several ministries such as the ministries of internal affairs, public health and justice. At present, there are three treatment systems, voluntary, compulsory and detention systems. A compulsory treatment patient is assigned to receive one of the treatment models in the treatment setting judged by the probation committee, i.e. non-control, loosely control or strictly control model. The treatment in detention system is for a substance dependent criminal to receive treatment in a special treatment prison. Several psychosocial interventions have been used, including Matrix programme, FAST (Family, Alternative treatment activity, Self-help and Therapuetic community) model, herbal treatment and Buddhist 12-step program. Methadone maintenance treatment is not officially approved however methadone detoxification and 45-day methadone treatment are available.

Fact and Vision: rehabilitation of alcohol use disorders in Korea

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Alcohol dependence is one of very important mental health problems in Korea. According to recent epidemiologic survey in 2006, lifetime prevalence of alcohol use disorders is 16.2 %(alcohol dependence 7.0%, alcohol abuse 9.2%). In Korea, traditionally other illicit drugs use should have been legally and strongly controlled. The current system of care for treating individuals with alcohol use disorders evolved during recent 20 years. It has roots in self-help groups (12 steps) and in medical and psychiatric treatment settings, and has been shaped by new care trends, national mental health strategies and uneven financing policies of national insurance system. This presentation reviews the past histories and perspectives about Korean psychosocial rehabilitation system for treating patients with alcohol use disorders. And the current psychosocial rehabilitation programs related to addiction field in Korea are introduced. Finally limitation of current Korean rehabilitation system and future directions are proposed.

Surveillance and rehabilitation of drug abuse in China

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Drug abuse has increasingly become a serious social and medical problem in China. From 1990 to 2004, the population of officially registered drug addicts has increased more than 16-fold from 70000 to 1140000. Since 1992, Chinese government has started the epidemiologic monitoring and investigation on pharmaceutical drug use and illicit drug abuse in addicts. The information on drug abuse cases, including (1) socio-demographic characteristics (e.g. age, gender, employment); (2) drug abuse characteristics (type of abused drug, age first used drugs, the reason for drug abusing, etc); and (3) the date of contact with the reporting institution, is collected through the National Network of Drug Abuse Surveillance, which covers 31 provinces, autonomous regions and municipalities directly under the Central Government. The National Surveillance Center on Drug Abuse collates and analyzes the data from "the Surveillance Form of Drug Abuse". The Annual Reports on Drug Abuse of China are published regularly on the trends and major characteristics of drug addiction. Although a general tendency of abusing new drug (e.g. MDMA, methamphetamine, and ketamine) may obviously be increasing, opiates, especially heroin, remain the most commonly used drugs in drug addicts. In China, treatment and rehabilitation system for drug abuse consists of mandatory (department of public security), reformatory (department of justice), and non-mandatory (department of public health). The therapeutic measures and rehabilitation programs include methadone maintenance treatment program, therapeutic community (Daytop), program of rehabilitation in resident area, self-help program, traditional Chinese medicine in the prevention of relapse, and the others. In 2007, the "Narcotics Control Law of the People's Republic of China" was adopted by Standing Committee of the National People's Congress, which can greatly improve the prevention of relapse of drug abuse.

Substance misuse treatment for Indigenous Australians

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This presentation is part of the symposium "Rehabilitation of substance use disorders in the Asia-Pacific Region" organized by Dr. Susumu Higuchi from the National Hospital Organization Kurihama Alcoholism Center, Japan.

Presentation Abstract

Substance misuse is a major public health problem for many Indigenous Australian peoples - in terms of death, disease, social and emotional wellbeing, and social and economic issues. Estimates of the burden of disease and injury for Indigenous Australians attribute 5.4% of the total to the net effects of alcohol consumption. In 2004, 15% of Indigenous Australians consumed alcohol at high-risk levels, compared with 2.8% of the non-Indigenous population.

In Australia, there have been two main responses to addressing Indigenous alcohol misuse. The first has been around the reduction and control of the supply of alcohol in specific regions. The second has been focused on demand reduction strategies. Demand reduction strategies aim to motivate users to consume less overall (or less per occasion), or by affecting specific population groups. The one feature that stands out in addressing Indigenous demand for alcohol is that there is considerable paucity of evidence showing effective intervention outcomes. This is partly because few interventions are evaluated, and those that are, have demonstrated poor outcomes.

Since the 1970s, the most popular approach to addressing Indigenous substance misuse has been through residential rehabilitation services. In 2002, there were 33 such services around Australia, each receiving a combination of Federal and State/Territory funding, and controlled and operated by Indigenous people themselves. In the early 2000s, there were 33 such services around Australia, each providing a range of services from cognitive behavioural therapies and harm reduction programs to abstinence based programs. However, concerns have been expressed regarding the effectiveness of residential treatment (including mandated to treatment services), although few have been evaluated. This presentation will discuss the outcomes of a four year National Health and Medical Research Council project that has examined the advantages and limitations of Indigenous residential treatment centres. The presentation will include a discussion about the outcomes associated with this form of treatment and the development of evaluation methodologies to allow organisations to assess client progress.

Cultural Differences and the Minimum Legal Drinking Age

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Three countries have the age of 21 as the legal age for drinking alcohol and three countries have 21 as the legal age for purchasing alcohol. In the USA, one of the countries with a 21 year age limit for legal drinking there is a group of university officials who want the legal age for drinking reduced to 18 (Amethyst Initiative). This paper summarizes the arguments for increasing and not increasing the legal drinking age and suggests that raising the legal drinking age alone may not have much effect on alcohol related problems. Other culturally based variables may be as important and should be considered in any decision to change a countries legal alcohol drinking age.

Gender and Age Differences on Alcohol Beverage Preferences in Thailand

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Introduction: Alcohol consumption in Thailand has been increasing since 1998*. This study provides the prevalence and the consumption of different beverage types by age and gender among Thais.
Methods:
Study design: National household survey conducted in 2007
Study subjects: Population aged between 12-65 years
Setting: Bangkok, municipal and non-municipal areas of Peripheral, Central, Northern, Northeastern and Southern regions
Measurements and data collection: Face-to-face structured questionnaire interview by trained interviewers
Results: Of the Thai population aged 12-65 years, 63% were abstainers and the prevalence of current drinking in the past 12 months was 48% among men and 12% among women. The most frequently consumed beverage was beer, followed by white spirits and whiskey.
Consumption by men of almost all types of beverages was more than in women, except for fruit cocktails, wine, and RTD (Ready-To-Drink). About 50% and 40% of men have consumed home brewed alcohol and illicit spirits. Moreover, 9 to 15% of men have consumed illegal spirits, illegal beer, or illegal wine.
The rate of lifetime drinking was high in all age groups for beer. Young drinkers preferred fruit cocktails and RTD; older drinkers (45-65 years) preferred white spirits, medicinal spirits, home brewed alcohol, illicit spirits, and Chinese spirits. While for whiskey, brandy and wine, consumption was highest among middle-aged adults (25-44 years).
Conclusions: Significant age and gender differences were found regarding the type of beverage consumed. Females and younger people are the main consumers of modern types of beverages. This situation should be observed with great caution because it may lead to future consumption of other types of alcoholic beverages.

Culturally specific drinking patterns and per capita consumption data: using different types of data in the development of policies to reduce alcohol related harms

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This paper discusses the analysis of alcohol consumption as described in per capita consumption data and as described in culturally distinct patterns of use. The numerous roles alcohol pays in a community are described to illustrate its cultural significance. Using data mainly from China the values and limitations of per capita consumption data are reviewed and discussed in light of the cultural significance of different drinking patterns. A model is proposed to assist policy makers in the evaluation of changing drinking patterns. This model and these data are then used to illustrate how data of these types can be helpful in the development of policies to reduce alcohol related harms.

Alcohol consumption among Indigenous Australians: opportunities for brief intervention

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Around the world Indigenous peoples that have been subject to colonisation have faced marginalisation, disempowerment and disadvantage. Furthermore policies of forced removal of children from parents in many countries have left legacies of trauma and grief. Together these risk factors place many Indigenous peoples at increased risk of alcohol and other drug problems. In Australian there are two distinct Indigenous groups: Aboriginals and Torres Strait Islanders, who together make up just over 2% of the population. Data on drinking patterns of Indigenous Australians are poor, but suggest more non drinkers than the general population, but among those who do drink, episodic heavy drinking is common. Seven out of ten men drink 7 or more standard drinks per occasion, and a similar proportion of women drink 5 or more drinks. In the same survey there appeared to be low levels of awareness of the levels of drinking which cause harm to health. To date Indigenous Australians have had limited access to modern treatment approaches for alcohol problems. There is no completed successful trial of clinical interventions for alcohol problems in the indigenous Australian setting. We found minimal data on clinical interventions for alcohol problems in indigenous peoples worldwide. It is not clear if current models of one-on-one intervention are the most appropriate in this setting, where family and broader community plays a particularly important role.

Here we report on a pilot study of community-based group education and brief intervention for alcohol problems. Approaches used and lessons learned are described.

Detoxification and management of alcohol withdrawal syndrome

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Alcohol withdrawal syndrome (AWS) can be a life-threatening condition therefore clinicians should pay more attention during the detoxification process in patient with alcohol dependence. In several studies, up to 50% of alcohol-dependent patients develop clinically relevant symptoms of withdrawal. The main objectives of the clinical management of AWS include: to decrease the severity of symptoms, prevent more severe withdrawal clinical manifestations and facilitae entry of the patient into a rehabilitation program in order to maintain the abstinence. Guidelines for the pharmacological treatment of the AWS often recommended the incorporation of standardized withdrawal asseessment scales (i.e. CIWA-Ar or CIWA-AD) into clinical practice. At present, benzodiazepines remain the treatment of choice for alcohol withdrawal, but these medications are not without risks. For that reason, individualized pharmacological treatment would be considered and symptom-triggered medication administration effectively treats AWS while reducing unnecessary medication exposure. Nowadays there is growing evidence to suggest that non-benzodiazepine compounds represent promising medications in the treatment of alcohol-dependent patients. We focus on research into non-benzodiazepine medications for the treatment of AWS in this presentation. Among them, carbamazepine, gabapentin and valproic acid are the most studied, and also the several preliminary data have suggested the possible utility of baclofen and topiramate although further evidence is needed.

Pharmacotherapy in alcohol dependence: anti-craving agents

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Alcohol dependence is a widespread psychiatric disorder. While relapse prevention alcohol dependence was dominated by psychosocial treatments for many years, recent reports documenting that naltrexone and acamprosate are more effective than placebo in the treatment of alcoholism justify clinical interest in use of these medications for alcohol-dependent patients. Whereas for acamprosate primarily abstinence maintenance has been demonstrated, studies with naltrexone have mostly focused prevention of heavy drinking. An action of acamprosate at N-methyl-D-aspartate (NMDA) receptors appears to account for many of its effects. There are conflicting data on this medication according to some recent US studies. However, overall, the evidence is good. Naltrexone, an opiate receptor antagonist, blocks the reinforcing effects of alcohol by preventing the stimulation of opioid receptors and the reduction of dopamine release in the ventral tegmental area (VTA). The efficacies of these medications are modest and the superiority of either one drug or over the other one cannot be determined as a general rule; it rather depends on the treatment goal. Benefits in the treatment of alcohol dependence might be optimized by matching the efficacy profiles of specific so-called anti-craving agents with the motivational status of alcohol-dependent patients. Pharmacological effectiveness also could be enhanced through improving medication adherence.

Pharmacotherapy of Co-morbid psychiatric disorders in Alcohol dependence

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Alcohol use disorders and psychiatric disorders commonly co-occur, and the relationship is complex and bidirectional. This complexity can lead to difficulties in diagnosis and management of co-morbid conditions.

The ideal approach to the pharmacological treatment of co-morbid conditions would be to use an agent that has no abuse potential, is safe and well tolerated, and is efficacious in both disorders.

This presentation contains an overview of the most common and clinically relevant co-morbid psychiatric disorders in alcohol dependence, such as schizophrenia, affective disorders, and anxiety disorders, and provides information on pharmacotherapeutic treatment options of above specific co-morbid conditions.

The development of scientific techniques which are capable of elucidating the common neurobiological pathways in co-morbid disorders is promising for the development of specifically targeted pharmacotherapeutic strategies.

KEY WORDS : Pharmacotherapy, Co-morbidity, Alcohol dependence

Co-morbid physical conditions

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Chronic intake of large quantities of alcohol causes damage to the liver. The longer the period of alcohol use and the greater the amount of alcohol consumed, the greater the likelihood of developing liver disease. Alcoholic liver disease still represents an important cause of death and disability in most well-developed countries and is becoming a leading cause of disease in developing countries. Alcoholic liver disease may take the form of acute illness, such as alcoholic hepatitis, or chronic illness, such as fatty liver, steatohepatitis, liver cirrhosis, hepatocellular carcinoma, and nutritional deficit. Alcoholic hepatitis is an important clinical entity, for reasons including the high short-term mortality rates and for being a well-documented precursor of cirrhosis. The actual stage of cirrhosis represents complications associated with portal hypertension, including upper gastrointestinal bleeding, ascites, spontaneous bacterial peritonitis, bacteremia, and hepatic encephalopathy. Diagnosis of alcoholic liver disease is performed by history taking, physical examination, laboratory tests, histopathology, and various imaging modalities such as ultrasonography and computed tomography. Treatments of alcoholic liver disease include alcohol withdrawal, nutritional support, anti-inflammatory drugs, anti-cytokine drugs, anti-oxidants, and liver transplantation. The prognosis for patient with alcoholic liver disease depends on the degree of pathologic injury, nutritional status, presence of complications of advanced liver disease, presence of other comorbid conditions, and the patient's ability to discontinue destructive patterns of drinking.

Gender differences in the genotype frequencies of the ADH2 and ALDH2 gene in Korean alcohol-dependent patients

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In the present study, the genotype frequencies of the ADH2 and ALDH2 gene polymorphisms in Korean men and women with alcohol dependence (AD) were compared with those of normal healthy (NH) Korean men and women who were determined to be at a low risk for alcoholism.

1) The frequencies of the ADH2*1/1 ($p < .001$) and ALDH2*1/1 ($p < .001$) genotypes were significantly higher in the AD men (n=180) than in the NH men (n=79). However, in the AD women (n=48) the frequencies of the ADH2*1/1 ($p < .001$) and ALDH2*1/2 or 2/2 ($p = .007$) genotypes were significantly higher than in the NH women (n=59).
2) When considering a combination of these two genes, 92.2% of AD men have the ALDH2 1/1 genotype, while 60.4% of AD women have the ADH2 1/1 genotype.

These results suggest that while the risk of alcoholism in Korean men is predominantly affected by the presence of the ALDH2 1/1 genotype, the risk of alcoholism in Korean women is primarily associated with the ADH2 1/1 genotype. It appears that these gender differences make it easier for alcoholic women to become intoxicated, thus making them more vulnerable to becoming alcoholic.

Pharmacokinetics and pharmacodynamics of acetaldehyde in Han Chinese carrying the ALDH2*2 variant gene allele

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Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are the principal enzymes responsible for metabolism of ethanol. Both ADH and ALDH exhibit genetic polymorphisms among racial populations. Functional variant alleles of ADH1B*2 and ALDH2*2 have been consistently replicated to show protection against developing alcohol dependence. Functional allele ADH1C*1, which is in linkage disequilibrium with ADH1B*2, appears insignificant in protecting against the disease as evidenced by relative haplotype analyses. A functional window has been proposed for assessing validity of potential candidate alcoholism genes in ADH family. Multiple logistic regression analyses suggest that ADH1B*2 and ALDH2*2 may independently influence the risk for alcoholism. It has been well documented that homozygosity of ALDH2*2 in East Asians almost fully protects against developing alcohol dependence and that the heterozygosity only affords a partial protection to varying degrees. To explore physiological basis for the full versus the partial protection against alcoholism by ALDH2 polymorphism, direct correlations of blood ethanol/acetaldehyde/acetate concentrations, cardiac and extracranial/intracranial arterial hemodynamic parameters, as well as subjective perceptions have been investigated in healthy male subjects with different ALDH2 allelotypes following a low (0.2 g/kg) to a moderate (0.5 g/kg) dose of alcohol for a period of 130 min. The pharmacokinetic consequences and pharmacodynamic effects indicate that acetaldehyde, rather than ethanol or acetate, is primarily responsible for the observed alcohol sensitivity reactions and suggest that the full protection by ALDH2*2/*2 can be ascribed to the intense unpleasant physiological and psychological reactions caused by persistently elevated blood acetaldehyde after ingesting a small amount of alcohol and that the partial protection by ALDH2*1/*2 can be attributed to a faster elimination of acetaldehyde and accordingly the lower accumulation in circulation.

Physiological basis for overcoming acetaldehyde-induced adverse reaction in ALDH2*1/*2 alcoholics

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It has been well documented that although homozygosity of the variant aldehyde dehydrogenese-2 (ALDH2) gene allele, ALDH2*2, in Asians almost fully protects against alcoholism, the heterozygosity only affords a partial protection to varying degrees. The partial protection against alcoholism has been ascribed to the faster elimination of acetaldehyde by residual hepatic ALDH2 activity and the lower accumulation in circulation in nonalcoholic heterozygotes. The physiological basis for overcoming the protection in ALDH2*1/*2 alcoholics, however, remains unclear. To address this question, we recruited a total of 27 Han Chinese alcohol-dependent men, matched by age and body-mass index, controlled for normal liver and cardiovascular functions, from a population base of 221 alcoholics. The subjects were divided into ALDH2*1/*1 homozygotes (n = 13) and ALDH2*1/*2 heterozygotes (n = 14). Following a moderate dose of ethanol (0.5 g/kg body weight), blood ethanol/acetaldehyde/acetate concentrations, cardiac and extracranial/intracranial arterial hemodynamic parameters, as well as self-rated subjective sensations, were measured for 130 min. ALDH2*1/*2 alcoholics exhibited significantly higher blood acetaldehyde levels as well as prominent cardiovascular effects and the subjective perceptions, compared with the ALDH2*1/*1 alcoholics. Comparable profiles of blood acetaldehyde were found between heterozygotic alcoholics and the previously reported nonalcoholic heterozygotes intaking the same dose of ethanol. ALDH2*1/*2 alcoholics revealed, however, significantly lower intensities in both physiologic and psychologic responses than did the nonalcoholic heterozygotes. These results indicate that acetaldehyde, rather than ethanol or acetate, is primarily responsible for the observed alcohol sensitivity reactions in heterozygotic alcoholics and suggest that physiological tolerance and/or innate low sensitivity may play a crucial role in overcoming the deterring response. A potential pharmacogenetic classification of acetaldehydism and alcoholism for alcoholics carrying the different ALDH2 genotypes is proposed.

Clinical implications on the alcohol metabolic gene

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The ALDH2*2 allele has been shown to be a protective factor against becoming alcoholics in normal population, due in part to the elevated blood level of acetaldehyde and its accompanying physiological discomforts after drinking. Despite the well-established link between ALDH2*2 allele and the physiological discomforts after drinking, very few is known regarding the psychological expectancies of drinking among alcoholics of different ALDH genotypes. We found that alcoholics with the ALDH2*1/*2 genotype had lower negative alcohol outcome expectancies. Specifically, they expected fewer negative outcomes in social/interpersonal, emotional and physical domains than did the ALDH2*1/*1 alcoholics. Moreover, the ALDH2*1/*2 group had higher positive alcohol outcome expectancies and they expected more positive outcomes in relaxation and tension reduction. Alcoholics with both genotypes did not differ in alcohol craving or consumption. We suggested that it is the reason why the ALDH inhibitors disulfiram and cyanamide do not always work. Alcoholics have higher positive and lower negative alcohol outcome expectancies with the same degree of craving and the same amount of alcohol consumption, even in the presence of acetaldehyde accumulation. Therefore, a role of acetaldehyde is implied in these effects, which seem to override the usual discomfort effects associated with protection against alcohol drinking.

Cloninger had proposed that personality dimensions distinguish the alcoholism into two subtypes (type I and type II) and may be related to dopamine and serotonin. However, the classification was equivocal for clinical diagnosis. Recently, anxiety–depressive alcohol dependence (ANX/DEP ALC) and Antisocial alcohol dependence (Antisocial ALC) has been posited as genetically specific subtypes of alcoholism. Its clinical characteristics were similar to individuals with type I and type II alcoholism, respectively. We found both Novelty seeking (NS) and Harm Avoidance (HA) were high in ANX/DEP ALC, but only high NS in Antisocial ALC. The association between NS and ANX/DEP ALC or Antisocial ALC existed in subjects with DRD2 TaqI A1+ allele (A1/A1 or A1/A2 genotypes) and in those with S/S genotype of 5-HTTLPR. With the stratification of DRD2 TaqI A1+ allele, high NS of ANX/DEP ALC or Antisocial ALC existed only in carriers of 5-HTTLPR S/S genotype. Moreover, ANX/DEP ALC was related to HA only in samples carrying 5-HTTLPR S/L or L/L genotype but not in Antisocial ALC. We suggested that Cloninger's hypothesis may require modification.

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UPDATE ON THE COLLABORATIVE STUDY ON THE GENETICS OF ALCOHOLIISM (COGA)

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Purpose: This presentation will focus on the recent findings related to the genetics of alcohol dependence and related conditions from the Collaborative Study on the Genetics of Alcoholism (COGA). Whole genome scan and candidate gene linkage and association findings based upon phenotypes derived from DSM-IV diagnoses and alcohol use behaviors will be presented

Methods: COGA is a six site study of the genetics of alcoholism being conducted in the US that uses an extended family study design. Probands were ascertained through inpatient and outpatient treatment facilities beginning in 1989. The sample now includes more than 15,000 individuals, ages 6-102 years old, representing more than 1800 families. More than 3500 adults have a lifetime diagnosis of alcohol dependence and most have provided a sample of DNA. The psychiatric history of each subject was assessed using the Semi-structured Assessment for the Genetics of Alcoholism (SSAGA), a highly reliable and valid psychiatric interview.

Results: Using several different analytical strategies, COGA has found evidence of linkage and association of several genes and SNPs from several different systems and phenotypes of alcohol use and alcohol dependence as well as endophenotypes based upon neurophysiological assessments. Genes related to the gaba system (GABRA2), alcohol metabolism (ADH4), nicotinic acetylcholine receptors (nAChR), the opiod system (OPRK1 and its ligand (PDYN), and taste sensitivity (TAS2R16) have been identified as increasing the susceptibility for alcohol dependence.

Conclusions: COGA has identified a number of genes in which variations are associated with the risk for alcohol dependence and with related phenotypes and endophenotypes. Several findings, particularly GABRA2, ADH4 and CHRNA5/CHRNA3, have already been replicated by other research groups. This is particularly notable for any complex medical or psychiatric disease

Alcohol Use during Pregnancy and Related Risk Factors in Korea

So Hee Lee
Korea

ABSTRACT

Objectives: Recently, women who drink alcohol and binge drink have increased remarkably in Korea. However, there have been few studies on the alcohol consumption among women who are pregnant or who might become pregnant. We examined the rates of self-reported alcohol use before and during pregnancy and identified maternal characteristics that were associated with drinking.

Methods: One thousand (1000) pregnant women who visited the Department of Obstetrics and Gynecology were given self-administered Questionnaires. The Survey asks about demographic characteristics and use of any alcohol, binge alcohol (≥ 5 drinks on an occasion) during 3 time periods ("in the year before pregnancy", "during this pregnancy" and "in the previous 30days") using Alcohol Use Disorder Identification Test (AUDIT)-C. It also includes items asking about common knowledge relating to alcohol drinking in pregnant women, history of pregnancy and smoking.

Results: We found that the rate of any alcohol drinking in pregnant women was 16.4%, that of any alcohol drinking in the previous 30days was 12.2% and that of binge alcohol drinking during pregnancy was 1.5%. Generally, the frequency of abstinence had a tendency to increase after pregnancy. The group of any alcohol during pregnancy showed a lower educational level, a lower rate of planned pregnancy, a lower level of common knowledge relating to alcohol drinking in pregnant women and a higher frequency of alcohol drinking in the year before pregnancy than the abstinence group. There was a significant negative correlation between "educational level/planning of pregnancy" and "any alcohol during pregnancy", and a significant positive correlation between "quantity and frequency of alcohol drinking in the year before pregnancy" and "any alcohol during pregnancy." However, only "educational level" and a "planning of pregnancy" could significantly predict "any alcohol during pregnancy".

Conclusion: In this investigation, the rate of refusal to the questionnaire was 26.1%. This is the first study to examine any alcohol and binge alcohol drinking during pregnancy in Korea. It warrant clinical attention and necessitates systematic studies on alcohol use in pregnant women as well as binge drinking among women of childbearing age.

