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IN THIS ISSUE

THE GENETIC EXPRESSION PROFILE AFTER ANTIDEPRESSANT TREATMENT INFORMS THE ANTIDEPRESSANT MOLECULAR CORE EVENTS

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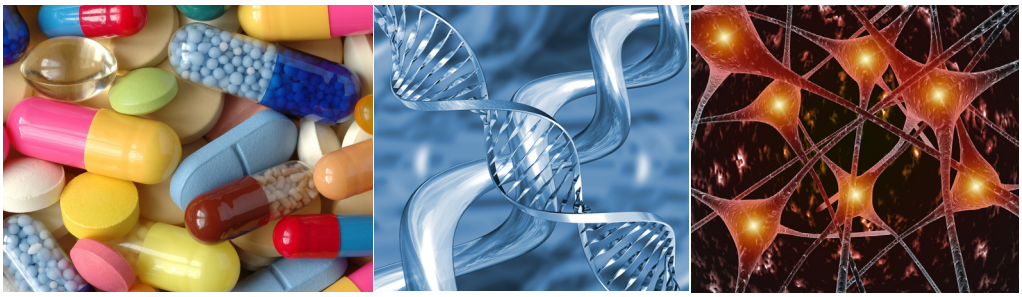

Abstract

Antidepressant pharmacological treatments are designed to interfere with the monoaminergic balance in the central nervous system. Nevertheless, the molecular mechanisms that drive the antidepressant effects are promoted but not exhaustively identified with the monoaminergic molecular pathways. In the present paper we review the most recent literature on the genetic expression profile of cells in the central nervous system of animals exposed to antidepressant drugs to identify the molecular cascades associated with the antidepressant mechanisms. As a result, genes involved in the prosurvival events (MAPK/ERK, BDNF), the glutamatergic and GABAergic balance (GAD67, VGAT), mitochondrial activity (Bcl-x), scaffolding proteins (PSDP95) and stress related events (AVPR1b) seem to be key elements of the antidepressant effects. The evidence involving the genes in antidepressant response is described and their possible role in the synthesis of new antidepressant compounds is discussed.

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LETTER FROM THE PRESIDENT

Dear Member,

Do you benefit from your membership?

We are thankful for your interest and dedication to the activities of the ISBD. With more than 800 members from 44 countries, we are the biggest and strongest international organization in the field of bipolar disorder. With your support, the Society continues to fulfill its mission of fostering on-going international collaboration on education and research with an objective to advance the treatment of all aspects of bipolar disorders, resulting in improvements in outcomes and quality of life for those with bipolar disorder and their significant others.

However, what do you get for your membership?

Two of the primary benefits of membership include reduced registration rates for our annual meetings (this year, from 13-16 June in Miami, Florida and next year, from 18-21 March in Seoul, South Korea) and the subscription to our journal Bipolar Disorders. Moreover, as a member, you can be active in our organization by participating in one of our task forces or committees. In addition to our annual scientific meetings, task forces are responsible for the majority of the Society's activities.

Nevertheless, we think we should provide you with more benefits, including additional educational activities. During the past two conferences, we organized several interesting preconference workshops and courses (registration for the workshops in Miami is still open!) and last year, we implemented the ISBD Mentorship Program: **http://www.isbd.org/education/mentorship-program.**

We are also proud to introduce ISBD's newest educational initiative in the form of periodic webinars. Each webinar will feature a presentation from a distinguished author, focusing on a recent body of his/her work. The first webinar will be launched in late April or early May. Please check your email for additional announcements. The Society is currently collaborating with the editors of our journal Bipolar Disorders on finding topics for future webinars. However, we invite you to share your suggestions and feedback on future topics and the webinar format in general!

In addition, we are pleased to announce that a printable version of the ISBD membership certificate is available to you through the Society's website. To access your membership certificate, please log into the Member Zone and click on the "Update My Profile" tab. From the dropdown menu on the right hand side of the page, select the year for which you wish the certificate printed. Should you prefer to have your certificate printed and mailed to you, please contact Mariya Dobrovinskaya at **dobrovinskayam@upmc.edu** to request this benefit.

Finally, if you are attending the 10th ICBD in Miami, we would also like to invite you to the ISBD Annual General Membership meeting to be held on Friday, 14 June, 2013 from 12 -1 PM at the Loews Miami Beach Hotel. At the meeting, we will share highlights of the business plan for the next two fiscal years 2013 and 2014, vote on significant changes to the ISBD Constitution, discuss plans and progress for Seoul 2014 and future meetings, highlight new awards, announce new Board Members and Chapters, review the output of the Task Forces over the past year, and much more. If you are attending, please do not forget to RSVP to Mariya Dobrovinskaya at: **dobrovinskayam@upmc.edu.**

I hope to see you in Miami!

Willem A. Nolen, MD, PhD
President, ISBD

SOCIETY UPDATES

Chad Daversa, ISBD Executive Director

The 10th International Conference on Bipolar Disorder (ICBD) meeting in Miami is now just a few months away, and we would encourage you to register for what will surely be an outstanding meeting. We have received over 300 submissions for posters and rapid communications, and the submissions for the oral symposia are of an exceedingly high caliber. Featuring a new collaboration with the Depression and Bipolar Support Alliance (DBSA) for the Saturday June 15th program, a new host city and venue, and the strong scientific program that has come to characterize the ICBD, the meeting is sure to be a success.

We are pleased to report that the ISBD Biomarkers Task Force paper entitled "Biomarkers in bipolar disorder: A positional paper from the International Society for Bipolar Disorders Biomarkers Task Force" has been accepted for publication at the Australia & New Zealand Journal of Psychiatry. The paper is the result of several years of work by ISBD-BIONET (biomarkers network from the International Society for Bipolar Disorders) led by Dr. Benicio Frey at McMaster University and Prof. Trevor Young at the University of Toronto, Canada. The paper seeks to examine potential biomarkers in the areas of neuroimaging, peripheral measurements, and genetics and outlines a research agenda based on the reported findings.

The Antidepressant Task Force, chaired by Prof. Eduard Vieta, has concluded over a year of lively debate on the topic, and the final manuscript has been submitted for publication with the authorship of over 50 of the leading bipolar experts in the field.

ISBD is also pleased to welcome a new chapter, The Austrian Society for Bipolar Disorders, led by Prof. Christian Simhandl. The organization has established outreach to 230 bipolar patients that are kept informed about the activities of the organization, and 150 people attended the last meeting on the 5th of October 2012 in Vienna. We also shortly anticipate the addition of the Italian Society for Bipolar Disorders, led by Prof. Carlo Altamura.

The organization is also making strides in our educational offerings. The ISBD mentorship program is providing opportunities to young clinicians and researchers from around the world to connect with senior investigators to develop the skills and training they need to succeed. To date, we have successfully paired 4 prospective mentees with mentors to develop a consultation based program of individualized training to support the goals of the mentee. If you would like to sign up to be a mentor or mentee, please contact **Mariya Dobrovinskaya** via email at: **dobrovinskayam@upmc.edu.**

Finally, if you have not had an opportunity to renew your ISBD membership, please login to the ISBD website to renew online or contact our office for further assistance.

Kind Regards,

Chad Daversa
Executive Director, ISBD

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ISBD Global Newsletter

Editorial Policies

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Authors: Please refer to the back cover for instructions on submitting material to the newsletter.

