FINAL PROGRAMME
ABSTRACT BOOK

European Bipolar Forum
EBF

THE 12TH INTERNATIONAL REVIEW OF Bipolar Disorders

21–23 May 2012 ▪ Nice ▪ France

International Review of Bipolar Disorders
IRBD

www.irbd.org

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WELCOME AND INTRODUCTION

The Annual Meeting of the European Bipolar Forum

The European Bipolar Forum is exactly that - an open forum for debate and discussion on all topics relating to Bipolarity and Bipolar Disorders. We welcome all individuals to join and comment, although the EBF is based in Europe it is FREE to join and as such is not limited to geographical divides. Please feel free to join in no matter where you are from.

The EBF offers an opportunity to access expert opinion; join in with peers with a common interest; and keep up to date on current thinking on treatments and management strategies. It also offers the opportunity to contribute to clinical research in simple, but effective ways.

The International Review of Bipolar Disorders (www.irbd.org), provides a forum for European Psychiatrists to meet on an annual basis, and provides the perfect stepping stone upon which to base an organization which encourages an ongoing dialogue between like-minded individuals.

The European Bipolar Forum seeks to establish itself as such an organisation. It provides the basis for individuals or National organisations to form like-minded International groups, and to drive common objectives, research and projects.

We welcome your ideas to start new initiatives, and look forward to working with you in the coming years.

International Review of Bipolar Disorders

IRBD is the world's largest Bipolar Disorders Conference. In 2011 over 60 leading experts and 1500 delegates attended with 40 countries represented making IRBD a truly international community. Add to that 6 sponsors, 1 webcast, 2 selective workshops and several advisory board and meet the expert meetings and the breadth and appeal of the IRBD conference becomes clear.

The 2012 International Review of Bipolar Disorders takes place at the Nice-Acropolis Convention Center, Nice, France with a 3 day programme from 21- 23 May 2012.

If you would like to help shape the future of IRBD join the International Scientific Advisory Committee. The committee already comprises nearly 40 highly respected professionals from across the world. However, we are always looking to extend that group.

The 2012 programme will be multi-tracked enabling it to offer a depth and range of information unparalleled in bipolar conferences. Expert review sessions will be delivered by the world's experts on new developments in bipolar disorder's epidemiology, diagnosis, pathology and treatment. New tracks for 2012 include Ground Breaking Research and Discussion and Debate ensuring that there is extensive material for discussion amongst all attendees.

We welcome the chance to form partnerships with other associations in this area to extend understanding and dialogue worldwide. With that in mind we invite regional societies and organisations to take advantage of our Associated Society Scheme.

Contact us if you have a suggestion for the 2012 conference programme, wish to sponsor or would like to keep up to date with the conference as it evolves.

We trust you will find the conference to be a memorable, informative and enjoyable event.

IRBD 2012 CONFERENCE OFFICIALS

President: Prof Jean-Michel Azorin (France)

Chairman: Dr Elie Hantouche (France)

Local Organizing Committee:

Prof J Allilaire (Nice)

Prof D Pringuey (Nice)

Dr P Robert (Nice)

The IRBD Secretariat is very grateful to the IRBD 2012 Conference Advisors:

Prof J Angst

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In Association with

Organisations that have taken the opportunity to link with the International Review of Bipolar Disorders and The European Bipolar Forum and receive the associated benefits are:

Bridging Eastern and Western Psychiatry
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Burning Issues in Psychiatry
Region: Worldwide

European Opiate Addiction Treatment Association
Region: Europe

Global Addiction
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A Message from the EBF Committee

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Recognition of Bipolar Disorders at an academic, clinical, and National level has increased in recent times. However a European-wide network of like-minded individuals or groups is still lacking.

The International Review of Bipolar Disorders (www.irbd.org), has provided a forum for European Psychiatrists to meet on an annual basis, and provides the perfect stepping stone upon which to base an International, regional, cross-cultural federation.

The European Bipolar Network seeks to establish itself as such an organisation. It provides the basis for individuals or National organisations to form like-minded International groups, and to drive common objectives, research and projects.

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Join the European Bipolar Forum

Membership of the EBF is FREE

The Role of the European Bipolar Forum is to:

1. Broaden the base of Bipolar Disorders in Europe
2. Raise the public and political awareness about the importance of Bipolar Disorder in Europe
3. Strengthen the standard, availability and uniformity of Bipolar Disorder treatments in Europe
4. Create and maintain continuing Medical Education accreditation
5. Support and encourage European Bipolar research programmes
6. Strengthen the standard quantity and equality of pre-graduate and post-graduate teaching and training
7. Strengthen WPA, AEP, ECNP, WCBP and EU relations
8. Strengthen the collaboration with professional and lay organisations

The EBF provides:

- An annual Meeting
- A network of esteemed psychiatrists, academic researchers and pharmaceutical companies involved in Bipolar Disorders
- The opportunity to contribute to ongoing research projects advancing the understanding and treatment options for Bipolar Disorders
- Membership of the EBF also entitles you to access the Online Learning Library

Members:

- Have the opportunity to join working parties, special interest groups, pressure groups or any other activity associated with the EBF
- Receive full information about EBF events
- Are entitled to unlimited collaboration requests

CME ACCREDITATION SERVICES

The European Bipolar Forum offers fully peer-reviewed CME accreditation rating services to organisations that are developing a programme for Bipolar conferences.

To have your programme assessed for CME point accreditation please contact: **Society Director • Russell Pendleton • +44 (0)7878 201 416** with the following information:

- The draft programme
- A brief biography of the speakers

We look forward to hearing from you.

CME Credits

Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. The EBFCME credit system is based on 1 EBFCME per hour with a maximum 18 credits.

GENERAL INFORMATION

Venue:

Nice-Acropolis Convention Center
1 Esplanade Kennedy, 06302
Nice Cedex 4,
France

Tel:+33 (0) 4 93 92 83 00

www.nice-acropolis.com

Registration Desk Hours

May 21, 2012

Registration for IRBD 2012 08:30 – 09:00

May 21 & May 22

General opening hours From 08:30 – 19:00

May 23

General opening hours From 09:00 – 13:30

Name Badges

Upon registering you will receive your conference bag and name badge. You are kindly requested to wear name badges during the conference. Please note that delegates without a name badge will not be allowed to enter the conference venue or sessions.

Language

The official language of the conference is English. Simultaneous translation into French is available in the main audiotorium.

Exhibition

The Exhibition will be open at the main foyer of the Convention Centre

Certificate of Attendance

Delegates will be able to receive their certificate of attendance from the registration desk.

Lunch, Refreshments and Breaks

Lunch bags will be provided on May 21 & May 22. Other refreshments will be provided according the programme in the main foyer of the Convention Centre.

Posters

The Electronic Poster boards are located in the main foyer of the Convention Centre. Posters will be available to view throughout the programme days. However, please note the specific poster viewing times according to the programme. Poster presenters may wish to make themselves available during those times.

Connectivity Cafe

An internet cafe will be free to use during the conference. With the following username and password:

Name : **irbd2012**
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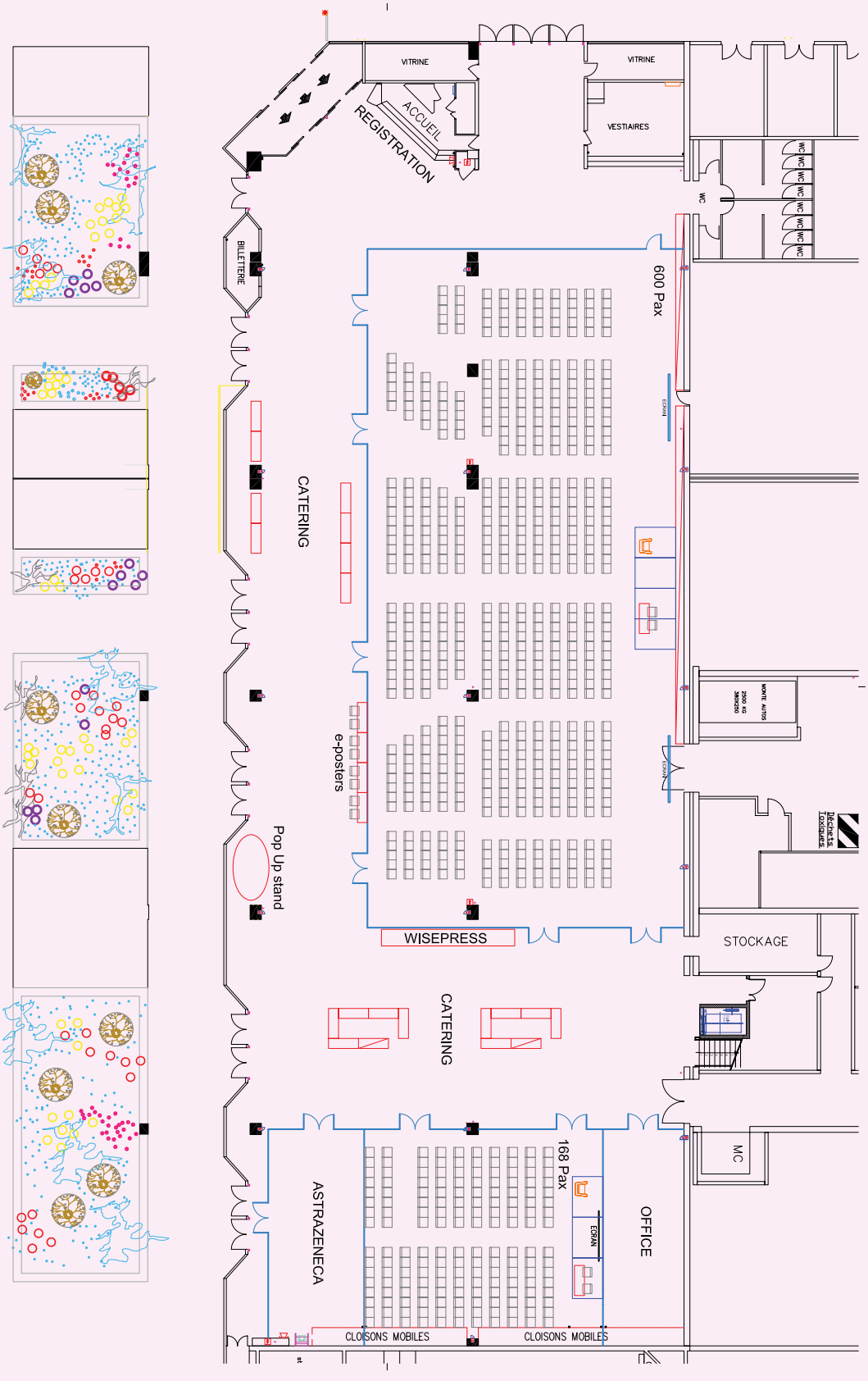
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DAY 1: Monday 21 May

08:30 - 09:00	Registration	
09:00 - 09:15	**WELCOME AND INTRODUCTION**	IRBD PLENARY ROOM
	President: Prof J M Azorin (Fr) Chairman: Dr E Hantouche (Fr) Local Chairs: Prof J Allilaire (Fr), Prof D Pringuey (Fr), Dr P Robert (Fr)	
09:15 – 10:15	**PLENARY SESSION**	IRBD PLENARY ROOM
	Plenary 1: **Bipolar spectrum: The BRIDGE and other international studies** Chair: Prof A Young (UK) Speaker: Prof J Angst (Ch)	
	Plenary 2: **Stress and Bipolar Disorder** Chair: Prof A Swann (US) Speaker: Prof A Young (UK)	
10:15 – 10:45	Coffee	
10:45 – 12:45	**SYMPOSIUM: European Bipolar Forum I**	IRBD PLENARY ROOM
	New Insights in Soft Bipolarity and Emotion Regulation Chairs: Prof J M Azorin (Fr)/Dr E Hantouche (Fr) Validating cyclothymia in youth Prof E Youngstrom (US) / Dr A Van Meter (US) The affective and emotional composite temperament model and scale (AFECTS): utility for the evaluation and treatment of mood disorders Dr D Lara (Br) Temperaments across the spectra of mood disorders Prof J Angst (Ch) Major Change in structured interviews in hypomania Prof E Karam (Lb)	
12:45 – 14:15	Lunch	ELECTRONIC POSTER VIEWING
14:15 – 14:40	**PLENARY SESSION**	IRBD PLENARY ROOM
	Plenary 3: **Subsyndromal Bipolar in the New Nosology** Chair: Prof E Karam (Lb) Speaker: Prof A Okasha (Eg)	
14:40 – 15:00	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Research Update I Chair: Prof E Karam (Lb) Can routinely collected data be used for research on bipolar disorder? Data from the St. Göran bipolar project Mikael Landén, Eleonore Rydén, Anette Johansson, Lennart Wetterberg, Joel Jakobsson, Erik Pålsson, Carl Johan Ekman, Carl Sellgren, Sara Olsson, Sophie Erhardt, Ulvi Bâve	
14:40 – 15:00	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Research Update II Chair: Prof G Perugi (I) Can sophisticated methods of evidence synthesis offer better clinical decision making tools for the treatment of bipolar mania? Aysegül Yildiz, Eduard Vieta, Mateusz Nikodem, Christoph U. Correll, Ross J. Baldessarini	
15:00 – 16:00	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Science Update 1: **Bipolar Disorders: Poised for discovery?** Chair: Prof J Allilaire (Fr) The Genetic Basis of Affective Temperament and the Bipolar Spectrum Prof J Kelsoe (US) New perspectives from research to care and prevention Prof M Leboyer (Fr)	
15:00 – 16:00	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Interactive 1: **Mania Phenotypes** Chair: Prof D Pringuey (Fr) Mania phenotypes: findings from cluster an analyses Prof J Azorin (Fr) Hyperthymic vs clyclothymic BP-I disorder Prof G Perugi (I)	