KEY WORDS: Pregnancy   Alcohol   Korean women

Researching the Prevalence of FASD in South Africa, Italy, and the United States: Implications for Other Countries

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Abstract

Researching the epidemiology and estimating the prevalence of fetal alcohol syndrome (FAS) and other fetal alcohol spectrum disorders (FASD) for mainstream populations anywhere in the world has presented a challenge to researchers. Three major approaches have been used in the past: surveillance and record review systems, clinic-based studies, and active case ascertainment methods. Previous conclusions about the prevalence of FAS and total FASD in the United States (U.S.) population are summarized. Active approaches which provide clinical outreach, recruitment, and diagnostic services in specific populations have been demonstrated to produce the highest prevalence estimates. Selected studies and results from in-school studies in South Africa, Italy, and the U.S. will be highlighted. The particular focus of this review is on the nature of the data produced from in-school methods and the specific prevalence rates of FAS and total FASD which have emanated from them. I will conclude that FAS and other FASD are more prevalent in school populations, and therefore the general populations of these countries, than previously estimated. My colleagues and I believe that the prevalence of FAS in typical, mixed-racial, and mixed-socioeconomic populations of the U.S. is at least 2 to 7 per 1,000. Regarding all levels of FASD, we estimate that the current prevalence of FASD in populations of younger school children may be as high as 2 to 5% in the U.S. and some Western European countries.

Brain and Behavior in FASD

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San Diego State University

Shortly after the identification of FAS it became clear that the developing brain was impacted by prenatal alcohol exposure. Early autopsies reported diffuse CNS disorganization, including microcephaly, migration errors, and, corpus callosum, basal ganglia, and cerebellar anomalies. However, magnetic resonance imaging (MRI) has indicated specific alterations in brains of individuals exposed prenatally to high doses of alcohol with and without a diagnosis of FAS. In early studies, reductions in specific areas of the cerebrum, the cerebellum, basal ganglia, and corpus callosum were noted. More recently, relative white matter hypoplasia has been observed and diffusion tensor imaging (DTI) studies suggest that white matter pathways are disorganized in FASD. Most recently, functional MRI (fMRI) has exposed changes in brain function in FASD during tests of spatial working memory, attention, verbal learning and memory, and response inhibition. Typically, increased frontal activation has been observed, although decreased activation has been observed in brain areas thought to mediate certain aspects of the tasks (e.g. caudate during response inhibition tasks). This may indicate inefficient neural networks or some form of compensation. Importantly, the changes in behavior and cognitive function seen in individuals with prenatal alcohol exposure are consistent with the functional and structural brain changes. Behaviorally, these individuals have executive function deficits, attention and motor problems, and various learning and memory deficits. Additional research will help to elucidate the relationships between brain changes and functional outcomes and hopefully lead to better intervention strategies.

Over-expression of GSK3 beta Sensitizes Neuronal Cells to Ethanol Toxicity

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The developing central nervous system (CNS) is particularly susceptible to ethanol toxicity. The loss of neurons underlies many of the behavioral deficits observed in Fetal Alcohol Spectrum Disorders (FASD). The mechanisms of ethanol-induced neuronal loss, however, remain incompletely elucidated. We demonstrated that glycogen synthase kinase 3β (GSK3β), a multifunctional serine/threonine kinase was involved in ethanol neurotoxicity. The activity of GSK3β is negatively regulated by its phosphorylation at serine 9 (Ser9). Ethanol induced dephosphorylation of GSK3β at Ser9 and the activation of Bax as well as caspase-3 in the developing mouse brain. These ethanol-induced alterations were ameliorated by the pretreatment of a GSK3β inhibitor, lithium. To determine the role of GSK3β in ethanol neurotoxicity, we over-expressed wild type (WT), S9A mutant or dominant-negative (DN) mutant GSK3β in a neuronal cell line (SK-N-MC). Ethanol only modestly reduced the viability of parental SK-N-MC cells, but drastically induced caspase-3 activation and apoptosis in cells over-expressing WT or S9A GSK3β, indicating that the high levels of GSK3β or the active form of GSK3β increased cellular sensitivity to ethanol. Contrarily, over-expression of DN GSK3β conferred resistance to ethanol toxicity. Lithium and other specific GSK3β inhibitors abolished the hypersensitivity to ethanol caused by WT or S9A over-expression. Bax, a pro-apoptotic protein, is a substrate of GSK3β. Cells over-expressing WT or S9A GSK3β were much more sensitive to ethanol-induced Bax activation than parental SK-N-MC cells. Our results indicate that GSK3β may be a mediator of ethanol neurotoxicity, and its expression status in a cell may determine ethanol vulnerability.

NrCAM and addiction

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We have shown previously that haplotypes associated with decreased NrCAM expression in brain are protective against addiction vulnerability for polysubstance abuse in humans and that Nrcam knockout mice do not develop conditioned place preferences for morphine, cocaine, or amphetamine. These results imply that NrCAM may have a role in a common pathway underlying polysubstance abuse. In order to gain insight into NrCAM involvement in addiction vulnerability, which may involve specific neural circuits underlying behavioral characteristics relevant to addiction, we evaluated several behavioral phenotypes in Nrcam knockout mice, including analgesia, development of alcohol preference, novelty seeking, anxiety, obsessive behavior in marble-burying test. We also screened molecule regulated by low expression of NrCAM in brain by gene expression array and by realtime PCR methods, as following pharmacological-behavioral tests using a specific inhibitor of the molecule detected. As results, we found that Nrcam did not affect analgesia, suggesting its major effects are only on reward-related function. Consistent with a potential general reduction in motivational function, Nrcam knockout mice demonstrated less curiosity for novel objects and for an unfamiliar conspecific, and paid less attention to marbles in home cage. Nrcam knockout mice also showed less anxiety in the zero maze, open field, or passive avoidance test. An enzyme was found regulated by NrCAM, which inhibitor could demonstrate similar behavioral phenotypes in mice as those in Nrcam knockout mice. In conclusion, these observations provide further support for a role of NrCAM in substance abuse vulnerability, possibly through its effects on behavioral traits that may affect addiction vulnerability, including novelty seeking and responses to aversive or anxiety-provoking stimuli.

Role of Dopaminergic Genes in Alcohol Dependence: First study from India

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Background: Dopamine is an important neurotransmitter involved in reward mechanism in brain and thereby influences development and relapse of alcohol dependence (AD). The dopamine D2 receptor (DRD2) gene on chromosome 11 (q22–q23) has been found to be associated with increased alcohol consumption through mechanisms involving incentive salience attributions and craving in alcoholic patients. Therefore, we investigated the association of three single nucleotide polymorphisms (SNP) in DRD2 gene with alcohol dependence in north Indian subjects.

Methods: In a retrospective analysis, genetic association of three polymorphisms from DRD2 gene with alcohol dependence was investigated using a case-control approach. Alcohol dependence was determined by DSM IV criteria. Odds ratio and confidence interval was calculated to determine risk conferred by a predisposing allele/genotype/haplotype. Logistic regression analysis was carried out to correlate various clinical parameters with genotypes, and to study pair wise interactions between SNPs.

Results: In the present study, a significant association of -141C Ins allele, and a trend of association of TaqI A1 allele of DRD2 with alcohol dependence was observed. Haplotype with the predisposing -141C Ins and TaqI A1 alleles (-141C Ins-A-A1) seems to confer ≈ 2.5 times more risk to develop alcohol dependence. A significant genotype-phenotype correlation indicated that subjects with -141C Ins/Ins genotype (of -141C Ins/Del polymorphism) had higher values of SGOT, SGPT, and GGT as compared to those with -141C Ins/Del and -141C Del/Del genotypes. On multiple logistic regression analysis (MLR), a significant association of SNP -141C Ins/Del in DRD2 gene was found with Alcohol Dependence. Further categorical analysis identified -141C Ins allele to be predisposing to AD.

Conclusions:
The study provides preliminary insight into genetic risk to alcohol dependence in Indian males. Two polymorphisms namely, -141C Ins/Del and TaqI A in DRD2 gene seem to have clinical implications among Indian alcoholic subjects.

Dopamine receptor polymorphisms and alcoholism in Korean Drinkers

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Backgrounds: Multiple dopamine receptors in the dopaminergic system may be prime candidates for genetic influence on alcohol abuse and dependence due to their involvement in reward and reinforcing mechanisms. Genetic polymorphisms in dopamine receptor genes are believed to influence the development and/or severity of alcoholism and co-morbid psychiatric conditions. Those possibilities were evaluated in this study.

Methods; To examine the genetic effects of the Dopamine Receptor gene family (DRD1–DRD5) in the Korean population, 11 polymorphisms in the DRD gene family were genotyped and analyzed in 535 alcohol- dependent subjects and 273 population controls. Alcohol Use Disorders Identification Test (AUDIT) and State- and trait anxiety scales also assessed.

Results; The DRD1 (DRD1 48A>G) gene was significantly associated with severity of alcohol-related problem, in a gene dose-dependent manner, i.e., 24.37 (±8.19) among patients with 48A/A genotype, 22.37 (±9.49) among those with 48A/G genotype, and 17.38 (±8.28) among those with 48G/G genotype (P = 0.002). The genetic effects of DRD1_48A>G were further analyzed with other phenotypes among alcohol-dependent subjects. Interestingly, the DRD1 48A>A genotype was also found to be associated with novelty seeking (NC), harm avoidance (HA), and persistence (P) (P = 0.01, 0.02, and 0.003, respectively). In DRD2, +32806 C>T and Block2-ht1 showed associations (in dominant models) with both the state anxiety level scale (STAI-S) and the trait anxiety level scale (STAI-T) (P = 0.004 and P = 0.003, and P = 0.01 and P = 0.005, respectively).

Conclusion; In Korean drinkers, DRD1 receptor polymorphisms were possibly linked to severity of alcoholism and DRD2 receptor polymorphisms were possibly linked to the anxiety symptoms in alcoholics.

The Genetics and Physiology of Co-morbid Depression and Alcoholism

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Major depressive disorder is a brain pathology which is estimated to affect almost 10% of the world population by the year 2020 (WHO). In developed countries, alcohol dependence (DSM IV) appears often as a co-morbidity with major depressive disorder and some researches have speculated that an etiologic link exists between depression and alcoholism. The most popular, current, theories which describe the etiology of major depressive disorder center attention on the cAMP signaling systems in brain (PKA, CREB, etc) and also focus on defects in brain cell regeneration via stem cells as a cause of depression. Perturbation, by ethanol, of cAMP signaling and stem cell survival has also been demonstrated. One of the less examined components of the cAMP signaling cascade has been the enzyme system that actually generates cAMP and the activity of which is intimately controlled by receptor systems which have been the targets of antidepressant medications (5-HT, NE, DA, CRF). There are 10 members of the adenylyl cyclase (AC) family which differ in their brain distribution and regulation characteristics. One of these AC isoforms is quite sensitive to activation by ethanol when it is simultaneously activated through Gs protein coupled receptors (e.g., CRF via the CRF-1a receptor subtype). This isoforms of AC is AC7. One of the most well-studied roles of CRF has been in the pituitary where it controls the synthesis and release of ACTH which in turn, activates release of adrenocortical hormone (cortisol in humans). We found AC7 to be co-localized with the CRF-1a receptors in the pituitary and we found that ethanol could potentiate the release of ACTH and corticosterone in mice. The effects of ethanol were more profound in female mice compared to males. Genetic manipulation of brain AC7 levels by creating knock-down or transgenic mice demonstrated that quantitative changes in AC7 levels could significantly change the ACTH and corticosterone response to ethanol. Excessive circulating corticosterone levels, can damage stem cell development and brain repair, as well as causing damage to neurons in the hippocampus, amygdala and cortex. We found a tetranucleotide repeat polymorphism in the human AC7 gene which influences transcription/stability of AC7. This polymorphism is in a haplotype which in our work was associated with major depressive disorder, particularly in women. Interestingly, the strongest association was in depressed subjects who were also alcoholic. We will present data that the length polymorphism in the 3' untranslated region of AC7 may control the transcription of this enzyme. The levels of the enzyme influence the response to CRF, and to ethanol if people drink. Higher circulating levels of cortisol in individuals with overactive AC7, damage neurons and stem cells and promote major depressive illness.

Cognitive Impairment in Alcoholism and Depression

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Patients who suffer from both a depressive disorder and alcoholism are at great risk of chronic impairment. Untreated alcoholism aggravates depressive states, decreases responsiveness to antidepressant, and increases the possibility of suicide and severe cognitive declines. Major depression and alcohol dependence are common in primary psychiatry care, yet little is known about the neuropsychological effects of alcohol problems in patients with depression or alcohol's effect on major depression. Neuropsychological studies of patients with alcohol dependence report that the frontal lobes, hippocampus, limbic system, and cerebellum are particularly vulnerable to damage. and proper treatment and cessation of alcohol drinking lead to the reversal of atrophy and cognitive decline. Neuropsychological impairment is well reported as a characteristics of depressive disorder. Many neuropsychological studies have demonstrated that cognitive deficits are seen across a broad range of cognitive domains, executive deficits associated with frontal lobe dysfunction. Structural and functional neuroimaging has provided evidence supporting some degree of neuropathological convergence of alcoholism and mood disorders. One of the most striking similarities is that, although pathology affects both neuronal and glial cells, effects on glia are more dramatic than on neurons in both alcohol dependence comorbid with depression.

Moreover, prefrontal cortical regions are commonly affected in both depression and alcoholism. So cognitive impairment is common to both major depression and alcoholism. Despite increasing recognition that people with both disorders represent a problematic cases, little is known about the possible additive effect of a dual diagnosis upon impaired cognitive function. My presentation will cover impairment of cognitive functioning in patients with alcohol dependence, or a dual diagnosis of depressive disorder and alcohol dependence.

Genetic Aspects of Alcoholism and Depression

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Japan

Major depression and addiction are mental health problems associated with stressful events in life. Further it is well known that a comorbidity of alcoholism and depression is high. However, a biological mechanism underlying those diseases and the comorbidity remains unknown. The presence of cannabinoid CB2 receptors is much fewer than that of CB1 receptors in brain, and thus, a role of neuronal expression of CB2 receptors had not been characterized yet. Therefore, we tested the hypothesis that genetic variants of CNR2 gene, encoding CB2 receptor, might be associated with depression and alcoholism in relation to stress response. In this symposium, we presented systematic research, including a genetic association study, a functional analysis of the gene, and pharmacol-behavioral study in mice.

Associations between Q63R polymorphism in the CB2 gene and both of depression and alcoholism were found. The risk allele appeared to cause a low function of CB2 receptor, demonstrated in artificially expressed CB2 receptors in cultured cells. Thus, the receptor with R63 allele showed weaker response to several cannabinoid receptor ligands in cells. The polymorphism has moderate linkage disequilibrium with another polymorphism in flanking region of the CNR2 gene that is associated with low expression of the receptor in human postmortem brain tissues. In mice, the Cnr2 gene is expressed in brains of naïve mice and its expression is modulated after exposure to stressors and administration of ethanol. Mice that developed an alcohol preference had reduced Cnr2 gene expression, and chronic treatment with CB2 agonist JWH015 enhanced alcohol consumption under chronic mild stresses (CMS). CMS changed corticosteron level in blood, which was altered by CB2 ligands in mice. Recently we found two isoforms of the gene, and either of those expresses differently in CNS and in the peripheral. Further investigation of the CB2 receptors in brain may provide novel mechanism in depression and alcoholism.

Dysregulation of neurogenesis in alcoholism and depression: possible approach to regulate neurogenesis by antidepressants in the damaged brain by ethanol

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The comorbidity of depression with alcoholism has been investigated in several large epidemiologic surveys. They report that patients with depression frequently have alcohol-related problems and that depression has a great influence on the prognosis of alcoholism. On the other hand, alcohol-related problems are more common in the patients with depression compared to the general population. Some clinical symptoms such as depressed or irritable mood and cognitive distortions are commonly observed in alcoholism and depression, and antidepressants medication usually show at least a modest beneficial effect for the patients with alcoholism and/or depression. These findings suggest that the comorbidity may reflect the common biological aspects of pathophysiology. Recent biological studies suggest that the impairment of neurogenesis is the key factor for the pathophysiology of alcohol-induced and depression-induced brain damage. Antidepressants have been reported to promote neurogenesis and neuronal survival. Neuroimaging studies revealed the possible relation between morphological brain changes and cognitive impairments in the clinical course of alcoholism and depression.

In the previous work, we have been analyzed the mechanism of neural network disruption by ethanol using cultured cells and postmortem human brain, and found the suppressive effect of ethanol on the neural stem cell differentiation to neurons. Antidepressants, which have neurotrophic action, reduced the suppression by ethanol of neuronal differentiation. We also observed the alterations of the NRSF/REST binding activity which regulate the neuronal gene expression.

Furthermore, we evaluated the effects of ethanol and antidepressants on p-CREB expression in neural stem cells. Ethanol decreased the phosphorylation of CREB significantly. Antidepressants diminished the ethanol-induced suppression of p-CREB, but the recovery effect differed by each antidepressant. Interestingly, antidepressants changed both CREB and NRSF/REST activities in a different proportion. These results suggest that the stimulatory effect of antidepressants on neurogenesis may be mediated through the increased CREB activity and the decrease NRSF activity, and that the transcriptional regulation by antidepressants may be an advanced approach to recover the alcohol-induced damage of neuronal network.

The prevalence and correlates of alcohol use disorders in the United States and Korea-A cross national comparative study

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The purpose of this study was to compare the prevalence rates of DSM-IV 12-month diagnoses of alcohol use disorders between the United States and South Korea using two large nationally representative surveys. Cross-tabulations were used to derive weighted prevalences of alcohol abuse and dependence, and odds ratio derived from linear logistic regression analyses were used to determine the relationships between alcohol abuse and dependence across sociodemographic characteristics of the general population samples. The prevalence of 12-month alcohol abuse was greater in the U.S. (5.3%) than Korea (2.0%) whereas the rate of alcohol dependence was greater in Korea (5.1%) compared with the U.S. (4.4%). The odds of abuse were significantly greater among men, respondents who were employed, widowed/separated/divorced and never married in both countries. There was increased of odd of 12-month dependence among men, and those who were never married in each country. Further, the rates of abuse and dependence in the U.S. and of abuse in Korea decreased as a function of age, a result that did not generalize to dependence among Koreans. The implications of the results of this study are discussed in terms of cultural differences between the U.S. and Korea as the result of gender roles, modernization, industrialization, and drinking patterns, and the need to understand the potential influence of the cultural applicability and specificity of psychiatric assessment interviews across cultures.
Keywords: Alcohol use disorder, cross-cultural, prevalence, sociodemographic correlates

Alcohol and other substance use disorders in a sample of Chinese-, Korean-, and White-American college students: Prevalence and correlates

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Epidemiologic studies find significant variation in alcohol and other substance use disorders across racial and ethnic groups. Ethnic and racial variation also is found for protective factors (aldehyde dehydrogenase *ALDH2*2* and alcohol dehydrogenase *ADH1B*2* alleles) and risk factors (e.g., conduct disorder) for alcohol use disorders. We assessed these protective and risk factors in 21-26 year-old Chinese-, Korean-, and White-American students attending the University of California, San Diego (N = 604; 50% women). As shown below, significantly more Chinese-Americans (52%) possessed an *ALDH2*2* allele than Korean-Americans (34%), and no White Americans (0%) possessed an *ALDH2*2* allele. Chinese- (92%) and Korean- (90%) Americans did not differ in their possession of an *ADH1B*2* allele, but White-Americans (5%) were significantly less likely to possess an *ADH1B*2* allele than either Asian subgroup.

	Chinese Men	Women	Korean Men	Women	White Men	Women
*ALDH2*2* (+)	49%	55%	34%	35%	0%	0%
*ADH1B*2* (+)	91%	92%	89%	91%	3%	6%
Conduct Disorder	10%	2%	28%	3%	14%	5%

Chinese-Americans had a lower rate of alcohol dependence (5%) than Korean- (14%) or White- (17%) Americans (shown below). In our previous research, we examined whether *ALDH2* status, *ADH1B* status, and conduct disorder mediate the relationship between ethnicity and alcohol dependence. *ALDH2* status (odds ratio, OR= 0.3, p < .05), *ADH1B* status (OR = 0.6, p < .05), and Chinese ethnicity (OR = 0.3, p < .05) were all independently associated with decreased risk for alcohol dependence. Conduct disorder (OR = 1.6, p < .05), being male (OR = 2.5, p < .05), and White ethnicity (OR = 2.1, p < .05) were all independently associated with increased risk for alcohol dependence. The relationship of ethnicity to alcohol dependence was mediated by *ALDH2* status and conduct disorder. Gender and *ADH2* status were no longer significant, but Chinese ethnicity remained significantly associated with alcohol dependence; no interactions were significant. Results suggest different rates of risk and protective factors partially account for ethnic differences in rates of alcohol dependence. Rates of nicotine dependence and marijuana dependence also differed across gender and ethnicity (shown below), but were not related to *ALDH2*2* or *ADH1B* allele status. We examined whether the relationship of conduct disorder to alcohol dependence, nicotine dependence,

and marijuana dependence was similar across gender and ethnicity. Conduct disorder was similarly related to each substance use disorder for all subgroups (ORs, from 1.2-1.6 for alcohol dependence, 1.3-1.8 for nicotine dependence, and 1.4-1.9 for marijuana dependence) but Chinese women. For this subgroup, the ORs were not even in the predicted direction for alcohol dependence (OR = 0.4, p = .922) or nicotine dependence (OR = 0.3, p = .858), and for marijuana dependence the relationship was slightly stronger (OR = 2.3, p < .05) than in the other groups. These results suggest that, despite different prevalence rates, the association between conduct disorders and substance use disorders are similar across gender and ethnic subgroups, with the exception of Chinese women. What affords this group greater protection from substance dependence remains to be determined.

	Chinese Men	Women	Korean Men	Women	White Men	Women
Alcohol Dependence	8%	2%	18%	8%	22%	12%
Nicotine Dependence	11%	7%	35%	14%	15%	11%
Marijuana Dependence	6%	4%	22%	4%	18%	9%

Changes in alcohol consumption and related harm including drink driving in Japan

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Despite alcohol-related problems are serious among Asia-pacific countries, the epidemiological features of alcohol in each Asia-pacific country is not well known. This presentation shows changes in alcohol consumption and related harm including drive under influence (DUI) of alcohol in Japan.

Data were primarily collected from statistics and survey results issued by the national government and articles published since 2000, identified by searching the MEDLINE and Igaku-Chuo-Zasshi databases. These data were assessed regarding their quality and summarized.

Alcohol consumption per capita among Japanese has tended to decline for nearly 15 years, but it still remains at a high level. Alcohol consumption in women has sharply increased, specifically in young women. That will probably result in increasing alcohol related problems in women in the future. Alcohol-related problems, especially health problems, have steadily increased over the past several decades.

Traffic accidents related to DUI is one of main social problems by drinking in many countries. It is notable that the number of accidents and fatalities related to DUI has sharply dropped for these several years. A part of that is because the punishments for DUI has become much more severe since 2002. In addition, an increase of public awareness after a tragic accident caused by drink driving killing three little children may have accelerated the downward trend.

The data provided in this presentation may be partly common in Asian-pacific countries and these may be useful to develop new alcohol control policies in Japan and in other Asian-pacific countries.

Introduction and overview: reducing alcohol consumption in the treatment of alcohol dependence

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One of the main features of alcohol dependence is the impairment of control over drinking. Both naturalistic and clinical long-term studies have indicated that relapse to uncontrolled drinking in a relatively short period of time can occur even after years of abstinence. Consequently, abstinence has been strongly recommended by clinicians as a goal for the treatment of alcohol dependence.

In recent years, however, there is a growing interest in harm reduction strategies in which reducing alcohol consumption is the primary goal for patients with alcohol dependence. Driving forces of the interest appear to be the following two reasons. First, cumulative evidence has suggested that a sizable percentage of alcoholics could benefit from reducing alcohol consumption by pharmacotherapy with new medications including off-label use of unapproved drugs. Second, brief interventions with the primary goal being reduction in alcohol consumption have been increasingly popular, and the target population of this treatment modality may include mild alcohol dependence.

The purpose of this symposium is to begin discussions as to whether reducing alcohol consumption can be applied as a treatment goal of alcohol dependence. Fierce controversies arose regarding controlled drinking in the treatment of alcohol dependence in the 1970s and 1980s. However, the definition of alcoholism and treatment methods including pharmacotherapy have substantially changed since then. Revisiting to the discussion on this issue at this time, therefore, may be fruitful for some types of alcohol dependence.

In this symposium, the pharmacotherapy aspect of the issue will be covered by two outstanding researchers. I will briefly summarize psychosocial approaches related to this issue, and will attempt to discuss which type of alcoholics could benefit from treatment targeted at reducing alcohol consumption.

Evidence-based pharmacotherapy of alcohol abuse and dependence

H. Alho, Professor of Addiction Medicine, MD, PhD,
University of Helsinki, Finland

Many specific psychosocial treatment methods have been scientifically documented as effective means to treat abuse and dependence on alcohol and drugs. However, 40% to 70% of the individuals treated with these methods relapse within 1 year. Medications that can enhance the effectiveness of psychosocial treatments are clearly needed.

For the official evidence-based recommendation for the treatment of alcohol dependency in Finland, 150 published randomized controlled trials assessing the effects of medication were evaluated. Essentially all drugs to treat alcohol dependence are covered by these assessments.