Yoga and Bipolar Disorder – Evidence and the Way Ahead

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Yoga is an ancient system of exercises that include postures (asana), breathing exercises (pranayama), and meditation (dhyana). Multiple mechanisms explaining the mental effect of yoga have been put forward, including reduction in the sympathetic and increase in the parasympathetic tone, which leads to emotional regulation, empathic response, and is associated with decreased levels of cortisol. Vagal activity also calms body's stress response system. In addition, an increase in melatonin, which has its own beneficial effects, has been observed (1). Increased EEG synchrony and coherence, increased heart rate variability, and respiratory sinus arrhythmia were also considered as possible effects (2).

Out of all psychiatric disorders, depression has been the best documented with regard to the rold of yoga with multiple trials showing benefit in mild to severe depression (3). Many studies also emphasize rhythmic breathing as an essential component of yoga. Although yoga has been found effective, it fails to achieve high remission rates by itself, and results from monotherapy are worse than the current pharmacotherapy and electroconvulsive therapy (4) . However, findings of Sharma et al confirm the effectiveness of yoga when used in addition to prescribed antidepressants (5). In fact, yoga is better than many other non-pharmacological adjuncts being used today, such as group therapy and psychoeducation (6).

Many of these studies, however, lack numerous basic details of trial methodology, and differences in yoga techniques used in the investigation prevent a general analysis. Still, seven out of nine randomized, controlled trials, demonstrate positive outcomes of yoga intervention (3). Multiple authors stress the fact that more standardized research is required in this field before yoga is accepted as a clear clinical adjunct. Some side effects have been noted in patients undergoing yoga with comorbidities like diabetes (7). Additionally, individuals who want to practice yoga must make sure that the technique they use is adequate for their physical profile. Same can be said for prenatal women. Yoga's impact on mental health is also being considered, with studies focusing on psychiatric diseases currently being conducted in various parts of the world. For instance, authors of an ongoing study at the RML hospital in New Delhi, India, have demonstrated a positive effect of yoga on patients with schizophrenia (8).

While there have been nine studies for Depressive disorder there is a distinct lack of clinical studies devoted to the investigation of beneficial effects of yoga on bipolar disorder. Similar findings were reported by Andreescu et al (9), when they were looking for alternative treatments for bipolar disorders. They found yoga to be better than other alternate treatments like herbs, which can cause serious pharmacological side effects (9). However, the lack of evidence hampered them from actively suggesting yoga therapy as a viable option. Nanda et al (10) found reduction in anxiety and depressive symptoms, as well as increased quality of life in yoga-practicing patients, but also mentioned the need for further research in this field. Another study found positive results in people with bipolar disorder, who followed a regular exercise regimen like yoga (11), but a few participants found the cost of practicing it high.

The difference between yoga's effects on depression and bipolar disorder must be understood. This is especially critical when it comes to certain types of yoga. For instance, Sudarshan Kriya Yoga, a subtype of yoga recognized as very effective in depression by three studies (4, 12 -13), was found to trigger mania in individuals affected with bipolar disorder, when they were practicing a Bhastrika breathing technique (2). Another case study cited instances of mania induced by meditation (14).

As a result, more research is needed on yoga, not only to identify it as a potential treatment adjunct but also to test its efficacy. Since many patients are likely to pursue this exercise regimen on their own, in addition to pharmacotherapy, we, as treating doctors, should be able to provide them with proper advice.

While there are many different forms of yoga, it is safe and relatively well-tolerated, resulting in very few side effects when practiced appropriately (15). In addition, yoga is gaining popularity and is widely accepted as a low intensity exercise course with 6.1% of the population of US practicing it in 2007 (16). Being a low intensity regimen, long term compliance is more likely; this is important, since bipolar disease is often life-long. The effects of yoga on diseases, such as hypertension, hyperglycemia and hypercholesterolemia, can counter the side effects caused by the drugs being given for bipolar disorder or prove helpful for patients with bipolar disorder and associated chronic conditions (17). A number of questions regarding the type of yoga to be used, the length and intensity of yoga treatment, and the psychiatric disorder it is most effective against remain unanswered. A concerted, focused research is needed to develop an effective program to integrate yoga with pharmacological treatment in order to harness its full benefits.

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THE GENETIC EXPRESSION PROFILE AFTER ANTIDEPRESSANT TREATMENT INFORMS THE ANTIDEPRESSANT MOLECULAR CORE EVENTS

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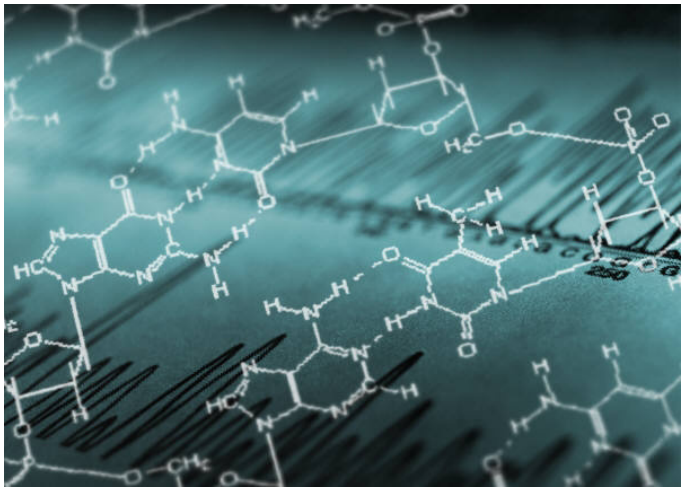
Introduction

Evidence from different regions of the world confirms that the trend of psychotropic drug prescription increased through the last decades. Antidepressants led this trend. People prescribed with antidepressants were 5.84% in 1996 and 10.12% in 2005 in the United States (1). Antidepressant prescriptions increased from 7.36% in 2004-2005 to 8.21% in 2005-2006 and to 9.39% in 2006-2007 in NewZeland (2). In Europe (Italy), antidepressant prescriptions increased 4-fold per year between 1998 and 2008 (3). In England, antidepressant prescriptions increased by an average of 10% a year, a total of 130% from 1998 to 2010 and antipsychotic prescriptions increased by 5.1% per year on average, a total of 66.1% during the same time period (4). Higher economical costs - antidepressants are some of the most expensive drugs in the market, and their cost raises faster compared to other drugs (5) - result from this trend. This situation raises concerns about the rationale, use and possible misuse of these compounds (6,7). Trial and error principle that guides the antidepressant prescriptions today may contribute to these trends. Personalized prescriptions could contribute to the decrease in economical costs of antidepressant treatments and personal sufferance of patients and their families by optimizing response and side effects. The scientific community has long searched for a biological tool able to identify a personalized antidepressant treatment for any specific patients. Unfortunately, a biological mark able to guide the antidepressant prescription in any specific case is yet to be discovered (8,9). Genetics and molecular biology may contribute to the identification of genetic variations that predict response to a certain drug, bringing evidence for both personalized treatments and understanding of the biological background of depressive disorders. New insights in the biological underpinnings of drug activity could then revamp the interest in the field, with important consequences for the global mental health. Investigation of the genetic expression changes that follow the administration of drugs is a classical approach to understanding the mechanisms of drug action. Identification of such genes in specific brain areas may help find the biological hallmarks of drug activity, which could inform the molecular mechanisms at the basis of mood and psychotic disorders and help identify subjects who will respond to specific treatments. The current paper investigates which genes change their expression profile after administration of an antidepressant or an antipsychotic.