DAY 1: Monday 21 May

16:00 – 17:00	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Interactive 2: **Management of difficult cases in Bipolar Disorder** Chair: Dr J Cookson (UK) Mania in neuropsychiatric disorders. Focus in post-stroke mania Prof M L Figueira (P) Management of difficult cases: Mania Dr J Cookson (UK) A Pharmaco-epidemiological Study of ADHD and Bipolar Disorder: Complete One Year Data from the Norwegian Population Dr V Syrstad/Dr K Odegaard (No) Postpartum Depression Dr J Masmoudi (Fr)	
16:00 – 17:00	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Science Update 2: **French Networks: Research on Affective Disorders** Chair: Prof F Bellivier (Fr) French Expert Centre Network: first data Prof C Henry (Fr) Functional brain imaging of unipolar and bipolar depression: differences and similarities Prof Fossati (Fr) Comorbid addiction in Bipolar Disorder: results from the French Expert Centre Network Prof F Bellivier (Fr)	
17:00 – 17:15	Break	
17:15 – 18:15	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Interactive 3: **Assessment of Hypomania: Methodological Issues** Chair: Prof E Karam (Lb) BP-II recognition in primary care Prof Z Rihmer (Hu) Correlates of under-diagnosis of Bipolar Disorders Prof E Karam (Lb) Intra-bipolar dichotomy: specificity of cyclothymia Dr E Hantouche (Fr)	
17:15 – 18:15	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Interactive 4: **Geriatric Bipolarity** Chairs: Prof J M Azorin (Fr) Behavioural markers of bipolarity Dr D Lara (Br) Treating late onset Bipolar Disorder Dr A Kaladjian (Fr)	
18:15 – 18:45	**PARALLEL PLENARY**	IRBD PLENARY ROOM
	Plenary 4: **Pathophysiology of psychosis and novel approaches to treatment** Chair: Dr J Cookson (UK) Speaker: Prof A Grace (US)	
18:15 – 18:45	**PARALLEL PLENARY**	IRBD BREAKOUT ROOM
	Plenary 5: **How much bipolar schizoaffective disorder is?** Chair: Dr A Martinez-Aran (Es) Speaker: Dr A Murru (Es)	
18:45 – 19:30	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Evening Lecture: **Tackling stigma through theatre - "That's Just Crazy Talk" by Victoria Maxwell** Speaker: Prof Erin Michalak (Ca)	

DAY 2: Tuesday 22 May

09:00 – 10:00	**SYMPOSIUM: European Bipolar Forum II**	IRBD PLENARY ROOM
	European Bipolar Forum II: **Bipolar Spectrum in special conditions** Chair: Prof L Dell'Osso (I) Sub-threshold Bipolar and reaction to stress and grief Prof L Dell'Osso (I) Affective temperaments and alcoholism Prof A Erfurth (At) Criminal conviction, impulsivity and course of illness in Bipolar Disorder Prof A Swann (US)	
10:00 – 10:30	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Science Update 3: **Risk and Bipolar Disorder** Chair: Prof L Dell'Osso (I) Speaker: Prof J Scott (UK)	
10:00 – 10:30	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Interactive 5: **Bipolar IIB – The Beneficial B Forum of Bipolar Disorder – the case of Dominique Straus-Khan and Mental Disorder** Chair: Prof A Erfurth (At) Speaker: Dr R Fieve (US)	
10:30 – 11:00	Break	ELECTRONIC POSTER VIEWING
11:00 – 11:45	**DEBATE FORUM**	IRBD PLENARY ROOM
	Lithium Use for Bipolar Disorder - does the LiTMUS trial change anything? Discussant: Prof A Young (UK) Speaker: Dr P Grof (Ca)	
11:45 – 13:15	**SYMPOSIUM: Sponsored by LUNDBECK**	IRBD PLENARY ROOM
	Bipolar I disorder: Early and accurate diagnosis and treatment Chair: Allan Young (UK) Clinically relevant subtypes of Mania Giulio Perugi (I) Taking a broader view: New perspectives on the functional outcome Lars Häggström (Se) Asenapine, a multifunctional antipsychotic. From pharmacology to clinical benefits Eduard Vieta (Es)	
13:15 – 14:15	Lunch	ELECTRONIC POSTER VIEWING
14:15 – 14:45	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Plenary 6: **Functional Remediation of Bipolar Disorder** Chair: Prof E Vieta (Es) Speaker: Dr A Martinez-Aran (Es)	
14:15 – 15:45	**SYMPOSIUM: Sponsored by ASTRA ZENECA**	IRBD PLENARY ROOM
	Bipolar disorder understanding: bridging evidence-based medicine and daily practice Chair: Prof Jean Michel Azorin (Fr) Wave BD: a 360 degree real world evidence bipolar disorder perspective ` Prof Eduard Vieta (Es) Bipolar depressive polarity care: the challenge of translating EBM in clinical practice Prof Philip Gorwood (Fr)	

DAY 2: Tuesday 22 May

14:15 – 15:45	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Oral Platform Session I Chair: Prof A Swann (US) **Temperaments as mediators of suicide risk, hopelessness and psychopathology in bipolar disorders** Maurizio Pompili **The association between impulsivity and behaviour in individuals who screen positive on the Mood Disorders Questionnaire** Burden, J. Corcoran, R. Morris, R. **Objective versus Self-Report Measures of Impulsivity and History of Suicide Attempt in Youth with Bipolar Disorder** Sally M. Weinstein, Woo-Young Ahn, Amy E. West, Mani Pavuluri **High nicotine dependence is a factor in the risk of suicide in Bipolar Disorder patients** Luis Gutiérrez-Rojas, Manuel Gurpegui, Francisco Soto, José María Martínez-Ortega, Lola Jurado **Bipolar affective disorders – investigations of the families** E. V. Gutkevich, E. D. Schastnyy, I. A. Zrazhevskaya **How the nitrergic output to large brain vessels from the pterygo-palatine ganglion could matter in BPAD too** Treviranus, Gottfried. M.D. **The dynamics of three-month bi-daily measures of global self-esteem functioning in bipolar disorder** Hugo Vachon, Julie Doron, Véronique Thomas-Ollivier, Marina Fortes-Bourbousson **Concept-matching, link-joy and bipolar disorders** Brian Bayly **Clinical typology of atypical depression and its relation to bipolar disorder A.S.Avedisova,** M.P.Marachev	
15:45 – 16:15	Break	
16:15 – 17:15	**PARALLEL SESSION**	IRBD PLENARY ROOM
16:15 – 16:45	Plenary 7: **A 3-year, open label study of adjunctive Memantine in Treatment-resistant Bipolar Disorder** Chair: Prof M Pompili (I) Speaker: Prof G Serra (I)	
16:45 – 17:15	Plenary 8: **Mixed states: diagnostic and therapeutic implications** Chair: Prof E Vieta (Es) Speaker: Prof I Pacchiarotti (Es)	
14:15 – 15:45	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Oral Platform Session II Chair: Prof A Erfurth (At) **Deterministic dynamics of daily mood over 5 years in a patient with affective disorder** João Guilherme Ribeiro, Carlos Lourenço **Creativity and Bipolar Disorder: Family Study of 300,000 Patients** Mikael Landen **Prevention of Postpartum Psychosis in Women at High Risk** Veerle Bergink, Paul F. Bouvy, Jeroen S.P.Vervoort, Kathelijne M. Koorengevel, Eric A.P. Steegers, Steven A. Kushner **Cognitive inhibition and affective priming effect in Major Depressive Disorder** B Gohier, D Denes, M Briere, CR Mesu, G Fournis, SA Surguladze, D le Gall, JB Garre **Mood Variability in Adult Women** Sarah Romans, David Kreindler, MD; Eriola Asllani MSc., Gillian Einstein, PhD; Sheila Laredo, MD; Anthony Levitt, MD; Brenda Toner, PhD; Donna Stewart, MD **Genome-wide study of CSF kynurenic acid in bipolar disorder implicates a molecular pathway underlying psychosis** C Sellgren1, M Kegel, CJ Ekman, SK Olsson, Camilla I Svensson, C Hultman, P Lichtenstein, SM Purcell, PF Sullivan, P Sklar, G Engberg, S Erhardt, M Landèn	

DAY 2: Tuesday 22 May

17:15 – 18:15	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Clinical Practice 1: **Selecting best treatment for the Bipolar Spectrum** Chair: Prof A Erfurth (At) Changes in DSM-V for Bipolar Disorder type II Prof O Pinto (Br) Antidepressant resistant depression and suicidal behaviour: the role of underlying bipolarity Prof X Gonda (Hu) Cognitive and temperamental correlates of lithium response Prof J Rybakowski (Pl)	
17:15 – 18:15	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Interactive 6: **Early Manifestations of Bipolarity: From Prodromes to Real Risk** Chair: Prof E Youngstrom (US) Paediatric Bipolar Disorder: an update Prof B Birmaher (US) Early interventions in Bipolar Disorder Prof P Conus (Ch) Advances in assessment: Fast and Frugal methods of detection without over diagnosis Prof E Youngstrom (US)	
18:15 – 18:30	Break	
18:30 – 19:00	**EVENING LECTURE**	IRBD PLENARY ROOM
	The Portrayal of Bipolar Disorder, Mental Illness and Mental Health Professionals in Films Chair: Dr E Hantouche (Fr) Speaker: Prof D Wedding (US)	

DAY 3: Wednesday 23 May

09:30 - 10:30	**PLENARY SESSION**	IRBD PLENARY ROOM
09:30 - 10:00	Plenary 9: **Receptor targets for antidepressant therapy in bipolar disorder: an overview** Chair: Dr J Cookson (UK) Speaker: Prof K Fountoulakis (Gr)	
10:00 – 10:30	Plenary 10: **The Potential Clinical Benefits of the Glutamate Neuromodulator N-acetylecysteine in Bipolar Disorders and Associated Psychotic Conditions** Chair: Dr J Cookson (UK) Speaker: Dr R McCarthy (US)	
10:30 – 11:30	**PARALLEL SESSION**	IRBD PLENARY ROOM
	Interactive 7: **Severe Bipolar Disorder - Pathology and Sequelae** Chair: Prof Z Rihmer (Hu) Suicide and Bipolar Disorder Prof P Courtet (Fr) Smoking, suicide and BP-II Prof Z Rihmer (Hu) The severe part of BP-II Spectrum Dr J Deltito (US)	
10:30 – 11:30	**PARALLEL SESSION**	IRBD BREAKOUT ROOM
	Clinical Practice 2: **Unmet Needs in Treating BP-II Spectrum** Chair: Dr E Hantouche (Fr) Think Effectively About Mood Swings (TEAMS): the science and practice of novel CBT in BDs Dr W Mansell (UK) Current role of psychodynamic treatment in Bipolar Disorder Dr R Bush (US)	
11:30 – 12:00	Break	
12:00 – 13:30	**ROUND TABLE**	IRBD PLENARY ROOM
	Clinical Neurobiology of Bipolar Disorder Chair: Prof K Fountoulakis (Gr) Relationship of body mass index, symptoms and cognition in mood disorders and schizophrenia Dr M Siamouli (Gr) Neurobiology of disability in bipolar disorder Dr M Mageiria (Gr) Bipolar disorder in the frame of dementia Dr D Kontis (Gr) Dopamine pathways in Bipolar disorder and Schizophrenia Dr E Tsapakis (Gr)	
CLOSE		

PRESENTATION ABSTRACTS

DAY 1: Monday, May 21, 2012

PLENARY SESSIONS

Plenary 1: Bipolar spectrum: The BRIDGE and other international studies

Chair: **Prof A Young (UK)**
Speaker: **Prof J Angst (Ch)**

Jules Angst, MD, is Emeritus Professor of Psychiatry at Zurich University and Honorary Doctor of University of Heidelberg (Germany).

He was Professor of Clinical Psychiatry and Head of the Research Department of Zurich University Psychiatric Hospital (the Burghölzli) from 1969 to 1994. Since then he has continued his work in epidemiological and clinical research at the University.

Awards: Jules Angst has received the Anna Monika Award (in1967 and in1969), the Paul Martini Prize for Methodology in Medicine (1969), the Otto Naegeli Prize (1983), the Eric Strömgren Medal (1987), and the Emil Kraepelin Medal of the Max Planck Institute, Munich (1992). He has also received the Selo Prize of NARSAD, USA (1994), the Mogens Schou Award for Research in Bipolar Disorder, USA (2001), the Burghölzli Award for Social Psychiatry (2001), the Lifetime Achievement Award of the International Society of Psychiatric Genetics (2002), the Wagner-Jauregg Medal (2007) and the Juan J. López-Ibor Award (2010).

Abstract

Bipolar spectrum: The BRIDGE and other international studies

Angst J. [1]), Gamma A.[1]), Azorin, J-M., Bowden Ch.L., Perugi G, Vieta E, Young A.H.

[1] Zurich University Psychiatric Hospital, Zurich, Switzerland
[2] University of Texas Health Center, San Antonio, USA -
[3] Hôpital de Sainte-Marguerite, Marseille, France –
[4] University of Pisa, Pisa, Italy –
[5] Hospital Clinic, University of Barcelona, IDIBAPS – CIBERSAM, Barcelona, Spain –
[6] Centre for Mental Health, Imperial College London, UK -

Introduction: There is growing evidence that an important group of patients with major depressive disorders (MDE), hitherto diagnosed as having pure depression (MDD), have conditions on a broader bipolar spectrum embracing subthreshold hypomania.

Method: The BRIDGE Study [Bipolar disorder: improving diagnosis, guidance and education] is a multicentre diagnostic study involving 18 countries (in Europe, North Africa and the Near and Far East) of 5635 patients seeking treatment for depression. Psychiatrists consecutively recruited all adults with a diagnosis of MDE according to DSM-IV and completed the questionnaire developed by the BRIDGE steering committee on patients' clinical features and socio-demographic variables. A more descriptive approach to diagnostic variables was applied, which allows the analysis of their validity.

Results: The current gate questions for hypomania (elated or irritable mood) were found too narrow and to exclude a large group of patients reporting increased activity. The minimum 4-day duration for a hypomanic episode was found to exclude many patients with episodes lasting 1 or 2–3 days. In addition, the rule excluding a diagnosis of bipolar disorder if patients with MDD manifest hypomania under an antidepressant, under other treatments, or in association with another medical condition, was not supported by our data. Application of a broader concept of bipolarity not only reduced the size of the group of patients with MDD but also the comorbidity of their disorder, especially the association with all substance use disorders, panic, phobia, OCD, ADHD and borderline personality disorder. These results accord with those reported by subsequent analyses of two large epidemiological studies, the EDSP and the NCS-R study.