The strongest evidence to treat alcohol dependence was found for naltrexone that has well-documented effects. Naltrexone significantly reduces alcohol abuse and particularly the relapse to heavy drinking. As a treatment goal reduction of alcohol consumption, preventing relapsing, seems to be as acceptable and effective as abstinence. Disulfiram is also documented as an effective method to reduce alcohol intake, but only when aiming to abstinence and used under supervision.

Two randomized controlled trials showed a significant effect from topiramate, an antiepileptic drug. Antidepressants (especially SSRIs) are effective in treating depression or anxiety in alcoholics. However, they have no confirmed effects on alcohol dependence.

There are several good methods for treating alcohol-related problems; the difficulty is adapting them to practical work and the lack of structured directives. The choice of drug combinations and possible new medications, such as CB1 receptor antagonists, will be discussed.

Challenges in Designing Alcoholism Clinical Trials and Analyzing Outcomes

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USA

Surveys by the WHO and other organizations show that alcohol abuse and alcohol dependence contribute significantly to morbidity, mortality and social problems throughout the world, including Asian Pacific regions. There is considerable active research to identify new and more effective treatments for alcoholism. However, there exist several methodological issues and controversies that make studying alcoholism treatment difficult and challenging. Some of the issues include: 1)marked heterogeneity of drinking patterns, desired outcomes and personal characteristics in patients with alcohol dependence; 2) bias in study recruitment and patient selection for clinical trials; 3) controversies over what should be the goals of alcohol dependence treatment (especially abstinence versus reduced drinking) and which are the best treatment outcome variables; 4) managing the "therapeutic" effects of study participation; and 5) choosing optimal statistical methods, as statistical significance can depend upon the methods of statistical analysis. Some of these issues may have contributed to the common observation of both positive and negative clinical trial outcomes in different alcoholism clinical trials that study the same treatment. For example, the results of placebo-controlled efficacy trials with pharmacotherapies such as acamprosate, baclofen and naltrexone differ across international sites and the different results cannot be easily explained. The issue of whether abstinence or reduced drinking over what should be the goals of alcohol dependence treatment engenders much controversy among patients and clinicians. Some believe (as does Alcoholics Anonymous in the US), that complete abstinence is the only viable treatment outcome. Others believe that a "harm reduction" approach to reduce alcohol consumption is a more realistic goal. Certain treatments, including the pharmacotherapies naltrexone and topiramate, may be more efficacious for the outcome of reduced heavy drinking than for the outcome of abstinence. The paper will discuss these several issues using examples drawn from several funded clinical trials. Disclosures: Dr. Swift is a member of the advisory board for Alkermes, Inc., Forest Laboratories and Ortho McNeil. He has received research funding from Eli Lilly and Bristol Myers Squibb.

A new anti-fibrotic mechanism of TRAIL through regulations of apoptosis and collagen production in hepatic stellate cells

Sang Ick Park
Korea National Institute of Health (KNIH)

Liver fibrosis occurs as a wound-healing response to a variety of chronic stimuli including chronic alcohol consumption. If left untreated, it could progress to liver cirrhosis. However, currently there are few treatment options other than liver transplantation and therapeutic options are limited to treat liver fibrosis. Liver fibrosis is characterized by excessive deposition of extracellular matrix (ECM) proteins such as type I, III and IV collagen. Activated hepatic stellate cell (HSC) is responsible for liver fibrosis and thus it have attracted much attention as an appealing target for antifibrotic therapy. In this study, we investigated antifibrotic effects of tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) in hepatic stellate LX-2 cells, taking the advantage of its unique characteristics inducing apoptosis preferentially in cancer cells but not in normal cells. Here we demonstrated molecular mechanism that TRAIL induced apoptosis of LX-2 cells by downregulating FoxO-dependent c-FLIP expression and led to decrease of collagen expressions (type I and III) at mRNA and protein levels via down-regulation of heat shock protein (Hsp)47, thereby reducing their extracellular secretion. Our study suggests that TRAIL could be an effective strategy for anti-fibrotic therapy in liver fibrosis.

Molecular Mechanisms of Organ Damage by Alcohol and Other Toxic Compounds

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USA

Although many toxic compounds including alcohol (ethanol) and high fat diets are known to increase oxidative stress and damage the target cells/organs, the underlying mechanisms of mitochondrial dysfunction, ER stress and cell death pathways are poorly understood. Therefore, we aim to investigate the role of increased oxidative stress in oxidative inactivation of key mitochondrial proteins and promotion of the cell death signaling pathway. Oxidatively-modified Cys residues of many mitochondrial proteins were specifically labeled by a redox proteomics method, purified with streptavidin-agarose, and analyzed by 2-D gel electrophoresis followed by mass spectral analysis for protein identification. More than 80 mitochondrial proteins were oxidatively-modified in alcohol-exposed rats. Alcohol-induced oxidative stress led to inhibition of mitochondrial aldehyde dehydrogenase (ALDH2), involved in the metabolism of acetaldehyde and toxic lipid aldehydes such as malondialdehyde and 4-hyroxynonenal, contributing to their elevated levels. The activity of ATP synthase (complex V) involved in the mitochondrial energy (ATP) production was markedly inhibited through oxidative modification (nitration) of the active site Tyr residues in alcohol-exposed animals compared to dextrose-treated controls. In addition, many enzymes involved in the peroxisomal and mitochondrial beta-oxidation of fatty acids were oxidatively-modified and inactivated, resulting in elevated levels of fatty acids. Based on these results, we conclude that oxidative modifications and inactivation of key mitochondrial enzymes contribute to mitochondrial dysfunction with energy depletion, fat accumulation and increased cell death observed in alcohol-exposed animals. Our results also showed that many cytosolic chaperone proteins such as protein disulfide isomerase (PDI) and GRP78 (Bip) were oxidized and inactivated, contributing to accumulation of unfolded proteins with signs of ER stress. Similar patterns of oxidative-modifications of many mitochondrial or cytosolic proteins and inactivation were observed in the animal models of non-alcoholic liver diseases such as ischemia-reperfusion liver injury or after exposure to acetaminophen (a major ingredient of Tylenol), carbon tetrachloride, or MDMA (ecstasy), a frequently-abused drug substance. Furthermore, oxidative stress caused by alcohol and other toxic compounds (e.g., staurosporine, etoposide and acetaminophen) activate the cell death-related protein kinases such as JNK and/or p38 kinase, which subsequently phosphorylate pro-apoptotic Bax, leading to its translocation to mitochondria to initiate mitochondrial permeability change, mitochondrial cytochrome c release and apoptosis. Site-directed mutagenesis and confocal microscopy of the mutant Bax proteins revealed that Thr167 is the critical site of JNK/p38

kinase-mediated phosphorylation. Significant activation of p38 kinase and mitochondrial association of Bax were also observed in the brains of individuals suffering from Alzheimer's disease. These results indicate that Bax, but not BimEL and Bcl-2 which are the previously-identified targets of p38 kinase-mediated phosphorylation in cultured cells, is a major protein phosphorylated by stress-activated protein kinases in in vivo conditions. These data also suggest that phosphorylated Bax is likely involved in mitochondrial permeability change, thus contributing to neurodegeneration in individuals with Alzheimer's disease. We believe that our data represent the molecular mechanisms for cellular/organ damage observed after exposure to ethanol and many other toxic compounds or in pathological conditions. Finally, some of the new data with the animal models of alcoholic and non-alcoholic fatty liver diseases will also be discussed.

Hepatic stellate cells mediate alcoholic fatty liver through the activation of hepatic CB1 receptors by endocannabinoids

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Alcohol-induced fatty liver, a major cause of morbidity, has been attributed to enhanced hepatic lipogenesis and decreased fat clearance of unknown mechanism. Here we report that the steatosis induced in mice by a low-fat, liquid ethanol diet is attenuated by concurrent blockade of cannabinoid CB1 receptors. Global or hepatocyte-specific CB1 knockout mice are resistant to ethanol-induced steatosis and increases in lipogenic gene expression and have increased carnitine palmitoyltransferase 1 activity, which, unlike in controls, is not reduced by ethanol treatment. Ethanol feeding increases the hepatic expression of CB1 receptors and upregulates the endocannabinoid 2-arachidonoylglycerol (2-AG) and its biosynthetic enzyme diacylglycerol lipase beta selectively in hepatic stellate cells. In control but not CB1 receptor-deficient hepatocytes, coculture with stellate cells from ethanol-fed mice results in upregulation of CB1 receptors and lipogenic gene expression. We conclude that paracrine activation of hepatic CB1 receptors by stellate cell-derived 2-AG mediates ethanol-induced steatosis through increasing lipogenesis and decreasing fatty acid oxidation.

Alcoholic Liver Disease in Korea, Present and Future

Dong Joon Kim, Heon Ju Lee, KASL ASG
Korea

Alcohol drinking is popular in Korea and Korean culture has a rather permissive attitude to the drunken state than western countries. In a recent survey 73.3% of adult men and 36.2% of adult women in Korea indicated that they drink alcohol more than once per month. Also, the quantity of alcohol consumption increased from 5.0 kg per person in 2001 to 5.6kg in 2004. A famous novelist describes Korea as "a society of drink recommending". Fast economic growth, named "a miracle of Han River", resulted in a sharp increase in alcohol accessibility. This kind of abundance of alcohol, noticeable in the recent 50 years, is an exception in the long 5,000 years of Korean history.

As alcohol consumption increased, the socioeconomic loss attributed to alcohol also increased from 2.58% of GDP in 2000 to 2.9% in 2004. In a 2007 national survey, alcohol-related death rate was 9.6/100,000 person and total liver disease-related death rate was 15.5/100,000 person. These statistics show the importance of alcoholic liver disease and alcohol-related problems in Korea. It is worth mentioning that alcohol-related death rate increases until the 40s and 50s, with a 11 times higher death rate in men. Considering the age of death and the role of the "man of the house", its impact may be more serious than just the statistics. For alcoholic liver disease, the disabled adjusted life year (DALY) of alcoholic cirrhosis was estimated to be 798.2 person-years (PYs) per 100,000 Korean men and 149.3 PYs per 100,000 Korean women in the 2000s. DALY of hepatocellular carcinoma (HCC) associated with alcohol was estimated to be 655.2 PYs per 100,000 Korean men and 126.2 PYs per 100,000 Korean women in the 2000s.

Although alcohol is one of the leading causes of chronic liver disease in Korea, only a few studies on alcoholic liver diseases have been published. In searching data from KoreaMed and KMBASE for the period 2004-2009, articles related to alcoholic liver disease were very low in number (31 articles) compared to hepatitis B (460 articles) and hepatitis C (232 articles). The scarcity in number is partly due to the lack of drugs which treat alcoholism efficiently. The fact that abstinence is influenced by many factors and frequently fail can also be discouraging factors to studying alcoholic liver disease in Korea.

The Korean Association for the Study of the Liver (KASL) recognized the significance of alcohol-related problems in Korea, and KASL launched the Alcohol Study Group (KASL ASG) in January 2009. Active members from 43 hospitals (42 university hospitals and National Medical Center) participate in KASL ASG. Three multi-center studies, "A restrospective study on the predicting the outcomes in patients with alcoholic liver disease", "Short-term survival in patients with severe alcoholic hepatitis treated with corticosteroid versus pentoxifylline: A non-inferiority trial", and "Compliance of psychiatric referral in patients with alcoholic liver disease" are just the beginning.

Besides studying alcoholic liver disease, KASL ASG has plans to implement collaborations with related field, such as psychiatry and sociology, in the near future.

Family problems and family treatment model to addiction

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Clinicians encounter family issues as they treat substance abuse. An increasing number of researchers and clinicians have examined family factors relevant to addictions, and the clinical applications of marital and family therapy have grown considerably over the last 40years. Family methods with empirical support are ready for clinical use so that we can improve our efforts to help substance abusers and their family. In this session, I briefly describe 1) the family problems; dysfunctional family dynamics, children and spouse problems, and co-dependence. 2) the historical roots of the family treatment model and its applications to addiction; psychodynamic model, sociological stress model, family disease model, family system model, behavoiral model, social network model, and so on. 3) the typical treatment goals, the structure of therapy session and the major techniques of treatment.

The intervention for the family of an addict

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The intervention for the family of an addict is not enough for the family to understand the characteristics of the addict's addiction. Also due to a lack of medical insurance, it does not allow the family to understand what the role of family means to the addict's recovering process in hospital settings.

Medical personnels like psychiatrists, nurses, and social workers in hospital settings have been helpful in giving confidence to addicts that allows them to believe that they can adjust to the community without drug or other problems.

The family of an addict can be served by professionals like social workers and nurses. These professionals are aware of the family's needs, and the environmental factors that impact the addict's life in the community.

Most importantly, the family of an addict should not only include wives, but it should also include children, parents and anyone who is concerned about the addict's wellbeing.

Communication skills training program (CSTP) for alcoholism families

Yong Jin Kim
Korea

The purpose of this study was to investigate the effects of the communication skills training program (CSTP) for alcoholism families in the study was carried out the group communication program which I had composed of using the Satir's communication family theory and skills. For this aim, a group counseling was conducted for 2 hours a week for 10 weeks in total, in application of theories and techniques of Satir's family therapy.

Case Management in Mental Hospital

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ABSTRACT

This subject will show case management in specialized hospital for alcoholics. In many cases, we face with various state of motivation, clinical states, clinical progress and outcome. Specially, in involutarily visited cases, we are required delicate motivational interviewing and active inpatient treatment approach. In the process of treatment, we need team approach of various specialists such as psychiatrist, medical doctor, nurse, addiction counsellor, social worker.
 Because of various cases of patients, various form of treatments needed like inpatient versus outpatient treatment, day hospital versus night hospital or partial hospitalization, Similarly, various form of aftercare program needed. for example, AA(alcoholic anonymous), abstinence meeting for men, abstinenece meeting for women, abstinence meeting for elderly, and family meeting of alcoholics.
 Providing continuous treatment program and service based on patient need, we can help progressive recovery of the patients and their family. Because it is not easy to participate in recovery program voluntarily, we must be a team and make a strong rapport with patients and their family and have to guide the patients to take continuous services. Finally, I will present a few cases of case management.

Case management of the Alcohol Counseling Center

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Daegu Catholic Alcohol Counceling Center / Director
Korea

Case management that is a concept of having been said at treatment in changing processes toward care is a service delivery method to satisfy needs, and to improve a social function to the client who had various and complex needs.

Also, case management is to organize a network of formal and informal of resources and activities of people who are experiencing multiple and concurrent problems, and to coordinate and to keep it.

Case management is known as very effective ways to service practice to target a chronic mental patient, the disabled, alcoholics, the aged who have complex needs.

Specially, case management can be regarded as the most critical and important role to practice alcohol problems in communities.

Recently, case management that has been used actively as in the field of alcohol and drug abuse, provide individualized support to clients and clients' family. and it change the client and surrounding environment in order to be able to cause functional recovery and improvement of a client who has had problems on a social function. and it is continuous and integrate intervening manner.

Case management that is performed in the alcohol counseling center of a community has a base to recover the client's desire and special problems solving of client and It is to support a client of continuity of care until endings in early interventions.

Case management process has several steps such as performed engaging, assessing, assessing resources, planning, coordinating, disengaing.

Alcohol problem intervention is a process that is multilateral and systematic including screening, assessed, service plans, care of medical and psychiatric, rehabilitation of psychological and social, and follow up.

In order to intervene agreed to individual biopsychosocial needs level of client in these processes, evaluation process of systematic and an efficient of screening, diagnosis, assessed and service plans shall be preceded.

Case management is supporting not only treatment or counseling of an addict but also all areas such as income, housing, employment, health, mental health, social needs, leisure, education etc.

Intervention principles for alcoholics is individualization of services, comprehensive services, maximizing the client's autonomy, continuity of care, and connectivity of services.

In the process, a case manager should be the role of counselor, coordinator, advocator and a case manager is emphasized as the role of administrator and clinician.

In the case management process of alcoholics, the importance of community connection is emerging as a very important part regarding follow up, consecutive Increase of treatment, and rehabilitation.

However, alcohol-related community resources are still poor, and treatment or rehabilitation process could not be activated situation. And the expansion of case management through connecting with community is true to has some limits to be practiced comparing with the importance.

Nevertheless, we continuously develop community resources, and strengthen connection, and we put an our effort to be more systematically performed with continuity of care, through prevention and treatment, rehabilitation of alcoholics.

Case Management in The Korean Research Foundation

AeRan, Park
Korea

Abstract

Alcoholism is complex primary physiological disease with unique therapeutic interventions, and neither a primary behavior disorder nor any symptomatic manifestation of any other disease process. And, it is highly prevalent disease with important impact on public health perspective. Therapeutic approach for alcoholism need to be organized by integrative and comprehensive systems, because that development and course of alcoholism are influenced by complex interaction between biological and environmental factors. The Korean Alcohol Research Foundation: KARF tried to developing effective intervening systems for alcoholism in the community by case management. The case management is the processes of alcoholism`s continuum care.

Case management of The KARF is one-stop service system of alcoholism. The KARF`s Treatment and Regional Rehabilitation System have KARF Hospital, Alcohol Counseling Center, Residential Facility, Rehabilitation Center and Halfway House for early discovery, treatment, rehabilitation and social recovery of alcoholics. The KARF`s case management should be developed based on continuum of care system in the community. First, the hospital should be detoxicate and link post-treatment management. Second, the alcohol counseling center should be provide counseling and program. Third, Residential Facility and Halfway House should be provide living conditions to maintain non-drinking and helping change the attitude of the alcoholics. Finally, Rehabilitation Center should be provide vocational rehabilitation. The KARF`s case management set up a system to support and organize alcoholism integrative systems is needed. It should be the process of the community environment that based on personal-family-A.A.-hospital-alcohol center-residential center and facility-community-national level state.

key words : alcoholism, case management, continuum of care, The Korean Alcohol Research Foundation (KARF)

The here and the hereafter of virtual reality based on computer technology.

Chanjong Park
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Korea

Virtual reality (VR) is a technology which allows a user to interact with a computer-simulated environment, whether that environment is a simulation of the real world or an imaginary world. Sometimes, special peripheral devices are used to stimulate various senses (auditory, olfactory, gustatory, tactile senses) more than visual senses to maximize immersion effects.

 In this session, the below subjects will be mentioned.

- Understanding of virtual reality technology..
- The functional features of virtual reality system.
- The components for virtual reality computer system.
- The application of virtual reality technology.
- Virtual reality market.
- The present and future of virtual reality.

What's the virtual reality aversive therapy for alcohol-dependent patients?

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Virtual reality (VR) is an evolving technology that is being applied to treat wide of medical and psychiatric diseases. A virtual reality therapy (VRT) with multisensory stimulation has been applied to patients with alcohol dependence (ADP). The virtual reality therapy (VRT) consisted of a series of scenes that were associated with relaxation, simulating a high-risk situation (virtual alcohol cues) and then an aversive stimulation. The aversive stimulation included visual, auditory and olfactory stimuli. The ingestion of a small amount of kefir, when seeing a vomiting-movie, encouraged patients to recollect unpleasant memories associated with frequent vomiting after excessive alcohol consumption. Kefir is a fermented milk drink and it's taste has been equated to being similar to that of vomitus. We hypothesized that the VRTP for alcohol dependence would reduce the craving for alcohol and increase alpha EEG activity in frontal areas of individuals with ADP. Twenty ADP and eighteen ADP were exposed to a series of 10 VRTP sessions (VRTP-ADP) and cognitive behavioral therapy (nVRTP-ADP), respectively. The VRTP-ADP exhibited a greater decrease in craving after the 10th VRTP session, when compared to the nVRTP-ADP after the 10th cognitive behavioral therapy. When the before and after treatment of VRTP were compared, the absolute EEG alpha power in Fp2-A2 and F8-A2 was increased significantly after the 10th session of VRTP. These results suggest that VRTP may be useful as an adjunct to treat alcohol dependence and may also serve as an evaluation tool to identify high-risk patients.

The comparisons between alcohol-dependent patients and healthy subjects in virtual cue exposure

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Introduction

In our previous report, alcohol dependent patients (ADP) with virtual reality treatment showed greater decrease in craving for alcohol and increase in alpha power of frontal lobe, compared to ADP with general treatment. For the showing different responsibility on alcohol consumption situation between ADP and healthy comparisons, we compared the change in craving and alpha waver in frontal lobe during virtual reality treatment for alcohol (VRT).

Methods

Thirty seven alcohol-dependent male inpatients diagnosed using DSM-IV and age- and education-matched 25 healthy adult males were recruited. We measured the changes in the craving and EEG activity between alcoholic patients and healthy control subjects during VRT.

Results

During the VRT, ADP reported higher craving for alcohol during the high risk situation and lower craving for alcohol during aversive situation, compared to healthy controls. The alpha wave of frontal lobe in ADP was decreased while that in healthy comparisons was increased from relaxation to HRS. In ADP, the changes of EEG (Fp1-A1 ($r=-0.48$, $p=0.04$), F7-A1 ($r=-0.49$, $p=0.03$), Fp2-A2 ($r=-0.46$, $p<0.05$), and F8-A2 ($r=-0.54$, $p=0.02$)) in frontal lobe were negatively correlated with the change of craving for alcohol.

Discussion

The present study demonstrated that the ready availability and the affinity of alcohol cues in ADP appear to be correlated with decreased function of frontal lobe.

Alcohol Consumption and Carotid Atherosclerosis According to Cardiovascular Risk Factors

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SunMi Kim, Sang Min Park MD,
Min Seon Park MD, Belong Cho MD*
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Abstract

Background: Moderate drinking has been known to have protective effect on cardiovascular disease. However, there have been few studies on the correlation between alcohol consumption and atherosclerosis formation in low-cardiovascular risk group, and protective effect of moderate drinking has not been established in low-cardiovascular risk group. Thus, we have evaluated the correlation between carotid intimal-medial thickness (IMT) and alcohol consumption in various subgroups grouped based on cardiovascular risk factors.
Methods: 525 normal subjects who visited one health care center and were free from cardiovascular disease were enrolled in this study. They answered to the questionnaire about lifestyle factors including alcohol consumption and underwent a complete blood chemical test for cardiovascular risk markers and the B-mode ultrasonography to assess carotid IMT.
Results: In the low cardiovascular risk group (young age, total cholesterol<200, LDL cholesterol<130, HDL>45, CRP<0.03), the subjects consumed only 1-2 drinks per week had lower carotid IMT than abstainers. The subjects who consumed over 3drinks had higher carotid IMT than abstainers and showed positive trend of increasing carotid IMT. In the high cardiovascular risk group (old age, total cholesterol>200 mg/dL, LDL cholesterol>130 mg/dL, HDL<45 mg/dL, CRP>0.03mg/100mL), the subject consumed alcohol had thinner carotid IMT than abstainers in all range of alcohol consumption (1 to 20 drinks per week). In the high cardiovascular risk group, the range of cardioprotective effect of drinking was wider and the negative correlation was more profound than that of low cardiovascular risk group.
Conclusion: In the high cardiovascular risk group, alcohol consumption had a different correlation with carotid IMT from in the low cardiovascular risk group. Thus, the term 'healthy drinking' needs new standards for both low cardiovascular risk group and high cardiovascular risk group.
Key words: alcohol, carotid atherosclerosis, cardiovascular risk, crp, hypercholesterolemia

Implications of executive dysfunction of frontal lobe among alcoholics : A Neuropsychological approach

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The purpose of this study is to explore the proposition that, by the evaluation of neuropsychological test, chronic alcohol use can be pinpointed as a cause for frontal lobe dysfunction and that this dysfunction has relationship with both denial and insight level.

We enrolled 55 patients who were admitted as inpatients in alcohol treatment programs at Incheon Christian Hospital. The subjects were evaluated according to sociodemographic and clinical characteristics. After 3 weeks of detoxification, denial and insight level were measured, and neuropsychological test including the following were administered : the Korean version of Wechsler Adult Intelligence Scale(k-WAIS) for assessing Intelligence Quotient(IQ) and the EXIT(Executive Intelligence Test) which consists of stroop, verbal fluency, figural fluency, and auditory verbal learning test for

assessing Executive Intelligence Quotient(EIQ).

Mean IQ was 96.16 and EIQ was 86.25. But EIQ was decreased from an assumed premorbid level more than that of IQ. According to insight level poor insight group showed lower EIQ but not on IQ. And among subtests medial and interference stroop and figural fluency showed the difference. Insight level was positively correlated with the denial. And EIQ and particularly among subtest figural fluency showed correlation with insight level but not in case of IQ and other subtests. Through simple regression test, EIQ can explain Insight level about 15.3%.

Cognitive impairment, especially executive dysfunction was identified. Denial itself is not correlated with cognitive function though. It seems that the more patient gaining insight, the more they admit their denial. The fact that Insight level is much more correlated with performance of EIQ, especially figural fluency test, than IQ reflect that Insight level is much more correlated with function of frontal lobe, particularly right hemisphere. Given this condition, level of cognitive function could be one of the factor that can evaluate a capacity for rehabilitation of patient, and concern over the need of neuroprotection from chronic alcohol use as well as cognitive rehabilitation as a part of alcoholism treatments should be increased.