Antidepressants, evidence from literature

Antidepressants (AD) change the expression profile of genes that could inform the biological mechanisms of antidepressant response. The administration of citalopram in animal models increased the expression of the MAPK (mitogen-activated protein kinases)/ERK (extracellular signal-regulated kinase) pathway (10). Once activated, ERK1/2 phosphorylates target proteins in the cytosol or nucleus to regulate proliferation, differentiation, apoptosis, and synaptic plasticity (11). ERK1 and ERK2 are pivotal to the correct neuronal development. The glutamatergic system could be also involved in the serotoninergic – ERK interplay. It has been suggested that serotonin suppresses NMDAR function through the activation of the 5-HT1A receptor, which triggers a mechanism dependent on microtubule/kinesin-based dendritic transport of NMDA receptors regulated by CaMKII and



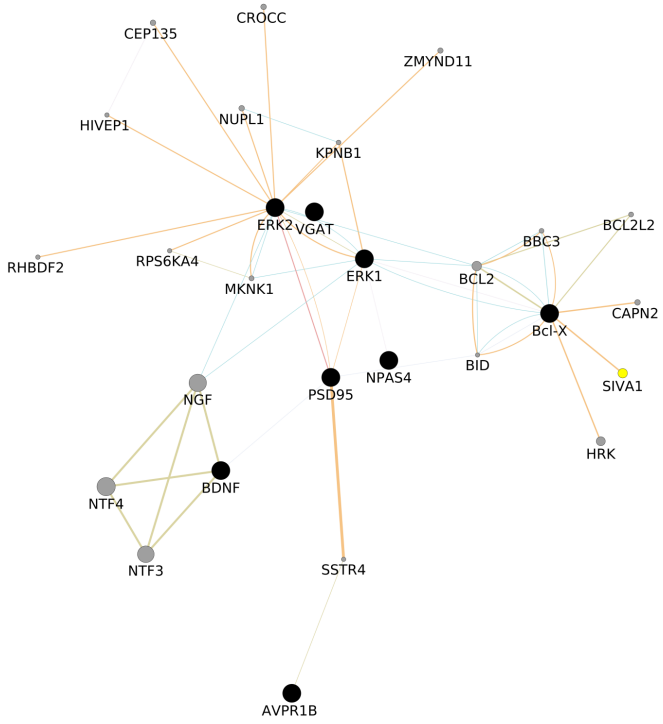
ERK signaling pathways (12). On the other hand, activation of the 5-HT2A/C counteracts this effect (13). Citalopram altered the expression of AVPR1b in the hippocampus and in the prefrontal cortex, key brain regions for mood disorders, involved in the retention of memory and in the eleboration of emotions (Kokras et al., 2011). The protein encoded by this gene acts as receptor for arginine vasopressin, which is inolved in the activation of the ACTH pathway during stress. A chronic stressful condition may elicit mood disorders, especially when it occurs during childhood (14). Genetic variations located in the AVPR1b have been consistently (14–16), even if not systematically (17), associated with psychiatric disorders. Citalopram decreased the expression of the serotonin transporter (SERT) (18) and venlafaxine increased the

expression of Bcl-xl and BDNF (19,20) and down-regulates the expression of Bax (20). SERT is the biological target of the action of citalopram and its down-regulation in the hippocampus is consistent with previous findings after chronic AD treatment (21,22). Interestingly, the down-regulation of SERT after AD treatment could be related to the BDNF. There is consistent evidence suggesting that the use of AD results into an increased BDNF concentration in various brain areas, and Deltheil and colleagues convincingly demonstrated that BDNF by itself increases the 5-HT tone in the brain of animals (23) so that the decreased SERT expression in the hippocampus of animals treated with AD could be the result of an adaptation to a decreased 5-HT tone induced by the increased BDNF concentration after AD treatment. Bcl-x codes for an enzyme that is found outer of the mitochondrial membrane, and regulates outer mitochondrial membrane channel (VDAC) opening. VDAC regulates mitochondrial membrane potential, and thus controls the production of reactive oxygen species (ROS), a potent inducer of cell apoptosis. Nevertheless, two alternatively spliced transcript variants, which encode distinct isoforms, have been reported for the Bcl-x. The longer isoform acts as an apoptotic inhibitor and the shorter form acts as an apoptotic activator. The down-regulation of Bax, a pro-apoptotic factor, induced by citalopram suggests that the overall effect of the AD drug is to promote cell survival in the hippocampus. Venlafaxine increased the expression of BDNF in the cortex of animals (19), while citalopram induced a change in the expression of PSD95 (postsynaptic density protein 95) and down-regulated the expression of Homer1a (10) in the same brain region. The PSDP95 is a key factor for the glutamatergic transmission. Homer are scaffolding proteins involved in the second messenger cascades. Fluoxetine was able to induce the expression of Reelin in the frontal cortex. Reelin encodes for a large secreted extracellular matrix glycoprotein that helps regulate processes of neuronal migration and positioning in the developing brain by controlling cell–cell interactions. Reelin also modulates synaptic plasticity by enhancing the induction and maintenance of long-term potentiation. Reelin deficit is associated with neurological defects and this gene has been associated with Autism (24). Duloxetine is a dual mode AD that acts both on the serotoninergic and noradrenergic tones. Its use was found to be associated with an increased expression of NPAS4, VGAT and GAD67 in the prefrontal cortex and in the hippocampus of animals (25). NPAS4 product belongs to a family of regulators of transcprition, which are involved in a wide range of physiologic and developmental events, VGAT is the vesicular GABA transporter and GAD67 encodes for a key enzyme in the synthesis of GABA from glutamate. The impact on the GABAergic system is of particular relevance in that the chronic hyper tone of the glutamatergic system, which could be counteracted by the activity of the GABAergic one, is thought to be a biological event related to the major depressive disorder (26).

Conclusions

Studies on animals showed that the genetic effect of AD is related to prosurviving events, GABA ergic and Glutamatergic changes in the brain and to the activity of scaffolding proteins. Results are reported in table 1. These findings point to a different understanding of the activity of AD drugs. Indeed, a paradigm shift from the relevance of the monoamines to the relevance of prosurviving events is happening

Fig 1. Molecuar pathway associated with the activity of genes directly impacted by AD treatments



- black circles represent genes whose activity is directly associated with the AD effects

in these years for the understanding of the activity of AD effects. This finding is of relevance in that there no current AD treatment that directly targets these proteins. Nevertheless, the lines of evidence reported in the present paper would suggest that these genetic targets would be worth a deep scientific investigation in preclinical trials in order to synthesize new and more efficacious AD treatments. A limit of this approach is related to the tranlsational effort that must be paid when discussing results on animal manipulation and bringing them to the human brain. There are important differences between the animal and the human brains. Nevertheless, the basics of neuronal adaptations and of the AD effect must be reasonably similar between species, or at least sufficiently similar to design studies able to investigate the potential of AD effect in directly targeting these genes.