Conclusions: The group of patients with DSM-IV MDD is heterogeneous: it includes a subgroup, comprising up to 40% of depressed patients, who also manifest subthreshold hypomanic syndromes. Their recognition is important for this will facilitate early diagnosis of bipolar disorders, earlier intervention and may prevent the development of secondary comorbidity and serious social consequences. MDD is over- and bipolar disorder is under-diagnosed.

These findings could have considerable implications for treatment, WHO cost/burden estimates and future research.

Plenary 2: Stress and Bipolar Disorder

Chair: **Prof A Swann (US)**
Speaker: **Prof A Young (UK)**

Professor Allan Young, MB, ChB, MPhil, PhD, FRCPsych, FRCP(C)

Professor Allan Young holds the Chair of Psychiatry at Imperial College London where he is also Director of the Centre for Mental Health within the Division of Experimental Medicine. He has held academic ap¬pointments at the Universities of Edinburgh, Oxford, Newcastle upon Tyne, (latterly holding the Chair of General Psychiatry at Newcastle) and UBC, Vancouver, Canada where he held the Leading Edge Endowment Fund En¬dowed Chair in Research in the Department of Psychiatry and was also the Director of the Institute of Mental Health. His research in¬terests focus on the cause and treatments for severe psychiatric illness¬es, particularly mood disorders. Professor Young has received research grant funding from the UK Medical research Council, the Wellcome Trust, the Stanley Medical Research Institute, the Canadian Institutes for Heath Research (CIHR), the National Institutes of Health (USA)

PRESENTATION ABSTRACTS

and numerous other funding agencies. He has published over 300 peer-reviewed publications and a number of books about Psychopharmacology and Affective Disorders including, **Bipolar Disorders: Basic Mechanisms and Therapeutic Implications (2nd Ed.)** with JC Soares and **Practical Management of Bipolar Disorder** with IN Ferrier IN and E Michalak, Cambridge University Press, 2010). Professor Young is a member of a number of editorial boards and is a member of numerous professional and scientific societies. He is currently Treasurer of the International Society for Affective Disorders and a Fellow and Member of the executive council of the CINP.

Abstract

Background: Bipolar disorder is a common, complex and costly mood disorder. The aetiopathogenesis of bipolar disorder is multifactorial and involves vulnerability genes and predisposing and precipitating environmental factors. The physiological systems involved in the "stress" response are implicated in both predisposing factors (early life adversity) and precipitating factors for bipolar disorder. Possible therapeutic mechanisms will also be discussed.

Methods: A semi structured systematic review of the published evidence base and relevant abstract proceedings.

Results: In common with other mood disorders early adversity, mediated via epigenetic mechanisms, may play an important predisposing role in the aetiopathogenesis of bipolar disorder. Stressful life events precipitate mania but the relationship is different from other mood disorders. New evidence confirms the possible benefits of stress hormone antagonists for cognitive impairment in bipolar disorder.

Conclusions: Stress plays an important role in multiple aspects of bipolar disorder and also the potential for new drug development.

SYMPOSIUM

European Bipolar Forum I: New Insights in Soft Bipolarity and Emotion Regulation

Chairs: **Prof J M Azorin (Fr)/Dr E Hantouche (Fr)**

Validating cyclothymia in youth

Prof E Youngstrom (US) / Dr A Van Meter (US)

Eric Youngstrom is a Professor of Psychology and Psychiatry at the University of North Carolina at Chapel Hill, where he is also the Acting Director of the Center for Excellence in Research and Treatment of Bipolar Disorder.

He is the first recipient of the Early Career Award from the Division of Child and Adolescent Clinical Psychology, and is an elected member of the American College of Neuropsychopharmacology. He has served as the Director of the Data Management and Statistical Analysis Unit and Research Methods Core of the Center for Research in Bipolar Disorder across the Life Cycle. He earned his doctorate in clinical psychology at the University of Delaware, and he completed his predoctoral internship training at Western Psychiatric Institute and Clinic before joining the faculty at Case Western Reserve University. Prof Youngstrom is a licensed psychologist who specializes in the relationship of emotions and psychopathology, and the clinical assessment of children and families. He teaches courses on assessment and therapy, developmental psychopathology, research design, and multivariate statistics, and has earned the Carl F. Wittke, Glennan Fellowship, and the Northeastern Ohio Teaching Awards. He also actively investigates ways of improving the use of clinical assessment instruments for making better differential diagnoses, predictions about future functioning, or monitoring of treatment progress – particularly with regard to bipolar disorder across the lifespan

Anna Van Meter is a clinical psychology doctoral student at the University of North Carolina at Chapel Hill. Her interests include the classification and assessment of pediatric bipolar spectrum disorders, with a special focus on subthreshold presentations. Ms. Van Meter is also interested in the intersection of emotion, temperament, personality, and mood, and in other risk factors related to early onset mood disorder.

Abstract

Objective: DSM-IV-TR defines four subtypes of bipolar disorder (BP): bipolar I, bipolar II, cyclothymic disorder and bipolar not otherwise specified (NOS). However, cyclothymic disorder in children is rarely researched, most often being subsumed in an "NOS" category, and little is known about its presentation. We present data from two studies investigating the criterion validity of cyclothymic disorder in youths. Youth diagnosed with cyclothymic disorder will be compared to youth with non-bipolar spectrum disorders and to youth with bipolar I, bipolar II, and bipolar NOS.

Method: We used components of the Robins and Guze (1970) framework to examine the validity of cyclothymic disorder as a distinct diagnostic subtype of BP. Using two youth (ages 5-17) outpatient clinical samples (N=894; N=827), participants with cyclothymic disorder (n=53; n=52) were compared to participants with other BP spectrum disorders and to participants with non-bipolar disorders. Constructs of interest include Irritability, Comorbidity, Sleep disturbance, Family history, Quality of life, Suicide and self injury, Treatment, and Overall functioning.

Results: Compared to youths with non-bipolar disorders, youth with cyclothymia had higher irritability ($p<.0005$), more comorbidity ($p<.0005$), greater sleep disturbance ($p<.005$), and were more likely to have a family history of BP ($p<.0005$). Cyclothymia was associated with higher levels of sexual abuse ($p<.05$) and neglect ($p<.05$). Youth with cyclothymic disorder have impaired functioning at school, including suspensions, expulsions, and special services. Families are greatly affected by having a child with cyclothymic disorder, with parents losing an average of 31 work hours due to their child's needs in the

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preceding three months. Youth with cyclothymic disorder are also at high risk for suicidal ideation, non-suicidal self-injury, and suicide attempt. Finally, the majority of youth with cyclothymic disorder are being treated with a psychotropic drug and/or are in psychotherapy, suggesting a high level of treatment utilization.

Comparisons between youth with cyclothymic disorder and youth with other bipolar spectrum disorders revealed no consistent differences.

Conclusions: Results support previous findings that cyclothymic disorder belongs on the bipolar spectrum. Epidemiological studies indicate that cyclothymia is not uncommon among young people, and that it causes significant impairment; the fact that it is rarely studied or diagnosed clinically suggests that many youth are being misdiagnosed. Failing to differentiate between cyclothymia and bipolar NOS limits our knowledge about a significant proportion of bipolar cases.

References:

Van Meter, A., Youngstrom, E. A., Youngstrom, J. K., Feeny, N. C., & Findling, R. L. (2011). Examining the validity of cyclothymic disorder in a youth sample. Journal of Affective Disorders, 132, 55-63.

Van Meter, A. R., Youngstrom, E. A., & Findling, R. L. (2012). Cyclothymic disorder: A critical review. Clinical Psychology Review, 32, 229–243.

The affective and emotional composite temperament model and scale (AFECTS): utility for the evaluation and treatment of mood disorders

Dr D Lara (Br)

Diogo R. Lara, MD, PhD

Clinical psychiatrist, PhD in Basic Neuroscience, Professor at Pontifical Catholic University of Rio Grande do Sul in Biochemistry and Psychiatry, coordinator of the Bipolarity program at São Lucas Hospital.

Abstract

Based on many temperament frameworks, we proposed an integration of emotional and affective temperaments (the AFECT model), forming a common substrate for mood, behavior, personality and part of cognition. Temperament is conceived as a self-regulated system with seven emotional dimensions: volition, desire, anger, inhibition, sensitivity, coping and control. The different combinations of these emotional dimensions result in 12 affective temperament types, namely depressive, anxious, apathetic, obsessive, cyclothymic, dysphoric, irritable, volatile, disinhibited, hyperthymic and euphoric. We also developed and validated a self-report scale to evaluate this construct, the Affective and Emotional Composite Temperament Scale (AFECTS).

Methods: exploratory and confirmatory psychometric analysis were performed with the Internet version of the AFECTS in 2,947 subjects (72% females, 35 ± 11 years old). The scale was also tested for other factors, such as presence of a mood disorder diagnosis.

Results: the factors interpreted as voliton, anger, inhibition, sensitivity, coping and control showed very good Chronbach's alphas for 5 dimensions (0.87–0.90) and acceptable alpha for inhibition (0.75). Confirmatory factor analysis corroborated this 6-factor structure when considering Inhibition as a second-order factor with fear and caution as first-order factors (SRMR = 0.061; RMSEA = 0.053). In the Affective section, all 12 categorical affective temperaments were selected in the categorical choice, with 99% of volunteers identifying at least one adequate description of their affective temperament. Mood disorders showed clear differences in emotional profile (low volition and coping and high sensitivity) compared to controls, and bipolar patients showed more anger and desire and less control and inhibition the depression patients.

Conclusions: the AFECT model provides an integrated framework of temperament as a self-regulated system, with implications for mental health, psychiatric disorders and their treatment. The AFECTS showed good psychometric properties to further study this model.

Temperament and the Spectrum of Mood Disorders

Jules Angst[1]), Michael Hengartner[1]), Alex Gamma[1]), Felix Angst[2]), Vladeta Ajdacic-Gross[1]) and Wulf Rössler[1])

1) Zurich University Psychiatric Hospital, Zurich, Switzerland

2) Rehabilitation clinic "RehaClinic" Zurzach, Bad Zurzach, Switzerland

Abstract

Introduction: First, a long-term prospective study will provide epidemiological data on personality characteristics, including temperament, in individuals with subtypes of major mood disorders; secondly, some data on temperament and mortality will be shown from a long-term cohort study of patients hospitalised for mood disorders.

Method: In the Zurich Cohort Study personality was assessed by the General Behavior Inventory (GBI) and by the Freiburg Personality Inventory (FPI). Impulsivity was assessed by the SCL-90 R. All major mood disorders met DSM-III R criteria for major depression and mania but BP-II disorders were defined by broader criteria for hypomania. In the patient study (began 1959) on long-term course (406 patients admitted for depression or mania) additional data on mortality were analysed repeatedly from 1985 to 2009. Temperament (melancholic, hyperthymic/manic and anxious) was assessed blindly in 1985 by von Zerssen's method applicable to record information and computed at the Max Planck Institute of Psychiatry, Munich.

Results: in the epidemiological study an anxious personality at school age was found in subjects with comorbid mood disorders and anxiety disorders. A hyperthymic temperament was more prevalent among

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men and a cyclothymic or depressive temperament among women. A cyclothymic temperament was twice as common in individuals with bipolar disorder as in those with MDD; hyperthymia was most frequent among subjects with mania and hypomania. Compared to controls, probands with bipolar diagnoses scored higher in aggressivity, extraversion and neuroticism, whereas those with depression took an intermediate position. Impulsivity was equally high in MDD and BPD, but ADHD traits were highest in the bipolar subgroups. In the patient study, in which 90% of the subjects had died, anxious personality traits in those with MDD were significantly associated with a longer life and an aggressive personality with a shorter life.

Discussion and conclusions: the results regarding temperament confirm the studies by Akiskal and others. Temperament and diagnostic subgroups of mood disorders corresponded systematically: anxious and depressed personality traits were associated with the depressive component and hyperthymic traits with the manic component right across the diagnostic spectrum of major and minor mood disorders. The finding that anxiety in depressed patients may be protective is of interest and needs replication by other studies.

Major Change in structured interviews in hypomania

Prof E Karam (Lb)

Prof. Elie Karam received his MD in 1974 and the American Board of Psychiatry and Neurology (USA) in 1979.

Prof. Elie Karam came back to Lebanon in 1980 and worked at the American University of Beirut and in parallel founded the Department of Psychiatry and Clinical Psychology at St. George Hospital Medical Center, Balamand University, Faculty of Medicine in Lebanon, of which he is currently Professor and Head since 2001. He had served too as the Head of Department of Psychiatry in the Lebanese University Medical School from 1995 till 2000.

Prof. Elie Karam founded IDRAAC (Institute for Development, Research, Advocacy and Applied Care) in 1985 and is currently the institution's Executive Director. IDRAAC is an institute solely devoted to Research and Field Services in Mental Health. (www.idraac.org). IDRAAC's research has addressed a variety of important regional and international issues such as violence (including war), depression, bipolar disorders, suicide, substance abuse, childhood disorders, burden and treatment of mental health disorders, temperament etc…

Abstract

The L.E.B.A.N.O.N. study, using the Composite International Diagnostic Interview (CIDI) instrument, has estimated the prevalence of Bipolar (BP) disorders at 2.4%. In order to reassess the prevalence rate of BP disorders in L.E.B.A.N.O.N. and other World Mental Health (WMH) studies, the research team at the Institute for Development, Research, Advocacy and Applied Care (IDRAAC) is investigating the hypomania and mania CIDI questions through different research activities:

1-SCID Changes:

IDRAAC has recently introduced changes, which have been approved by the SCID authorities, to the Structured Clinical Interview for DSM-IV (SCID) for better detection of hypomania and mania.

2- Saudi Arabia Validation Study:

The revised version of the SCID will be used as a gold standard to validate the CIDI for bipolar disorders in the newly launched WMH study in Saudi Arabia.

3-Correlates of Bipolar Disorder in Lebanon:

IDRAAC has studied the flow of questions in the diagnosed instrument, and identified the gate questions in the "screener" and "mania" sections. Then, three groups were created:

1-Reference
2-Screened out inappropriately
3-Continue the mania section: Prevalence and characteristics of Major Depressive Episodes (MDE) (suicide attempt, having one episode of MDE for more than 2 weeks, age of onset (AOO) of MDE, AOO less than 18 years old and age of worst MDE), presence of other disorders (impulse, substance, and anxiety) were analyzed for possible correlations with the three identified groups.