The Alcohol and Substance problems of Male North Korean Defectors in South Korea

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The number of North Korean defector is increasing and there's many study about their psychiatric problems. But their is limited study about their alcohol and substance problem. The purpose of this study is to investigate the alcohol and substance problem of Male North Korean Defectors in South Korea.

The sample consisted 365 Male North Korean Defectors who entered South Korea from April, 2008 to February, 2009. We investigates their demographic characteristics and the severity of alcohol and drug problem.

We use Morey's Personality Assessment Inventory(PAI) to evaluate their Alcohol and Drug Problems. There's 40 people(11%) that their ALC score is more than 70. And there's 96 people(26.5%) that their DRG score is more than 70. ALC score is significantly correlates with their ANX score ($p=0.000$), ARD score($p=0.000$), DEP score($p=0.000$), AGG score($p=0.000$), STR score($p=0.000$). DRG score is significantly correlates with their ANX score($p=0.000$), ARD score($p=0.000$), DEP score($p=0.000$), AGG score($p=0.000$). The PAI score indicated that some of North Korean defectors they have a alcohol and drug problem and their problems might be related their anxiety and stress during their defecting from North Korea.

Groping for the Addictions Policy in Korea, Separated vs. Unified.

Kyung Seung Kim,
Addiction Center of Motherth Hospital
Ulsan Alcohol Counselling Center

Objectives : There are various kinds of addictions, including from alcohol and substance use disorders to many kinds of so called behavioral addictions, such as pathologic gambling, internet addiction, etc. In Korea the government agencies for the various addictions are not unified but separated into several different ones. For example, the administrative policies about the alcohol related problems are developed and performed by the Ministry for Health, Welfare, and Family Affairs, those about the drug abuse by the Food and Drug Administration, and , those about the gambling problems by the Ministry of Culture Sports and Tourism. In this study, I investigated the advantages and disadvantages of the separated vs. unified governmental policies for the various addictions problems and tried to draw a tentative conclusion about which approach would be desirable.

Main subject : Various kinds of addictions may be said to be different forms of the same category of disorder, because similar neurobiological findings have been being revealed and similar treatment approaches applied. Pharmacological agents for the various addictions are alike and psychosoical approaches are substantially the same. So the unified and integrated governmental approach for the various kinds of addictions would have several following advantages in comparison with the separated and individualized one. 1) Prevention of overlapping budget and wasting of limited mental health professional power 2) Maximizing the effectiveness and efficiency of treatment especially for the co-addicts 3) Easy accessibility for the service consumers 4) The development of effective and integrated policies for prevention and rehabilitation

Conclusions : I propose various kinds of addictions be managed by one governmental agency and its service providing facility to develop effective and systematic administrative policies and to provide convenient and integrated treatment.

Internet Addiction and its Treatment

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Excessive Internet use by young children and the youth is emerging as a serious social issue. Internet addiction is "a state in which excessive Internet use creates withdrawal and tolerance that cause various impairments in the Internet user's daily life." Internet addiction has various forms such addiction to games, chatting, pornograph or sex, gambling, shopping, and vandalism including surfing. Block(2008) suggests three subtypes: excessive gaming, sexual preoccupation, and e-mail/text messaging. Asian counties, Korea, Chain, Taiwan, count Internet addiction to gaming as its most serious issue compared to western countries including USA

Korean Association of Adolescent Psychiatry under my leadership carried out the three-year project "**Health Network of Treatment & Rehabilitation for Severe Internet Addicted Adolescents (HN-TRSIAA) (2005 – 2007)**" funded by Korea National Youth Commission.

They had high rates of predisposing/co-morbid psychopathology: ADHD, ODD/conduct disorder, depressive disorder, anxiety disorder. One half - one third of subjects drop out in the early period of intervention. They were reluctant to visit "psychiatric" facilities. Involvement of parents & whole family in any kind intervention are essential, for example, parental education on internet, how to supervise internet use, improving relationship & communication with adolescents. For the severe IA children and adolescents with psychiatric co-morbidity and serious family dysfunctions, usual individual treatment approaches do not seem to be effective; they require multimodal treatment approach in a highly structured therapeutic-educational milieu for an extended period of time. Preventive measures, such as parent education, school counseling, early interventions of predisposing psychopathology & strengthening family functions, are the best treatment.

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Psychomotor Stimulant Addiction: Basic to practice

Genetics of Addiction Disorders in Korean Population: Does Ethnicity really matter?

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Since Wolff described that ethnic differences in alcohol sensitivity are related to variations in autonomic reactivity, the genetic polymorphisms in alcohol-metabolism genes have been believed to be influencing drinking behavior and development of alcoholism. Individuals possessing high-active *ADH2*2 (ADH1B*47His)* and *ADH3*1 (ADH1C*349Ile)* alleles generate acetaldehyde much more rapidly after alcohol consumption, and the inactive *ALDH2*2 (ALDH2*504Lys)* allele delays the clearance of acetaldehyde, both protect against alcohol abuse. Those protective alleles are found almost only in Asian population including Korean, though *ADH1B*3* in African and native American also have been reported to have protective effect against alcohol dependence. In contrast with s allele in other population, L allele of *SLC6A4 (5-HTTLPR)* has been reported to be associated with alcoholism in Korean population. Other dopaminergic, serotonergic, GABAergic and cholinergic genes, known to be polymorphic in alcoholism, found to be not so polymorphic in Korean alcoholics.

In regard to susceptibility to tobacco addiction, glutamatergic, dopaminergic, cholinergic and other genes have been studied to be associated with tobacco dependence in other population, also not clear in Korean population. A1/A1 or A2/A2 genotype of DRD2 TaqI A in Korean smokers, in contrast to only A2/A2 genotype in European American, is the factor to predict more abstinence after bupropion treatment. Though s allele and s/s genotype of *SLC6A4* are associated with adolescent smokers in Korea, L/L genotype is another favorable factor for bupropion treatment in Korean smokers. *SLC6A4* s/s genotype is associated with tobacco addiction in Caucasian population, though L allele is more correlated with smoker.

Dopaminergic, serotonergic and noradrenergic genes are known to contribute to the risk of pathologic gambling in other ethnic groups. Higher s/s genotype frequency of *SLC6A4* polymorphism was reported among Korean male adolescents who use internet excessively.

Low level of response to alcohol has been indicated as the cause of increased risk for alcoholism in Koreans in contrast to Chinese. Epigenetic differences and microRNAs may explain the ethnic as well as individual discrepancies between the genetic polymorphisms and phenotypic manifestations of addiction disorders. Copy number variations from different ethnic groups also can identify the ethnic differences in the genetic polymorphisms of addiction disorders. The genome-wide association study is another future direction of genetic study in addiction disorders, which may

solve the problems of ethnic differences in addiction disorders.

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Morphine withdrawal syndrome and its amelioration

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Many researchers have recently proposed an anti-oxidative action for the compounds on tolerance and withdrawal syndrome of drugs. We recently found that oxidative stress-related gene glutathione peroxidase (GPx) was commonly modulated by morphine, butorphanol, and nalbuphine through the results of microarray in brain cortex of these opioid treated mice. Based on these results, it confirmed that the expression of GP1 and 3 was induced after morphine withdrawal in the brain of mouse and then we used to GPx and catalase (Cat) double knock out (-/-) mouse. This study investigated whether the oxidative stress affects the morphine withdrawal syndrome in the neuron of brain using GPx/Cat(-/-) mice. The naloxone-induced morphine withdrawal syndrome by jumping test was increased in the GPx/Cat(-/-) mouse than wild type mouse, but the psychological dependence by conditioned place preference (CPP) was not affected. Therefore, blocking the oxidative damage might be a useful strategy for the development of a new therapy for the amelioration of morphine withdrawal syndrome. In addition, we synthesized the serotonin receptor agonist and evaluated biological activity of 3,4,5-trimethoxyphenyl acrylamides as novel antinarcotic agents. It was found that compounds exhibited good inhibitory effects on the morphine withdrawal syndrome in mice and their binding affinities on serotonergic 5-HT1A receptors.

Methadone Maintenance treatment for treating heroin addicts in Malaysia

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In Malaysia, substance misuse, in particular heroin addiction contributes to health and social problems. Although effective medical treatment was available, earlier efforts confined the treatment of heroin addicts to community in-house rehabilitation which required them to be estranged from the community and their families for 2 years. Implemented since the 1980s, the community in-house rehabilitative programme has produced low abstinence rates. Furthermore being 'absent' meant that many heroin addicts faced employment problems and family relationship difficulties upon completing their in-house rehabilitation stay. Faced with these problems and acknowledging that heroin addiction is a medical illness, various government and non-government organisations set up a national drug task force to address the heroin addiction problem. At present, methadone substitution programmes have been offered as part of treatment programme for heroin addicts in Malaysia. The introduction of methadone maintenance treatment (MMT) programs to treat heroin addiction has provoked resistance from individuals who viewed the program as changing one drug dependence to another. Furthermore, the MMT program also faced additional problems such as the new uptake of amphetamines in heroin addicts who had stopped heroin use. On the other hand, the reported good retention rates and the reduction in risky behaviour among clients attending the MMT program have encouraged further upscaling of the program. This presentation thus attempts to discuss the findings and issues raised when operating a methadone maintenance treatment program and aim to suggest the scientific basis of some of the findings. Overall, this new MMT programme has been shown to be effective in treating heroin addiction in Malaysia.

Effectiveness of VIVA QS® for Nicotine Addiction

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Nicotine dependence associated with tobacco use, particularly cigarette smoking, results in devastating effects including lung cancer, ischemic heart disease and chronic obstructive pulmonary disease. Efforts have been made to identify new agents for smoking cessation. The use of herbals as an alternative to current treatments is still limited. To our knowledge, this is the first randomised, double-blind, placebo-controlled trial in Malaysia using a herbal preparation for smoking cessation. We evaluated the effectiveness of VIVA QS®, a herbal supplement consisting of twelve herbs, for the management of nicotine addiction. Smokers meeting study criteria were recruited upon consent and followed up was for 6 months, with three assessment time points for smoking status and withdrawal symptoms. Brief counselling was provided at each follow-up via telephone call at week 4 and 12. At week 24, self-reported abstinence was validated by measuring expired carbon monoxide level and cotinine in urine and/or saliva samples. Results: Of 155 smokers recruited, mean age = 35.2 ± 8.36 years. Mean baseline Fagerström test for nicotine dependence (FTND) score = 5.03 ± 1.39. Biochemically verified 7-days point prevalence abstinence at week 24 showed significant difference in quit rates between both groups (Viva QS® = 30.7% vs. placebo = 13.9%; p = 0.015). Significant differences in quit rates between groups were showed in 7-days point prevalence abstinence at week 4 (Viva QS® = 42.7% vs. placebo = 26.2%; p = 0.038) and week 12 (Viva QS® = 32.0% vs. placebo = 16.7%; p = 0.031). Adverse events reported were similar in both groups. Conclusion: VIVA Qs ® at least doubled the smoking cessation rate vs. placebo in smokers with moderate to high level of nicotine dependence.

Background: Different smoking cessation programmes have been developed in the last decade, but developing new concepts are at important states. We established a mobile smoking cessation service to reach smokers at workplaces. With difficulties in getting smokers to attend quit smoking clinics in Malaysia, the existence of such service is vital. As most adults spent about one third of their day in workplace environment, therefore workplace is a suitable setting to reach a large group of smokers to promote smoking cessation. To our knowledge, this is the first mobile smoking cessation service ever established in Malaysia.

Objective: To assist and motivate smokers to quit and to provide pharmacotherapy whenever necessary.

Method: Team consists of pharmacists and physicians. Service targeted smokers aged 18 to 60 at worksites. Trained health professionals provided motivational talk and supplied pharmacotherapy when required. Pharmacotherapy given was based on randomized double blind placebo control study using Viva QS® an herbal medicine as intervention and placebo as control. Smokers were required to fill self-administered demographic and smoking history forms at baseline. Subjects were randomized to either intervention or placebo groups. Follow-up was undertaken for 6 months at three time points to assess smoking status and withdrawal symptoms. Brief counselling was provided during follow-up via telephone call at week 4 and 12. At week 24, self-reported abstinence was validated by measuring expired carbon monoxide level and cotinine in urine and/or saliva samples.

Result: From November 2007 until April 2009, 12 industrial worksites have been reached. A total of 205 smokers attended motivational talk at baseline; 155 smokers agreed to receive intensive smoking cessation service. Mean age of smokers was 35.2 ± 8.36. On average, baseline Fagerström test score for nicotine dependence (FTND) was 5.03 ± 1.39. 7-days point prevalence quit rates at week 24 was statistically significant (quitters, 22.4% [Viva QS 30.7% vs. placebo 13.9%]; smokers, 77.6%; $P = 0.15$; OR = 2.74; CI = 1.197-6.282).

Conclusion: We observed that workers working at industrial sites were highly addicted to tobacco and faced difficulty to quit. Our findings suggested that a flexible-duration and easy-to-reach programme can doubles the abstinence rates for this group of smokers. Mobile smoking cessation service is an advantage to assist these smokers to quit. The intervention was found to be acceptable and welcomed by the employers. Thus, this service can improve the hard-to-reach population to promote smoking cessation.

Casino Employees and Gambling Problems

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Gambling is a popular form of entertainment throughout the world. The gambling industry can provide jobs and be an important source of tax revenue when it flourishes. However, casino employees are at greater risk for a variety of health problems compared to the general work force. They are exposed to, become familiar with, and have ready access to gambling, alcohol, and tobacco. Casino workers have increased proximity to and knowledge of gambling. At the same time, casino employees are at the front line for detecting and preventing pathological gambling (PG). Casino employees have opportunities to give information about PG to their clients. Therefore, we can hypothesize that gambling problems will influence how employees report their mental health and social attitudes toward PG. Employee gambling-related experience might be a crucial factor to determine whether responsible gambling programs intended to prevent and reduce any gambling related harms is going to operate well within casinos. In this regard, looking through the mental health problems (i.e., gambling, alcohol problems and tobacco use) and identifying employee's social attitude differences toward gambling will give us an idea how to make the program of public mental health education about gambling problems.

Issues in Effective International Scientific Research Collaboration with the U.S. NIH/NIAAA

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The U.S. National Institutes of Health is the world's largest public sector health research agency, and as such plays a major role in international research collaboration. While the overall NIH budget of $30 billion USD is primarily dedicated to support U.S. domestic science, in fiscal years 2004/2005(the latest available data), NIH invested approximately 3% ($570 million) of its total research budget in foreign research. As part of NIH, the National Institute on Alcohol Abuse and Alcoholism (NIH) has an active international research program. This program is based on three elements: 1) Direct grant awards to foreign Principal Investigators; 2) Funds for foreign components of U.S. domestic grant awards; 3) Research training through exchange of scientists/fellows. NIAAA is one of the few NIH institutes to have a special mechanism (PAR-08-004) to fund international scientific collaborations. The presentation will give an overview of NIAAA's current foreign research investment with special emphasis on collaborations with scientists in Asian countries. NIAAA's international collaborative alcohol research mechanism will be described. Finally, the essential elements of successful collaborations gathered from data on productive projects will be presented.

Human Study for Methamphetamine Abusers in Korea

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In this symposium, the presenter will summarize three articles that his center has published this year.

1) Dose-dependent frontal hypometabolism on FDG-PET in methamphetamine abusers.(J Psychiatr Res. 2009 Apr 22)

Resting brain FDG-PET revealed significant hypometabolism in the left inferior frontal white matter (Talairach coordinates (x, y, z): -34, 7, 31) in MA dependent patients compared to the control subjects (corrected p=0.001, peak Z=5.37, voxel number 201). The nearest gray matter region was the left inferior frontal cortex (Brodmann area 9). There were negative correlations between the relative regional cerebral metabolism for glucose (rCMRglc) in the left inferior frontal white matter and the total cumulative dose of MA (r=-0.57, p<0.01). MA dependent patients completed significantly fewer categories (3.8+/-2.2) and made more perseveration errors (21.3+/-11.8) and total errors (43.5+/-19.5) on the Wisconsin Card Sorting Test (WCST) when compared to the control subjects (p<0.01).

2) Reduced corpus callosum white matter microstructural integrity revealed by diffusion tensor eigenvalues in abstinent methamphetamine addicts.(Neurotoxicology. 2009 Mar;30(2):209-13)

Results showed significantly reduced fractional anisotropy (FA) in the genu of the corpus callosum (CC) in MA-dependent subjects compared with controls. Furthermore, the eigenvalues offered a unique opportunity to assess the microstructural source of abnormal changes in the genu of the CC. The relationships between WCST performance and the values of tensor measures also suggest that altered myelination is a possible source of FA reduction observed in the genu of the CC in MA abusers.

3) Frequency of osteoporosis in 46 men with methamphetamine abuse hospitalized in a National Hospital.(Forensic Sci Int. 2009 Jul 1;188(1-3):75-80)

The mean Bone mineral density (BMD) value was lower in methamphetamine abusers (mean+/-SD, 0.71+/-0.07 g/cm(2)) than in the controls (mean+/-SD, 0.98+/-0.14 g/cm(2)). The frequency of osteoporosis was 22% according to WHO diagnostic guidelines, and osteopenia at the lumbar spine was 76%. The correlation between the extent of methamphetamine abuse and BMD was very clear.

Preclinical and Translational Identification of Novel Pharmacotherapeutic Strategies for Psycho stimulant Abuse Treatment

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Psychostimulant (methamphetamine [METH] and cocaine) abuse continues to present profound socioeconomic, legal and medical problems worldwide. In addition, it is a significant comorbid factor for other psychiatric disorders, e.g., schizophrenia, bipolar disorder, and adversely affects their clinical courses and treatment responses. Various drugs have been tested as monotherapies against this disorder without consistent success; therefore, there is a critical unmet medical need for the development of more robust treatment strategies. Our recent research using animals models have demonstrated that combinations of a psychostimulant or a non-abused "substitute" agonist (e.g., pergolide) with a $5-HT_3$, $5-HT_{2A/2C}$, or NK-1 antagonist can: (1) reverse previously-established behavioral sensitization; (2) attenuate cocaine self-administration under a progressive ratio paradigm; and (3) attenuate cocaine- or METH-induced psychostimulant self-administration reinstatement. These behavioral effects are accompanied by parallel normalization of selected neurobiological marker changes in various regions of the brain. Importantly, the two drugs must be given 3.5 hours apart; and (2) monotherapies using either agonists or antagonists are ineffective. Experimental analyses of these behavioral and neurobiological marker changes have identified novel medication development targets. My symposium presentation will describe selected examples of our ongoing preclinical and bench-to-bedside development efforts seeking to identify novel therapeutic strategies based on the above experimental analyses.

THE ROLE OF ERM PROTEINS
IN PSYCHOMOTOR STIMULANT ADDICITON

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Drug addiction can be viewed as a form of neuronal plasticity that involves structural as well as functional changes of target areas or molecules to the drugs. The ezrin-radixin-moesin (ERM) proteins have been implicated in cell-shape determination by crosslinking F-actin to plasma membranes. Here we show that the phosphorylation levels of ERM protein are dose- and time-dependently decreased in the NAcc by a single injection of either cocaine or amphetamine. Further, we show that the amount of active RhoA, a small GTPase protein, is significantly reduced in the NAcc by cocaine, while the phosphorylation levels of ERM protein are also decreased by bilateral microinjections in this site of the Rho kinase inhibitors, Y27632 or RKI II. Together, these results suggest that psychomotor stimulants reduce phosphorylated ERM levels in the NAcc by making down-regulation of RhoA-Rho kinase signaling, which may importantly contribute to initiate synaptic morphological changes in the NAcc leading to drug addiction.

Epidemiological trends of drug abuse in Korea and drug hair testing.

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In Korea, eleven chemicals including 2C-B and Benzylpiperazine have been added as psychtropic substances or narcotic precursor as results of five series of revisions of Narcotics Control Act of Korea between January 12 of 2000 and March 28 of 2008. For last one year (2008 and 2009), surprisingly enough, twenty two new chemicals were added to the control list due to rapid increase in new misused or abused chemicals.

The following characteristics of abused chemicals, however, make disclosure and enforcement difficult in Korea. First, the chemicals are many kinds with various shapes. Second, channels of distribution and hiding skills are dexterous. Third, they spread very rapidly due to the internet and advanced transportation technologies.

Furthermore, most of these newly listed chemicals are not developed for the purpose of medical uses, users including even misusers do not have proper information about dosages, effects, toxic character, side effects and interactive effects. Therefore, the level of social danger due to increased misuse and abuse of these chemicals becomes more serious than ever before.

Drug abuse has become a significant medical and social problem in Korea. Chemical testing of biological specimens from individuals is generally accepted to be the most objective method for determining drug abuse. Hair Analysis for drugs of abuse provides a possible long-term measure of drug abuse not possible with urinalysis. Many drug and metabolites have been detected in hair. Analysis of human hair is purported to provide evidence of the drug of abuse. The extent and timing of drug exposure may also be estimated. Segmental hair analysis can yeild the information about the time course of the drug abuse. Hair test results for drug abuse have recently been entered more frequently as evidence in the courts and have generated much interest and controversy in the forensic drug testing.

Enhanced analytical techniques with increased sensitivity and selectivity and new methods of sample preparation and extraction have improved detection limits of drugs. These advanced analytical techniques have highly improved the ability to detect numerous drugs in hair.

However, the differences in hair growth rate depending on anatomical region, age, gender, ethnicity and individual variability, mechanism of drug incorporation are not simple, not yet understood in full details and need not be evaluated exactly in all cases. The hair sampling, sample preparation and analytical procedures are also very important for final results. Futhermore interpretation of parent drug or/and metabolite concentrations in hair is not easy. The comprehensive information on circumstances of the case examined should be taken into account during interpretation. There are still remaining pitfalls in hair analysis and more scientific understanding and further research are necessary in this developing technology.

Poster Session

12 November (Thu) 2009

Patterns of club-drug use in Chiang Mai city

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Background: Drugs had been broadly used for entertaining. Club drug uses were rarely seeking help from medical care facility. Most of them occasionally use drug and refusing of any serious dependence problems. Their patterns of use and related behaviors are not well exposed.

Objectives: To determine club-going young adult patterns of club drug use in Chiang Mai Municipality and identify associated risk factors.

Method: Time-space sampling generated a sample of 170 club-going young adults (ages 18–38) who provided data on their use of four key club drugs: ecstasy, ketamine, cocaine, and methamphetamine crystal, as well as data on their gender, alcohol behavior, and other demographic variables. The data collection using a pocket PC was done for three-months in 2009. The tool enabled a smooth and effective gathering of the sensitive data among this population.

Results: Club-going young adults reported a high prevalence (76%) of lifetime illicit drug use. Among these ever-users, 57 % reported recent club drug use and 32% reported use of multiple drugs. Club drugs were used before entering, while at, or after leaving an entertainment place. It was used before entering an entertainment place to increase the fun. Multiple drug users had, on average, used amphetamine and cannabis 2−4 years before using any other drugs. No significant association found between illicit drug use and gender, educational levels or occupation.

Conclusion: Three-fourths of club-going youths in Chiang Mai city were lifetime illicit drug users. Multiple drug use were common. No factors showed significant association with the use of drugs.

Alcohol Use Disorders and Inadequate Knowledge about Drinking and Driving among Japanese DUI Offenders

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Purpose: Driving under the influence of alcohol (DUI) is a serious public health concern. However, little is known about drunk drivers in Japan. This study presents data on Japanese DUI offenders.

Methods: The subjects were 1,279 males and 66 females who participated in traffic schools conducted by the Kanagawa Prefectural Police because they had their driver's license revoked. They completed self-report questionnaires on sociodemographic information, experiences of DUI and arrests due to DUI, patterns of alcohol consumption, times that they should wait before driving after drinking, and several screening scales on problem use of alcohol such as AUDIT, CAGE and KAST.

Results: Arrests due to DUI were reported by 39.2% of males and 30.3% of females. Among DUI offenders, 23.8% of males and 22.2% of females scored 20 points or higher in AUDIT, 36.9% of males and 45% of females scored 2 points or higher in the CAGE test, and 39.5% of males and 36.8% of females scored 2 points or higher in KAST. In addition, DUI males reported significantly shorter times that they should wait before driving after drinking than those without a history of DUI.

Conclusion: These results and recent literature suggest that the prevalence of alcohol use disorders among DUI offenders is much higher than that in the general Japanese population. In addition, drunk drivers have inadequate knowledge about drinking and driving. We conclude that provisions of treatment programs for drunk drivers and promotion of public education are necessary for further reducing DUI in Japan.

Perceived factors contributing to non-completion of treatment in patients with substance use disorder at in-patient treatment facility

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The study was conducted at National Drug Dependence and Treatment Centre, All India Institute of Medical Sciences, Ghaziabad, India, during 2007-2008.

