



IDARS NEWS

Newsletter of the International Drug Abuse Research Soci-

Volume 1 Issue 8

Fall 2011

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IDARS President
George F Koob

Past-President
Michael Kuhar

Executive Officer
Syed F. Ali



Dr. George F. Koob

As IDARS moves forward, many exciting developments from the last two biannual meetings held in Seoul, South Korea and in Istanbul, Turkey, raises our enthusiasm and optimism for our creative IDARS initiative to continue our International conferences across the globe and share novel advances in drug abuse and addiction. The third IDARS meeting in Istanbul was very successful with significant milestones, and the scientists and clinicians from 14 different countries that attended the meeting, attests to the truly International flavor and diverse presentations at the meeting. This meeting also marked the inauguration of the

Michael Kuhar travel award that was presented to Dr. David Matuskey (see award picture in page 2 of this newsletter). Also incorporated in the Istanbul meeting were specific symposia in different areas, highlighting, "Recent frontiers and advances in drug abuse and addiction". One particular highlight from these meetings has become the final session with Chairpersons from the different panel symposia which has become an important and critical panel discussion to summarize the different sessions and make suggestions and recommendations for the way forward. An emerging area that is important for future symposium in IDARS meetings will be the inclusion of symposia exploring the role of epigenetics in the vulnerability to drug abuse. There are however some lingering challenges, including recruiting more members into IDARS and a charge for members to pay their dues.

I am looking forward to seeing you at this year's society for neuroscience meeting in Washington DC, where IDARS will have a booth and a social event. At the social event and dinner, there will be a presentation by Professor Barry Everitt, from the Behavioral and Clinical Neuroscience Institute, of Cambridge University in UK. His presentation is "An after dinner view of drug seeking habits". See you there.

Yours Truly
George F. Koob, Ph.D.

The Michael Kuhar Travel Award-

Dr. David Matuskey presented the award by Dr. Michael Kuhar.



Dr. David Matuskey

David joined the city tour of Istanbul



From left, Dr. Ali, Dr. Koob and far right Dr. Kuhar congratulates Dr. Matuskey as the first Kuhar travel awardee.

The Michael Kuhar Travel Award– During the third IDARS meeting in Istanbul in Turkey, Dr. David Matuskey from the Department of Psychiatry, Yale University School of Medicine, New Haven, USA was awarded the Kuhar's Travel Award by IDARS as shown above and he presented a lecture on the sub-cortical D3/D2 receptor binding in cocaine dependent humans.

George F. Koob
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San-Diego, CA, USA

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Kiyofumi Yamada
Nagoya,

Japan

Newsletter Editor
Emmanuel S. Onaivi
Wayne, NJ, USA

Website:
WWW.IDARS.org

Third IDARS meeting Report

IDARS-ISN satellite meeting entitled “Recent Frontiers and Advances in Drug Addiction” was held in Turkey, Istanbul from August 22-26, 2011.



The meeting was opened by the invited lecture delivered by Dr. George Koob followed by different symposia on dopamine, alcoholism and drug addiction potential treatment targets, with coffee breaks. Pictures from the first day symposium and during the coffee break.

Third IDARS meeting Report



PHOTO GALLERY FROM SYMPOSIA

Representative pictures from thirteen different symposia: From top left to right are Antonio Noronha and Alfreda Stadlin and others with Susan Schenk at bottom right.

Third IDARS meeting Report



PHOTO GALLERY FROM COFFER BREAK

Bonnie Robinson in the middle right picture takes care of registration of arriving IDARS members for the conference.