The above analysis has been conducted in Lebanon. Results will be presented; hinting strongly that BP disorder is under-diagnosed in the CIDI based L.E.B.A.N.O.N study.

4-International Study about Correlates of Bipolar Disorder:

The IDRAAC team will be conducting soon analyses, in collaboration with Harvard University and other WMH parties, across several countries included within the WMH Initiative with the aim of assessing the impact of under-diagnosis of hypomania and mania in field studies.

PLENARY SESSIONS

Plenary 3: Subsyndromal Bipolar in the new Nosology

Chair: **Prof E Karam (Lb)**
Speaker: **Prof A Okasha (Eg)**

Prof Ahmed Okasha MD, PhD, FRCP, FRCPsych, FACP(Hon.)

Professor and Director of WHO Collaborating Center for Training and Research in Mental Health, Okasha Institute of Psychiatry – Ain Shams University, Cairo.

- President Egyptian Psychiatric Association.
- Hon.President Arab Federation of Psychiatrists.
- President World Psychiatric Association (2002 – 2005)
- President of the Egyptian Society of Biological Psychiatry, of WFSBP.
- Chairman of WPA Review Committee

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- Editorial Advisory Board of 20 International Scientific Journals.
- Honorary Fellowship of many Psychiatric Associations
- Published More Than 276 Original Articles in National and International Journals.
- Supervised 80 Doctorate Thesis and 147 Master Thesis
- Editor and contributor of 47 national and International books in the field of psychiatry and psychology in both the Arabic and English languages.
- Awarded the highest honors in Egypt, State Merit award in creativity in medicine (2000), State Merit award for Medical Sciences (2007), Nile (Mubarak) Award for Medical Sciences (2010) from the Egyptian academy of science.

Abstract

The aim of this presentation is to highlight the importance, prevalence, morbidity and disability caused by Bipolar syndromal disorders. The entity of these disorders is blurred and should be included in our future classification either in ICD11 or DSMV.

The addition of the dimensional approach may encompass these disorders instead of adding more entities. Bipolar disorder is underdiagnosed, misdiagnosed and undertreated. The emphasis now is on the bipolar spectrum including subsyndromal and the management is under continuous revision. The recent change in conceptualization of bipolar disorder has changed the lifetime prevalence, the difficulty in diagnosis, the syndromal and functional outcome. The bipolar spectrum encompasses many psychiatric disorders which require a change in the attitude and management. Subsyndromal in bipolar disorder impairs functioning and diminishes quality of life. A reassessment of bipolar-spectrum disorders including patients with subsyndromal revealed at least fivefold greater prevalence than found with traditionally defined syndromal diagnoses. Appropriate therapeutic interventions should be considered even when threshold level symptoms are absent.

A dimensional concept (from normal to pathological) was proposed for schizophrenia (schizothymic – schizoid – schizophrenia); and for affective disorders (cyclothymic temperament – cycloid 'psychopathy' – manic-depressive disorder). The term 'spectrum' was first used in psychiatry in 1968 for the schizophrenia spectrum, which integrated schizoid personalities. In 1977 Akiskal proposed a cyclothymic- bipolar spectrum and in 1981 Klerman suggested a mania spectrum. As long as Subsyndromal bipolar has no place in our classification and their needs are unmet, we are depriving a considerable percentage of those patients from alleviating their suffering. The inclusion of subsyndromal bipolar in a mood or bipolar dimension a cluster or spectrum is required.

PARALLEL SESSION

Research Update I

Chair: **Prof E Karam (Lb)**

Can routinely collected data be used for research on bipolar disorder? Data from the St. Göran bipolar project

Mikael Landén, Eleonore Rydén, Anette Johansson, Lennart Wetterberg, Joel Jakobsson, Erik Pålsson, Carl Johan Ekman, Carl Sellgren, Sara Olsson, Sophie Erhardt, Ulvi Båve

Objective: The pathophysiology of bipolar disorder remains obscure. This is partly due to the fact that the DSM diagnostic categories are insufficient tools to describe phenotype. Moreover, the episodic and recurrent nature of bipolar disorder makes relapse prevention a primary goal of treatment. But to date, most studies of , e.g., cognitive function and brain imaging have been retrospective, cross-sectional in nature, or with a short follow-up period. We thus lack knowledge of which patients develop cognitive dysfunction, or develop morphological brain changes and whether these changes worsen during the course of illness. We are therefore unable to offer specific treatment to prevent this from happening. To help answering important pathophysiological questions facing the field, controlled experimental studies (such as PET-studies) need to be complemented with naturalistic longitudinal studies of clinical cohorts. In order to be informative, such studies need to collects an extensive array of endophenotypes. The St. Göran study fill this gap by providing extensive baseline and follow-up data.

Method: This multi-center study enrolls patients from two Bipolar Clinics in Sweden who are diagnosed with bipolar disorder type 1, 2, or NOS, cyclothymia, or manic-type schizoaffective disorder. The baseline investigations are carried out when the patients are in remission. Tests are taken under standardized conditions: the fasting patient arrives at the clinic at 08.00, where a somatic status is taken, followed by blood work, lumbar puncture and Magnetic Resonance Imaging (MRI) scans of the brain. The neuropsychological test battery includes tests of general intelligence, memory functions, and executive function. The key clinical assessment instrument used in this study, The Affective Disorder Evaluation, was developed for the NIMH-sponsored Systematic Treatment Enhancement Program of Bipolar Disorder (STEP-BD). Age- and sex-matched healthy, randomly-selected population controls are collected from Statistics Sweden (SCB). Controls undergo the same set of investigations as the patients. To date, more than 330 patients and 120 matched controls have been investigated.

Results: This presentation will summarize the published results from this project including, e.g., elevated level of cerebrospinal fluid (CAF) kynurenic acid and interleukin-1ß in bipolar disorder; micrometer-sized structures in CSF from bipolar patients revealed by scanning electron microscope; MRI gray-matter reductions associated with manic episodes; sex steroid levels and related genes

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associated with paranoid ideation.

Conclusion: The St. Göran Project is built as a clinical follow-up program with yearly follow-ups feeding data back to the treating physicians. This secures long term follow-up data. This project shows that structuring the clinical work-up can yield valuable research data with minimal effort. To date, the project has been used for cross-sectional studies. Currently, 6-year follow-up data are collected that will be used to study prognostic factors.

Additional Information: These are publications from the St. Göran project that will be summarized during the talk.

1. Rydén E, Thase ME, Stråht D, Åberg-Wistedt A, Bejerot S, Landén M. A history of childhood attention-deficit hyperactivity disorder (ADHD) impacts clinical outcome in adult bipolar patients regardless of current ADHD. Acta Psych Scand. 2009;120(3):239-46.

2. Rydén E, Johansson C, Blennow K, Landén M. Lower CSF HVA and 5-HIAA in bipolar disorder type 1 with a history of childhood ADHD. Journal of Neural Transmission. 2009;116:1667-74.

3. Olsson SK, Samuelsson M, Erhardt S, Engberg G, Nordin C, Landén M. Elevated levels of kynurenic acid in the cerebrospinal fluid of patients with bipolar disorder. Journal of Psychiatry and Neurosci. 2010 May;35(3):195-9.

4. Båve U, Landén M, Nybom R, Wetterberg L: Morphology of structures by scanning electron microscope (SEM) in early fractions of cerebrospinal fluid (CSF) in 59 patients with bipolar disorder. Bipolar Disorders. 2010 May;12(3):298-305.

5. Ekman CJ, Lind J, Ingvar M, Rydén E, Landén M. Manic episodes are associated with grey matter volume reduction - a voxel-based morphometry brain analysis. Acta Psych Scand. 2010 Dec;122(6):507-15

6. Söderlund J, Olsson SK, Samuelsson M, Walther-Jallow L, Erhardt S, Landén M, Engberg G. Elevation of cerebrospinal fluid interleukin-1ß in bipolar disorder. Journal of Psychiatry and Neuroscience. 2011(36):114-8. doi: 10.1503/jpn.100080.

7. Johansson AGM, Nikamo P, Schalling M, Landén M. AKR1C4 gene variant associated with low euthymic serum progesterone and a history of mood irritability in males with bipolar disorder. J Affect Disord. 2011 Sep;133(1-2):346-51. Epub 2011 May 12.

8. Backlund L, Nikamo P, Hukic DS, Ek IR, Träskman-Bendz L, Landén M, Edman G, Schalling M, Frisén L, Osby U. Cognitive manic symptoms associated with the P2RX7 gene in bipolar disorder. Bipolar Disord. 2011 Aug-Sep;13(5-6):500-8. doi: 10.1111/j.1399-5618.2011.00952.x

9. Johansson AGM, Nikamo P, Schalling M, Landén M. Polymorphisms in AKR1C4 and HSD3B2 and differences in serum DHEAS and progesterone are associated with paranoid ideation during mania or hypomania in bipolar disorder. European Neuropsychopharmacology. In Press.

PARALLEL SESSION

Research Update II

Chair: **Prof G Perugi (I)**

Can sophisticated methods of evidence synthesis offer better clinical decision making tools for the treatment of bipolar mania?

Aysegül Yildiz, Eduard Vieta, Mateusz Nikodem, Christoph U. Correll, Ross J. Baldessarini

Objective: Needs on development of decision-analytic cost-effectiveness models and dearth of head-to-head trials prompted use of evidence synthesis techniques which can obtain numerical results on never conducted trials by use of indirect methods borrowing strength from conducted trials (1). This technique is called multiple treatments/comparisons meta-analysis (MTM). A MTM applied to bipolar mania has recently promoted haloperidol as one of the best anti-manic drugs (2). In this article, we aim to explore validity of the underlying assumptions of the MTM technique and of the utilized network structure of anti-manic agents, investigating their potential impact on the ranking of treatments.

Method: We included single-agent-trials with random assignment to treatment-arms that prospectively compared a test-agent with placebo or a standard comparator for treatment of mania (through January 20, 2012). We conducted standard pair-wise meta-analysis (SPM) by weighted inverse variance approach using Comprehensive Meta-Analysis-version 2.2 as well as Bayesian approach, to facilitate consistency checking with the whole MTM conducted within a Bayesian framework.

Results: Previously detected differences in patient and study characteristics as well as placebo response rates ranging from –19% to +38% in the trials of acute mania raised concerns on the validity of underlying assumptions of the MTM technique (3,4). However, statistical tests of consistency could not detect any significant indication of incoherence within the network structure on single-agent-trials. SPM across 54 single-agent-trials of 17 anti-manic drugs in 13,747 manic patients indicated superiority over placebo (based on standardized mean difference as Hedges' g [SMD]) for: tamoxifen (2.30), risperidone (0.66), carbamazepine (0.61), haloperidol (0.54), cariprazine (0.51), paliperdone (0.49), olanzapine (0.48), asenapine (0.42), ziprasidone (0.42), quetiapine (0.40), lithium (0.39), aripiprazole (0.31), and valproate (0.27), with a lack of efficacy for lamotrigine, licarbazepine, topiramate, and verapamil. Results of MTM across single-agent-trials confirmed these findings. There were notable differences on the SMD values of carbamazepine (+0.20), olanzapine (+0.10), risperidone (+0.16), valproate (+0.14), and ziprasidone (+0.13) in comparison to placebo detected with MTM across the network of single-agent versus single-agent plus add-on trials (2). Likewise, the validity of conclusions from the initial network analysis (2), indicating haloperidol as the best anti-manic treatment,

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was challenged when further analyses on a more inclusive and homogenous network structure were conducted. The present network analysis indicated greater short-term anti-manic effects of risperidone than aripiprazole, quetiapine, ziprasidone, lithium, valproate; and olanzapine than lithium, valproate. Available direct evidence validated these findings.

Conclusion: A network analyses on a mixture of studies with different study and patient characteristics, as shown in the particular case of mania, may introduce different risks of bias and may lead to inconsistent networks and questionable validity of the results. These biases may be harder to detect and guard against in the case of MTM. We recommend that factors in addition to apparent ranking of drugs by efficacy should be considered in developing clinical therapeutic recommendations. For the treatment of bipolar disorder, these might well include consideration of effects on full clinical recovery, functional status, cognition, neoroprotection, and risk of suicide as well as adverse metabolic effects.

Additional Information: *To be considered for '30 minute oral session' or '10 minute oral platform'.

References:

1] Salanti G, Higgins JPT, Ades AE, Ioannidis JPA. Evaluation of networks of randomized trials. Statistical Methods in Medical Research 2008;17:279–301.

2] Cipriani A, Barbui C, Salanti G, Rendell J, Brown R, Stockton S, Purgato M, Spineli LM, Goodwin GM, Geddes JR. Comparative effi cacy and acceptability of antimanic drugs in acute mania: a multiple-treatments meta-analysis. Lancet 2011. E-pub ahead of print, 17August 2011; doi::10.1016/S0140-6736(11)60873–8.

3] Yildiz A, Vieta E, Leucht S, Baldessarini RJ. Efficacy of anti-manic treatments: Meta-analysis of randomized controlled trials. Neuropsychopharmacology 2011a;36(2):375–389. E-pub ahead of print, 27 October 2010.

4] Yildiz A, Vieta E, Tohen M, Baldessarini RJ. Factors modifying drug and placebo responses in randomized trials for acute mania. International Journal of Neuropsychopharmacology 2011b;14(7):863–875. E-pub ahead of print, 7 Feb 2011.

PARALLEL SESSIONS

Science Update 1: Bipolar Disorders: Poised for discovery?