Introduction

Patients who get admitted in ward for treatment of their addiction problems often leave the inpatient facility without completing their treatment. The aim of this study was to find out the perceived reasons for the same so that proper preventive measures could be taken to improve treatment completion rate.

Methodology

Different techniques which were used to know about the perceived reasons for leaving the inpatient treatment facility prematurely included reviewing files of patients who got discharge on disciplinary grounds (DDG), discharge on request (DOR), leave against medical advice (LAMA) ; interviewing persons in hospital who were related to the treatment, interviewing patients who were receiving treatment currently in the ward, who came in touch with the patients leaving prematurely, identifying the patients who had past h/o leaving the ward prematurely from their files and interviewing them regarding the reasons of the same. Out of 32 such patients who left the ward before completion of treatment in one month files of 16 such patients could be reviewed; five doctors, three nurses, two social workers and two security guards could be interviewed; four patients who came in touch of patients who left prematurely could be interviewed; seven patients who left the ward without completing the treatment in the past could be interviewed.

Results

Review of files showed that in more than half of the cases the reasons for such behaviors had not been explained. Few patients reported tobacco smoking related restrictions, uncontrolled withdrawals and personal problems as the reasons. Craving was mentioned as the main factor by

the persons involved in treatment. Interviewing patients revealed tobacco related restrictions in the ward was the factor in majority of the patients.

Conclusion
Craving for the drug of choice and tobacco were probably the biggest perceived factors which led to leaving the ward without completing the inpatient treatment.

PA-E04

Recovery from alcohol and drug dependence in welfare recipients in Japan

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Key words ; alcohol dependence, drug dependence, welfare, rehabilitation, recovery

Background: Recovery from alcohol and drug dependence does not imply sobriety. Universally recognized as being multidimensional, it involves more than the mere elimination of substance use. In Japan, since we do not know the criteria of recovery from alcohol and drug dependence, the basic actual situation has not yet been grasped.
Method: The purpose of this study was to investigate the recovery from alcohol and drug dependence in welfare recipients in Japan. We dispatched and collected a questionnaire of investigation to 976 welfare offices by mail. In the questionnaire, we enquired about the real situation and recovery from alcohol and drug dependence of welfare recipients in the area. During data analysis, we used two tentative definitions of recovery from alcohol and drug dependence, developed on the basis of the definition proposed by the Betty Ford Institute Consensus Panel.
Results: In our criteria, 12% of welfare recipients recovered from alcohol and drug dependence with a comparatively wide definition; however, only 3% with a comparatively narrow definition. In addition, the staff of the welfare office considered the personal element of alcohol and drug dependence to be important for recovery. Although they tended to perceive the relationship with alcohol and drug dependence as difficult, they did not undergo adequate training for alcohol and drug dependence.

Conclusion: Medical care facilities should be in conjunction with welfare offices in the treatment of alcohol and drug dependence. We need to examine the factor and support required for recovery from alcohol and drug dependence in the future.

PA-E05

Alcohol-related adverse experiences among high school students within the past 12 months

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Introduction
Alcohol consumption is common in youth and subsequently causing other consequences such as deadly accidents, quarrels and sexual problems. Effective surveillance and intervention programs to prevent these problems are therefore necessary.

Objective
To study the alcohol-related experiences among high school students in Thailand

Subjects and Methods
A cross-sectional survey was conducted among students from high-school years 7, 9 and 11 and vocational school year 2 in 201 schools from 40 randomly selected provinces throughout the country. The students were asked to complete a self-administered, voluntary and anonymous questionnaire. The total number of students was 50,033, 46% males and 54% females.

Results
39.8% of male and 24.5% of female students ever consumed alcohol in their lifetime while 25.1% and 14.0% of male and female students did so within the past 12 months. The most common adverse experiences found in past-year drinking students themselves were being nauseous/vomiting, driving a car/motorcycle after drinking and having a hangover (49%, 43% and 42% among males and 44%, 29% and 34% among females, respectively). Experiences caused by other drinking students in their school included being disturbed while studying and sleeping, being blamed on and attacked, participating in brutal fights, and having to assist drunk fellow students (21%, 20% and 18% among males and 20%, 13% and 14% among females, respectively).

Conclusions

Alcohol consumption in students clearly has negative effects on themselves and others, and these problems are becoming more severe. Parents and teachers should pay close attention to prevent inappropriate behaviors and promoting proper ones.

PA-E06

Prevalence of problem alcohol use, nicotine dependence, internet addiction and gamble addiction among Japanese adults

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In order to determine the prevalence of problem alcohol use, nicotine dependence, internet addiction, and gamble addiction among Japanese adults using four screening tests simultaneously.

Japanese adults were selected using two stage stratified random sampling method from entire Japan. Survey method was home- visit interview. The survey period was June, 2008. The questionnaires were collected from 4,123 people (response rate=55.0%). The questionnaire contained some screening tests for alcohol dependence (AUDIT, CAGE, KAST, new KAST), experience of drink-driving, nicotine dependence, internet addiction, and gamble addiction.

Prevalence of people who drank during one year was 83.1% for male and 60.9%, whereas the figures in 2003 were 85.3% and 61.8%, respectively. In the younger age groups, the gender difference is narrowing.
The proportion of heavy drinkers (>=60g pure alcohol/one drinking day) was 12.0% for male (6.0 million, 12.7% in 2003), and 3.1% for female (1.7 million, 3.7% in 2003). Comparing 2008 results with 2003, the narrowness of gender difference in 20-24 was observed.
Using cut-off point as 13 mark of AUDIT, the prevalence of problem drinking was 8.7% for male and 1.2% for female. In the case of CAGE, the rate was 5.3% and 1.6% , respectively.
The prevalence of nicotine dependence was 5.1% for male and 0.6% for female, gambling dependence was 9.6% and 1.6%, internet dependence was 8.3% and 7.7%, respectively.
The internet dependence was frequent in younger age groups, and gender difference was small. Alcohol dependence and nicotine or gambling dependence was more likely to merge, but not for internet dependence. The positive relationship was found in each dependence among women. Four dependences were associated mutually, however the characteristic of each distribution was

different by sex and age group. In near future, the accumulation of problematic behaviors should be analyzed in detail.

PA-E07

Pattern and health impact assessment of kratom (Mitragyna speciosa Korth.) users in upper southern Thailand

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Background: Kratom (Mitragyna speciosa Korth.) is a tropical tree indigenous to Thailand, especially in the southern part. Kratom leaves have been used by native people as an herbal drug or a mild stimulant to help them enduring hard work and tolerant to sunlight for decades. Thai government enacted the Narcotics Act B.E. 2522, placing kratom along with marijuana in Category V of a five-category classification of narcotics. The pattern of use has been changed recently among teenagers from chewing fresh leaves to drinking kratom cocktail, which is a mixture of krathom leaf extract with other substances such as coca-cola, benzodiazepines and mosquito-repellant sticks. This study aimed to determine the pattern and health impacts of kratom use.

Methods: A cross-sectional survey, using a face-to-face interview was conducted among 522 household residents in Ranong and Nakornsrithammarat provinces between April 2008 and April 2009.

Results: 48.5% ever used kratom leaves in their lifetime while 26.8% ever used krathom cocktail and 16.3% were currently using kratom leaves. Among those who ever used kratom 12.2% admitted that they were addicted to it as they had difficulties or restlessness when no kratom available. The most common health consequences of chronic kratom or kratom cocktail use included fatigue, joint and muscle pains, sleepiness and yawning, dizziness, feeling lazy and amotivational symptoms, all of which were more frequent among cocktail users than were in pure kratom users.

Conclusion: Chronic kratom use is associated with some health consequences, which are more severe and frequent among cocktail users.

PA-E08

Prevalence of substance dependence including alcoholism among homeless people in a district of the Tokyo metropolitan area

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Objectives
It is widely believed that substance dependence including alcoholism is prevalent among homeless individuals in Japan. However, the actual situation has not been clearly studied. We clarified the actual condition of patients among homeless individuals who suffer from these diseases, and examined the necessity for support and treatment.

Methods
This study involved a cross-sectional survey. The survey period was from December 30, 2008 through January 4, 2009, and the respondents were individuals who were located within a 1 km radius from a station during this period. We defined a homeless person as an individual not living in a room with a roof during the investigation period. For the diagnosis of a mental disease, we used a questionnaire created according to the Mini International Neuropsychiatric Interview (MINI) and another questionnaire devised by ourselves that involved aspects regarding the living conditions of the participants.

Results
Out of 115 persons who were requested to participate, 80 (70%) responded to the survey. The average age of the participants was 50.5 (SD 12.3) years. The number of participants that were diagnosed as having mental disease was 50 (64%), that for depression was 33 (41%), and that for alcoholism was 12 (15%). The substance dependence excluding alcoholism was only one person. Mental disease symptoms such as hallucinations or delusions in 12 persons (15%) were identified by the psychiatrist.

Conclusion

The Japanese homeless(roofless) number is estimated at about 30,000. If a number that an alcoholism is 15% is correct, there will be 4,500 alcoholism of non-treatment.
It is clear that there are many homeless people who should be urgently supported because of the prevalence of mental disease and alcoholism who are non-treatment.

PA-E09

Questionnaire survey of drink-driving directed at the treating and/or the mutual-aid- groups-attending alcoholics.

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Recently, drink-driving is taken up as one of the largest social troubles by the mass media in Japan. As a result, it proceeds drink-driving measures in the direction of making to the severe punishment. However, it is not effective in the extermination of drink-driving in making to the severe punishment alone, and it is pointed out the importance of the treatment and measures to alcoholics, which is being acknowledged gradually at present. Then, to examine the situation of the alcoholics patients' drink-driving, we did the questionnaire survey of drink-driving in the alcoholics who attend to the mutual help group and/or who are treated.
We did the questionnaire survey by using the survey slip of self-registering unsigned. The questionnaire objects were made an alcoholics who were treating in the hospital and/or commuted to the mutual help group (AA or Danshu-kai, unique mutual help group to Japan). We explained that their privacy was protected, and the data was not used by the purposes other than the research by oral, and the answer was gotten only from the persons who had won consent.
We obtained the answers from 251 people. 82% of the treating alcoholics and/or the ones reformed by mutual aid groups experienced drink-driving, and the 26% repeated drink-driving. The majority of drink-driving offender understood that it was a violation and drove while intoxicated. Moreover, there were a lot of people who had caused the accident in drinking and driving. There were a lot of the alcoholics who had enumerated the introduction of making to the severe punishment and interlock as a method of settlement of drink-driving.

Benzodiazepine Misuse Problem and Development to Narcotic Drug in Rural Province Thailand

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Background: benzodiazepine is one of sedative and hypnotic drugs. Increasing of its misuse and abuse makes it play an important role as narcotic drugs in Thai society.

Study design: A qualitative research was conducted for this research.

Source of data and key informant: 18 key informants willing to participate in this study were drawn from a population based survey of sedative and hypnotic drug use in rural area, northeastern region of Thailand. As misuse and abuse drug users, key informants were identified in accordance with international standard criteria of DSM IV (revised version 1994).

Method: An in-depth interview of misuse experiences was implemented. Data analysis was performed using content analysis and triangulation methods.

Result: Most frequently used Benzodiazepine drugs were Diazepam, Lorazepam and Alprazoram. Most misused group was women who were housewife. Usually drug misuse begins with medical treatment and then drug addiction is slightly developed. Most of key informants were patients who habituated drug used reflected that benzodiazepine in their lives is harmless. Some user used Benzodiazepine as narcotic drugs, second line drugs and used involved with cannabis, alcohol and methamphetamine. Drug users can easily find out Benzodiazepine from hospitals and some of them bought from nightclubs and smugglers from Thai-Lao free trade border.

Conclusion: Sedative and hypnotic drugs in Benzodiazepine group have been increasing misuse until becoming abuse. Medical Law need increased strictly control and medicine dispensation of medical treatment in public health system should be seriously considered.

Clinical profile of patients with Inhalant abuse in India: data from a tertiary care de-addiction centre.

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Background: Even though inhalant abuse is relatively uncommon, it warrants attention owing to its impact on the adolescent population. However, data regarding the clinical profile of this condition is relatively sparse.

Methodology: This study is a retrospective data analysis of individuals who presented to the National Institute of Mental Health And Neurosciences, Bangalore, India, with inhalant abuse as the presenting problem. Overall 43 patients had presented between January 1999 to July 2009 with an ICD 10 diagnostic code of F18 and their records were subjected to analysis.

Results: The mean age of the sample was 19.25 years. They predominantly came from urban background (97%) and the mean years of education was low (7.65 years). All the individuals in the sample used volatile solvents, of which trichloroethylene was predominantly abused (69.8%). The mean age of onset of use is 16.3 years and the mean duration of use being 37.62 months. Withdrawal symptoms were experienced by 88.4% of the sample. Co-morbidity of depressive symptoms, psychosis and externalizing symptoms were 9.3%, 37% and 65% respectively. The subgroup of patients with inhalant abuse as apart of polysubstance use (22 subjects) when compared to pure inhalant abuse (21 subjects) differed significantly in the parameters of presence of withdrawal symptoms (chi=5.4,p=0.020),depressive symptoms (chi=4.2,p=0.040), aggression(chi=5.8,p=0.016) and externalizing symptoms (chi=5.3,p=0.021).

Conclusions: Inhalant abuse was found mainly in adolescents and had a high rate of psychiatric co-morbidity. Individuals with inhalant abuse with polysubstance dependence are different as a group compared to pure inhalant abusers, with the former group having greater externalizing diathesis and psychiatric co-morbidity.

Comparison of behavioral, psychological characteristic features and severity between gamblers using legal and illegal gambling places.

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Korea

This study investigated whether the pathological gambling severity, motivation, irrational gambling belief and depressive mood varied between gamblers using legal and illegal gambling places.

A sample of 890 adults was collected at legalized gambling places, illegalized gambling places, or normal general people and divided into three groupings: gamblers both using (legal and illegal gambling places), gamblers only using legal gambling places, and gamblers only using illegal gambling places.

Results revealed that the prevalence of pathological gambling was the highest in the both using group, and the lowest in the only using legal group. The motives for avoidance, monetary, excitement, and socialization and irrational belief, severity of anxiety, depression were increased in the gamblers both using group. This results suggested that if some people could have more chances to gamble anywhere, it will be the risk factor for pathological gambling.

The Temperament and Character Profiles of Drinking, Smoking and Over-using Internet in middle school students

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Internet addiction is a newly appeared addiction phenomenon. The purpose of this study was to survey the present conditions of adolescents'internet use and to investigate the relationship of internet addiction with depression, temperament or character trait.

Four hundred and twenty-five middle-school students were included in the study, each of whom completed self-rating questionnaires including demographic data, Korean version of Young's Internet Scale, the BDI (Beck's Depression Inventory) and the TCI (Temperament Character Inventory).

In this study, prevalence of high-risk group of internet addiction is 11.5 %, and male students had significantly higher score of internet addiction than females. Alcohol experienced group had significantly higher scores of NS(Novelty Seeking) and RD(Reward Dependence) and lower score of HA(Harm Avoidance) than inexperienced group. Cigarette experienced group had significantly higher score of NS and lower score of SD(Self-directedeness) than inexperienced group.

High-risk internet addiction group had significantly higher score of HA, and significantly lower scores of RD, P(Persistence), SD, CO (Cooperativeness) in the TCI than no risk group. High-risk addiction group also had a high score of depression in the BDI than no risk group.

The scores of NS of alcohol or cigarette experienced group were high but the score of NS of internet addiction group was not high. It suggests that temperament and character of the internet addiction group is different from that of other addiction group. Different and discrete therapeutic approach different from alcohol or nicotine dependence will be needed to resolve this type of addictive problem.

Further study will be needed to investigate the relations between addictive behavior, problematic mood and temperament of internet addiction group.

A Study on the treatment and barriers of drug offenders in compulsory treatment system in Korea

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The objectives of this study were to analyze the present status of compulsory treatment system and to explore the barriers of pre-existing compulsory treatment system to drug offenders.

A survey was conducted with 42 drug offenders in mental hospital to treat drug offenders in Korea.

Major findings of this study were as follows :
The main barriers of compulsory treatment system are insufficient information of drug abuse treatment system, prejudice to compulsory mental health treatment system, and insufficient infrastructures in the community.

To facilitate the compulsory treatment system, we need advertisement to inform the compulsory treatment system, collaboration efforts improvement of legal-social system, construction of community based drug center and evaluation of compulsory treatment system.

Key words : drug offenders, compulsory treatment, barriers of treatment

The Social Context of Alcohol Consumption in American Samoa

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The authors present results from qualitative interviews and focus groups on the cultural context of alcohol use in American Samoa . These data were collected for a NIAAA translational research grant, with assessment instruments (SSADDA, FHAM) to identify alcohol-related traits and phenotypes in Samoans. Our research suggests that heavy alcohol use and alcohol use disorders may be highly prevalent in Samoans; however, little information has been available about the alcohol consumption and the cultural context of drinking in American Samoa. Therefore we conducted 12 individual interviews with community leaders and 6 focus groups with low-to-moderate or heavy alcohol users (8 persons per group) to understand the cultural context of alcohol use. Interview and focus group data were transcribed from recordings; some data were translated from Samoan into English. Transcripts were analyzed with NVivo 7 software.

Several themes have recurred in the focus groups and interviews including the following: There is a preference for a locally produced, high alcohol content beer. Women tend not to drink as often as men, and women and men tend not to drink together, although these patterns are changing among younger drinkers. Higher socio-economic status Samoans drink in bars while those of lower status drink outdoors in hidden spaces, such as under trees and behind stores. High alcohol consumption is normative for certain groups, such as fish cannery workers. Stress, often a result of Fa'alavelave, labor and money demands from the extended family for lifecycle events, are connected to alcohol consumption. These events require significant donations of money or time and are central to Samoan culture.

The findings about stress and alcohol are of interest because stress has previously been related to diabetes and other chronic disease in this population. In related work we found that such stressors were impediments for improving self-care among those with type 2 diabetes and in large representative community samples. In future etiologic and intervention research we plan to disentangle the cause and effect relationships between alcohol consumption and familial and community stressors.

PA-E16

A Comparative Study of Involvement and Motivation among Casino Gamblers

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Objective The purpose of this paper is to investigate three different types of gamblers (which we label "non-problem," "some problem," and "probable pathological gamblers") to determine differences in involvement and motivation, as well as differences in demographic and behavioral variables.

Methods The analysis takes advantage of a unique opportunity to sample on-site at a major casino in South Korea, and the resulting purposive sample yielded 180 completed questionnaires in each of the three groups, for a total number of 540. Factor analysis, ANOVA and Duncan tests, and Chi-square tests are employed to analyze the data collected from the survey.

Results Findings from ANOVA tests indicate that involvement factors of importance/self-expression, pleasure/interest, and centrality derived from the factor analysis were significantly different among these three types of gamblers. The "probable pathological" and "some problem" gamblers were found to have similar degrees of involvement, and higher degrees of involvement than the non-problem gamblers. The tests also reveal that motivational factors of escape, socialization, winning, and exploring scenery were significantly different among these three types of gamblers. When looking at motivations to visit the casino, "probable pathological" gamblers were more likely to seek winning, the "some problem" group appeared to be more likely to seek escape, and the "non-problem" gamblers indicate that their motivations to visit centered around explorations of scenery and culture in the surrounding casino area.

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Conclusion The tools for exploring motivations and involvements of gambling provide valuable and discerning information about the entire spectrum of gamblers.

PA-E17

Recovery Experiences of Korean Alcoholics: Being Reborn

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Objectives: The purpose of this study was to develop a practical theory through an analysis of recovery experiences among alcoholics. **Methods**: Strauss & Corbin's grounded theory(1998) was employed as a primary method. The time spent for collecting data spanned from June, 2006 to November, 2006. Total of eight men and three women who were diagnosed with alcohol dependency participated in the study. **Results** : The core category that emerged from the comparative analysis was "being reborn". Eighty concepts, twenty two sub-categories, and fourteen categories were emerged from the comparative analysis by open coding, axis coding, and selective coding. And then, a situational model was made after analysis of pattern and process. It was in the process of the central phenomena. The recovery experiences of Korean alcoholics is a phenomenon based on action/interaction results from a personal-family-A.A. –alcohol center-community-national level chain. **Conclusions** : There is a need for local society and government to modify the old policies and create new ones to prevent and improve of Korean alcoholic and alcoholism.
Key Words : alcoholic and alcoholism, recovery.

Validation study of Kim's smoking cessation motivation scale and its predictive implications for smoking cessation

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Purpose: The purpose of this study was to develop a scale to measure motivation for smoking cessation. The motivation for smoking cessation may be an important variable that can predict the success of smoking cessation attempts. The reliability of the scale was assessed and its predictive validity for smoking cessation was evaluated.

Methods: We recruited 333 men aged 20 to 70 that visited smoking cessation clinics at seven public health centers that wanted to stop smoking. A smoking cessation motivation scale was developed with 10 questions based on the theory of motivation enhancement therapy. The Kim's smoking cessation motivation scales(KSCMS) were administered to participants in the study and maintenance of smoking cessation was measured at the sixth week after providing nicotine replacement therapy. To verify the cross-validity of Kim's smoking cessation motivation scale, Korean version of the stages of readiness for change and eagerness for treatment scales version 8.0(K-SOCRATES), Korean version of nicotine dependence insight scale(K-NDIS), Korean nicotine dependence syndrome scale(K-NDSS) were performed.

Results: Through factor analysis, four factors were identified for measurement: the precontemplation level of motivation, the contemplation level of motivation, the preparation level of motivation 1, and the preparation level of motivation 2. The preparation level subscale was divided into the slightly forwarding contemplation level and an action level. The internal consistency for the four factors was .537, .480, .666, and .481, respectively. The internal consistency for the total items was .679. The split half reliability of the scale was .431. The results of the correlation analysis of the KSCMS and K-SOCRATES subscales conducted to verify the validity of the motivation scale, precontemplation showed that it was positively related to recognition ($r=.227$, $p<.001$) and negatively correlated with ambivalence ($r=-.277$, $p<.001$) from the K-SOCRATES. The contemplation level from the KSCMS was positively related to recognition ($r=.398$, $p<.001$) and to taking steps ($r=-.162$, $p<.001$). The preparation level of motivation 1 was positively correlated with recognition ($r=.328$, $p<.001$). In addition, the preparation level of motivation 2 was positively related

to taking steps (r=.346, p<.001) and ambivalence (r=.207, p<.05). Moreover, the preparation levels of motivation 1 and 2 had a significant correlation with stereotypy in the K-NDSS (r=.133 p<.05 and r=.128, p<.05 respectively). According to the results of the analysis, although higher level of motivation for smoking cessation and insight into smoking as a problem could lead to a higher likelihood of trying to stop smoking, they were found to have an inverse correlation (r=--.434, p<.001). This result could be interpreted as being due to the discriminant validity of the scale being high. The logistic regression analysis showed that the precontemplation level from the KSCMS and the continuity and stereotypy from the K-NDSS significantly predicted the success rate of smoking cessation. Therefore, a higher level of motivation during the precontemplation stage, a higher level of stereotypy and a lower level of continuity of the smoking patterns resulted in a higher success rate for smoking cessation.

Conclusion: The smoking cessation motivation scale with 10 questions that was developed in this study was a highly reliable and a valid scale for the prediction of success for smoking cessation for those who wanted to stop smoking.

PA-E19

Demand for Voluntary Counseling and Testing Among Intravenous Drug Users, Thailand

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Introduction: The problem is: if we can not encourage IDUs to access care, we are not able to control the spread of TB and HIV/AIDS in this group in the future. This research aimed to study 1) the demand of voluntary counseling and testing (VCT) among IDUs, 2) the willingness to pay for VCT and 3) their condom use behavior.

Methodology: This is a cross section study. We interviewed 361 IDUs who did not have access to the ART program and they continuously used drugs.

Results: Ninety three percent of IDUs were male.69 percent of IDUs have shared needles with other people. The illicit drugs which are injected are mostly heroin (55 %) . 79 percent of the subjects have been tested for HIV and 22 percent know that they are already infected. The willingness to pay for VCT and screening tests by IDUs was less than the standard price of 200 baht. The cost of VCT and blood testing would be free if an IDU had at risk behavior, such as unsafe sex or injecting drugs.77 percent of IDUs use condoms regularly when they had sexual relations with commercial sex workers, and 86 percent had used condoms in their last sexual encounter.

Conclusion: Most IDUs know about VCT and ART, and if they test positive for HIV/AIDS they want to join an ART program. We have to implement an outreach program in communities to educate them, and also keep a good quality of life by providing continuing care.

Cigarette Smoking and Suicidal Ideation

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Objective:
Smoking has been implicated as a possible risk factor for mortality from suicide. However, it is unclear if this association is due to cigarette smoking itself or due to other confounders such as depression and alcohol use. This study aimed to examine that cigarette smoking is a independent risk factor for suicidal ideation.

Methods
A total of 1262 soldiers (male; age range, 19-29 years) participated in this study. Self-reported questionnaire was administrated. Questionnaire included demographic data, smoking, alcohol use, BDI, STAI, AUDIT as well as questions about suicidal ideation. Participants were divided into 4 groups according to smoking status (non-smoker, past smoker, light smoker, heavy smoker).