Third IDARS meeting Report

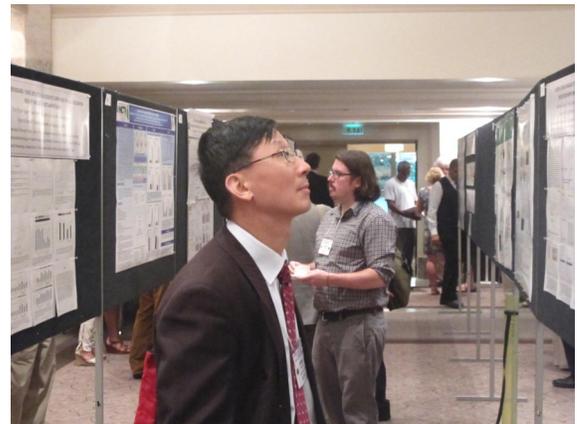
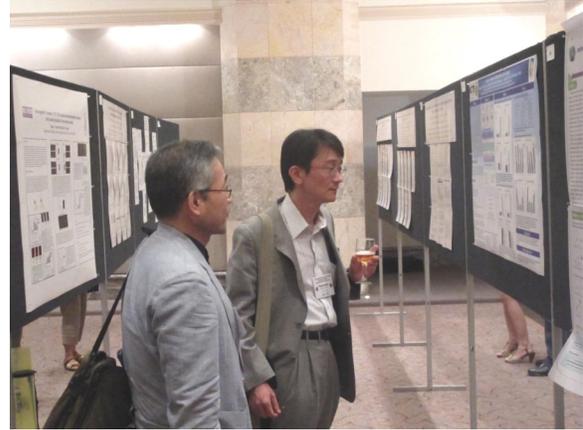


PHOTO GALLERY FROM LUNCH BREAK

IDARS members continue to network during lunch and update on new frontiers in addiction research and therapeutic approaches.

Third IDARS meeting Report

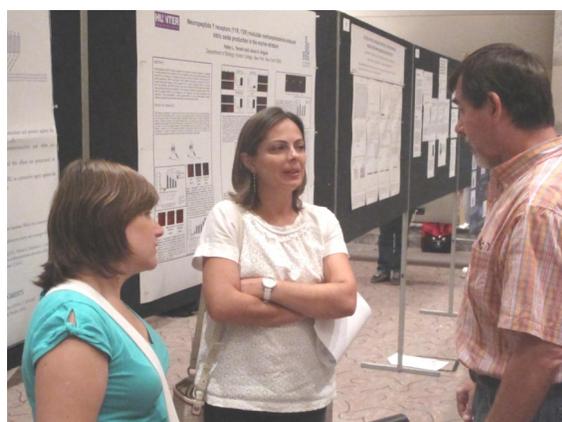
Photo Gallery from poster session 1



Poster session 1 was the odd-numbered posters moderated by Drs. Zbigniew Binienda and Ashraf Virmani.

Third IDARS meeting Report

Photo Gallery from poster session 11



Poster session 11 was the Even-numbered posters moderated by Drs. Frederico Periera and Eun-Joo Shin.

Third IDARS meeting Report

Photo Gallery from Lunch Break



Participants and attendees during lunch.

Third IDARS meeting Report



IDARS Members on the cruise

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IDARS Members on the cruise

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IDARS Members on the cruise

Third IDARS meeting Report



IDARS Members Dinner on the cruise

Third IDARS meeting Report



Photo gallery from Istanbul city tour

Third IDARS meeting Report



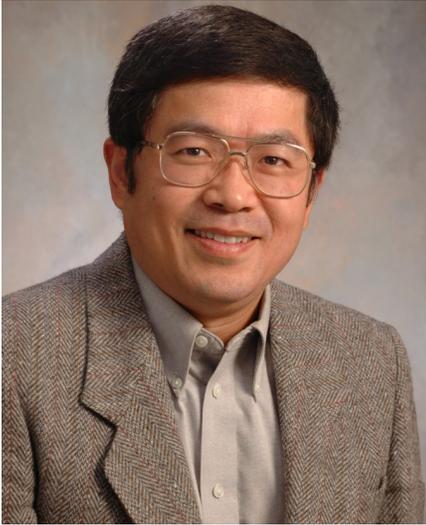
Photo gallery during IDARS Istanbul city tour and lunch.

Third IDARS meeting Report



Photo gallery during IDARS Istanbul city tour with lunch and visit to a carpet factory.

Neurobiology of cocaine abuse



Cocaine is purified from the leaves of the *Erythroxylum* coca bush. This plant grows in South America. Abusers can snort, inject or smoke cocaine. Cocaine is a powerful stimulant of the central nervous system. Cocaine is euphoric and reduces fatigue but also increases blood pressure, heart rate and body temperature. According to the [National Survey on Drug Use and Health](#), in 2009, 4.8 million Americans age 12 and older had abused cocaine and 1.0 million had abused crack cocaine at least once in the year prior to being surveyed.