Chair: **Prof J Allilaire (Fr)**

The Genetic Basis of Affective Temperament and the Bipolar Spectrum

Prof J Kelsoe (US)

Prof J Kelsoe, Professor of Psychiatry, Director, Laboratory of Psychiatric Genomics, University of California, San Diego, CA, Director, STEP Clinical Research Center, Veterans Affairs San Diego Healthcare System, San Diego, CA

Research Focus

Dr. Kelsoe's longstanding research focus has been the genetics of psychiatric illness, bipolar disorder in particular. As the director of the Laboratory of Psychiatric Genomics at the University of California, San Diego, his work has focused on using a variety of molecular genetic methods to identify the specific genes that predispose to bipolar disorder. He has pursued this primarily by using positional cloning methods such as linkage and association in families in which the illness is genetically transmitted. He has also employed animal models of bipolar disorder in order to identify possible candidate genes that can then be tested in clinical populations. This approach has led to the identification of the gene for G protein receptor kinase 3 (GRK3) as a likely gene for bipolar disorder on chromosome 22. Dr. Kelsoe is currently actively engaged in genome wide association studies of bipolar disorder. He directs the Bipolar Genome Study (BiGS) which is a 13-site consortium focused on identifying genes for bipolar disorder and their relationship to clinical symptoms. He also co-directs the Psychiatric GWAS Consortium for Bipolar Disorder (PGC-BD) which is an international collaborative effort designed to identify genes for bipolar disorder in a sample of over 10,000 patients. These large new technological approaches promise great advances in understanding the causes of bipolar disorder.

Clinical Focus

Dr. Kelsoe's primary clinical focus is the treatment of refractory mood disorders. He is the Medical Director of the NIMH clinical research center Special Treatment and Evaluation Program (STEP) at the Veterans Affairs San Diego Healthcare System where he specializes in the treatment of chronic and refractory mood disorders. Patients at this clinic receive a thorough diagnostic evaluation and are eligible to participate in longitudinal research studies of the ability of genes to predict course, outcome, and treatment response.

Abstract

John R. Kelsoe[1,2], Tiffany A. Greenwood[1], Hagop S. Akiskal[1], Kareen K. Akiskal[1] and the Bipolar Genome Study

[1]Department of Psychiatry, University of California San

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Diego, La Jolla, USA; [2]Department of Psychiatry, VA San Diego Healthcare System, La Jolla, CA, USA

Though much data exists to support the strong role of genes in bipolar disorder, the relationship between genes and presentation is complex. Family studies and molecular studies suggest that different forms of bipolar disorder may be partially genetically distinct. On the other hand, a portion of the genes for bipolar disorder also play a role in several other psychiatric disorders. This picture is further complicated by the observation of a spectrum of manifestations of bipolar disorder that vary in severity and the observation of mild manifestations of the bipolar trait in healthy relatives of bipolar patients. This raises the hypothesis that genetic variation in affective temperament may be the primary aspect of genetic transmission that in turn predisposes to episodes of illness. Bipolar disorder that develops in the context of different affective temperaments have also been reported to have different clinical characteristics, further emphasizing the importance of temperament. We have explored the genetic basis of temperament in bipolar disorder using family methods, as well as, genetic linkage and association studies. We report a genomewide association study of temperament as assessed using the TEMPS-A in 1263 bipolar I subjects. These subjects were genotyped at 1M DNA markers and analyzed for association to each of five affective temperaments. Genomewide significance was obtained for two genes, MDM1 and FBLN1, to the hyperthymic temperament and one region on chromosome 1 to the irritable temperament. These studies suggest that specific temperaments are heritable in bipolar disorder, may be the result of distinct gene effects, and that temperament is a powerful phenotype for genetic studies of bipolar disorder.

Bipolar disorder: New perspectives from research to health care and prevention

Marion Leboyer[1,2,3]

[1] Professeur de Psychiatrie, Université Paris-Est, Pôle de Psychiatrie du GH Mondor, AP-HP

[2] INSERM U 995, Laboratoire de Psychiatrie Génétique, Créteil, France

[3] Fondation FondaMental

Marion Leboyer, M.D., Ph.D., is currently appointed as Professor of Psychiatry at the faculty of the University of Paris East in France. She is head of the University-affiliated department of Psychiatry (Groupe Hospitalier Mondor, Assistance-Publique-Hôpitaux de Paris). She also runs a Psychiatry Genetic laboratory belonging to INSERM (Paris). Since 2007, she is the executive director of the FondaMental Foundation, recently created by the French Ministry of Research. This Foundation is dedicated to creating a network of expert centres for bipolar disorders, schizophrenia and high-level autism, to promoting research in Psychiatry, to assuring professional education in Psychiatry and to increase public awareness of psychiatric diseases. Dr. Leboyer has authored or co-authored more than 230 scientific articles and book chapters, as well as 5 books on a range of topics focusing on bipolar disorder, autism and schizophrenia. Marion Leboyer's research efforts contributed to a better identification of relevant phenotype for genetic studies. She has been able to produce prominent findings such as in autism the identification of the first mutations of genes implicated in synaptogenesis.

Abstract

High rates of misdiagnosis, delayed diagnosis, lack of recognition and treatment of comorbid conditions often lead patients with bipolar illness to have a chronic course with high disability, unemployment rates, and mortality. Despite the recognition that long term outcome of bipolar disorder depends on systematic assessment of both inter-episodic dysfunctional domains and comorbid psychiatric and medical conditions, treatment of bipolar disorder still mostly focuses primarily on alleviation of acute symptoms and prevention of future recurrences. We will review the evidence offering a modern view of bipolar disorder defined as a chronic and progressive multi-system disorder, taking into account characteristics of each patient in order to help design personalized treatments (Leboyer and Kupfer, 2010).

Current guidelines advocate the use of more or less similar treatment algorithms for all patients, ignoring the clinical, pathophysiological, and lifetime heterogeneity of bipolar disorder. Systematic assessment of clinical characteristics such as age at onset, polarity of first episode, staging, and of inter-episodic dimensions, such as abnormal emotional reactivity, sleep and circadian rhythm disturbances, cognitive impairment, along with a systematic screening for comorbid medical and psychiatric disorders as well as risk factors should be performed along the life cycle in order to plan specific and personalized pharmacological, medical, and psychosocial interventions tailored to the needs of each patient.

This new comprehensive framework should guide the search to identify biomarkers and etiological factors (Leboyer et al, 2012) and should help design a new policy for health care including early diagnosis and prevention, treatment, and training. A description of the newly created French bipolar network of expert centres is given as it offers systematic, comprehensive, longitudinal, and multi-dimensional assessments of cases, building personalized treatment (Henry et al, 2011).

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PRESENTATION ABSTRACTS

PARALLEL SESSION

Interactive 1: Mania Phenotypes

Chair: **Prof D Pringuey (Fr)**

Mania phenotypes: findings from cluster analyses

Prof J Azorin (Fr)

Jean-Michel Azorin, MD, is Professor of Psychiatry at the Mediterranean University School of Medicine and Chief, Psychiatry Service, Sainte-Marguerite Hospital in Marseille, France. He is a member of several national and international scientific associations.

Professor Azorin studied medicine and psychiatry at the University of Marseille Medical School. He was also trained in biological psychiatry at the University of Geneva.

He has been interested in the study of affective symptoms in schizophrenia and involved in the conception and implementation of rating scales devoted to assess anxiety and depression in schizophrenia.

He participated, as a member of review committee, to an International Survey of Depression In Schizophrenia designed to evaluate how depression is currently being treated in clinical practice.

Professor Azorin is an expert for the French National Drugs Agency and contributed to the French Consensus Treatment of Schizophrenia.

He has conducted with H. Akiskal and E. Hantouche national collaborative studies on the clinical characteristics of bipolar mania and depression in France.

He participated to the design of worldwide multicenter BRIDGE studies devoted to the systematic screening for hidden bipolarity in patients with major depression.

Professor Azorin has been principal investigator for many studies of newer antipsychotics and particularly the French/ Canadian Clozapine Risperidone Study.

He has published 200 papers on schizophrenia and mood disorders, is the author of one book on vulnerability models in schizophrenia and the co-editor of one textbook on second-generation antipsychotics.

Abstract

Cluster analysis is a multivariate statistical technique which is aimed at defining discrete groups (clusters) of patients within a population, which are defined by measurable patient characteristics. It permits to classify patients in distinct groups, on the basis of clinical variables judged to be relevant for this classification. It could therefore help identify more accurate phenotypes for a clinical entity. Five cluster analytic studies of mania have already been published (Dilsaver et al, 1999; Swann et al, 2001, Sato et al, 2002; Haro et al, 2006; Azorin et al, 2008). Classic (also called “pure” or “typical” mania), as well as psychotic mania, were identified in all studies. Depressive (or “mixed”) mania was obtained in four analyses. A cluster labelled “irritable” or “aggressive” was identified in two studies. Finally, dual mania was found in two of these cluster analyses. Differences found between studies may be related to the characteristics of the population included and to the nature of variables available for analysis. For example, some studies included both in-and out-patients whereas others were conducted on manic patients during their hospitalization and one of them concerned only patients participating in a clinical trial. In three of these studies, cluster analysis was based on mere factor scores following a principal component analysis of a rating scale, whilst in two others it involved a series of clinical, psychological, and illness course characteristics.

In the study conducted on the French National EPIMAN-II Mille Cohort (Azorin et al, 2008) four clusters were identified: “classic mania” (29% of patients) with less severe mania; “psychotic mania”(22.7%) with psychotic symptoms, more severe mania, younger age and social impairment; “depressive mania” (30.4% characterized by female gender, suicide attempts, high number of previous episodes and residual symptoms ; and “dual mania” (17.6%) characterized by male gender, substance use, earlier onset and poor compliance. Patients groups also differed in manic symptoms, marital status, prior diagnoses, first episode polarity, stressors preceding illness onset, and temperamental characteristics. Based on the three latter characteristics, age at onset and other moderating variables we propose a vulnerability-stress model for the outbreak of bipolar I disorder, as well as its further development and genetic underpinnings.

*Department of Psychiatry, Ste Marguerite Hospital, 13274 Marseille Cedex 9 France Email: jazorin@ap-hm.fr

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Eur Arch Psychiatr Clin Neurosci 258: 497-504

Hyperthymic vs clyclothymic BP-I disorder

Prof G Perugi (I)

Dr Giulio Perugi is Professor of Clinical Psychiatry and Psychopharmacotherapy at the University of Pisa, Italy and Director of the Institute of Behavioural Sciences "G De Lisio", Pisa, Italy.

Dr Perugi received his medical degree at the University of Pisa in 1981 and he trained in Psychiatry until 1985. He works as the co-director of the Day-Hospital unit of the Department of Psychiatry of the University of Pisa. Dr Perugi is professor of Clinical Psychiatry and Psychopharmacotherapy at the University of Pisa, Italy. From December 2000, Dr Perugi has been the director of the Institute of Behavioural Sciences "G. Delisio" in Pisa. He is involved in the International Research Project on Mood Disorders in collaboration with the University of South California in San Diego. In this field he has developed and directed many research projects on Mixed States, Mania, Anxious-Bipolar Co-morbidity and Atypical Depression-Bipolar II-Borderline connection. In the field of anxiety disorders he has directed several studies on clinical features and long-term naturalistic treatment of Panic Disorder-Agoraphobia, Obsessive-Compulsive Disorder and Social Phobia. He is part of the editorial board of the Journal of Affective Disorder and other 5 International Journals. He is the author of 3 books and over 350 papers, published in national and international Journals (about 120 peer reviewed), on psychopathology, clinical psychopharmacology, and pharmacotherapy of affective disorders.

PARALLEL SESSION

Interactive 2: Management of difficult cases in Bipolar Disorder

Chair: **Dr J Cookson (UK)**

Mania in neuropsychiatric disorders. Focus in post-stroke mania

Prof M L Figueira (P)

Prof Figueira is Professor of Psychiatry at the Faculty of Medicine, University of Lisbon, and Head of the Psychiatric Department of the Hospital Santa Maria, University of Lisbon, Portugal.

Prof Figueira's area of scientific research is clinical and experimental psychopathology (bipolar disorders) and clinical psychopharmacology. Prof Figueira has been involved in the organisation of various meetings including the 1997 European College of Neuropsychopharmacology (ECNP) regional meeting, the 17th European Congress of Psychiatry that took place in Lisbon 2008 and International Symposia on Bipolar Disorders (1994-2009) since 1997 in cooperation with Hagop Akiskal - Honorary President (Univ. San Diego). Between 1996 and 2005 she was involved as a principal investigator in many pharmacological clinical trials including six phase III studies and four phase II studies. Professor Figueira has been a fellow of the Collegium Internationale Neuro-psychopharmacologicum (CINP) since 1978, the European Association of Psychiatry (EAP) since 2002 and the International Society of Affective Disorders (ISAD) since 2003. She has published over 100 manuscripts in national and international peer-reviewed journals.

Abstract

Post-stroke mania should be considered in any manic patient who presents concomitant neurological focal deficits and is older than expected for the onset of primary mania. Mania is a rare consequence of stroke and according to the sparse published information it is difficult to describe. We performed a systematic review of all cases of mania and stroke to describe those characteristics. More frequently, these patients were male, without psychiatric antecedents or subcortical atrophy, with vascular risk factors and right infarct. There is a significant relationship between post-stroke mania and right hemispheric lesions causing a dysfunction in the ventral limbic circuit that involves the right orbitofrontal and basotemporal cortices, dorsomedial thalamic nucleus and head of the caudate nucleus. The orbitofrontal circuit is a complex functional network that includes the orbitofrontal cortex, the basotemporal region, the thalamus and the caudate nucleus and is a central circuit in mood regulation and social behaviour. Robinson and colleagues [10, 15] suggested that mania was associated with a genetic predisposition and/or subcortical atrophy. This was not supported by the present systematic review .We could not detect a significant role of subcortical atrophy.

The clinical profile of post-stroke mania is very similar to primary mania, characterized mainly by elevated mood/euphoria, pressured speech, and flight of ideas, grandiosity and insomnia. The follow-up of these patients was described in a minority of cases and some of these had recurrence of mania or presented hypomania.

A variety of psychotropic drugs have been used to treat post-stroke mania, mainly mood stabilizers, typical antipsychotics and atypical antipsychotics with variable outcome. Lithium was frequently used with favourable results, but its use is controversial in cases with cerebral lesions. Antipsychotics were used in cases of severe mania with psychotic symptoms. Nevertheless, the lack of placebo-controlled and double-blind trials and the differences in efficacy between the same or similar drugs in different cases reinforces doubts about the role of pharmacological treatment and impedes the definition of targeted and evidence-based treatment guidelines.

Although rare, the results of a systematic study of mania in acute stroke with follow-up and data from diffusion MR or

PRESENTATION ABSTRACTS

perfusion CT in a multicenter study with a central database would be relevant.