Table 1. Genes whose regulation was found to be impacted by AD and their counterparts in a molecular pathway (Cytoscape, GENEMANIA)

Gene Name	annotation name
CAPN2	The calpains, calcium-activated neutral proteases, are nonlysosomal, intracellular cysteine proteases. The mammalian calpains include ubiquitous, stomach-specific, and muscle-specific proteins. The ubiquitous enzymes consist of heterodimers with distinct large, catalytic subunits associated with a common small, regulatory subunit.
BDNF	The protein encoded by this gene is a member of the nerve growth factor family. It is induced by cortical neurons, and is necessary for survival of striatal neurons in the brain. Expression of this gene is reduced in both Alzheimer's and Huntington disease patients. This gene may play a role in the regulation of stress response and in the biology of mood disorders. Multiple transcript variants encoding distinct isoforms have been described for this gene
KPNB1	Nucleocytoplasmic transport, a signal- and energy-dependent process, takes place through nuclear pore complexes embedded in the nuclear envelope. The import of proteins containing a nuclear localization signal (NLS) requires the NLS import receptor, a heterodimer of importin alpha and beta subunits also known as karyopherins. Importin alpha binds the NLS-containing cargo in the cytoplasm and importin beta docks the complex at the cytoplasmic side of the nuclear pore complex.
MAPK1	activation of MAPKK activity
HRK	positive regulation of cellular component organization, apoptotic mitochondrial changes, positive regulation of organelle organization, regulation of protein oligomerization, release of cytochrome c from mitochondria, mitochondrion organization, regulation of mitochondrion organization, positive regulation of mitochondrion organization, positive regulation of protein oligomerization, anti-apoptosis, positive regulation of protein complex assembly, regulation of release of cytochrome c from mitochondria, positive regulation of release of cytochrome c from mitochondria
CROCC	Major structural component of the ciliary rootlet, a cytoskeletal-like structure in ciliated cells which originates from the basal body at the proximal end of a cilium and extends proximally toward the cell nucleus. Contributes to centrosome cohesion before mitosis
ZMYND11	apoptotic signaling pathway, regulation of apoptotic signaling pathway, negative regulation of apoptotic signaling pathway
SSTR4	Somatostatin acts at many sites to inhibit the release of many hormones and other secretory proteins. The biologic effects of somatostatin are probably mediated by a family of G protein-coupled receptors that are expressed in a tissue-specific manner. SSTR4 is a member of the superfamily of receptors having seven transmembrane segments and is expressed in highest levels in fetal and adult brain and lung
BCL2	organelle outer membrane, outer membrane, apoptotic signaling pathway, regulation of mitochondrial membrane potential, regulation of apoptotic signaling pathway, apoptotic mitochondrial changes, induction of apoptosis by intracellular signals, mitochondrial outer membrane, release of cytochrome c from mitochondria, mitochondrion organization, anti-apoptosis, mitochondrial membrane organization, negative regulation of apoptotic signaling pathway, activation of pro-apoptotic gene products
MAPK3	positive regulation of cellular component organization, interleukin-1-mediated signaling pathway, activation of MAPKK activity, positive regulation of histone acetylation, positive regulation of organelle organization, positive regulation of peptidyl-lysine acetylation
CEP135	This gene encodes a centrosomal protein, which acts as a scaffolding protein during early centriole biogenesis, and is also required for centriole-centriole cohesion during interphase. Mutations in this gene are associated with autosomal recessive primary microcephaly-8
RPS6KA4	positive regulation of cellular component organization, interleukin-1-mediated signaling pathway, positive regulation of histone acetylation, positive regulation of organelle organization, positive regulation of peptidyl-lysine acetylation
NGF	positive regulation of cellular component organization, activation of MAPKK activity, tumor necrosis factor receptor superfamily binding, death receptor binding, anti-apoptosis
BID	protein localization in membrane, organelle outer membrane, outer membrane, positive regulation of cellular component organization, tumor necrosis factor receptor superfamily binding, apoptotic mitochondrial changes, positive regulation of organelle organization, regulation of protein oligomerization, induction of apoptosis by intracellular signals, mitochondrial outer membrane, release of cytochrome c from mitochondria, mitochondrion organization, regulation of mitochondrion organization, positive regulation of mitochondrion organization, positive regulation of protein oligomerization, death receptor binding, regulation of release of cytochrome c from mitochondria, positive regulation of protein complex assembly, activation of pro-apoptotic gene products, positive regulation of release of cytochrome c from mitochondria
BBC3	organelle outer membrane, outer membrane, positive regulation of cellular component organization, apoptotic mitochondrial changes, positive regulation of organelle organization, regulation of protein oligomerization, induction of apoptosis by intracellular signals, mitochondrial outer membrane, release of cytochrome c from mitochondria, mitochondrion organization, regulation of mitochondrion organization, positive regulation of mitochondrion organization, positive regulation of protein oligomerization, mitochondrial membrane organization, T cell apoptosis, regulation of release of cytochrome c from mitochondria, positive regulation of protein complex assembly, activation of pro-apoptotic gene products, positive regulation of release of cytochrome c from mitochondria
SIVA1	tumor necrosis factor receptor superfamily binding, anti-apoptosis, T cell apoptosis
DLG4	protein localization in membrane
HIVEP1	This gene encodes a transcription factor belonging to the ZAS family, members of which are large proteins that contain a ZAS domain - a modular protein structure consisting of a pair of C2H2 zinc fingers with an acidic-rich region and a serine/threonine-rich sequence. These proteins bind specifically to the DNA sequence motif, GGGACTTTCC, found in the enhancer elements of several viral promoters, including human immunodeficiency virus (HIV), and to related sequences found in the enhancer elements of a number of cellular promoters.
NTF4	This gene is a member of a family of neurotrophic factors, neurotrophins, that control survival and differentiation of mammalian neurons. The expression of this gene is ubiquitous and less influenced by environmental signals. While knock-outs of other neurotrophins including nerve growth factor, brain-derived neurotrophic factor, and neurotrophin 3 prove lethal during early postnatal development, NTF5-deficient mice only show minor cellular deficits and develop

	normally to adulthood
AVPR1B	The protein encoded by this gene acts as receptor for arginine vasopressin. This receptor belongs to the subfamily of G-protein coupled receptors which includes AVPR1A, V2R and OXT receptors. Its activity is mediated by G proteins which stimulate a phosphatidylinositol-calcium second messenger system. The receptor is primarily located in the anterior pituitary, where it stimulates ACTH release. It is expressed at high levels in ACTH-secreting pituitary adenomas as well as in bronchial carcinoids responsible for the ectopic ACTH syndrome
BCL2L1	protein localization in membrane, organelle outer membrane, outer membrane, apoptotic signaling pathway, regulation of mitochondrial membrane potential, regulation of apoptotic signaling pathway, apoptotic mitochondrial changes, induction of apoptosis by intracellular signals, mitochondrial outer membrane, release of cytochrome c from mitochondria, mitochondrion organization, regulation of mitochondrion organization, anti-apoptosis, mitochondrial membrane organization, regulation of release of cytochrome c from mitochondria, negative regulation of apoptotic signaling pathway
RHBDF2	Rhomboid protease-like protein which has no protease activity but regulates the secretion of several ligands of the epidermal growth factor receptor. Indirectly activates the epidermal growth factor receptor signaling pathway and may thereby regulate sleep, cell survival, proliferation and migration
NPAS4	NXF is a member of the basic helix-loop-helix-PER (MIM 602260)-ARNT (MIM 126110)-SIM (see SIM2; MIM 600892) (bHLH-PAS) class of transcriptional regulators, which are involved in a wide range of physiologic and developmental events
NTF3	The protein encoded by this gene is a member of the neurotrophin family, that controls survival and differentiation of mammalian neurons. This protein is closely related to both nerve growth factor and brain-derived neurotrophic factor. It may be involved in the maintenance of the adult nervous system, and may affect development of neurons in the embryo when it is expressed in human placenta
BCL2L2	anti-apoptosis
MKNK1	This gene encodes a Ser/Thr protein kinase that interacts with, and is activated by ERK1 and p38 mitogen-activated protein kinases, and thus may play a role in the response to environmental stress and cytokines. This kinase may also regulate transcription by phosphorylating eIF4E via interaction with the C-terminal region of eIF4G. Alternatively spliced transcript variants have been noted for this gene
SLC32A1	The protein encoded by this gene is an integral membrane protein involved in gamma-aminobutyric acid (GABA) and glycine uptake into synaptic vesicles. The encoded protein is a member of amino acid/polyamine transporter family II.
NUPL1	This gene encodes a member of the nucleoporin family that shares 87% sequence identity with rat nucleoporin p58. The protein is localized to the nuclear rim and is a component of the nuclear pore complex (NPC). All molecules entering or leaving the nucleus either diffuse through or are actively transported by the NPC. Alternate transcriptional splice variants, encoding different isoforms, have been characterized