Results
Of all participants, current smoker were 458 (36.8%). Persons with suicidal ideation were 9.7% in non-smokers, 5.8% in past smokers, 6.1% in light smokers, 15.7% in heavy smokers. Heavy Smoking was a risk factor for suicidal ideation (p=0.015, unadjusted odds ratio, 1.8; 95% confidence interval, 1.12-2.90). This association was not significant after controlling for depression, alcohol use, anxiety (p=0.09).

Conclusion:
This study suggests that cigarette smoking itself is not a independent risk factor for suicidal ideation.

PA-O01

ECONOMIC COST OF ALCOHOL CONSUMPTION: A HOUSEHOLD SURVEY IN KHONKAEN, THAILAND

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This household survey aimed to obtain the economic costs of alcohol consumption incurred to users in Khon Kaen province, Thailand. Our study targeted the population aged 12-65 years old in both rural and urban areas. The study applied multistage sampling to obtain information during February-March 2007 using structured interview. The economic cost comprised (a) Expense on treatment, (b) Productivity losses, and (c) Other costs. Descriptive statistics were performed using Excel and SPSS. Multivariate analyses were performed using SPSS and STATA.

Among 1053 respondents, lifetime drinking was 53.2%, with proportion in male was 2.7 times greater than that of female. The rate of alcohol drinking in the past 12 months was 43.6%. Among these, about 20% were classified as high to very high risk drinkers. In past 12 months, the rate of having health problems and accident occurred were 4.0% and 5.3% among current drinkers, whilst 0.2% and none among abstainers. It was found that risk behaviors and social consequences were increased regarding drinking risk level. Considering economic cost, it was found that 16.3% of them had cost incurred and varied greatly. The largest proportion of cost was individual productivity loss, following by relatives' productivity loss. The major cost contributors were very high risk, frequent-inconsistent drinkers, and adolescent. Multivariate regressions revealed that perceive of good health, male, frequent drinker, and frequencies of binge drinking were significant determinants of drinking risk level. Age was found to have negative effect on drinking risk level, but not significant. Considering determinants of cost, having health problems and having accident had very high significant positive effects. Drinking risk level and male gender had high positive effects, while age and living in urban area had negative effects on cost incurred.

The estimated overall 1 year private cost of alcohol consumption in KhonKaen was US$ 19.8 million (95%CI 4.4, 35.1 million). This study urge for promoting social recognition of safe-drinking, reducing binge drinking behavior, targeting young adult male drinkers.

PA-O02

Hostility and Impulsivity of Nicotine Dependence

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Objectives: This study investigated the independent risk of hostility and impulsivity of smokers in military populations, and examined risk differences among non -smokers, light smokers and heavy smokers. Subjects and Method: A total of 550 airmen participated in this study. They completed questionnaires including demographic data, a smoking history, the Beck Depression Inventory (BDI), the State-Trait Anxiety Inventory (STAI), the Alcohol Use Disorders Identification Test (AUDIT), Dysfunctional Impulsivity Scale (DIS), Buss &Durkee Hostility Inventory (BDHI), Fagerström Test for Nicotine Dependence (FTND), and the Nicotine Dependence Syndrome Scale (K-NDSS). Results: All of the subjects were male; 543 individuals, with a mean age of 21.0±1.1. Most of them were single; 541 people, 99.6%. 29.5% or 160 of the subjects were smokers. Demographics and smoking-related characteristics of non-smoker and smoker were similar. The Trait Anxiety Inventory, DIS, and BDHI are more significant differences between light smokers and heavy smokers, and less significant differences between non-smokers and light smokers. The mean differences of STAI (F=3.379, P<0.05), DIS (F=8.186, P<0.001), and BDHI (F=10.332, P<0.001) between light smokers and heavy smokers were higher than that between non-smokers and light smokers. We found significant correlations between FTND and BDHI (r=0.208, P<0.05), initiation (r=-0.260, P<0.01), duration (r=0.206, P<0.05) and amount (r=0.546, P<0.001) among smokers. NDSS is related to BDHI (r=0.198, P<0.05), initiation (r=-0.280, P<0.001), duration (r=0.259, P<0.01) and amount (r=0.421, P<0.001). Conclusion: In this study, we found that there is a significant correlation between hostility and smoking status and nicotine dependence scales. Impulsivity has no relation with nicotine dependence scales, but was related to smoking status.

Attitudes of Japanese psychiatrists toward the clinical practice of alcoholism: an online questionnaire survey

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Alcohol consumption has increased considerably in Japan. Correspondingly, alcohol related problems are getting more and more serious and prevailing. In spite of such increasing social demand, Japan continues to face a serious shortfall in this field's workforce. In this study, we conducted a survey to investigate the perceptions, experiences, and interests of psychiatrists in alcoholism.

The subjects of this study were 182 psychiatrists in Japan. The mean age and clinical psychiatric experience of them were 33.1±4.5 years and 5.43±3.5 years, respectively. We created an online questionnaire system and e-mailed the URL and login password to all subjects. Most questions required an answer indicating a degree of agreement scored on a nine-point scale.

On a nine-point scale (with nine being the highest), experience and desirability of specialist in alcoholism were scored 3.38±1.9 and 3.71±1.9, respectively; further, these two factors showed significant correlation (r=0.776, p<0.001). The mean scoring of the subjects' confidence in their ability to appropriately treat alcoholism was notably low, 3.83±2.2. Only 35.5% of the respondents answered that they believed the possibility of complete recovery from the alcoholism, while 60.5% of them were concerned the possibility of the recurrence of alcohol related problems.

Our results demonstrated that the subjects of this study self-evaluated their clinical abilities for alcoholism as insufficient, and their experiences and desirability of specialist in alcoholism

correlated significantly. Therefore, in order to provide appropriate interventions to alcoholics, we need to expose psychiatrists to sufficient cases and explore the factors that could attract them to this field.

PA-O04

Factors influencing drinking behavior during pregnancy in Korean women

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Introduction: Drinking alcohol during pregnancy can result in fetal alcohol spectrum disorder, malformation of the fetus, diverse behavioral problems in newborns, attention deficit hyperactivity disorder, and learning disorder. Nevertheless, few studies have been conducted in Korea to investigate alcohol consumption and factors influencing drinking behavior during pregnancy in Korean women. Therefore, a survey was conducted on pregnant women to investigate whether they drank alcohol and to identify factors predictive of drinking behavior during pregnancy.

Method: Pregnant women at less than 30 days before expected delivery who visited 3 obstetric and gynecology hospitals (a university hospital, a specialized hospital, and a clinic) were asked to complete a self-report questionnaire. Demographic (age, education, job, income, religion etc.) and obstetric characteristics (primipara or multipara, whether they wanted the pregnancy or not), and smoking history (cigarette smoking before and after the realization of pregnancy, frequency of smoking, average amount smoked and family history of smoking) were investigated, as were alcoholic history (consumption of alcohol before and after the realization of pregnancy, frequency of drinking, average amount consumed, and awareness that consuming alcohol during pregnancy is harmful).

Results: 1) Six hundred and ninety five subjects of average age 30.8±3.8 years were enrolled. 2) One hundred forty one subjects visited to a university hospital, 496 subjects visited to a specialized clinic, and 58 subjects visited to a clinic. 3) Of these subjects, 74.6% had completed up to high school education and 37.6% had a job. 67.9% were primiparous, and 99.4% were aware that

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consuming alcohol during pregnancy is harmful. 4) Five hundred seventy eight (83.2%) and 173 subjects (24.9%), respectively, consumed alcohol before becoming pregnant and after they were aware of being pregnant. 5) Ninety seven (14.2% of 685 subjects) and 20 subjects (2.9% of 689 subjects), respectively, smoked before becoming pregnant and after they were aware of being pregnant. 6) Those that had consumed alcohol before becoming pregnant (χ^2=107.21, p<0.001, OR=68.85), those that smoked before becoming pregnant (χ2=4.98, p=0.025, OR=3.31) and those with a family history of smoking (χ2=8.06, p=0.004, OR=2.29) were found to be more likely to drink alcohol when pregnant.

Conclusion: This study shows that a quarter of pregnant Korean women aware of their status consume alcohol, and that 3 factors, alcohol drinking before becoming pregnant, cigarette smoking before becoming pregnant and family history of cigarette smoking, are predictive of drinking behavior during pregnancy. These results strongly suggest that an anti-drinking educational strategy should be devised to target women of childbearing potential, in particular, those at high risk.

PA-O05

Telescoping effects in female alcoholic patients in Korea

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Introduction: Previous studies have shown that alcohol dependence develops in a shorter period of time in female alcoholics than in male alcoholics, even though female alcoholics start drinking at an older age. Such a phenomenon is generally referred to as a telescoping effect. However, there has been no report of a telescoping effect in female alcoholics in Korea. The goal of this study was to investigate whether there are telescoping effects unique to female alcoholic patients by comparison with male alcoholic patients in Korea.

Methods: A semi-structured interview was used to obtain information on the demographic characteristics and alcoholic histories of 229 alcoholics (167 male and 62 female alcoholics).

Results: 1) Although there were no differences in the age at onset of alcohol-related problems (ARP) and the age at first admission to a psychiatric hospital for ARP between the female (hereinafter female group) and male (hereinafter the male group) alcoholic patients, the female group started drinking at a significantly older age than the male group (p<.001). 2) The period from the age at which drinking started to the age at onset of ARP or to the age at first admission to a psychiatric hospital for ARP was significantly shorter in the female group than in the male group (p=.015, p<.001). 3) In the female group, the average age of the patients was younger (p=.038), the average number of drinks per drinking day during the 12 months before the present admission was smaller (p<.001), the number of patients with a history of severe alcohol withdrawal symptoms was greater (p<.001), and the number patients with a family history of alcohol dependence in a first-degree relative was greater (p=.045) than in the male group.

Conclusion: The results of the present study show that there is a telescoping effect in female alcoholic patients in Korea. Therefore, it is suggested that physicians, family members, and community members should pay more attention to female drinkers.

PA-T01

Healing Effects of the Forest Experience on Alcoholics

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   Purpose: The purpose of this study was to explore and describe healing effects of the forest on alcoholics through a forest experience program. **Methods:** The qualitative data was gathered from one focus group discussion with 6 alcoholics and individual interviews with 8 alcoholics. They had all participated in a "healing forest" program. All interviews were recorded and transcribed according to thematic content analysis processes. **Results:** The four main themes on the attributes of forest were "a lively living being", "placidity and tranquility", "acceptive atmosphere", and " beautifulness as it is" which revealed the participants' perceived nature of the forest which was attributed to the healing effects. Eight other themes on participants' positive changes included "revived senses", "aspired to live", "relieved and relaxed from being tense", "gaining insight on self", "having an acceptive attitude", "becoming compliant with his/her life", "learning that life is being together" and "recognizing the value of one's existence" **Conclusion:** The findings of the study illustrated the participants' self-healing processes through interactions with the nature of the forest. Nursing interventions utilizing healing atmospheres such as "healing forest" programs can be considered helpful in providing a venue to alcoholics to reflect on their lives affirmatively.

   Key word: Qualitative Research, Focus Groups, Individual Interview, Alcoholics, Forest

The Reliability of Measurment the Effectiveness of Therapeutic Community Programs to Alcoholics'Recovering.

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Objective: This study was conducted to test the reliability of Korean□version CAI(Client Assessment Inventory), CAS(Client Assessment Summary) and SAS(Staff Assessment Summary), which are the scales of the effectiveness of therapeutic community programs and, ultimately, to contribute to the utilization of the scales in measuring the effectiveness of Korean therapeutic community programs and to the development of therapeutic community programs in Korea. Methods: The subjects of this study were 224 alcoholics at 3 residential institutions with therapeutic community programs applying the DAYTOP model. The questionnaires used were CAI , CAS , and SAS. Internal consistency for testing the reliability of the instruments was measured in Cronbach`s alpha and total item correlation. Multiple comparison was made through one□way ANOVA. Results: In the results of the analyses, CAI had 87 questions in 13 sub areas, and both CAS and SAS had 14 questions. The reliability of the instruments was all over .06 except 'Emotional Skills' among the sub□areas of CAI. Overall reliability was .95 for CAI, .86 for CAS, and .94 for SAS. The results of one□way ANOVA indicate that both client and staff instruments reliably differentiate client clinical changes during treatment. Conclusions: With regard to areas and questions excluded from this study, further research is suggested through exploratory factor analysis on cultural differences of the assessment tools and their safety and through confirmatory factor analysis on the construct validity of the tools. In addition, because the overall reliability of CAI, CAS and SAS scales are considered applicable in Korea.

PA-T03

Assessing planning ability may help predict adaptability in patients with alcohol dependence

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Background: Since alcohol abuse leads to intellectual impairment, testing of cognitive function is important. Ito et al. (2008) reported that the Clock Drawing Test (CDT) is suitable for assessing alcoholics' cognitive function and that patients who drew the clock as planned had lower scores on Wechsler Memory Scale-Revised (WMS-R). This study examined the relation between drawing the clock in CDT and WMS-R.

Methods: Subjects were 378 male inpatients who participated in the alcoholism rehabilitation program for three months. The mean age was 48.22 years (SD = 9.26), and subjects had completed mean 12.84 years (SD = 2.64) of education. All subjects were tested using CDT, Mini-Mental State Examination (MMSE) and WMS-R approximately 9 weeks after admission. In this study, planned drawing of the clock was defined as drawing the dial showing 12, 3, 6 and 9 and hands from the center of the clock face. One hundred and forty subjects showed high CDT scores (> 8 points) and drew the clock as planned, while 52 subjects with high CDT scores but drew the clock unplanned.

Results: Comparisons using t-tests showed that 140 subjects had higher index scores of WMS-R than the 52 subjects. The former patients also had higher scores on 8 WMS-R subtests, especially "Mental Control" and "Logical Memory 1 and 2".

Discussion and Conclusions: Patients with high scores on CDT showed differences in WMS-R scores based on drawing the clock. Especially WMS-R subtests, which require ability to manage information, showed conspicuous differences. These subtests are related to ability to comprehend

various phenomena. In addition, many alcoholics showed impaired frontal lobe function early in alcohol abuse. These results suggested that measuring planning ability reflected in the frontal lobe could help assess alcoholics' cognitive function impairment and predict their adaptability to daily life.

PA-T04

A capacity building program for health-care professionals in southern Thailand in providing screening and brief intervention for harmful substance use

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Substance abuse is associated with multiple physical, emotional health and interpersonal problems. Only a small number of substance abusers, who need treatment, actually receive it in Thailand. Research has demonstrated that screening and brief intervention can promote significant reductions in alcohol and tobacco use and suggested some benefit for illicit or prescription drug use as well. The WHO Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) was developed in 1997 by the World Health Organization and specialist addiction researchers and has undergone significant testing in several countries, including Thailand. In response to the overwhelming public health burden associated with substance use in Thailand, the Southern Academic Network for Substance Abuse Research (SANSA), Prince of Songkla University has initiated a research and development project in 2008 with the aim to build the capacity of health-care professionals who work with substance abusing patients in hospitals in lower southern Thailand in providing screening and brief intervention for patients with harmful substance use. Fifteen nurses from community hospitals, substance abuse treatment and rehabilitation centers and a psychiatric hospital in five provinces of lower southern Thailand were invited to participate in the project as a core development team. A two-day training workshop on the administration of ASSIST-screening and brief intervention was held at the beginning of the project. All nurses then tried out the screening and brief intervention with outpatients in their hospitals. Meetings among nurses and research team were held every 2-3 months to discuss problems encountered in the use of ASSIST-screening and brief intervention in their actual practice. At the end of the initial study phase, a two-day meeting was held again to summarize the project and revise the Thai-translated ASSIST-

screening test and brief intervention manual to ensure that it is feasible, flexible, culturally relevant, and covers all commonly substances used in Thailand. All core development team nurses were challenged to find out the way to integrate ASSIST-screening and brief intervention in the routine clinical practice of their hospital, which is the ultimate goal of the project.

Poster Session

13 November (Fri) 2009

BA-G02

Effects of Alcohol and Acetaldehyde on Sustained Attention: Findings from the Alcohol Clamping in Healthy Japanese

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Previous studies have shown that alcohol impairs performance on a variety of complex tasks with divided attention. However, results of prior studies that examined the effects of alcohol on sustained attention are inconsistent.

It is well known that the inactive form of aldehyde dehydrogenase-2 (ALDH2), encoded by ALDH2*2, is a genetic protective factor for the development of alcohol dependence due to accumulation of acetaldehyde in the blood.

This background led us to hypothesize that the Continuous Performance Test (CPT), a popular method for evaluating sustained attention, can be used to examine the effect of alcohol and/or acetaldehyde on sustained attention. We also used the alcohol clamp method to administer alcohol and compared results between absence and presence of ALDH2*2. Alcohol clamping is a technique that maintains a constant breath alcohol concentration (BrAC) (50 mg %) for 3 hours by intravenous infusion of an ethanol solution.

Subjects were 102 healthy nonalcoholic Japanese. All participants provided written informed consent. CPT was administered before and one hour after start of infusion. Correct detections, made when a subject responded correctly to the target stimulus, were attributed to sustained

attention abilities. The number of correct detections was significantly decreased and the number of omission errors was significantly increased in subjects with ALDH2*2 when compared with those without ALDH2*2. In subjects without ALDH2*2, there were no significant differences in the number of correct responses and omission errors before and after infusion. These results indicate that acetaldehyde rather than alcohol affects sustained attention at this moderate blood alcohol concentration. However, because alcohol might affect sustained attention at higher blood alcohol levels, further studies are needed to reach firm conclusions.

BA-G03

Genetic association of DRD2 polymorphisms with anxiety scores among alcohol-dependent patients.

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The dopaminergic neurotransmission system is one of the major factors in development of alcoholism and also contributes to anxiety and depression. In this study, the associations of the dopamine receptor type 2 (DRD2) polymorphisms with the symptoms of anxiety were analyzed. A total of 573 alcoholics and 273 controls were enrolled in the study from the Korean population. Five DRD2 SNPs, including -32869 A>G, -32768 insdel C, +11890 C>G, +11915 C>T, and +32806 C>T, were genotyped using a TaqMan assay and analyzed with various alcoholic phenotypes. Although no DRD2 polymorphisms were associated with the risk of alcoholism, +32806C>T and Block2-ht1 showed associations (in dominant models) with both the state anxiety level scale (STAI-S) and the trait anxiety level scale (STAI-T) (P=0.004 and P=0.003, and P=0.01 and P=0.005, respectively). In addition, the -32768 insdel C also showed positive association with both anxiety level scales in recessive models (P=0.01 and P=0.02, respectively).

BA-G04

Gene expression profiling analysis involved in alcohol and naltrexone responses in murine hippocampus and prefrontal cortex

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Naltrexone is an opioid receptor antagonist to prevent alcohol craving and relapse. To elucidate action mechanism of naltrexone for the reduction of alcohol consumption, we have investigated gene expression profiling of mice with ethanol treatment for one month (with and without naltrexone) using Mouse gene 1.0 ST array (Affymetrix). All mice were supplied water and 10% alcohol with self-administration. Naltrexone (16 mg/kg) had been injected at every 3 days during the experiment. We have observed that naltrexone treated mice had taken less amount (50%) of alcohol. After one month we performed microarray experiment using RNA isolated from hippocampus and prefrontal cortex. The expression of 394 and 566 genes were changed of hippocampus and prefrontal cortex, respectively. We have obtained a few genes (including pkcd gene) which are upregulated in prefrontal cortex but not changed in hippocampus with naltrexone treatment in alcohol via IPA pathway analysis. Protein kinase C (PKC) helps to shape the level for

sensitivity to alcohol's behavioral effects through its interaction with GABA-A receptor. Naltrexone influences PKC neuronal signaling system in prefrontal cortex. In conclusion, naltrexone alters gene expression profile in the mice hippocampus and cortex that related to reduce alcohol consumption. The significant gene lists and pathways involved will be further examined in an attempt to elucidate the mechanism of action of nlatrexone.

BA-I01

Reduced activity in the anticipatory reward system and white matter abnormalities in pathological gambling: An event-related fMRI and DTI study

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Objective: The reward system has been considered involved in the pathophysiology of pathological gambling (PG). We examined the functional brain activity specific to the anticipation phase of situations involving rewards using event-related functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) to detect white matter abnormalities in patients with PG.
Method: Ten drug-naive patients with PG and 14 age-, and IQ-matched healthy controls participated in a modified monetary incentive delay task, in which visual cues predicted that a rapid button-pressing response during a brief target presentation would result in monetary gain, monetary loss, or no consequences during fMRI scanning. Symptom severity was assessed with Yale-Brown Obsessive Compulsive Scale for pathological gambling and the South Oaks Gambling Screen.
Results: Patients with PG showed reduced activation in the ventromedial caudate nucleus and the anterior cingulate cortex and increased activation in the posterior cingulate cortex when anticipating gain, and decreased activation in the anterior insula when anticipating loss. Reduced white matter fractional anisotropy in the brain regions consisting of dopaminergic mesolimbic circuits were also observed among those with PG.

Conclusions: Our results indicate that patients with PG might be less sensitive to anticipating positive and negative consequences; these findings were supported by white matter abnormalities in dopaminergic mesolimbic circuits.

BA-I02

PARAHIPPOCAMPAL-GYRUS ATROPHY IN PATIENTS WITH ALCOHOL-RELATED DEMENTIA

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Background: Alcohol dependence is one of the leading causes of disability worldwide and an epidemiological study for nursing home residents has showed that alcohol related dementia (ARD) is more common than previously thought. Although ARD is supposed to derive from direct ethanol intoxication and/or coexisting nutritional deficiency, liver disease, cerebrovascular disease or trauma, the biological basis of ARD has not been fully studied. Recent neuropsychological studies have demonstrated the both executive control and memory tests are impaired in ARD patients, suggesting the involvement of cortical and subcortical neuropathology. Here we conducted a study to clarify the contribution of parahippocampal atrophy to neurocognitive function in alcoholic patients.
Methods: Fifty alcoholic patients and age-matched 28 normal controls as well as 33 disease controls including 24 AD and 9 amnestic MCI patients were examined. Alcoholic patients were categorized into 4 groups: patients with normal cognitive function (n = 10), those with amnesia (n = 20), those with ARD including Korsacoff's syndrome (n = 10) and those with AD (n = 10) according

to MMSE scores and Clinical Dementia Rating Rating scale (CDR). Alcoholics with AD were defined as alcoholic patients who developed their cognitive decline even after abstinence and/or showed high CSF-tau levels. MRI was performed to estimate parahippocampal atrophy by using the Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD), developed as a diagnostic tool for early stages of AD. VSRAD is software based on SPM2 and gives mean Z-scores by region-of-interest analysis of the parahippocampal area as compared with age-matched standard brains. Serum folate levels were measured to assess nutritional status

Results: Alcoholic patients had higher Z-scores than normal controls subjects (2.3 ± 1.4 vs. 0.9 ± 0.4, $p < 0.0001$ by post-hoc after ANOVA). These high scores in alcoholic patients were comparable to those in AD (vs. 2.7 ± 1.0, p = NS.) and depended on the severity of cognitive decline (alcoholic patients with normal cognition: 1.2 ± 0.4, those with amnesia: 2.1 ± 1.0, with ARD: 3.0 ± 1.9 and with AD: 3.7 ± 1.5, $p < 0.0001$). Serum folate levels were more decreased in alcoholic patients than in AD (6.4 ± 3.5 vs. 10.5 ± 4.4 ng/mL, p = 0.004). However, the cognition status of alcoholic patients was not influenced by folate levels (alcoholics with vs. without cognitive deficits: 6.3 ± 3.4 vs. 7.5 ± 4.4 ng/mL, p = NS.).

Conclusions: Although alcoholics and AD patients have different pathological background, parahippocampal atrophy on MRI would be a powerful indicator for their cognitive deficits. Further, the remaining parahippocampal area may determine the reversibility of cognitive function in alcoholic patients by treatment including abstinence and nutritional repletion.

BA-M01

Influence of alcohol consumption on atherosclerosis in the hospitalized-based population

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Objective: To study the association between alcohol consumption and atherosclerotic risk factors in high risk group.

Participants: Consecutive 706 Japanese patients who were examined for carotid arterial findings by ultrasonography in our hospital [mean age, 68.3 ± 10.8 (range, 28-90) years, male/female = 508/198].

Measurements: Patients' characteristics, medical history, complications, biochemical markers, carotid arterial mean and max intima-media thickness (IMT), and questionnaire about alcohol habit.