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Management of Difficult Cases: Mania

Dr J Cookson (UK)

Consultant and Honorary Senior Lecturer in Psychiatry at The Royal London Hospital in London, England, UNITED KINGDOM. John Cookson obtained a doctorate in pharmacology at Oxford, and studied clinical medicine at University College Hospital in London. His higher training in Medicine was in London and in Psychiatry was at St. Bartholomew's and the Maudsley Hospitals. He is responsible for a catchment area service comprising a community mental health team and a general psychiatric ward, with access to a Home Treatment Team, an Early Intervention Service and an Assertive Outreach Team. He was consultant for a Psychiatric Intensive Care Unit from 1988-2007, and for a Specialist Addictions Unit from 1981-1996. Dr. Cookson's research interests are in psychopharmacology and the use of drugs in psychiatry, particularly in relation to the treatment of bipolar disorder. He has participated in the development of new drugs for bipolar disorder, schizophrenia, depression, social phobia, and panic disorder. He serves on the editorial boards of The British Journal of Psychiatry, International Clinical Psychopharmacology, and Advances in Psychiatric Treatment. He coauthored the fourth and fifth editions (2002) of Use of Drugs in Psychiatry: The Evidence from Psychopharmacology, published by the Royal College of Psychiatrists. He participated in the British Association for Psychopharmacology Guidelines for Bipolar Disorder.

Abstract

Mania is treated in the first instance usually with an antipsychotic, preferably an atypical to reduce the likelihood of extrapyamidal side effects.

Antipsychotics vary in their effectiveness in mania, the most efficacious being haloperidol, followed by risperidone and olanzapine, with quetiapine and aripiprazole being less efficacious.

In severe agitation, an antipsychotic is combined with a benzodiazepine, often given by injection intramuscularly. A barbiturate may occasionally be required to achieve sedation.

For mania that has not responded to an adequate dose of haloperidol, the addition of lithium or valproate is the next step. Blood levels of lithium up to 1.4 mM/L provide more efficacy than lower levels in mania, but patients must be observed carefully to avoid the development of neurotoxicity.

Carbamazepine has value in severe mania but involves pharmacokinetic interactions with certain antipsychotics.

Careful nursing within a psychiatric Intensive Care Unit may be needed including, in some cases, seclusion.

Occasionally electroconvulsive therapy provides fast and effective improvement. Lithium and anti-epileptic drugs should be withheld before ECT is administered.

Depot injections of antipsychotic medication, particularly clopenthixol decanoate, can achieve control in some instance where oral medication has not been adequate.

Clozapine has a limited base of evidence for efficacy as an adjunctive medication is resistant mania.

A Pharmaco-epidemiological Study of ADHD and Bipolar Disorder: Complete One Year Data from the Norwegian Population

Vigdis E.G. Syrstad[1,2], Anne Halmoy[3], Steven C. Dilsaver[4], Øivind Hundal[1,5], Trond Riise[6], Anders Lund[1,2], Hagop S. Akiskal[7,8], Jan Haavik[3,9], Ole B. Fasmer[1,2] Ketil J. Oedegaard[1,2]

[1] Moodnet Research Group, Haukeland University Hospital, Norway

[2] Department of Clinical Medicine; Section of Psychiatry, University of Bergen, Norway

[3] Department of Biomedicine, University of Bergen, Bergen, Norway

[4] Comprehensive Doctors Medical Group, Arcadia, Ca, USA

[5] Haukeland Hospital Pharmacy, Apotekene Vest HF, Bergen, Norway

[6] Research group for Lifestyle Epidemiology, Dept. of Public Health and Primary Health Care, University of Bergen, Bergen, Norway

[7] Department of Psychiatry, VA San Diego Healthcare System, CA, USA

[8] Department of Psychiatry, University of California San Diego, CA, USA

[9] Division of Psychiatry, Haukeland University Hospital, Bergen, Norway

Dr. Vigdis Elin Giaever Syrstad, MD
Senior consultant Haukeland University Hospital, department of emergency psychiatry, (tertiary referral center) Bergen, Norway. Also finalizing a Master of health administration at University of Oslo. Main interest of research is in the field of bipolar disorder, temperaments, vagal nerve stimulation. Speaker and co-chairing at several national and international conferences with main focus on bipolar disorder. Since 2006 member of the board of the Norwegian society of bipolar disorder. Member of the board of education and certification, specialist committee of the Norwegian Medical association since 2002-2009, since 2006 as co-chair.

Member of Moodnet Research Group, Prevention of Psychosis project, POP, Pharmacogenomics of Mood Stabilizer Response in Bipolar Disorder (PGBD), USCD NIMH funded multicenter study, clinical investigator, European Bipolar Forum; Board member and member advisory committee and scientific sercretariat from 2008. ISBD Membership committee from 2011, Participating in the research group of prof.dr. med Ole Bernt Fasmer and

PRESENTATION ABSTRACTS

dr.med Ketil Oedegaard.

Has received either grants, participated in clinical trials from various pharmaceutical companies such as Desitin Pharma, Glaxo Smith Kline, Pharmacia Upjohn, AstraZeneca, Pfizer.

Ketil J. Oedegaard, MD PhD, Specialist in Psychiatry. Chief or Research Division of Psychiatry, Health-Bergen, and Head of the Department of Mood Disorders, same place. Assoc. Professor Department of Clinical Medicine, University of Bergen, Norway. Chairman of the Norwegian Society of Bipolar Disorders since 2004, board member of the International Society for Bipolar Disorders (ISBD; Research committee) and the European bipolar forum; Chairman Migraine phenotype work group Bipolar Genome Survey: NIMH Genetics Initiative for Bipolar Disorder Consortium. Main research interests have been clinical, epidemiological and genetic studies of affective disorders. Currently the Principal Investigator of the following studies: 1. SIPEA-project (Cohort of 6000 patients admitted to the acute department of Psychiatry followed up since 2005). 2. Prevention of Psychosis Project (POP) (PI, Health-Bergen). 3. The Norwegian Randomized controlled study of ECT in bipolar depression (PI Health- Bergen). 4. The Pharmacogenomics of Moodstabilizer response in bipolar disorder (PI, Norway).

Abstract

Background: Attention-deficit/hyperactivity disorder (ADHD) and Bipolar Disorder (BD) have been associated with one another in epidemiological, clinical and genetic studies. However, it is not known if or how such associations are reflected in the concurrent use of medications for these disorders in the general population.

Methods: Data from the Norwegian Prescription Database for 2006 were analysed for the purpose of ascertaining how drugs used to treat ADHD and mood stabilizers used to treat BP (lithium, carbamazepine, valproic acid, lamotrigine) are concurrently prescribed to the same patients in the general population. Data were subjected to analysis testing deviation from unity for the OR performed by logistic regression tests.

Results: In the total Norwegian population (N = 4640219) anti-ADHD drugs were prescribed to 18481 persons (0.40%), 19517 (0.45 %) were prescribed a mood stabilizer for a BD, and 343 persons were prescribed both types of drugs (0.008%). The overall OR for having received both ADHD medication and mood stabilizer was 5,13 CI (4.61:5.72) p. <0.001 The association was significantly stronger for women OR 7,97 CI (6.83:9.29) p compared to men OR 4,17 CI (3.58:4.85)]

The association was significantly increased for all mood stabilizers (Lithium (n=37): OR: 2,4185, CI 1,784-3,3455; Carbamazepine (n= 22): OR: 4,1910, CI 2.7476- 6.39; Valproate (n= 70): OR: 9.1989, CI 7.2402- 11.6875; Lamotrigine (n= 183): OR: 14.6506, CI 12.6065- 17.0261) when controlled for age and gender. The association was stronger for lamotrigine compared to all other mood stabilizers (p< 0,001).

Conclusion: Concurrent use of bipolar mood stabilizing medications was found to be increased in patients diagnosed with ADHD in the general population. However, the relation varied significantly between different mood stabilizer, and the association was strongest for the use of lamotrigine, and least pronounced for lithium, possibly revealing a pattern in the pharmacological management of patients with ADHD and BD of clinical and pathophysiological importance.

Key words: ADHD, Bipolar Disorder, co-morbidity, medication, epidemiology, the Norwegian Drug Prescription Registry.

Acknowledgements: This research was sponsored by an unrestricted grant from Moodnet Research Group, Haukeland University Hospital, Institute of Clinical Medicine; Section of Psychiatry, University of Bergen, Norway.

Postpartum Depression

Dr J Masmoudi (Fr)

Professor of Psychiatry, Service de Psychiatrie « A », CHU Hédi Chaker Sfax Tunisie

Abstract

Post partum depression (PPD) is a frequent psychiatric condition, but little is known about its potential bipolar nature and the implication of affective temperaments. The goal of this is to estimate the prevalence of the PPD and assess the affective temperamental profile of those affected.

Method: The study was conducted in the department of Gynecology and Obstetrics of the CHU of Sfax, Tunisia. The selected population included all 213 consecutive admissions (mean age=29 years). Post partum depressive symptomatology (SPPD) was assessed during the first week after delivery by using the EPDS (Postnatal Edinburgh Scale Depression) in its Arab version. TEMPS-A was simultaneously used to assess affective temperaments.

Results: Forty and one women (19,2%) had a score higher than 9 on the EPDS (group D+). Lower educational level, lower social and family support, dysfunctional marital relationship, problems with accepting the pregnancy, and prior psychiatric disorders were significantly more present in the D+ group. The majority of the affective temperaments, excepted hyperthymic, were correlated between them. The EPDS scores were correlated with all temperamental scores, except for hyperthymic. Higher scores on the depressive, irritable, anxious and cyclothymic temperaments were observed in the group D+.

Women belonging to the 3rd and 4th quartiles of the depressive, cyclothymic and irritable temperaments, and those belonging to the 4th quartile of the anxious temperament, were significantly more depressed. Cyclothymic and depressive temperaments seemed to influence the pregnancy acceptance. Other interactions

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were observed between SPPD, temperamental profiles and quality of marital relation, family support. The opposite seems true for the hyperthymic temperament, which could be protective against SPPD through better psychosocial conditions. Multivariate regression analysis showed that cyclothymic and anxious temperaments are significant risk factors independently from psychosocial factors such as problems with accepting the pregnancy, which seemed to be the most important risk factor.

Conclusion: PPD represents a frequent disorder, which needs to be correctly screened and recognized especially with its temperamental attributes combining anxious, irritable, depressive, and cyclothymic traits. This complex unstable temperament should be considered as a predisposing factor, which interacts also with other common risk factors of post-partum depression.

PARALLEL SESSION

Science Update 2: French Networks: Research on Affective Disorders

Chair: **Prof F Bellivier (Fr)**

French Expert Centre Network: first data

Prof C Henry (Fr)

Chantal Henry, MD, PhD, Professor of Psychiatry, University of Paris-Est and Chenevier Hospital, Creteil, FRANCE

Chantal joined the faculty of the University of Paris-Est in September, 2008 as Professor of Psychiatry after 14 years at the Bordeaux hospital. Dr. Henry's research focuses on the assessment and treatment of mood disorders, with a particular interest on emotional reactivity to define mood episodes and intercrisis period. She works also on the identification of relevant phenotypes for genetic studies on bipolar disorders.

Since 2008 in charge of the organisation of french networks of expert centres on bipolar disorders, schizophrenia and Asperger. She coordinates also an european project: ENBREC (European Network of Bipolar Research Expert Centres). Dr. Henry has authored or co-authored more than 90 scientific articles, book chapters and books.

Abstract

In France, a huge duration of untreated illness is observed for bipolar disorders, with patients waiting in means 9 years between their first major mood episode and the initiation of a mood stabilizer. This delay can be explained by low care accessibility, misdiagnosis and lack of awareness of current guidelines. Efforts to provide optimal care by general practitioners and psychiatrists are undermined by the complexity of the disorder and difficulties in applying clinical practice guidelines. A national network of bipolar expert centres was established under the aegis of Fondamental Foundation with fundings from the Ministry of Research and Ministry of Health. Each centre has established strong links to local health services and provides support to clinicians in delivering personalized care plans derived from systematic case assessments undertaken at the centre. The network has adopted a common set of diagnostic and clinical assessment tools. All data are collected using a web application, e-bipolar© and are shared between centres through a national anonymized database. We will present here the rationale for setting-up this network and the first descriptive results obtained for the included patients.

Functional brain imaging of unipolar and bipolar depression: differences and similarities

Prof Fossati (Fr)

Dr. Fossati is a graduate of the University of Lille II School of Medicine. He did his adult psychiatry training in Paris (University of Paris VII). He is currently a Full Professor of Psychiatry and chief of a mood Treatment Center for Adults at the Pitié-Salpétrière Hospital and the University of Paris VI, Pierre & Marie Curie. Dr Fossati was a post-doctoral Research Fellow at the Rotman Research Institute, Baycrest center for geriatric care (Toronto) under the supervision of Pr H Mayberg. He defended his PH. D in 2001 in paris. His main clinical and research interests include the self, memory and emotion in depression and healthy subjects. This includes exploring with functional fMRI the neural correlates of emotional and cognitive impairment in depression and the changes in brain activity induced by antidepressant treatment and the neurobiological mechanisms of social cognition, self-awareness and psychotherapy.

Abstract

Mood disorders are very heterogeneous clinical conditions with unipolar depression on one side and bipolar disorder on the other side. There are not clear clinical and neuropsychological features that allow to distinguish bipolar depression from unipolar depression. Being able to differentiate these two forms of depression would be useful for supporting the presence of distinct biological underlying processes. In this talk we will review from functional and structural MRI studies evidence for difference and similarities between unipolar and bipolar depression. Both unipolar and bipolar depression are usually conceptualized within the framework of emotional dysregulation, an impaired ability to self-regulate emotion resulting from abnormal interaction of emotional and cognitive processes. Emotional dysregulation is associated with impaired cortical and limbic interaction. Bipolar depression is associated with abnormal ventrolateral prefrontal cortex activity whereas unipolar depression is characterized by an increased dorsomedial prefrontal activity. Unlike unipolar depression, bipolar depression increases the sensitivity to negative and positive emotional stimuli, a finding consistent with structural changes in amygdala described in bipolar disorder. Finally clinical and theoretical significance of these findings will be discussed.