*in bold genes directly associated with AD activity

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The Dialogue on Diabetes and Depression (DDD)

Roger S. McIntyre, MD, FRCPC

Professor of Psychiatry and Pharmacology, University of Toronto,

Head, Mood Disorders Psychopharmacology Unit, University Health Network, Toronto, ON, Canada

During the past decade it has become abundantly clear that individuals with bipolar disorder (BD) are differentially affected by being overweight, obesity, abdominal obesity, type II diabetes mellitus, and metabolic syndrome. The robust corpus of descriptive data across multiple countries, cultures, and ethnic/racial groups indicates that there are a host of broad-based and specific factors that conspire to increase the risk of metabolic abnormalities in individuals with BD. The immediate clinical implications of metabolic morbidity in BD is the observation that metabolic comorbidity acts as a "mood destabilizer", decreases cognitive performance, and contributes to excess and premature mortality (1,2). For example, it is now established that the presence of type II diabetes mellitus is associated with a more complex BD illness presentation, lower rate of recovery, higher rate of recurrence, as well as fostering a "depression-prone" illness course (3). Preliminary results also indicate that metabolic abnormalities in BD contribute to cognitive impairment in BD; a principle determinant of psychosocial outcome in BD (1). Like most other mental disorders, BD begins prior to the age of 25 in most affected individuals. Conceptually, it is now believed that "progression" of illness occurs in a large subset of individuals with BD. Available evidence provides rationale for hypothesizing that type II diabetes mellitus may accelerate illness progression in BD, resulting in further "off-trajectory" development for affected individuals.

Fortunately, the robust descriptive literature has now been yoked to endeavors that broadly aim to elucidate mediators of the BD-metabolic association as well as interventional efforts to treat and prevent metabolic comorbidity. For example, iatrogenic factors are well established as risk factors for type II diabetes mellitus in BD as are family history, and co-existing medical comorbidity (e.g., obesity) (4). The observation from longitudinal studies that type II diabetes mellitus and mood disorders may predate each other indicates that type II diabetes mellitus may not only be consequential but may also be causative of mood disorders in some cases (5-7). It is tempting to speculate, now supported by a modicum of data, that type II diabetes mellitus in BD changes brain structure and function resulting in a "metabolic connectopathy"; a pathophysiological nexus of sorts wherein convergent mechanisms implicated in the pathophysiology of BD and type II diabetes mellitus affect central nervous system function.

A major (modifiable) contributor to elevated risk for metabolic disorders in BD is insufficient access to primary, preventative, timely, and coordinated health care. All of us have lamented at how suboptimal physical health care in general has been for individuals with BD particularly as it relates to medical comorbidity with direct implications on bipolar outcome (e.g., type II diabetes mellitus). Replicated evidence indicating that most individuals with BD do not receive general health advice, risk factor modification (e.g., treatment of hypercholesterolemia), physical examinations, and or surveillance for the presence of metabolic comorbidity (despite taking weight-gain promoting agents!) leaves us all with a sense of disquiet (8,9). There clearly is a need to disseminate knowledge as it relates to the interface of BD and type II diabetes mellitus with a particular focus on the clinical ecosystem across multiple settings, cultures, and countries. Against this background, it would be opportunistic to partner with an organization that has established the foregoing as its clarion call.

The Dialogue on Diabetes and Depression (DDD) has been inspired by the observation of a bidirectional relationship between mood and metabolic disorders. The goals of the DDD have been endorsed by well over a dozen national and international non-governmental organizations and its activities include the coordination of research, the development of training materials, the organization of symposia and training courses, the production of reviews of knowledge, as well as the facilitation of collaboration in matters related to the prevention or reduction of problems of comorbid diabetes and depression among countries, organizations, and experts (10,11). The Chairman of the DDD is Norman Sartorius, and Larry Cimino serves as the program director.

Continued from previous page.

The International Society for Bipolar Disorders (ISBD) endorses the goals of the DDD broadly encompassed by the aim to improve outcome of illness and quality of life of persons with comorbid mood disorders and diabetes with a plan to participate in its activities and agreed to be recognized as a participating organization on the materials that concern the DDD's work and the publications that the DDD will produce. As a North American Representative for the ISBD as well as someone who has been working with the DDD, I am pleased to serve as the liaison for establishing and promoting this partnership.

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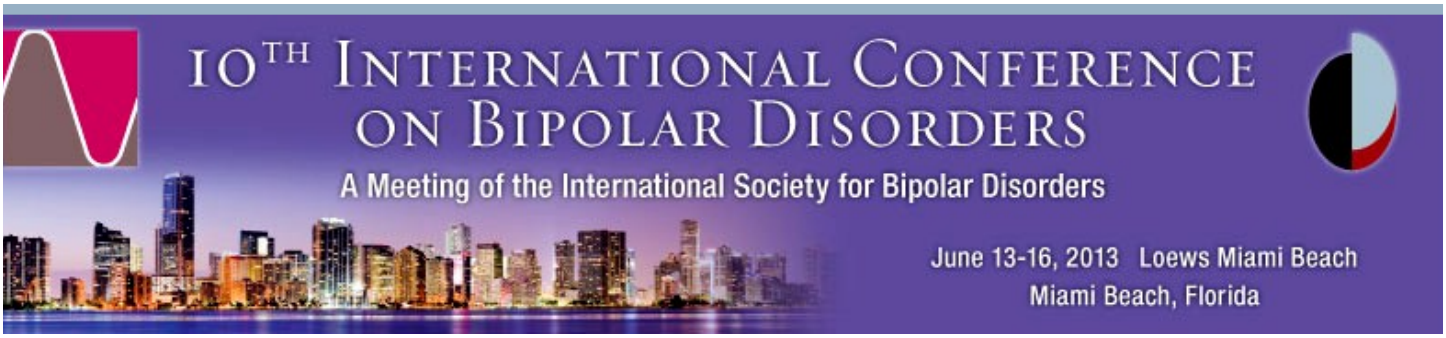

SAVE THE DATE!

Chapter Updates: ISBD Korea

Chapter Officers: Yeon Ho Joo *(President),* Hyun-Sang Cho *(Vice President),* Yong Min Ahn *(Treasurer),Tae Hyon Ha (Secretary)*

At the general membership meeting of the ISBD Korea, Yeon Ho Joo, MD, PhD (University of Ulsan College of Medicine, Asan Medical Center) was re-elected as the 2nd President, and all of the former officers (Vice president Hyun-Sang Cho, Treasurer Yong Min Ahn, and Secretary Tae Hyon Ha) were reappointed. The Executive Committee decided on whom to recommend to join the Regional Organizing Committee for the 2014 Annual Conference of the ISBD that will be held in Seoul.

We have two main activities: the monthly research meeting and the Annual Conference. In the previous year, young researchers have discussed their new findings, as well as potential ways on how to collaborate with each other at the monthly research meetings. The 2012 Annual Conference of the ISBD Korea was held on October 6, 2012 at Korea University Hospital, where we discussed two main topics, "Understanding of Bipolar Depression" and "Subthreshold Bipolarity". Willem Nolen, the President of the ISBD, gave an invited lecture, "Bipolar II depression: Should it be treated as bipolar I depression or as unipolar depression?" at the Conference.