Results: Fifty-five percent of the patients abstained from alcohol, 17.1% consumed fewer than 20 g of ethanol/day, 21.5% consumed 20-80 g/day, and 6.4% more than 80 g/day. The rate of obesity (0/0-20/20-80/80- g/day = 16.2/24.0/33.6/22.2%, P = 0.0002), hyper uremia (29.1/36.4/37.5/48.9%, P = 0.0216), history of ischemic heart disease (25.5/29.8/37.5/48.9%, P = 0.0016), and ischemic stoke (15.7/17.4/25.7/40.0%, P = 0.0002) were significantly elevated with the increase of alcohol consumption. A significant positive correlation was also found between alcohol consumption and serum triglyceride (P = 0.0040), uremic acid (P = 0.0008), ferritin (P < 0.0001), and hemoglobin level (P < 0.0001). Compared to the 0 or 0-20 g/day group, mean and max IMT were higher in the

20-80 or 80- g/day group (mean IMT = 0.88 ± 0.46/0.84 ± 0.43/0.96 ± 0.52/0.98 ± 0.58 mm, P=0.0492; max IMT = 2.34 ± 1.15/2.31 ± 1.10/2.63 ± 1.39/2.35 ± 1.20 mm, P = 0.0552). Conclusions: Alcohol consumption is associated with the multiple risk factors for arteriosclerosis progression in the hospitalized population. These findings support the recommendations that the alcohol consumption should not exceeded 20 g /day in the high risk group for atherosclerosis.

BA-N01

Disruptive effects of protein synthesis inhibitors on behavioral sensitization to single morphine exposure by Hsp70 in the mouse Nucleus Accumbens: mouse cAMP/Ca2+ signaling pathway RT-PCR array analysis

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Molecular accounts of neuroplasticity implicate the necessity of new protein synthesis for long-lasting changes in neuronal function. Behavioral sensitization to single exposure to addicting drugs is thought to be neuroplasticity, but little is known about the importance of new protein synthesis in behavioral sensitization. This study was to investigate the effects of protein synthesis inhibitors actinomycin D (AD) and cycloheximide (CHX) on behavioral sensitization to single morphine exposure in mice. In combination with behavioral experiments, changes of the gene expression in NAc were analyzed by RT-PCR array containing 84 genes and Western blot. Behavioral sensitization was well established in mice pretreated only once with morphine at the doses of 20 and 40 mg/kg, instead of 5 and 10 mg/kg. Mice pretreated only once with morphine (20 mg/kg) and challenged with the lower dose (5 mg/kg) after 4, 7, 14, 21 days, rather than 1, 2, 3 days of washout showed increased locomotion. At the doses that did not affect locomotion in mice, AD and CHX blocked the development, but not the transfer, of behavioral sensitization dose-dependently.

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Moreover, CHX, but not AD, significantly inhibited the expression of behavioral sensitization to single morphine exposure. RT-PCR array and Western blot indicated that the changes of Hsp70 expression in the NAc of mice were associated with the development of behavioral sensitization induced by single morphine exposure. Together, these findings suggest that the development of behavioral sensitization to single morphine exposure is protein synthesis-dependent, potentially involving Hsp70 expression in the NAc of mice.

BA-N02

Multifaceted Intervention for a case with Multiple Substance Abuse with Higher Cerebral Dysfunction

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This case report is about multiple drug abuse with higher cerebral dysfunction, for which the multifaceted approach was effective in a Japanese setting.

The subject is a 37-year-old male. He was brought up in a middle class family with both parents and two siblings. He started habitual drinking from the age of 17. He dropped out of high school. He started habitual thinner consumption between the ages of 18-20. He developed delusion and scoptophobia when he was 19. Year X-11, he was screaming on the street after an excessive amount of alcohol consumption and was involuntary admitted to a psychiatric hospital. From X-9 to X-7, he was in prison for using cannabis followed by DARC program. X-4, he returned to his hometown, but he started to drink alcohol, blackout and have severe behavioral problems then. X-1 family members left him home and the house was sold. X, March, he moved into an apartment alone and lived with limited financial support. He was able to keep his house clean and cook everyday meal but he also drunk often. March, X he was hit by car when walking drunk.

April X, he visited our outpatient clinic to get treatment for alcohol addiction. Although he was not drunk, he behaved arrogant and irritable. He expressed memory impairment and difficulty concentrating. However, he said he is perfectly healthy.

He was diagnosed as having multiple substance addiction with sequelae and higher cerebral dysfunction. Risperidone was effective for the irritability. However, since there was higher cerebral dysfunction, he was not able join any rehabilitation program for addiction. The welfare staff and the hospital implemented a rehabilitation program for him by using financial support, visiting and psychoeducation at the outpatient clinic. Multifaceted approach for both addiction and higher cerebral dysfunction was effective for his recovery.

BA-N03

The stem cell therapy as a possible new treatment for alcohol-induced brain damage

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Recently, it has been elucidated that cerebral morphological change is the key mechanism of various clinical conditions of psychiatric diseases including alcohol related disorders. The neurogenic and neurotrophic effects of psychotropics are considered to contribute to the prevention of reduction in brain volume. However, the precise mechanism and the way for suppression of brain morphological change have not yet cleared.

  In the previous study, we have reported the relations of deficits of neural network to the psychiatric disorders such as depression, schizophrenia, and alcohol-induced brain damage. We demonstrated the potentials of various kinds of emotional drugs and antipsychotics on the neuronal survival and neural stem cell (NSC) differentiation, and behavioral recovery of fetal alcohol spectrum disorder (FASD) and schizophrenia model rat by the NSCs transplantation, which is one of the promising new treatment strategies for treatment-resistant psychiatric disorders. We revealed that intravenously administrated NSCs were detected in the damaged brain area by visualizing a fluorescent marker. We also showed that NSC transplantation ameliorated behavioral abnormalities of these model rats.

In the present study, we analyzed the differentiation of transplanted NSCs to each phenotype of cells by immunofluorescence assay. We found that transplanted NSCs had the potential to differentiate to neurons and glias. We also investigated the maturation of neurons in the brain those were differentiated from transplanted NSCs. We indicated the synaptic formation of transplanted cells by showing the dendritic spine morphogenesis using antibody for microfilament-associated protein, drebrin. Furthermore, we investigated the effect of exogenous NSCs on the neuronal survival and NSC differentiation in vitro, and suggested the trophic factor signaling change in neurons and NSCs without cell-cell contact, which may be suggested a mechanism of contribution to the neural network repair by the NSC transplantation in vivo.

These results may suggest that the NSC transplantation may be a possible approach to recover the brain damage of neuronal network and CNS dysfunction in psychiatric disorders including FASD, and the intravenously transplanted NSC could contribute to the neural network repair through the functional cells and trophic effects in the brain.

BA-N04

Molecular mechanisms of alcohol-induced neuronal damage to the developing brain: The role of neuron-restrictive silencer factor (NRSF/REST)

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Background: Alcohol is a well-known cytotoxic agent which causes various kinds of neuronal damage. Fetal alcohol spectrum disorders (FASD) are a cluster of behavioral and morphological abnormalities observed in children born to mothers with histories of heavy alcohol consumption during pregnancy. Fetal alcohol syndrome (FAS) is the most clinically recognizable form of FASD and is characterized by a pattern of minor facial anomalies, prenatal and postnatal growth retardation, and cognitive and behavioral abnormalities. In this study, we investigated the molecular mechanisms underlying the altered cell viability and inhibited neuronal differentiation induced by the alcohol treatment by using neural stem cells (NSCs). Further, we examine the effects of lithium, a mood stabilizer, against such inhibitory effects of alcohol.

Methods: The cells were cultured from Wistar rat embryos. The effects of ethanol on the differentiation from NSC into neuron were evaluated by cell counting after immnostaining with neuronal markers, MAP-2 or Tuj-1, and also with their ELISA which is a less complicated and more objective measure to assess neuronal differentiation. The binding activity of neuron-restrictive silencer factor (NRSF), a transcription factor that mediates negative regulation of neuronal genes, was measured by using a NoShift transcription factor assay system (Novagen). The expression of

NRSF, and molecules on the extracellular regulated kinase (ERK), a member of the mitogen-activated protein (MAP) kinase family, were investigated by using Western blot analysis.

Results: Ethanol enhanced NRSF binding activity and decreased neuronal differentiation in a concentration dependent fashion at doses which did not affect cell survival. Western blot analysis revealed that ethanol suppressed phosphorylation of ERK without affecting expression of total ERK. Lithium itself increased neuronal differentiation and decreased ethanol-induced suppression of neuronal differentiation of NSCs. Furthermore, lithium reduced the DNA binding activity and protein level of NRSF enhanced by ethanol.

Discussion: Ethanol is a deleterious agent that causes various kinds of neuronal damage, especially to the developing brain. Ethanol inhibited neuronal differentiation, decreased phosphorylation of ERK and elevated NRSF binding activity. Our previous studies demonstrated that the inhibition of ERK with an inhibitor of MEK (U0126) suppressed neuronal differentiation and potentiated NRSF binding activity. These results suggest that the enhancement of NRSF binding activity underlies the mechanism of ethanol inhibition of neuronal differentiation and decreased neurogenesis, i.e. generation of new neurons. The neuroprotective effects of lithium against neurotoxic agents have been demonstrated in various in vitro and in vivo studies. In our studies, lithium reduced the DNA binding activity and the protein level of NRSF enhanced by ethanol exposure. Taken together, we speculate that lithium may be efficacious in the treatment of ethanol-induced neurological deficits and mood disorders observed in the subjects with alcohol related problems.

BA-N05

Small heat shock proteins regulated by alcohol on the differentiation of mouse embryonic neural stem cells

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Neural stem cells (NSCs) from neuroepithelium differentiate along one of three central nervous system (CNS) cell lineages, neurons, astrocytes, and oligodendrocytes. In this study, the differentiation potential of NSCs from forebrain of embryonic day 15 (E15) mouse embryos was analyzed using immunocytochemistry. And then NSCs were early differentiated in the presence and absence of ethanol (50 mM) and gene expression patterns among NSCs, differentiated cells and ethanol-treated differentiated cells were observed using the microarray and real-time PCR. We found that genes related to Wnt signaling pathway including Ctnna1, Wnt5a, Wnt5b, Wnt7a, Fzd3, and Fzd2, genes related to cell adhesion including Cadm1, Ncam1, and Ncam2, and genes of small heat shock proteins including Hspb2, Hspb7, and Hspb8 were up-regulated at both differentiated cells in the presence and absence of ethanol as compared to NSCs. Especially, Hspb2 and Hspb7

were more increased at ethanol-treated differentiated cells than at differentiated cells. Also, we analyzed the gene expression of heat shock transcription factors (HSF), proteins regulating the transcription of heat shock genes. Hsf2 and Hsf5 were increased at both differentiated cells in the presence and absence of ethanol as compared to NSCs. Of them, especially Hsf5 at ethanol-treated differentiated cells was higher up-regulated than that at differentiated cells in the absence of ethanol. These results imply that Hspb2 and Hspb7 known as small heat shock proteins showing tissue-restricted expression may be up-regulated by ethanol during early differentiation of NSCs and might in part be in connection with defective astroglial and neuronal functions in fetal alcohol syndrome.

Keywords: neural stem cells, alcohol, differentiation, small heat shock protein, heat shock transcription factor.

BA-N06

Acetaldehyde Metabolism During Maintenance of Constant Blood Alcohol Levels by the Alcohol Clamping

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Alcohol and acetaldehyde metabolism is a biological determinant that can significantly affect drinking behavior and alcohol-related organ damage. Aldehyde dehydrogenase-2 (ALDH2) is regarded as responsible for the oxidation of most of the acetaldehyde generated in alcohol metabolism. In many Asians, the inactive form of this isozyme exists and leads to a high concentration of acetaldehyde in the blood following alcohol consumption, which causes an intense flushing response. It is well known that the inactive form of ALDH2, encoded as ALDH2*2, is a genetic protective factor for the development of alcohol dependence.

In most previous studies on alcohol metabolism, subjects were administered alcohol orally. However, single oral alcohol administration can not keep blood alcohol levels constant and it differs from actual drinking behavior in most drinkers. In typical actual drinking behavior, blood alcohol levels might be maintained at certain levels for a while. Therefore, we kept blood alcohol levels constant by alcohol clamping, measured blood acetaldehyde concentrations and compared acetaldehyde levels between subjects with ALDH2*2 and those without ALDH2*2.

Alcohol clamping is a technique that maintains a constant breath alcohol concentration (BrAC) (50 mg %) for 3 hours by intravenous infusion of an ethanol solution.

Subjects were 38 healthy nonalcoholic Japanese. All participants provided written informed consent. Genomic DNA was extracted from peripheral leukocytes using the standard method and genotyping of ALDH2 was performed using polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP). Blood was drawn before infusion and 30, 60, 120 and 180 minutes after start of infusion to determine blood acetaldehyde concentration using by head-space gas chromatography.

In subjects with ALDH2*2, blood acetaldehyde levels were more than five times higher than those without ALDH2*2 at each time point. In subjects with ALDH2*2, blood acetaldehyde levels increased in proportion to increasing alcohol levels until 30 minutes after start of infusion. However, it decreased even though blood alcohol concentrations were maintained within 50 ± 5 mg%.

As far as we know, this is the first study which examined acetaldehyde levels while keeping blood alcohol levels constant. We assume that induction of ALDH2 might occur during maintenance of constant blood alcohol levels. However, we need further studies including expression of ALDH2 to reach firm conclusions.

BA-N07

DNA methylation of the Serotonin transporter promoter in Alcohol dependence.

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Psychiatric disorders such as Depression, Anxiety disorder and alcohol dependence are thought to be associated with serotonin metabolism. We assessed 5-HTT promoter methylation level of the Alcohol dependence patients and Controls. Fifteen male patients who met the Diagnostic and Statistical Manual of Mental Disorder IV (DSM-IV) criteria for alcohol dependence were compared with 27 controls. Bisulfate modification were done and PCR assays were designed to amplify a part of the CpG islands in the 5HTT gene. Pyrosequencing were done and methylation level of seven site of CpG island were measured. We found no difference in the methylation patterns of the serotonin transporter promoter region between the alcohol dependence and control. However it has been reported that trend of an increased average methylation from l/l type to s/s genotype are evident only after 5HTTLPR genotype is taken into account. Our negative finding may due to 5HTT epigenetic variation as fine regulation mechanism of Serotonin receptor expression.

Increased plasma brain-derived neurotrophic factor and nerve growth factor in the patients with alcohol dependence

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Alcohol has a neurotoxic effect on the brain, such as learning and memory impairment. Brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) are thought to be related to neuroprotection in cell culture and animal studies. Our aim is to verify the changes in human plasma BDNF and NGF concentrations induced by chronic alcohol use.
Forty-one male patients with alcohol dependence were sampled within 24 hours after last drink and compared with 41 healthy male subjects. Plasma BDNF and NGF were assayed using an enzyme-linked immunosorbent assay (ELISA).
Mean plasma BDNF level was significantly higher in the patients with alcohol dependence (3502.21 ± 1726.9 pg/ml) compared with the healthy subjects (861.75 ± 478.9 pg/ml) (p=0.000). Mean plasma NGF level was also significantly higher in patients with alcohol dependence (137.64 ± 32.7 pg/ml) than in healthy subjects (112.61 ± 90.2 pg/ml) (p=0.012).
Increased plasma BDNF and NGF in alcohol-dependent pat

BA-N09

Increased transforming growth factor-beta1 in alcohol dependence

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Ethanol and its metabolite acetaldehyde increase TGF-β1 expression in animal studies. TGF-β1 is related with the hepatic stellate cell (the key element of hepatic fibrogenesis) and the radial glia (the key element of neuronal migration). We aimed to find the increase of TGF-β1 in human alcoholism blood plasma. Blood samples were collected from 41 patients with alcohol dependence, TGF-β1 levels measured by ELISA were compared with 41 normal subjects. Plasma TGF-β1 levels in the patients with alcohol dependence (1653.11 ± 532.45 pg/ml) were significantly higher than those of healthy subjects (669.87 ± 366.53 pg/ml) ($p = 0.000$). This is the first evidence in human that increased TGF-β1 in alcoholics may mediate deleterious effect of alcohol such as hepatic fibrosis and suppressed neuronal developments.

Ethanol consumption is decreased by downregulation of NK1R using RNA interference.

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Neurokinin 1, a biologically active peptide belonging to the tachykinin family, is highly expressed in brain areas involved in stress responses and drug reward. Recent findings suggest that blockade of NK1Rs might modulate alcohol self-administration. We tried to specifically induce knockdown of NK1R gene in mouse brain using RNA interference (RNAi) and examined the effect on alcohol consumption. Lentiviruses expressing either a shRNA targeting NK1R or a control shRNA were injected into mouse brain. And we examined for ethanol consumption in a two-bottle choice experiment. One month after shRNA induced specific knockdown of NK1R mRNA and protein in the brain, voluntary alcohol intake by NK1R shRNA injected mice was markedly lower than that by control. RNAi induced specific knockdown of genes related with alcoholism. Our result suggests

that RNAi technology may provide the basis of therapeutic potential for alcoholism treatment.

BA-N11

Changes in plasma brain-derived neurotrophic factor levels in smokers after smoking cessation

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Several studies have reported that brain-derived neurotrophic factor (BDNF) might be associated with nicotine dependence. However, there are few studies on BDNF levels in humans with nicotine dependence. In the present study, we compared the differences in plasma BDNF levels in patients with nicotine dependence and in healthy nonsmokers, and we investigated serial changes in plasma BDNF levels in patients with nicotine dependence following smoking cessation. Forty-five voluntary smokers and sixty-six nonsmokers were recruited in this study. Of the 45 smokers, 12 were taking varenicline, 21 were using a nicotine patch, and 12 were unaided in their cessation effort by their own choice. Plasma BDNF levels were measured at baseline using an enzyme-linked immunosorbent assay (both smokers and nonsmokers) and at week 4 and week 12 after smoking cessation (abstinent smokers only). A total of 19 smokers were able to remain abstinent during the entire study period. Baseline plasma BDNF levels were significantly lower in smokers compared to nonsmokers (F=4.410, P=0.002). The plasma BDNF levels in the abstinent smokers significantly increased from baseline after four weeks of smoking cessation (z=-2.86, p=0.004) but had a tendency of decrease in the period between weeks 4 and 12. We could not find differences in the plasma BDNF levels among the three smoker subgroups at week 12 following cessation. Changes

in plasma BDNF levels might be related to the process of abstinence and the pathophysiology of nicotine dependence.

BA-N12

The effect of BDNF on alcoholism and diabetes

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Background: It was well reported that both alcoholism and type 2 diabetes were related to a decreasing level of BDNF. Also, there were many clinical researches that chronic alcohol consumption contributed to an increase of the incidence of type 2 diabetes. According to this information, we hypothesized that BDNF may be the main factor which elevates the risk of diabetes in alcoholic models.

Methods: Therefore, we used 10-week-old male OLETF rats which have type 2 diabetes and non-diabetic control male LETO rats of similar weight. The rats were randomized by weight into four treatment groups (n=13-15): 1) OLETF-Control (n=15), 2) OLETF-Alcohol (n=15), 3) LETO-Control (n=14), 4) LETO-Alcohol (n=13). Rats in the alcohol-fed group were fed with a liquid alcohol diet over 6 week period. And control rats consumed an isocaloric liquid diet with a liquid control diet. We used pair-feeding control with a synchronized pellet pair-feeding apparatus in order to regulate different caloric intake. After 6 week feeding, we did Intraperitoneal Glucose Tolerance Testing (IP-GTT) to elucidate the deterioration of type 2 diabetes and evaluated the blood BDNF level.

Results: According to IP-GTT data, fasting glucose level of alcohol-fed groups was a little less than that of control group. However, 30 minute-glucose levels showed different pattern from each group.

The glucose level of OLETF-Alcohol group is significantly higher than OLETF-Control group (mean +_ SD 95.154+- ### mg/dl, mean+_SD 102.179mg/dl respectively, p<0.05). And after 120 minutes, the glucose level of OLETF-Alcohol group was not reduced to the baseline and remains higher (150.533mg/dl, p<0.05). Also, the level of BDNF in OLETF-Alcohol group was significantly lower than other groups(p<0.05).

Conclusions: We determine that this data means chronic alcohol consumption deteriorates the type 2 diabetes but showed different characteristic of diabetes from normal type 2 diabetes. Also, we inspect that the main factor which regulates this pattern is BDNF.

BA-N13

AMP-activated protine kinase antagonizes TGF-b-induced fibrogenic responses of hepatic stellate cells

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Hepatic stellate cell (HSC) is a key cellular element involved in the development of liver fibrosis. In response to chronic alcohol consumption-induced liver injury, quiescent HSCs undergo transdifferentiation from lipid-storing pericytes to activated myofibroblast-like cells producing extracellular matrix components. Activation of adenosine monophosphate-activated protein kinase (AMPK) is closely related with the modulation of HSC activation, but the molecular mechanism remains to be elucidated. We here report that AMPK modulates the fibrogenic property of HSCs by targeting p300 transcriptional co-activator. In human and rat HSC line, pharmacological activation of AMPK by treatment with 5-aminoimidazole-4-carboxamide-1-beta-4-ribofuranoside (AICAR), metformin, or adiponectin decreased the expression of extracellular matrix proteins type I alpha collagen (COL1A1) and myofibroblast phenotype marker alpha-smooth muscle actin (a-SMA) in the presence or absence of TGF-beta stimulation. Transient transduction of constitutive active AMPK (caAMPK) was sufficient to attenuate the expression of COL1A1 and a-SMA, whereas AMPK inhibitor considerably abrogated the antagonistic effect of AICAR on COLA1A2 promoter activity, demonstrating that active AMPK antagonizes the fibrogenic responses of HSCs. AMPK activators

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significantly suppressed TGF-beta-induced transcription driven by Smad-binding elements (SBE); however, it failed to prevent TGF-beta-stimulated phosphorylation, nuclear localization and DNA binding affinity of cellular Smad. We found that AMPK interrupts the physical interaction between Smad3 and p300 by a direct association with p300, resulting in decline of subsequent acetylation and transcriptional activity of Smad3. AMPK also decreased p300 protein levels via post-transcriptional regulation. Collectively, these results suggest that AMPK modulates TGF-beta-induced fibrogenic responses by targeting p300 transcriptional co-activator in HSCs.

BA-N14

Identification of post-transcriptional and post-translational regulatory mechanisms in the synaptic proteome of human, cirrhotic-alcoholic brain

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Hepatic complications are a common side-effect of alcoholism. Without the detoxification capabilities of the liver, excess alcohol induces changes in protein expression throughout the body and brain. Proteomics was used to identify these protein changes in the brain. We utilised post-mortem human brain tissue from the superior frontal gyrus (SFG) of six cirrhotic-alcoholics, six uncomplicated alcoholics and six non-alcoholic and non-cirrhotic controls. Synaptic proteins were used in two-dimensional differential in-gel electrophoresis coupled with mass spectrometry. Many expression changes occurred only in either cirrhotic or non-cirrhotic alcoholics when compared to controls, suggesting that that an alcoholic with cirrhotic complications may be responding to excessive drinking in a different manner to non-comorbid alcoholics. This was reiterated with the

additional comparison of cirrhotic to non-cirrhotic alcoholics which showed that protein expression profiles within the SFG of these two alcoholic types were very different. There were many proteins identified in more than one spot on the 2D-gel indicating the presence of multiple protein isoforms caused by either post-transcriptional (i.e. splice variants) or post-translational regulation (i.e. protein modification). For some of these proteins, isoforms showed alcoholic-type-specific expression changes. For example, two isoforms of 70 kDa heat shock protein 1 were identified; one isoform was altered only in cirrhotic alcoholics when compared to controls, while the other was altered only in non-cirrhotic alcoholics. These types of proteins will be discussed in relation to post-transcriptional and post-translational regulatory mechanisms at work on proteins in the human alcoholic brain. (Supported by NIH-NIAAA AA12404).

BA-N15

Quantification of the expression of N-methyl-D-aspartate receptor NR1 splice-variants in the cortex of human alcoholics.

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Ethanol is a modulator at the N-methyl-D-aspartate class of glutamate receptors (NMDAR) in the brain. NMDAR consists of a combination of NR1 and NR2 subunits. The NR2 subunits are encoded by a number of different genes to generate diversity. In contrast a single gene with a number of splice-variants encodes the NR1 subunit. These variants are generated by the absence or presence of exons 5, 21, 22 and 22' and have been shown to influence the response of NMDAR to ethanol. In animal studies the receptor adapts to sustained ethanol exposure through altered expression of the subunits that make up the receptor complex. We used real-time RT-PCR, interpolated to known standards, to assay the 4 C-terminal splice variants of the NR1 subunit mRNA in superior frontal and primary motor cortex tissue obtained at autopsy from chronic alcoholics with and without co-morbid cirrhosis of the liver, and from matched controls. The level of expression of the NR1-2 variant was significantly lower than all other variants independent of area or pathology. The NR-3 and NR-4 variants were the most highly expressed. All variants were expressed at a markedly lower level in alcoholics compared to controls in both areas. This was also seen for the cirrhotic alcoholics with the exception of the NR1-4 variant in the motor cortex where levels were similar to controls.

These data show that chronic alcoholism can influence the expression of NR1 subunits and that, in contrast to our previous findings; cirrhosis only has a minor influence.