Dopamine is a brain chemical messenger (or neurotransmitter) associated with pleasure and movement in reward circuits -

in the brain. Cocaine blocks dopamine and other neurotransmitters from being reabsorbed. The resulting buildup between brain cells causes euphoria or feeling high. With repeated use, cocaine can cause long-lasting changes in the brain's reward system leading to addiction. Addiction is characterized by the compulsive seeking and taking of cocaine despite known adverse consequences. Once acquired, it is long-lasting and difficult to extinguish. Relapse to drug-taking is the main obstacle to long-term treatment and cure for drug addiction in humans.

Research has found that memories of drug experience and drug-associated environmental cues can elicit drug seeking and taking behaviors. Dopamine works in reward learning through its receptors, and drugs of abuse can pathologically change reward-related learning circuits in the brain's dopamine system. Using behavioral, pharmacological, genetic, imaging, anatomical and molecular biological methods, researchers have been investigating the key molecules including dopamine receptors and related intracellular mediators that are involved in reward-related learning induced by drugs of abuse. It has been found that several dopamine receptor molecules, including dopamine D1, D2 and D3 receptors mediate the various effects of cocaine. Their work also shows that the glutamate system, another neurotransmitter in the brain, is involved in the development of cocaine addiction.

Cognitive-behavioral therapy has been shown to be effective for decreasing cocaine use and preventing relapse. FDA-approved medications for treating cocaine addiction are not yet available. The development of effective treatment of drug addiction relies on a more thorough understanding of the neurobiological mechanisms underlying the compulsiveness and persistence of drug-induced behaviors as well as susceptibility to relapse.

By Ming Xu, PhD
University of Chicago,
Chicago, Illinois USA.

Methamphetamine abuse and astrocyte activation in caudate-putamen

Methamphetamine (METH), a potent indirectly acting sympathomimetic amine, is a powerful addictive stimulant that has high potential for widespread abuse because it is inexpensive, available in many different forms, and can be easily made in clandestine laboratories from relatively inexpensive, over-the-counter ingredients. Amphetamine-type stimulants (ATS), including METH, represent the only widely administered class of drugs that predominantly release neurotransmitters, in this case principally monoamines (dopamine, noradrenaline and serotonin), by a non-exocytic mechanism. In addition to euphoria, effects sought by METH abusers include a heightened sense of attentiveness, increased energy



and curiosity, elevated interest in environmental stimuli, and, initially, hypersexuality and decreased anxiety. Human binge abusers typically take large METH doses every few hours, resulting in a sustained plasma concentration because of the long half-life of METH (~12 hr). Medical problems associated with excessive dosages include cerebral hemorrhage, stroke, seizure, hyperthermia, arrhythmias, coma, and death.

Drugs of abuse, including ATS have long been known to produce complex adaptations in caudate-putamen, many of which resemble those observed in the more extensively studied nucleus accumbens (NAc). Caudate-putamen, along with the globus pallidus (GP; internal GPi and external GPe), the substantia nigra (reticulate SNr and compacta SNc) and the subthalamic nucleus (STN) are considered the core structures of the mammalian basal ganglia (BG). There has been a resurgence of interest in the role of caudate-putamen in addiction based on its likely role in habit-based learning that may drive compulsive drug seeking. For example, it was suggested that although the caudate-putamen may have only a minor role in the acute reinforcing effects of psychostimulant drugs it has a chief role in the transition to compulsive use. Dopamine neurotransmission in the caudate-putamen may be a fundamental component in drug addiction. Astrocytes, playing a major role in neurotransmission, including DA dynamics, may also contribute to the synaptic and structural plasticity associated with drug addiction.