This year, ISBD Korea has planned "Bipolar Academia for Young Researchers" as its new activity. Sponsored by AstraZeneca, the academia will be held from May to July. Participants will have the opportunity to learn how to design and execute studies of animal model, neurocognition, neuroimaging and genetics. We hope these opportunities will recruit potential investigators to our society and strengthen the research network of the ISBD Korea.

ISBD Announcements

Post-doctoral fellowship – molecular psychiatry - biomarkers of mood disorders

The Center of Excellence on Mood Disorders at the Department of Psychiatry and Behavioral Sciences, University of Texas Medical School at Huston, Texas, is looking for a post-doctoral fellow. This individual will focus on research that attempts to identify biological targets for psychiatric illnesses. The individual should hold a PhD degree and have broad experience in molecular biology and biochemistry. The ideal person will have experience in western blotting, spectophotometry techniques, ELISA assays. For this position, an interest in biology and translational research is essential. We are looking for a candidate with excellent communication and interpersonal skills to integrate successfully into an interdisciplinary team. Ability to write scientific manuscripts in English is required.

For information, please contact:
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International Society for Bipolar Disorders: Save the Date!

Dear ISBD Member:

We are pleased to announce that the International Society for Bipolar Disorders will hold its annual general membership meeting on Friday, June 14th, 12-1 PM EDT at Loews Miami Beach Hotel (Room TBA) during this year's 10th International Conference on Bipolar Disorders (ICBD) in Miami, Florida. The meeting will include updates on activities from the past year as well as key decisions taken regarding the Society's future; a light lunch will be provided.

Please RSVP to **Mariya Dobrovinskaya** at **dobrovinskayam@upmc.edu** at your earliest convenience, but no later than Tuesday, April 30th, 2013.

Hours & Location:

Friday, June 14th, 2013
12 -1 PM EDT
Loews Miami Beach Hotel (Room TBA)
Miami, FL
For more information about the conference, please visit: **www.10thbipolar.org**.

A Look at the Literature

Vivek Singh, MD
Associate Professor, Department of Psychiatry,
University of Texas Health Science Center at San Antonio
ISBD Global Editor-in-Chief
ISBD Board Member

REVIEW I

Vancampfort D, Vansteelandt K, Correll CU, Mitchell AJ, De Herdt A, Sienaert P, Probst M, De Hert M. Metabolic Syndrome and Metabolic Abnormalities in Bipolar Disorder: A Meta-Analysis of Prevalence Rates and Moderators. Am J Psychiatry. 2013 Jan 30. doi: 10.1176/appi.ajp.2012.12050620. [Epub ahead of print]

The prevalence of cardiovascular disease among patients with bipolar disorder (BD) is significantly higher than those in the general population and this accounts for premature mortality seen in this group of patients. Metabolic syndrome, a collection of risk factors for cardiovascular morbidity and type II diabetes, such as abdominal obesity, hypertension, dyslipidemia, and dysfunctional glucose metabolism, is associated with higher risk of cardiovascular mortality. This meta-analysis aims enumerate the rate of prevalence and moderators of metabolic syndrome in patients with BD. The authors secondarily aimed to compare the rate of metabolic syndrome between patients with BD and age-and gender-matched healthy cohort. Based on meta-analysis of 37 studies involving close to 7,000 unique BD patients using standardized criteria for metabolic syndrome, 37.3% of patients with BD met criteria for metabolic syndrome. Compared with general population groups, bipolar patients had higher metabolic syndrome rates (odds ratio=1.98; 95% CI=1.74-2.25). Patients from Australia and New Zealand had the highest rate of metabolic syndrome, 64%, while the prevalence rate among patients in North America was 49%. Patients in South America, Europe and Asia had prevalence rates of 38%, 34% and 30% respectively. Higher mean age of study participants was associated with higher rates of metabolic syndrome. Patients who had received treatments with antipsychotics were more likely to have metabolic syndrome compared to those who had not. Metabolic syndrome was significantly more prevalent in patients who were currently receiving treatments with antipsychotics (45.3% versus 32.4%: odds ratio=1.72)

Vivek Singh, MD: Despite limitations of the meta-analysis, findings from this study provide further evidence of the high prevalence of metabolic syndrome in patients with BD. Given the associated cardiovascular morbidity and mortality associated with metabolic syndrome, it is essential BD patients be monitored for cardio-metabolic risk factors and referred for more specialized management of these risk factors. Findings from this meta-analysis implicate an association of treatment with antipsychotics with higher rates of metabolic syndrome. Clinicians should be aware of the risks associated with the use of antipsychotics in a patient population already at a higher risk for metabolic syndrome.

REVIEW II

Nierenberg AA, Friedman ES, Bowden CL, Sylvia LG, Thase ME, Ketter T, Ostacher MJ, Leon AC, Reilly-Harrington N, Iosifescu DV, Pencina M, Severe JB, Calabrese JR. Lithium treatment moderate-dose use study (LiTMUS) for bipolar disorder: a randomized comparative effectiveness trial of optimized personalized treatment with and without lithium. Am J Psychiatry. 2013 Jan 1;170(1):102-10. doi: 10.1176/appi.ajp.2012.12060751.

The last 2 decades have seen an expansion in the pharmacological options in the treatment of bipolar disorders (BD). Prior to the 1990's, lithium formed the mainstay of treatment for BD but its use has declined significantly due to factors associated with limited tolerability at higher doses and the availability of better tolerated pharmacological agents. Since lithium, even at lower doses, has shown to possess neuroprotection and may provide synergy when used in conjunction with other medications, this study aims to assess and compare the effectiveness of personalized, flexible medication regimen (optimized personalized treatment- OPT) with or without moderate dose of lithium in the acute and continuation treatment of patients with BD. Outpatients with BD I (n=216) and II (n=67), currently symptomatic were randomly assigned to treatment with open, flexible, moderate dosages of lithium plus OPT or to OPT alone for 6 months. Primary efficacy measures included the Clinical Global Impression Scale for Bipolar Disorder-Severity (CGI-BP-S) and "necessary clinical adjustments" defined as the number of medication adjustments made per month); secondary efficacy was measured by mood symptoms and functioning. The study also assessed the proportion of patients who attained remission, defined as a CGI-BP-S score ≤2 for at least 2 months and the proportion of patients who received treatment with second-generation antipsychotics. This study did not demonstrate any difference between between the lithium plus OPT group and the OPT alone group on the primary efficacy measures, on CGI-BP-S scores and necessary clinical adjustments. No differences were seen between the two groups in the rates of remission or on measures of mood and functionality. Patients in the lithium plus OPT were less likely to be treated with a second generation antipsychotic than those assigned to the OPT alone group (48.3% and 62.5%, respectively).

Vivek Singh, MD: This comparative effectiveness study did not demonstrate superiority of moderately dosed lithium over treatment with OPT alone on any of the primary or secondary efficacy measure though patients in the lithium group were less likely to be exposed to treatment with secondary generation antipsychotics. This study through low rates of sustained remission in both the groups, highlight the poor long term responseto treatments in patients with BD and is a sobering reminder of the substantial limitations of currently available treatment modalities in BD.

REVIEW III

Singh V, Bowden CL, Gonzalez JM, Thompson P, Prihoda TJ, Katz MM, Bernardo CG. Discriminating primary clinical states in bipolar disorder with a comprehensive symptom scale. Acta Psychiatr Scand. 2013 Feb;127(2):145-52. doi: 10.1111/j.1600-0447.2012.01894.x. Epub 2012 Jul 7.