PRESENTATION ABSTRACTS

Comorbid addiction in Bipolar Disorder: results from the French Expert Centre Network

Prof F Bellivier (Fr)

Frank Bellivier is the Professor of Psychiatry at the psychiatric unit at Mondor Hospital, Creteil, France.

He undertook his degree in Medicine at the C.H.U Cochin-Port-Royal, Paris V and having obtained a qualification in Psychiatry from Hospital Pitié-Salpêtrière, Paris went on to become a senior practitioner, followed by Professor of Psychiatry at the Psychiatric unit of Mondor Hospital, Creteil. He also holds a Masters Degree in statistics and genetic epidemiology and a Ph.D in Neuroscience. He has been awarded the University Paris XII research prize in 2000, the Jules Baillarger research prize in 2003 and the NARSAD independent investigator award in 2004. His main research focus is on the genetics of bipolar disorders and suicidal behaviors. He has published over 70 research papers and been a contributing author to a number of texts on psychiatry genetics.

Abstract

Authors: R. ICICK[1], M. BARDE[1], A. DESAGE[2,3], S. GARD[2,3], S. GUILLAUME[4], F. MATHIEU[5], C. HENRY[3,5,6], F. BELLIVIER[3,5,6]

[1]AP-HP Hôpital Fernand-Widal, Université Paris Diderot, Inserm U705, Paris, France;

[2]Centre Expert Bipolaire CHS Charles Perrens, Bordeaux;

[3]Fondation FondaMental, Hôpital Albert Chenevier, Créteil;

[4]Inserm U1061, Université Montpellier 1, CHU Montpellier, Montpellier, France;

[5]Inserm U955 - Équipe 15, Université Paris Est, Faculté de médecine, Créteil, 94000

[6]AP-HP, Hôpital H. Mondor - A. Chenevier, Service hospitalier, Créteil, 94000,

Bipolar disorder (BPD) is a chronic, disabling and frequent illness characterized by relapses and recurrences of mood swings with intervals of symptomatic remission. It is highly comorbid with many somatic and psychiatric disorders, especially substance use disorders (SUD), another chronic and relapsing condition.

The lifetime prevalence of SUD is around 50% in subjects with BPD, which makes them 3 to 5 times more likely to suffer from SUD than the general population. Yet knowledge is scarce about the course, the possible mechanisms, the optimal treatment and even diagnosis issues raised by that co-occurrence.

Our objective is to provide a comprehensive review of the existing literature about comorbid BPD-ADD. We also present the analysis of 718 patients bipolaires: 528 without SUD and 190 with SUD (26.5%). Multivariate analyses showed that male gender, early age at onset, onset polarity were associated with a lifetime history of SUD. SUD was also associated with a positive history of childhood trauma. Affective instability and affective hyper-reactivity, core dimensions of bipolar vulnerability, as well as impulsivity were also associated with SUD. No association was observed between SUD and scores at the Buss and Durkee Hostility Inventory.

Keywords: Bipolar disorder – addiction – substance use disorder – pathological gambling – comorbidity

PARALLEL SESSION

Interactive 3: Assessment of Hypomania: Methodological Issues

Chair: **Prof E Karam (Lb)**

BP-II recognition in primary care

Prof Z Rihmer (Hu)

Prof. Zoltán Rihmer, MD, PhD, DSc, received his medical diploma at the University of Pécs, Hungary in 1971. From 1971 to 1973 he worked at the Institute of Psychiatry, Pomáz, Hungary. From 1973 till 2007 he worked at the National Institute for Psychiatry and Neurology, Budapest, Hungary as the Director and Head (from 1983) of the In-and Outpatient Department of Psychiatry No. III. of that institute. From 2005 he is a professor of psychiatry at the Department of Psychiatry and Psychotherapy, Semmelweis Medical University, Budapest, where he works currently at the Department of Clinical and Theorethical Mental Health.

Professor Rihmer has three special examinations: psychiatry (1976), neurology (1979) and clinical pharmacology (1990). He received his PhD at the Hungarian Academy of Sciences in 1993, and his DSc in 2004. As a full-time clinician, his special interest is the clinical and biological/genetical aspects of mood and anxiety disorders, with particular regards to prediction of treatment response, prediction and prevention of suicide, the role of helath-care systmem in suicide prevention, the relationship between affective temperaments and major mood disorders, and the interface between mood and cardiovascular disorders. He has published more than 350 scientific articles/book chapters (more than 180 in English) and four books. He is a regular reviewer of 4 Hugarian and almost 20 international psychiatric journals. Professor Rihmer is deeply involved in graduate and postgraduate training of professionals and in the last 15 years he is also a regularly invited speaker at numerous international scientific meetings. He received the Brickell Suicide Research Award of the Department of Child and Adolescent Psychiatry, Columbia University, New York (1999), the NyírőGyula Award of Hungarian Psychiatric Association (1987), the Award of the Medicina Publishing House (1987) and the Life Work Award of the Hungarian Psychiatric Association (2005).

Abstract

Major depressive episode is common condition in primary health care service and many depressed patients first

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consult their general practitioners. The current prevalence of major depressive episode in the primary care practice is between 8 and 12%, and earlier studies reported that only a minority of these cases are recognized and treated adequately by GPs. Fortunatley, most recent studies reported much higher (62-85%) recognition and treatment rates. However, GPs have still some difficulties in correct diagnosis and treatment of depression and it is particularly true for bipolar depression. Recent studies show that between 1 and 2 percent of patients visiting their GPs have bipolar (type I and II) disorder. As bipolar patients (and particularly bipolar II ones) seek help in primary care almost exclusively with depressive symptomatology, the misdiagnosis of bipolar patients as unipolar depressives is quite common in primary care. In addition, most recent studies show that more than one-third of DSM-IV diagnosed (unipolar) major depressive disorder patients have subthreshold hypoanic symptomatology, indicating that they belong to the bipolar affective spectrum. As antidepressant-resistance, antidepressant-induced worsening of depression and antidepressant-associated (hypo)manic switches are quite frequent in (overt and covert) bipolar depressives, antidepressant monotherapy (a standard treatment of unipolar depression) should be avoided in bipolar I, II and bipolar spectrum disorder patients. The importance of correct identification of bipolar disorders in primary care will be also discussed.

Correlates of under-diagnosis of Bipolar Disorders

Prof E Karam (Lb)

Professor and Head, Department of Psychiatry and Clinical Psychology, St George Hospital University Medical Center, Balamand University Medical School, IDRAAC, Lebanon

Abstract

There is clear evidence that Bipolar Disorder is frequently misdiagnosed (69%) and with about two third of them for more than 3 years of first seeking treatment[1]. Additionally, new data from the BRIDGE study proposes robust criteria for Bipolar Disorder[2]. Data from population country-wide and national epidemiological study, the L.E.B.A.N.O.N., highlights a third problem, which lies in most instruments that we have used in international studies. Diagnosing Bipolar Disorders (& mostly Hypomania) will no doubt improve with these new insights.

[1]Hirschfeld et al., J Clin Psychiatry 2003; 64: 161-174.

[2]Angst et al., Arch Gen Psych, 2011; 68 (8): 791-8.

Intra-Bipolar Dichotomy: Specificity of Cyclothymia

Elie G. Hantouche, MD

Dr Hantouche is considered as top expert for bipolar disorders and OCD. He is also involved to be the scientific advisor of the AFTOC (French Association of Patients with OCD), ARGOS (bipolar patients), and BICYCLE (parents of bipolar children). Currently, Dr Hantouche is the director of CTAH, Anxiety and Mood Center (since 2006)

He have published more than 200 papers (74 cited in Pubmed*) and his the author of 14 books on OCD, Cyclothymia, Bipolar OCD, Juvenile bipolarity, Creativity, Psychoeducation for Cyclothymia, Trilogy of fears and phobias. In April 2005, he chaired the 5th International Experts Meeting for Bipolar Disorders and launched the European Bipolar Forum. He is reviewer for many international journals. He was the co-chair of the first "Burning Issues in Psychiatry" meeting (Beirut oct 2011) and the chair of the 12th IRBD.

Abstract

Among mood disorders, cyclothymia has received less attention despite the growing evidence of its high prevalence in general population and in clinical samples (depression, OCD, anxiety, eating and impulsive disorders).

Cyclothymic depression is probably the most frequent expression of major depression (33%), and represents a distinct entity (compared to other bipolar forms) with early onset, more recurrence, irritable ("dark") hypomania and high suicide risk (EPIDEP study). In a large sample of 2322 patients with recurrent and/or resistant depression, results showed that about 60% are positive for hypomania screening (by hypomania checklist 20), and Cyclothymia appears to be the most robust precursor of BP-II disorder.

The clinical approach must evolve beyond manic and depressive episodes, and look for specific and robust criteria evoking bipolarity in terms of basic temperaments, age of onset, pattern of stability and cyclicity (endogenous vs exogenous), clinical picture of episodes, comorbidity, and reactivity to drugs.

In this approach, bipolar disorders including BP-I, BP-II, BP-NOS, Recurrent MDD, could be classified in two major groups: "stable-hyperthymic episodic" group vs "instable-cyclothymic" group.

Recent data from several studies will be presented in favor the specificity and validity of cyclothymia as:

- Most frequent form of bipolar depression
- Distinct subtype of pediatric bipolarity
- Marker of mixed and "dark" hypomania
- Predictor of instability, rapid switching and depressive recurrence
- Risk factor for suicide and self-harm behaviors
- Significant indicator of complex comorbidity (anxiety, eating and personality disorders)
- Robust dimension linked with activation and destabilization induced by antidepressants
- Significant trait taping psychiatric disorders in family

Clinical practice is in favor of the "intra-bipolar" dichotomy, which appears more significant and useful than the confusing concept of "soft bipolar spectrum". In 2007, "CTAH project" was launched in order to face the challenging issues of cyclothymia:

- Explore the role of cyclothymic temperament
- Improve definition criteria of cyclothymic disorder

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- Develop adequate psychoeducation (learning cyclothymia, monitoring, mood repair via positive routines and cognitions)
- Enhance appropriate choice of mood-stabilizers
- Build better psychotherapies (surviving life-schemas, adjustment to illness, goodness of fit…).

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- Hantouche EG "Dealing with BP-II Complexity: Toward Simplexity" - IRBD, 2011, Rome.

PARALLEL SESSION

Interactive 4: Geriatric Bipolarity

Chairs: **Prof J M Azorin (Fr)/Dr P H Robert (Fr)**

Behavioural markers of bipolarity

Dr D Lara (Br)

Diogo R. Lara, MD, PhD
Clinical psychiatrist, PhD in Basic Neuroscience, Professor at Pontifical Catholic University of Rio Grande do Sul in Biochemistry and Psychiatry, coordinator of the Bipolarity program at São Lucas Hospital.

Abstract

Akiskal (2005) advanced the field of differential diagnosis of mood disorders by focusing on behavioral markers distinctively associated with bipolarity. Based on extensive clinical observations and case records, he listed several behaviors that are relatively rare, but when present, strongly indicate a putative bipolar disorder. These biographic signs and behaviors followed the pattern named as "rule of three" given their repeated and cyclic nature (e.g. three or more weddings, religions, foreign languages…). Also, the "red sign" denoted a tendency of individuals with bipolarity to prefer items with vibrant colors. The underlying hypothesis is that certain predisposition to particular states (e.g. hypomania), may also be manifest at the trait behavioral level.

Methods: we have developed a web-based system (the Brazilian Internet Study on Temperament and Psychopathology - BRAINSTEP) to anonymously evaluate the general population, aiming to have a large sample with a thorough assessment of behavioral, psychological and psychiatric measures. We then investigated the behavioral markers and temperament variables distinctively associated with bipolar individuals in comparison to controls and individuals with major depression. The sample was 36,742 subjects, with 9,977 males (27.2%, 31.4 ± 10.4 yrs) and 26,765 females (72.8%, 31.2 ± 10.2 yrs). The prevalence of mood disorders diagnoses received by a mental health professional in males and females was 10.9% (n=1,085) and 18.2% (n=4,883) for major depression only, 1.8% (n=182) and 2.6% (n=703) for both depression and bipolar disorder diagnoses, and 1.4% (n=137) and 1.5% (n=389) for bipolar disorder only, respectively.

Results: all thirty-three behavioral markers were able to differentiate THE bipolarity group in at least one sex from the depression group. The most robust differences (OR>4) were in day-night switch, speeding up of the mind at night, having high debts, religion changes, illicit drug experimentation, having more marriages (or living together), cheating the partner regularly, having ≥60 lifetime sexual partners, pathological love, heavy cursing, speaking ≥3 foreign languages, and having ≥2 apparent tattoos. When applicable, in most cases the "rule of three" was the best cutt-off number.

Conclusion: Behavioral markers clearly differentiate bipolarity from controls and unipolar depression, confirming Akiskal's observations.

Treating late onset Bipolar Disorder

Dr A Kaladjian (Fr)

Arthur Kaladjian is professor of Psychiatry at the University of Reims Champagne Ardenne.

Abstract

Growth in life expectancy in the general population yielded in the last decades is likely to have allowed the emergence of an increasing number of late-onset bipolar illness (LOBI) cases and therefore a renewed interest for this pathology.

The presentation of LOBI appears to be roughly similar to

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that of early onset but classically with less severe clinical features. In addition to etiologic and nosographic questions raised by considering LOBI as a specific entity, there is some debate on the management of this disorder, in a context of a limited evidence base for its treatment.

In choosing between the different treatment options, one has to keep in mind that pharmacokinetic and pharmacodynamic changes that occur with ageing, associated with frequent concomitant medical illnesses and their treatments, are likely to increase the risk of adverse events. In all cases, the management of LOBI must then be associated with thorough medical assessments in search for neurological and/or medical conditions that may be treated in parallel.

Current data on treatment of bipolar disorder in the elderly suggest that anticonvulsants such as valproate and lamotrigine may be of benefit and better tolerated as mood stabilizers than lithium, which may require lower target serum levels. Valproate and atypical antipsychotics in monotherapy could be firstline drugs for mania, with combination being proposed only if monotherapy fails. In the treatment of bipolar depression, monotherapy with a mood stabilizer is reasonable, as well as quetiapine, but also the combination of olanzapine and fluoxetine. ECT may be useful in patients who are refractory to drug treatment and in those who need rapid resolution of symptoms.