In vivo studies of METH administration to rodents have undisputedly shown that besides DA homeostasis disruption, astrocytic caudate-putamen activation is a hallmark of METH neurotoxicity. In fact, single-day regimen of both single high-dose or multiple METH injections and self-administration models exhibited significant activation of astroglia in caudate-putamen. Additionally, METH addicts showed structural and chemical abnormalities on magnetic resonance (MRI), proton magnetic resonance spectroscopy (1H-MRS) particularly in basal ganglia brain that could underlie glial alterations. However, the mechanisms of caudate-putamen astrocytic perturbation by METH remain elusive. Bearing in mind that dopamine is one of the several factors modulating astrogliosis, one could hypothesize that dopamine induces astrocytic activation under a METH neurotoxicity setting. Briefly, activation of astrocytes may be prompted by DA either by DA astrocytic metabolism and autoxidation following DA astrocytic uptake (aberrant DA extracellular levels-acute METH effects). Further astrogliosis could be led through DA signaling (DA depletion-long-term METH effects). In both cases, activated astrocytes would synthesize a pleiad of pro-inflammatory cytokines, including TNF- α . The impact of METH *per se* on the striatal astrocytic activation is far from being known. Although astrocytic reactivity might be prompted as a neuroprotection strategy to resolve the neurotoxic insult, it can ultimately aggravate the disruption of dopamine homeostasis in caudate-putamen. Further studies should be conducted so that the role of astrocytes in METH abuse could be better elucidated. These studies will be instrumental to design pharmacological tools that could help to recover the caudate-putamen following METH intoxication.

By Frederico C. Pereira, PhD
University of Coimbra, Portugal.

Dopamine in the addicted brain



Drug addiction is a brain disorder caused by the repetitive use of various chemicals which alter normal functioning of the central nervous system with consequent behavioral abnormalities. In the search to understand which neurotransmitter systems play upon this behavioral pathology, dopamine has long been thought to play a '*prima donna*' role. However, its primary role is commonly and erroneously attributed to the increase in activity after acute administration of addicting drugs.

On the contrary, the mesolimbic dopamine transmission appears to be drastically reduced in its tonic activity when measured in animal models, which mimic the human condition of drug addiction, and in the available human studies conducted in addicted subjects. Various experimental approaches such as electrophysiological, biochemical, behavioral, biomolecular and even anatomical, show that dopamine neurons work insufficiently in the crucial phases of the entire drug addiction cycle such as withdrawal from chronic treatment. This 'hypodopaminergic state' is viewed as one of the main causes that triggers drug-seeking and taking, even after prolonged drug-free periods, perpetuating the vicious cycle. In addition, albeit reduced in its activity, the system remains hyperresponsive to abused drugs conferring long-lasting vulnerability to the system. We propose that decreased dopamine function in addicted subjects results in a decreased interest to non drug-related stimuli and increased sensitivity to the drug of choice. The reduction in physiological activity of the DA system leads to the idea that an increment in its activity, to restore pre-drug levels, may yield significant clinical improvements (reduction of craving, relapse and drug-seeking/taking). Targeting the dopamine system with pharmacological (and non) agents, not necessarily classic receptor-oriented drugs, aimed at restoring a deficient dopamine transmission may reveal useful new avenues in the treatment of this socially debilitating brain pathology.

Suggested readings: Melis et al., 2005 The dopamine hypothesis of drug addiction: hypodopaminergic state. *Int Rev Neurobiol.* 63: 101-154.

By Marco Diana (PhD, University of Sassari, Italy).

Editorial Corner: Welcome to our Newsletter*

Emmanuel Onaivi, Ph.D., Newsletter Editor for IDARS is delighted to publish our electronic newsletter, with information about the society and opportunities for our members. The intention of this newsletter is not only to communicate to you, but also, for you to be able to respond with suggestions for how IDARS may increase its role in your research. Please send us feedback, and get involved! As editor of this newsletter, I invite you to contact me with ideas for articles in future editions, or to volunteer to write an article yourself and special thanks to Drs. XU, Pereira and Diana for their contributions to IDARS Biomedical report in this issue on pages 18-20.

COMMITTMENT TO IDARS MISSION

The President, Dr. Koob, in his column, noted that the final session with Chairpersons from the different panel symposia has become an important and critical panel discussions to summarize the different sessions and make suggestions and recommendations for the way forward, not only for IDARS members but also across the globe to share novel advances in drug abuse, addiction and treatment targets. The picture shows the panel's discussions at the close of the meeting moderated by Dr. Syed Ali—IDARS executive officer.

Newsletter Editor*:

Emmanuel S. Onaivi

Onaivie@wpunj.edu

Home Web Site

www.idars.org

Office email

Syed.ali@fda.hhs.gov

Office Telephone

870-543-7123

Office Fax

870-543-7745



IDARS MEMBERS IN ISTANBUL