There is limited data on the spectrum of symptomatolgy that characterize syndromal mood states in patients with bipolar disorder (BD). The application of DSM-IV TR criteria limit a comprehensive assessment of the symptomatic manifestation of syndromal mood states associated with BD which negatively impact the differentiation of syndromal mood states. This study aims to assess the sypmptomatic manifestations of different clinical states in BD and the spectrum and severity of symptoms that differentiate these clinical states using the Bipolar Inventory of Symptoms Scale (BISS). The BISS is a new, semi-structured rating scale developed to assess the spectrum of reported and observed behaviors/symptoms associated with BD. A total of 116 patients who met DSM-IV-TR criteria for BD with DSM-IV defined depressed, manic/hypomanic, mixed episode, or recovered state were interviewed using the BISS. BISS Depression and Manic subscales differentiated syndromal episodes from recovered status as well as between clinical states. Patients in mixed states had a higher illness severity than those in manic/hypomanic or depressed episodes. Level of depression in mixed states was similar to level of depression in depressed episodes and higher than in episodes of mania/hypomania. The severity of mania was not different between mixed and manic hypomanic episodes. The majority of BISS depression and manic symptoms differentiated between clinical states. Irritability-reported and affective lability were more severe in mixed episodes that in episodes of mania/hypomnia while hyperactivity, energetic, grandiose, sharpened thinking, delusions, and

impaired insight were significantly more severe among in episodes of mania/hypomnia than in mixed episodes. Anxiety symptoms were of greater severity in patients with mixed episodes.

Vivek Singh, MD: Findings from this study highlight the limitations of the DSM-IV TR criteria and traditional rating scales used in BD in differentiating between mixed episodes from depressive or manic/hypomanic episodes. The study also enumerates a small set of manic/hypomanic and anxiety symptoms that can aid in the diagnosis of mixed states in BD. The BISS appears to have utility in its ability to distinguish between different clinical states in BD.

Disclosure: Vivek Singh is an author in the article reviewed.

REVIEW IV

Fornaro M, McCarthy MJ, De Berardis D, De Pasquale C, Tabaton M, Martino M, Colicchio S, Cattaneo CI, D'Angelo E, Fornaro P. Adjunctive agomelatine therapy in the treatment of acute bipolar II depression: a preliminary open label study. Neuropsychiatric Disease and Treatment. 2013 Feb; 2013 (9): 243-251. doi: 10.2147/NDT.S41557.

There is considerable evidence to implicate the role of circadian rhythm in bipolar disorder (BD). Thus melatonion, through resetting of the circadian rhythm, may play a role in regulation of mood in BD. Depression in BD, particularly BD II, is the predominant mood manifestation in BD with few effective pharamacological treatments available. Agomelatine, a serotonin antagonist and melatonin agonist, is a norepinephrine and dopamine disinhibtor and has efficacy in depressive episodes associated with unipolar depression. This study aims to assess the safety and efficacy of adjunctive agomelatine in depression associated with BD II. Patients (N=28) who were currently taking valproate (n=12) or lithium (n=12) were treated with open label adjunctive agomelatine for 6 consecutive weeks followed by an optional treatment extension of 30 weeks. Primary efficacy measure was the proportion of patients who attained a 50% or greater reduction on the 17-item Hamilton depression scale. Eighteen patients (64%) demonstrated a response by the end of 6 weeks (71% in valproate group, 55% in lithium group) while 86% of patients showed a response by 36 weeks (82% in valproate group, 91% in lithium group). Adjunctive agomelatine treatment also led to a small reduction in body mass index and Pittsburgh Sleep Quality Index scores. Treatment with agomelatine was well tolerated: 4 patients switched to hypomania.

Vivek Singh, MD: Pharmacological options in the treatment of depression associated with BD are limited. This study demonstrates the efficacy, safety, and tolerability of agomelatine as an adjunct to lithium or valproate in the treatment of depression associated with BD II. Small sample size and the non-controlled nature of the study limit deriving definitive conclusions from findings of this study. Larger, well-controlled studies are needed to demonstrate more definitive evidence for efficacy and tolerability of agomelatine in the treatment of depression associated with BD.

Australasian Society for Bipolar & Depressive Disorders Ltd

2013 ASBDD Conference

"New, newer, newest - the mood spectrum"

3 - 5 October 2013, Melbourne, AUSTRALIA

Venue: Melbourne Brain Centre, Kenneth Myer Building, The University of Melbourne

Keynote Speakers: **Professor Pim Cuijpers, Professor of Clinical Psychology, VU University Amsterdam, The Netherlands**

Carlos A. Zarate, M.D., Chief Experimental Therapeutics, Mood and Anxiety Disorders Program, National Institute of Mental Health, George Washington University, USA

For further information and registration form, please contact the Conference Organisers at asbdd2013@bipolardisorders.com.au or visit the ASBDD website at www.bipolardisorders.com.au

Message from the Conference Convenor

The Organising Committee has pleasure in announcing the Australasian Society for Bipolar & Depressive Disorders (ASBDD) Conference that is to be held in Melbourne, Australia, from 3 to 5 October 2013. In addition, there will be a one day pre-conference workshop on preventing common mental disorders.

This will be the sixth conference under the aegis of the ASBDD, which was formerly constituted in 2004. ASBDD is affiliated with the International Society of Bipolar Disorders, and now addresses depressive illness as well as bipolar disorders.

The 2013 ASBDD Conference will be based at the new Melbourne Brain Centre of The University of Melbourne (on campus) Royal Parade, Parkville. This is at the heart of the Parkville neuroscience precinct, the centre of basic research through to clinical application. Breakfast and dinner meetings will be held in the historic University House facilities on campus.

The Conference will bring together researchers and clinicians from the scientific community worldwide to highlight the latest developments in knowledge on depressive illness and bipolar disorder, as well as treatments to improve clinical outcomes. This will not just focus on biology, but will also emphasise psychological factors and psychosocial rehabilitation and prevention.

The 2013 ASBDD conference is open to the entire spectrum of mental health professionals including basic and clinical researchers, psychiatrists, pharmacologists, psychologists, social workers, psychiatric nurses, students, trainees, interested lay groups and individuals.

We hope you will join us and be an active participant in this Conference. We also hope that you will use this as an opportunity to see what is happening in science in Melbourne and enjoy this fine city.

The 2013 ASBDD Conference website will be available shortly. From this website you will be able to gain information on the program, speakers, submit abstracts and register.