BA-N16

State alcohol craving is associated with plasma leptin and craving for smoking

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Appetite-regulating and stress hormones have received much attention in alcohol research in recent years, due to their potential involvement in the regulation of alcohol consumption patterns and craving level. Blood leptin concentration is positively correlated with self-reported alcohol craving [1–3], but the relationship between craving states for alcohol, smoking, food and water with leptin levels have not been explored. We examined the associations among these craving states, and with cortisol and leptin concentrations, in alcoholics in early withdrawal. Alcohol-dependent subjects (46 males, 35 females; 60 were smokers) were recruited during detoxification treatment. On day 4 of withdrawal, subjects were instructed to fast overnight. A self-report state measure, Alcohol Urge Questionnaire (AUQ), was used to measure craving for alcohol on the next morning, before breakfast. Craving scores for smoking (smokers only), food and water were concurrently assessed using an AUQ-derived questionnaire. Saliva and fasting blood samples were collected immediately afterward. To date, cortisol and leptin levels have been determined for 26 and 17 subjects respectively by ELISA. Alcohol craving was significantly correlated with smoking craving ($r = 0.338$;

P = 0.008), but alcohol correlations with food and water craving were negative and nonsignificant (r = -0.149, -0.192; P = 0.185, 0.082). A significant correlation was found between levels of craving for food and water (r = 0.248; P = 0.026). BMI-corrected plasma leptin level showed a positive linear correlation with alcohol craving, but not with other craving measures. Salivary cortisol levels did not significantly correlate with any craving measure, nor with plasma leptin levels. These preliminary results suggest that state alcohol craving may be positively correlated with smoking craving and plasma leptin level in alcoholics during early withdrawal. A correlation between cortisol level and state alcohol craving was not supported. Supported by NIAAA; AMC is a UQIPRS scholar.

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BA-N17

ASSOCIATION BETWEEN ALCOHOL-RELATED GENE POLYMORPHISMS AND ALCOHOLIC LIVER CIRRHOSIS IN KOREAN POPULATION

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Aim: Recent studies have implicated that genetic susceptibility play a major role in development of alcoholic liver cirrhosis (LC) in alcohol-dependent patients. We investigated the possible association between allelic variants of Glutathione S-Transferase M1 (GSTM1), Cytochrome p450 2E1 (CYP2E1), Manganese Superoxide Dismutase (MnSOD), Aldehyde Dehydrogenase 2 (ALDH II) and Alcohol Dehydrogenase 2 (ADH II) genotypes and alcoholic liver cirrhosis.
Method: Peripheral blood samples were collected and white cell genomic DNA was extracted from 146 alcohol-dependent patients (with or without hepatic cirrhosis) and 150 healthy controls, which was then studied for the genotypes GSTM1, CYP2E1, MnSOD, ALDH II and ADH II and the occurrence of allelic variants using allele-specific polymerase chain reaction amplification and restriction fragment length polymorphism (RFLP) analyses.
Results: Demographic and clinical characteristics did not significantly differ between LC patients and non-LC patients regarding variables, such as age, sex, tobacco use and age of withdrawal symptoms underwent initially. C1/C1 of CYP2E1, V/V of MnSOD and 1 * 1 of ALDH II

polymorphisms were presented frequently in Korean population with statistical significance. Furthermore, no evidence was observed that the distribution of the GSTM1, CYP2E1, MnSOD, ALDH II or ADH II genotypes differed between the subjects with LC patients and non-LC patients, but with normal controls altogether, alcohol-dependent patients were associated with ALDH II and ADH II genotypes.
Conclusion: These findings indicate that the alcohol-related genetic polymorphisms currently suggested, were not associated with the development of alcoholic hepatic cirrhosis in Korean alcohol-dependent patients.

BA-N18

Useful Smoking Biomarkers for Studies of Human Exposure to Secondhand Smoke

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Background: Nicotine and its major metabolite cotinine are commonly used as smoking biomarkers, and they can be determined in various biological specimens including urine, saliva, serum, and hair. Direct measurement of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), a potent carcinogen in tobacco smoke, in human urine was recently introduced as a useful biomarker of carcinogen exposure. Here we introduce sensitive methods for the simultaneous determination of nicotine and cotinine in hair, and for NNAL in urine.

Methods: For hair nicotine and cotinine, one mg of hair was cut into fine segments and extraction was done with 2 mL of diethyl ether. The extracts were evaporated under 0.3% of methanolic HCl

and dissolved in 50 µL of mobile phase comprised of methanol/water. For NNAL, 5 mL of urine was extracted and reconstituted in 125 uL of 10% methanol containing 12 mM HCl. Finally, these extracts were analyzed on the LC-MS/MS (API 4000). The limit of detection (LOD), limit of quantification (LOQ), precision, and recoveries of each method were assessed.

Results: For hair nicotine and cotinine, LOD/LOQ were 0.16/0.28 ng/mg hair, and 0.07/0.10 ng/mg hair, respectively. The coefficients of variation (CV) were 6.6~13.4% for nicotine and 4.6~10.2% for cotinine, respectively. Recoveries were 93.5~102.6% for nicotine, and 77.2~105.0% for cotinine, respectively. For NNAL, LOD/LOQ were 0.19/0.44 pg/mL, CVs were 3.1~10%, and recoveries were 94.2~99.5%.

Conclusions: Our methods allow a very sensitive and reliable measurement of nicotine and cotinine in hair, and NNAL in urine. Thus, these would be very useful tools for studies of human exposure to secondhand smoke.

BA-N19

Exposure to Paternal Smoking at Home in Neonates, Children, and Their Mothers

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Background: Exposure to secondhand smoke (SHS) is a major risk to human health, and the home is the greatest single source of SHS in children. Here, the authors investigated SHS exposure to paternal smoking in neonates, children, and their mothers.
Methods: Subjects were included as trios of fathers, mothers, and children. Sixty-three trios for neonatal exposure, and two hundred-five trios for children's exposure were enrolled in this study, respectively. Nicotine concentrations in hair were measured using liquid chromatography-tandem mass spectrometry to determine long-term exposure to SHS.

Results: For neonatal exposure, the difference between neonatal nicotine concentrations in the smoker and nonsmoker groups was not statistically significant. However, in the indoor-smoker group, neonatal nicotine concentrations were significantly higher than in the outdoor and nonsmoker groups. For children's exposure, differences between the smoker group and nonsmoker group in nicotine levels were statistically significant in both children and their mothers. However, difference between the indoor-smoker group and outdoor-smoker group was marginally significant in children and was not significant their mothers. In the indoor-smoker group, preschool children and their mothers had nicotine concentrations about twice as high as school children and their mothers, respectively. In the outdoor-smoker group, however, differences between two age groups in nicotine levels were significant in children, but not their mothers.

Conclusion: These findings indicate that paternal smoking at home leads to significant exposure to SHS in neonates and children as well as their spouses, which is not completely prevented by smoking outside. Especially, young children and their mothers appear to be most at risk for SHS exposure among nonsmoking household members.

BA-N20

The effects on the human body from the cessation of smoking

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Purpose: Cigarette smoking has clearly been identified as an independent major risk factor of atherosclerosis, coronary heart disease and myocardial infarction. Epidemiological studies have also shown that smoking cessation reduces morbidity and mortality from coronary heart disease. Smoking has also been shown to be associated with insulin resistance in non-diabetic as well Type 2 diabetic subjects, impaired oral fat tolerance, impaired intravascular lipolysis and dyslipidemia that is characterized by an atherogenic lipoprotein phenotype, with increased triglyceride and low high density lipoprotein cholesterol concentrations(HDL) and a preponderance of low density lipoprotein cholesterol(LDL). However there was little study for the effect of smoking cessation on lipid profile and the results were also inconsistent. We evaluated whether smoking cessation had an effect on insulin resistance, lipid profile, and hormonal changes in healthy male Korean smokers.

Methods: 20 male volunteers aged 28-52 years (mean 39) entered this study. A modified form of semi-structured interview based on the Diagnostic Statistical Manual of Mental Disorder IV was conducted by 2 board-certified psychiatrists. All the participants had no alcohol, illegal drugs, mental, or physical illness except for nicotine dependence. The severity of nocotine dependence was evaluated by Fragerstom Test for nicotine dependence. In order to minimize the influence of

alcohol and caffeine on lipid profile, all participants were instructed not to drink more than 5 standard drink a week and one cup of coffee a day and not to change their eating habits during the study period. All the study period, non of them had taken any medication or nicotine patch. During the study period, smoking abstinence was evaluated through a self-report and the urine cotinine level. The urine cotinine levels of all subjects were monitored three times, before cessation, after 1 month, and after 2 months. Among 20 participants, 12 smokers succeeded in quitting smoking (validated by urine cotinine level = 40?/?) whereas 8 smokers did not. Thus analyzed subjects were only 12 smokers. Blood sampling was withdrawn from the participants twice, at the baseline and after 2 months. At 7:00 a.m. after overnight fast, a sample of blood taken from all subjects to measure levels of plasma glucose, HDL, total cholesterol, and triglyceride.

Using the fasting glucose and insulin data obtained , we calculated the Quantitative Insulin Sensitivity Check Index(QUICKI) and the homeostasis model assessment-insuline resistance(HOMA-IR) as measures of insulin action. Insulin secretion was assessed by homeostasis model assessment β-cell function (HOMA-β) from data obtained at fasting state.

Results: The body weight increased during smoking cessation (2 months) (P=0.029) and waist circumference increased (P= 0.020), the fat component increased among the compositions of body more than muscle. LDL level decreased significantly (p=0.028) after smoking cessation, however change of HDL and triglyceride not significantly. The level of albumin and total protein were significantly lower after smoking cessation than before. During the smoking cessation , HOMA- IR and HOMA-β increased , QUICKI decreased significantly. Also insuline secretion increased.

Conclusion: Initial stage of smoking abstinence, it showed that Body weight , fat composition of body, insulin resistance, insulin sensitivity increased. Otherwise insulin secretion increased and LDL decreased therefore disadvantage after smoking cessation could be offset by increased insulin secretion and lowering LDL. For the reinforcement of smoking cessation , it could be need that patient was educated by the diet control, muscle and aerobic exercise.

BA-N21

In vivo evidence for long-term CNS toxicity associated with chronic binge use of methamphetamine

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The aim of this study was to examine disturbances in regional cerebral blood flow (rCBF) associated with methamphetamine abuse. Using Single Photon Emission Computed Tomography,

rCBF was measured in 20 men who had previously injected methamphetamine intravenously for over 30 months and who were now abstinent for a minimum of 9 months and for an average of 2 years. Values were compared with those in 12 healthy men who had never injected methamphetamine. Whole brain CBF was significantly reduced in the former methamphetamine users, although rCBF was significantly and disproportionately reduced in subcortical and dorsal cortical brain regions, including the striatum, thalamus, cingulum, mesiodorsal prefrontal cortex, and pons (all t's>8.3 after global normalization, corrected p's<0.001). Binge use of methamphetamine produces long-term changes in global and regional blood flow. Likely representing severe and enduring neural toxicity of monoaminergic neurotransmitter systems in the brain, producing a pattern of hypoperfusion that resembles patterns reported previously for persons with atypical Parkinson's disease. These findings suggest that methamphetamine abusers may be at increased risk for neurodegenerative diseases later in life.

BA-N22

Up-regulation of cocaine- and amphetamine-regulated transcript (CART) in the rat nucleus accumbens after repeated electroconvulsive shock

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Cocaine- and amphetamine-regulated transcript (CART) peptide regulates appetite, reward, and mood. CART expression is regulated via the protein kinase A (PKA) pathway, and electroconvulsive shock (ECS), an efficient antipsychotic and antidepressant measure, activates PKA-related signaling. Thus, we hypothesized that ECS may regulate the expression of CART. ECS given daily for 5 consecutive days increased the mRNA and protein of CART in the rat nucleus accumbens (NAc), accompanied by an increase in CREB phosphorylation. Our results suggest that ECS-induced CART up-regulation could be associated with PKA-CREB signaling, whereas the causal relationship remains to be elucidated in future studies.

Key words:
CART, CREB, depression, electroconvulsive shock, nucleus accumbens

BA-N23

The regulation of ERK, GSK3β and AKT after acute ethanol exposure and withdrawal in SH-SY5Y human neuroblastoma cell-line

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Objectives: The aim of this study was to demonstrate the activity/phosphorylation changes of intracellular signal transduction molecules such as extracellular signal regulated kinase (ERK), glycogen synthase kinase 3β (GSK3β) and AKT induced by acute ethanol treatment and withdrawal conditions in SH-SY5Y neuroblastoma cell line.

Methods: For acute treatment, SH-SY5Y cells were exposed to 100mM ethanol and the samples were taken 30, 60 minutes and 24 hours after the beginning of the treatment. Ethanol withdrawal session was initiated 24 hours after a continuous ethanol treatment, and the samples were taken at 30 and 60 minutes. Kinase phosphorylations were assayed by the immunoblot analysis using phosphor-specific antibodies, and quantified by optical densitometry.

Results: Ethanol treatment induced transient increase in the phosphorylation of GSK3β and AKT at 30 minutes, but failed to change the level of phosphorylation of ERK. Withdrawal of ethanol induced transient increase of phosphorylation of ERK at 30 minutes, but had no effect on phosphorylation of GSK3β, AKT.

Conclusions: The results indicate that ethanol induced cellular response includes ERK, GSK3β, AKT systems. Especially, ERK pathway may play a role in acute withdrawal response. It also suggests that relatively short exposure of ethanol, that is 24 hours in this study, can induce the functional adaptation of cell.

Key words: ethanol, treatment, withdrawal, ERK, GSK3β, AKT, phosphorylation

BA-N24

Effect of N-methyl-D-aspartate Glutamate Receptor Antagonist, Memantine, on Alcohol Intake in C57BL/6 Mice

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Introduction: Previous studies reported that the N-methyl-D-aspartate (NMDA) receptor is associated with the development of withdrawal or tolerance in alcohol-dependency. However, it is controversial whether NMDA receptor antagonists are effective in preventing relapse in alcohol-dependent patients or not. The purpose of this study was to investigate the effect of memantine, a NMDA receptor antagonist, on alcohol intake in alcohol-preferring C57BL/6 genetically modified mice.

Method: We used alcohol-preferring C57BL/6 mice previously acclimated to a limited access procedure. Mice received the vehicle, naltrexone 1.0 mg/kg, or memantine at 5mg/kg, 25mg/kg, or 50 mg/kg i.p. respectively for twelve days. Following the twelve-day treatment phase, measurements collected included the intake of alcohol in a 2-hr period; 22-hour water intake, 24-hour food intake and body weight.

Result: 1) A repeated measures ANOVA revealed significant medication by day interactions for all medication groups for the 2-hour alcohol intake measure (naltrexone, df=4, F=11.827, p=0.002, memantine 5 mg/kg, df=4, F=7.999, p=0.009; memantine 25 mg/kg, df=4, F=6.199, p=0.014; memantine 50 mg/kg, df=4, F=10.522, p=0.003). 2) In all three of the memantine groups, there was no significant medication by day interaction with vehicle group in the 22-hour water intake, 24-hour food intake and body weight measures. 3) Naltrexone and vehicle groups showed a significant medication by day interaction in body weight, but not in 22-hour water and 24-hour food intake.

Conclusion: These results show that memantine treatment reduces alcohol intake in mice. These results suggest that a pure NMDA receptor antagonist might be effective in preventing relapse in alcohol-dependent patients.

BA-N25

A Mu Opioid Receptor Gene Polymorphism (A118G) and Naltrexone Treatment Response in Adherent Korean Alcoholics

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Objectives: There have been previous studies investigating the relationship between genetic polymorphisms of the μ opioid receptor gene (OPRM1) and response to naltrexone treatment. The Asp40 variant genotype previously shown to be associated with naltrexone treatment response is known to be relatively common among Koreans. This study was conducted to prospectively investigate the relationship between genotype and response to open label naltrexone treatment in Korean alcohol dependent subjects.

Methods: Sixty-three alcohol dependent subjects were prescribed naltrexone for 12 weeks in combination with cognitive behavioral therapy (CBT). Thirty-two subjects were adherent, taking the medication at least 80% of the treatment days (16 Asn40 (A/A) patients and 16 Asp40 variant (A/G or G/G) patients).

Results: Subjects adherent to naltrexone treatment with one or two copies of the Asp40 allele took significantly longer time than the Asn40 group to relapse (p=0.014). Although not significant, the Asn40 group treated with naltrexone had a 10.6 times greater relapse rate than the Asp40 variant group. There was no significant difference between the Asn40 group and the Asp40 variant group treated with naltrexone in rates of abstinence.

Conclusion: These results from a clinically derived sample coincide with previous study results that naltrexone shows a higher therapeutic effect with the Asp40 variant genotype than the Asn40 genotype in Korean alcohol dependent subjects. The results will help identify alcohol dependent patients who might show the most effective treatment results with naltrexone.

BA-P01

Phenomenology and antipsychotic use for alcohol induced psychotic disorder at a tertiary care centre: a retrospective chart review

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Background: Alcohol induced psychotic disorders are a cluster of psychotic phenomena that have been documented to occur during withdrawal in patients with alcohol dependence [AD]. Though common in clinical practice, this entity has been sparsely studied with regard to phenomenology and indications for antipsychotic use.

Methods: We reviewed case records with an ICD-10 diagnosis of alcohol induced psychotic disorder (F 10.5 and F 10.75), registered between August 2008 to August 2009, at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India. Out of 110 records screened, 48 were included in the analysis, after excluding records with co-morbid substance dependence (except nicotine) and psychotic disorders.

Results: The mean age of onset of psychosis was 36.41 (SD 8.54) years, while that of AD was 28.33 (SD 7.11). Family history of AD was present in 31 (64%) of the subjects. Second person auditory hallucinations were the most common phenomena documented (58.3%), followed by delusion of persecution (52.1%). Antipsychotics were used in 25 subjects (52.1%) and were initiated 2.32 (SD 4.34) days after detoxification. Risperidone was the most common antipsychotic used (43.8%). Most specific indications were delusional misinterpretation ($p = 0.012$) and delusion of infidelity ($p = 0.014$), which did not subside with detoxification.

Conclusions: In this study, predominantly hallucinatory and delusional subcategories of alcohol induced psychotic disorder were seen, of which half the cases were severe enough to warrant addition of antipsychotics. This demonstrates the need for further research in this area to establish lucid treatment guidelines for this condition.

BA-P02

The efficacy of atomoxetine in treating co-morbid attention deficit hyperactivity and substance use disorders: Findings from an open label clinical trial.

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Bangalore, India.

Background

Attention Deficit Hyperactivity Disorder (ADHD) and Substance Use Disorders (SUD) frequently occur together and share a bidirectional relationship. Addiction in such patients tends to be of greater severity and of a longer course. Externalizing/ADHD symptoms appear to be an underlying diathesis in patients with SUD. Despite this, the number of clinical trials which have focussed on drug therapy in this population of patients is limited.

Aim

In this study, we sought to examine the effect of atomoxetine in treating co-morbid SUD (more than one substance) and ADHD.

Methodology

Study subjects were recruited from the outpatient services of the Deaddiction Centre, NIMHANS, and assessed for ADHD/externalizing symptoms, substance use and quality of life. The past maximum period of well being was noted and the scales were applied retrospectively for that period. Subjects received atomoxetine at dosages of 25 to 50 mg / day. After starting the drug, patients were followed up regularly on an average over 17 weeks. Post atomoxetine period and the past period of maximum well being were compared by the paired t test.

Results
ADHD scores had significantly reduced on atomoxetine (p=0.000). The maximum period of well being was significantly longer (p=0.003), the turnaround time was significantly shorter (p=0.001), and the quality of life was significantly better with atomoxetine (p=0.000).

Conclusions
Atomoxetine is useful in treating patients with comorbid SUD and ADHD, probably by targeting the underlying diathesis of externalizing symptoms.

BA-P03

The effect of low-nicotine cigarette smoking on the craving after smoking cessation: a pilot study

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Objectives: Nicotine addiction is regarded as the primary reason why so many smokers find it extremely difficult to stop smoking. On this basis, low-nicotine cigarettes were developed and marketed by tobacco industries as a healthier substitute for regular or full-flavor cigarettes. Many smokers believe that these low-nicotine cigarettes reduce craving and withdrawal and thus help to quit smoking. However, this belief is not substantiated by solid evidence up to now. We tried to test the hypothesis that long-term low-nicotine cigarette smoking reduce craving during the acute abstinence period.

Methods: Fifteen male participants were divided into two groups based on their favorite cigarettes during the past year: low-nicotine cigarette (10 subjects) and regular cigarette group (5 subjects). All the participants gathered and stayed together in a comfortable place. They were instructed to abstain from smoking from 4:00 pm to 10:00 am the next day (18 hours). The degree of craving was repeatedly measured by Visual Analog Scale and Tobacco Craving Questionnaire. The temporal change patterns of the craving were compared between the two groups.

Results: The degree of craving was continuously increased during the whole abstinence period. The temporal change patterns were much similar between the two groups. No statistically significant difference between the two groups could be found in any of the measurements except the baseline VAS score. We could not find any evidence that low-nicotine smoking help to reduce craving.

Conclusion: Low nicotine cigarettes currently marketed in Korea have no benefit in terms of craving reduction during acute abstinence period. The advertisement or promotion of low-nicotine cigarette as an aid to stop smoking should be discouraged based on lack of solid scientific evidence. Low nicotine cigarette cannot be the rational alternatives to stop smoking.

Key words: Smoking, nicotine, low-nicotine cigarette, craving, withdrawal

Congress Main Venue

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303: Meeting Room
304A: Secretariat
304B: Preview Room

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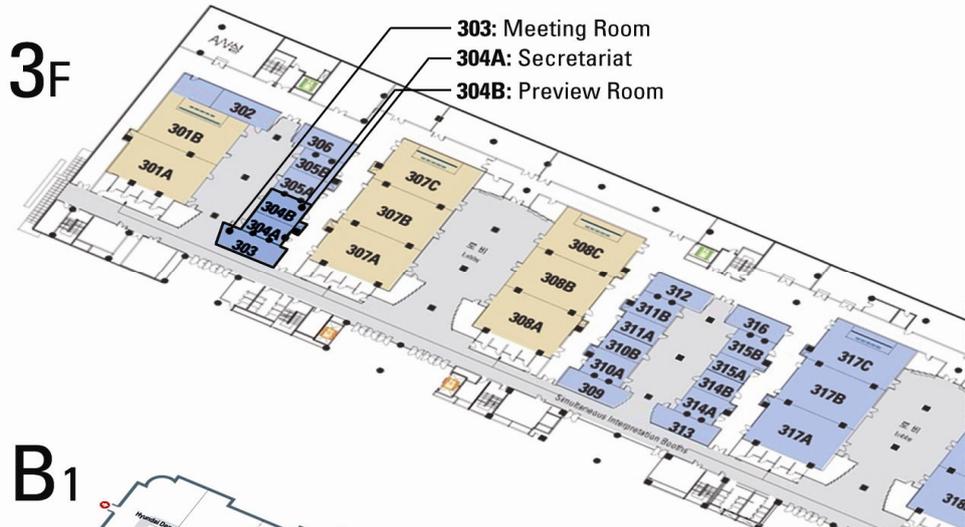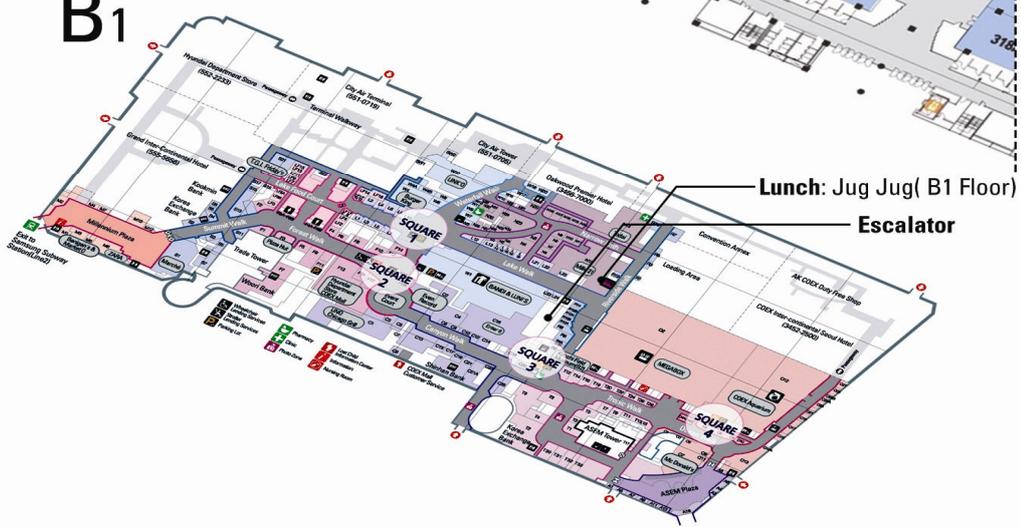
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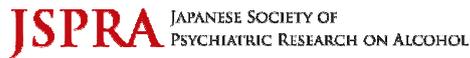
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