Emeritus Professor John Tiller
Convenor

SAVE THE DATE

5th International Foum: Innovation in Psychiatry
6 - 8 May 2013
Milan, Italy
Website: www.innopsy.it/ProgrammaINNSY2013.pdf

CINP 2013 Thematic Meeting
21 - 23 April 2013
Jerusalem, Israel
Website: www.cinp.org/congress/2013-thematic-meeting-jerusalem/

American Psychiatric Association 166th Annual Meeting
18 - 22 May 2013
San Francisco, CA
Website: www.psych.org/annualmeeting

10th International Conference on Bipolar Disorders
13 - 16 June 2013
Miami, FL
Website: www.10thbipolar.org

World Psychiatric Association International Congress
19 - 23 June 2013
Istanbul, Turkey
Website: www.wpaistanbul2013.org

11th World Congress of Biological Psychiatry
23 - 27 June 2013
Kyoto, Japan
Website: www.wfsbp-congress.org

2013 ASBDD Conference
3 - 5 October 2013
Melbourne, Australia
Website: www.bipolardisorders.com.au

26th ECNP Congress
5 - 9 October 2013
Barcelona, Spain
Website: www.ecnp-congress.eu

World Psychiatric Association International Congress
27 - 30 October 2013
Barcelona, Spain
Website: www.wpaic2013.org

ADVOCACY RESOURCES AROUND THE WORLD

ABRATA: The Brazilian Association of Families, Friends, and Sufferers from Affective Disorders. *www.abrata.com.br*

BIPOLAR Education Foundation (BEF): Takes a community based approach towards Bipolar disorder and Depression education, through programs which engage our key stakeholders and partners including: high schools, sporting clubs, local communities, workplaces, healthcare professionals and governments. *www.bipolar-edu.org/*

Bipolar Network News (BNN): Provides updates in the latest clinical and research information on bipolar disorder. *www.bipolarnews.org.*

Child & Adolescent Bipolar Foundation (CABF): Educates families, professionals, and the public. *www.bpkids.org*

Depression Alliance: UK charity offering help to people with depression, run by sufferers themselves. *www.depressionalliance.org*

Depression and Bipolar Support Alliance (DBSA): Educates patients, families, professionals, and the public. *www.dbsalliance.org*

Dutch Association for Manic Depressives: Sponsors psycho-educational courses to provide information and coping skills. *www.nsmd.nl*

Fubipa: In Argentina, is a grass roots organization offering self-help groups, workshops run by psychiatrists, and lectures. *www.fubipa.org.ar*

GAMIAN Europe: Global Alliance of Mental Illness Advocacy Networks is a non-political, non-sectarian organization dedicated to publishing and promoting information and awareness concerning the incidence and treatment of mental illness. *www.gamian.eu*

Iberoamerican Network for Bipolar Disorder (IAN-BD): Provides collaboration and exchange between groups and independent investigators from the Iberoamerican area, under the institutional support of ISBD. *www.ian-bd.com*

IDEA: In Italy, IDEA works to overcome the stigma and prejudice surrounding depression and bipolar disorders. *www.tin.virgilio.it* (in Italian)

International Bipolar Foundation: Educates caregivers, consumers and the public, supports research, and advocates for the elimination of stigma. *www.InternationalBipolarFoundation.org*

Leading Education and Awareness for Depression Pittsburgh (LEAD): A community advocacy nonprofit that promote collaboration throughout the community to address the standard of depression care as a common concern. *www.leadpittsburgh.org*

Mood Disorders Society of Canada (MDSC): A national non-profit, volunteer-driven organization committed to improving quality of life for people affected by bipolar disorder and related disorders. *www.mooddisorderscanada.ca*

Public Initiative in Psychiatry: Founded in Russia in 1996 by the doctors and nurses of the Mental Health Research Center of the Russian Academy of Medical Sciences. Member of GAMIAN Europe. Website is also in English. *www.pubinitpsy.da.ru*

Stanley Medical Research Institute: A nonprofit organization dedicated to eliminating barriers to the timely and effective treatment of severe mental illnesses. *www.stanleyresearch.org*

THE INTERNATIONAL SOCIETY FOR BIPOLAR DISORDERS
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2013 MEMBERSHIP APPLICATION & RENEWAL FORM

Please complete this form and mail or fax to the above address.

Title: ❑ Dr ❑ Prof ❑ Assoc Prof ❑ Mr ❑ Mrs ❑ Miss ❑ Ms ❑ Other _____

Name: _____ ❑New Member ❑Renewing Member
(Please print legibly or type) *(Please check one)*

Preferred mailing address:
_____
_____
Country: _____

Office Phone: _____
Home Phone: _____
Fax: _____
E-mail: _____

Professional Information: ❑ MD ❑ PhD ❑ Master's Level ❑ Bachelor's Level
❑ Resident/Trainee ❑ Consumer level ❑ Student

Area of Specialty: _____ (psychiatry, psychology, pharmacology, etc.)

Would you be interested in writing an article for *ISBD Global*, the Society Newsletter? ❑Yes ❑No
If so, how may we best contact you? ❑Office Phone ❑Home Phone ❑E-mail ❑Fax

MEMBERSHIP TYPES

(Please see breakdown of dues by country on the following page to determine your dues rates.)

❑ Professional 1 Year
❑ Professional 2 Year
❑ Professional Online (Area 1 & 2 only)
❑ Lifetime $3,000.00 (one time fee)
❑ Patient or Family Member $35.00/year

PAYMENT INFORMATION

❑ Check (in US dollars made payable to International Society for Bipolar Disorders or ISBD)
❑ Credit Card: ❑American Express ❑Mastercard ❑Visa ❑Discover
Card Number: _____ Expiration Date (00/00): _____
Card Security Code: _____
Name as it appears on Card: _____
Billing Address: _____
_____
Signature: _____

THANK YOU FOR YOUR SUPPORT!

INTERNATIONAL SOCIETY FOR BIPOLAR DISORDERS
2013 MEMBERSHIP DUES BY COUNTRY

Area 1 – Professional Membership: $150/year or $285/2 years

Professional Online Membership: $75/year

Bangladesh
Egypt
Ethiopia
Georgia
Ghana
India
Indonesia
Kenya
Nigeria
Pakistan
Philippines
Tanzania
Uganda
Ukraine
Yemen
Zimbabwe

Area 2 – Professional Membership: $200/year or $380/2 years

Professional Online Membership: $100/year

Argentina
Azerbaijan
Brazil
Bulgaria
Chile
China
Colombia
Ecuador
Iran
Malaysia
Mexico
Panama
Peru
Romania
Russia
South Africa
Tukey
Uruguay
Venezuela

Area 3 – Professional Membership: $250/year or $475/2 years

Australia
Austria
Belgium
Canada
Croatia (Hrvatska)
Denmark
Finland
France
Germany
Greece
Hong Kong
Hungary
Ireland
Israel
Italy
Japan
Korea, South
Netherlands
New Zealand
Norway
Poland
Portugal
Saudi Arabia
Singapore
Spain
Sweden
Switzerland
Taiwan
United Kingdom
United States

If you cannot locate your country of residence to the left, please see the complete list of country classifications online at:

http://www.isbd.org/images/PDF/Dues_by_Country_List_2013_Full.pdf

Please feel free to contact the Society offices regarding any membership or dues questions that you may have.

Thank You to All ISBD Members

With a membership representing approximately 50 countries and a scientific board representing 15 countries, the ISBD reflects the democratic spirit of an international organization.

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Contribute to the ISBD Global Newsletter

The newsletter of the *International Society for Bipolar Disorders* is a member service. As such, it prints information about the operation and activities of the organization, member news, feature articles, advocacy issues, letters to the editor, notices of events of interest to the membership, advertisements and other information relevant to both professional and lay members interested in all aspects of bipolar disorders.

We encourage you to send any materials that support and reinforce this function. The newsletter is published quarterly. Deadlines for submission of materials for 2013 are as follows: March 1, June 1, September 1, and December 1.

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Instructions to Authors

Submissions should be typewritten, double-spaced and may be submitted via e-mail in a format compatible with Microsoft Word to Mariya Dobrovinskaya at mariyad@isbd.org. Please follow APA style for any in-text citations and style questions and arrange the list of references in the order of their occurrence in the text. Please send any photo image files in a high resolution .tiff, Photoshop, or comparable format. The *ISBD Global* reserves the right to edit a manuscript to its style and space requirements and to clarify its presentation.