In the specific context of LOBI, it is worth mentioning that the appropriate treatment of bipolar symptoms can contribute to improve mood, behavior, and cognition in both bipolar type pseudomentia and dementia with secondary mood instability. However, if drugs targeting dementia may also be useful in the latter, they have no action on the former or could even aggravate the clinical picture. Further research could contribute to better disentangle the effects of treatment on the mood symptoms and cognitive dysfunction encountered in this illness.

PARALLEL PLENARY

Plenary 4: Pathophysiology of psychosis and novel approaches to treatment

Chair: Dr J Cookson (UK)
Speaker: Prof A Grace (US)

Dr. Anthony A. Grace is a Distinguished Professor of Neuroscience and a Professor of Psychiatry and Psychology at the University of Pittsburgh in Pittsburgh, PA. He received his Ph.D. from Yale University School of Medicine with Dr. Benjamin S. Bunney and had postdoctoral training with Dr. Rodolfo Llinas in the Department of Physiology and Biophysics at New York University School of Medicine. Dr. Grace has been involved in translational research related to the dopamine system for over 30 years. His early work pioneered the identification and characterization of dopamine-containing neurons, and was the first to provide a means to quantify their activity state and pattern in a way that is the standard in the literature, all while working as a graduate student. His current work involves looking at the interactions of several brain regions with known involvement in schizophrenia and drug abuse, including the hippocampus, prefrontal cortex, and amygdala, and how these interactions are disrupted by stress. Dr. Grace has received several awards for his research, including the Paul Janssen Schizophrenia Research Award and the Lilly Basic Scientist Award from the International College of Neuropsychopharmacology, the Efron Award from the American College of Neuropsychopharmacology, as well as a NIMH MERIT award, a Distinguished Investigator award from the National Alliance for Research in Schizophrenia and Depression, the Judith Silver Memorial Investigator Award from the National Alliance for the Mentally Ill, and appointment as a Distinguished Professor of Neuroscience at the University of Pittsburgh. Dr. Grace was also recently elected as a Fellow in the American Association for the Advancement of Science. He is also a past member of the governing council of the American College of Neuropsychopharmacology and editor on numerous leading journals in the field. Dr. Grace's work has had a substantial impact on the field that has spanned basic neuroscience and clinical research. His work is unique in providing a systems neuroscience approach to the understanding of complex psychiatric disorders in humans. Most significantly, he is one of a handful of individuals that not only performs important basic research, but has the ability to integrate this work into testable models of relevance to the human condition.

Abstract

Psychosis is a common feature across a number of disorders, including bipolar disorder, schizophrenia and drug abuse. Studies have consistently identified the dopamine system as playing a major role in psychosis, and drugs that are effective at treating psychosis are typically dopamine antagonists. Using a developmental disruption model, we found that insults to rats during gestational day 17 by administration of the mitotoxin methyl azoxymethanol acetate (MAM) lead to a disruption of hippocampal activity and an increase in dopamine neuron responsivity. Specifically, there was a decrease in parvalbumin interneurons in the hippocampus (similar to that observed with temporal lobe epilepsy and schizophrenia), leading to ventral hippocampal hyperactivity. This increase in ventral hippocampal activity led to a disinhibition of mesolimbic dopamine neuron firing, causing a near doubling in the number of ventral tegmental area dopamine neurons that were firing spontaneously. Since only dopamine neurons that are firing spontaneously can be phasically activated by stimuli, the result was an increase in the responsivity of the dopamine system to external events. This hyperactivation correlates with increased behavioral response to amphetamine administration.

Interestingly, stressors, which can precipitate or exacerbate bipolar disorder, also cause a hippocampal-driven increase in dopamine neuron activity. Currently, treating psychosis is done by administering dopamine-blocking

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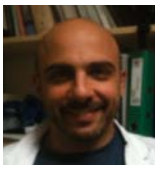
antipsychotic drugs. While in normal subjects the dopamine receptor blockade produced by antipsychotic drugs can be overcome by feedback activation of the dopamine system, in cases in which the dopamine system is hyperactive further blockade of dopamine receptors leads to overactivation and the induction of dopamine neuron depolarization block; a state in which neurons are so depolarized they cease firing. While this will decrease the number of dopamine neurons firing, this is achieved not by attacking the pathology at its source in the hippocampus, but instead is working at least 5 synapses downstream from the deficit. In contrast, we have used a novel GABA A alpha 5 positive allosteric modulator drug that has selective GABA potentiating actions in the hippocampus. This drug selectively attenuates hippocampal hyperactivity, and restores dopamine neuron firing back to baseline levels and reverses the behavioral hyper-responsivity to amphetamine, without affecting control rats. Therefore, by understanding the pathophysiology of psychosis with respect to alterations in dopamine neuron firing, more effective pharmacological approaches to treatment can be realized.

PARALLEL PLENARY

Plenary 5: How much bipolar schizoaffective disorder is?

Chair: Dr A Martinez-Aran (Es)
Speaker: Dr A Murru (Es)



Andrea Murru is Bachelor´s Degree in Medicine and Surgery at University of Cagliari, Italy. He specialized in Psychiatry cum laude at the University of Cagliari. He completed a Master en Neuroscience at the University of Barcelona.

He currently works as a Researcher of the Fundació Clínic in the Barcelona Bipolar Disorders Program of the Hospital Clínic, focusing on different research projects. He co-authored the Catalan Guidelines to the Clinical Management of Bipolar Disorder. He focuses his research on long-term treatments and adherence to treatment in patients affected by bipolar disorder and schizoaffective disorder.

Abstract

The issue of the diagnostic consistence and reliability of Schizoaffective Disorder (SAD) represents one of the oldest controversies in psychiatry and it has been highly debated over time. It is hard to understand the respect that modern nosology still pays to the taboo of comorbidity between the two protagonists of the Kraepelinian dichotomy, schizophrenia and bipolar disorder, of which SAD has been traditionally seen as an intermediate form. This choice appears as one of the most longevous contradictions in psychiatric nosology, considering that Kraepelin himself was perfectly aware of intermediate clinical presentations. Despite this, there is still no consensus whether it has to be considered as an independent diagnostic category or an extreme phenotype in schizophrenia or bipolar disorder.

Efforts for operational definitions of SAD in the official nosology have up till now failed to produce in their latest incarnations (DSM-IV and ICD-10) reliable diagnostic criteria, being the boundary between SAD bipolar type and psychotic bipolar disorder especially blurry in the classification of the World Health Organization.

Most of the recent advances in clinical and genetic research seem to point towards quantitative, rather than qualitative, differences in genetic, clinical, neuroimaging and treatment features of SAD versus bipolar disorder. The Task Force for the DSM-5 was at first oriented towards abolishing the diagnosis of SAD, opting for keeping it as a specifier for schizophrenia, bipolar disorder or unipolar depression, but then a diagnostic category of SAD has been kept.

Few studies specifically aimed at SAD are available, so that scant evidence may help clinicians in the management of patients with schizoaffective features. Specific evidence on treatment is also scarce, but present, but still ineffective in guiding clinical practice to sort out the complex treatment regimens that these patients normally need.

In the present speech, critical issues and future directions in research will be discussed, as well as an overall update on scientific evidence will be presented.

PARALLEL SESSION

Evening Lecture: Tackling stigma through theatre - “That’s Just Crazy Talk” by Victoria Maxwell

Speaker: Prof Erin Michalak (Ca)

Dr. Erin Michalak is an Associate Professor in the Department of Psychiatry at the University of British Columbia in Vancouver, Canada. Her background is in psychology, with a PhD awarded from the University of Wales College of Medicine in the United Kingdom. Her research interests are in bipolar disorder, knowledge translation, self-management, seasonal and nonseasonal depression, quality of life and the development of outcome instruments for mood disorders. Dr. Michalak’s research has been supported by the Canadian Institutes of Health Research (CIHR), the Michael Smith Foundation for Health Research and the Canadian Psychiatric Research Foundation, amongst others. She leads the ‘Collaborative RESearch Team for the study of psychosocial issues in Bipolar Disorder’ (CREST.BD, www.crestbd.ca), a CIHR-funded Canadian network designed to foster psychosocial research and knowledge translation in BD. She has published over 50 scientific articles and several books and book chapters.

Abstract

Presenter: Erin Michalak, Associate Professor, Department of Psychiatry, University of British Columbia, Vancouver, Canada.

Co-authors: Sagar Parikh, Department of Psychiatry, University of Toronto, Canada, James D. Livingston, BC

PRESENTATION ABSTRACTS

Mental Health and Addiction Services, Vancouver, Canada, Victoria Maxwell, That's Just Crazy Talk, Canada.

Mental illness stigma represents a major barrier to health and quality of life in people with bipolar disorder. Emerging evidence suggests that an effective multi-faceted strategy to prevent and reduce stigma would include creative arts and contact-based approaches. The power of the creative arts lays its potential to reach and speak to an audience that may not be responsive to conventional methods for addressing stigma. This presentation will share findings from a study that examined the impact of a contact-based theatrical performance on the attitudes of healthcare service providers (n=84) and people with bipolar disorder (n=80) in Toronto and Vancouver, Canada. The 1-hour performance – designed and delivered Victoria Maxwell, an actress and playwright who lives with bipolar disorder – used dramatic narrative to convey the narrator's experiences of stigma into a vivid, often humorous and sometimes troubled, portrait of life lived with bipolar disorder. Participants completed quantitative attitudinal measures immediately before and after the performance. The measures included Day's Mental Illness Stigma Scale (DMISS), the Mental Illness: Clinicians' Attitudes Scale (MICA-4), and the Internalized Stigma of Mental Illness (ISMI) scale. Paired-sample t-tests revealed significant pre-post improvements in healthcare providers' attitudes toward bipolar disorder (DMISS total score: $t(83)=5.55, p<.001; d=.58$). Positive change was also demonstrated on the MICA-4, but the results were not statistically significant ($t(81)=1.56, p>.05; d=.17$). Among people with bipolar disorder, pre-post scores on the DMISS ($t(79)=1.76, p>.05; d=.19$) and ISMI ($t(75)=1.00, p>.05; d=.13$) revealed non-significant improvements; however, significant shifts were observed on several subscales. Participants' perceptions about the performance were also positive, with strong ratings of its educational and emotional impact. The study findings support the inclusion of the creative arts and contact-based approaches in strategies that seek to foster positive attitudes among healthcare providers toward people with bipolar disorder. Pre-recorded excerpts from the performance - 'That's Just Crazy Talk' - will be shown during this conference session.

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Day 2: Tuesday, May 22, 2012

SYMPOSIUM

European Bipolar Forum II: Bipolar Spectrum in special conditions

Chair: **Prof L Dell'Osso (I)**

Sub-threshold Bipolar and reaction to stress and grief

Prof L Dell'Osso (I)

Liliana Dell'Osso, MD, Claudia Carmassi, MD, PhD, Paola Rucci, Dstat, Antonio Ciapparelli, MD, Ciro Conversano, PhD, and Donatella Marazziti, MD

Liliana Dell'Osso is full professor of Psychiatry and Director of the School of Residency in Psychiatry at the University of Pisa (Italy). Prof. Dell'Osso is also Director of the 1st Unit of Psychiatry of the Azienda Ospedaliero-Universitaria Pisana, Pisa (Italy). Since 1995 she has been active member of the Spectrum Project, an international collaborative research project including clinicians and researchers of the Universities of Pisa (Italy), Pittsburgh, Columbia N.Y. and California at San Diego (USA), which is aimed at assessing spectrum symptomatology of mental disorders. In the framework of this project she has worked at the development and validation of instrument aimed at assessing the spectrum of mood (MOODS-SR), panic (PAS-SR), obsessive-compulsive (OBS-SR), social anxiety (SHY-SR), psychotic (PSY-SR) and more recently post-traumatic stress (TAL-SR) disorders. In these fields she has also developed and directed many research projects with a particular focus on the issues of comorbidity, clinical manifestation and treatment outcome. Prof Dell'Osso is director of the Tuscan section of the Italian Society of Psychiatry (SIP). She is author of more than 400 publications on national and, international journals (index medicus, current contents, excepta medica).

Abstract

Introduction: The aim of the present study was to explore the relationship between subthreshold mood symptoms and suicidality in patients with complicated grief (CG).

Methods: Fifty patients with CG were included in the study and evaluated by the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Axis-I disorders, the Inventory of Complicated Grief, and the Mood Spectrum Self Report (MOODS-SR) lifetime version, to evaluate the subthreshold mood symptoms.

Results: Twenty-eight patients (56%) reported lifetime suicidal ideation and 11 patients (22%) reported suicide attempts. Subthreshold depressive and rhythmicity/vegetative functions items of the MOODS-SR were significantly associated with increased suicidal ideation and attempts, while subthreshold manic items were associated with suicidal ideation only. Relationships were confirmed after controlling for Axis-I disorders comorbidity.

Conclusion: The results of the present study suggest the usefulness of exploring lifetime subthreshold mood symptoms in CG patients, in order to promptly identify those who may be more prone to suicidality.

Affective temperaments and alcoholism

Prof A Erfurth (At)

Prof Erfurth is Head of Clinical Psychopharmacology and the Bipolar Spectrum Disorders Program, Division of General Psychiatry, Medical University of Vienna, Austria.

He was educated at the Conservatorio di Musica di Santa Cecilia, Rome, Italy, the Richard-Strauss-Konservatorium, Munich, Germany and the Medical School, University of Munich, Germany. He was resident in psychiatry at the University of Munich, Germany and was research fellow at the Laboratory of Neuroendocrine Regulation, Department of Brain and Cognitive Sciences, M.I.T., Cambridge, Massachusetts, U.S.A. Hospital appointments include the University of Munich and the University of Muenster, Germany, where he wrote his habilitation thesis. He was co-founder and secretary of the German Society for Bipolar Disorders. He is currently a member of the Scientific Secretariat of the European Bipolar Forum and of the Verein für Psychiatrie und Neurologie, Vienna. His particular interest is in the diagnosis, neurobiology and therapy of affective disorders.

Abstract

Andreas Erfurth[1,2], Benjamin Vyssoki[2], Dagmar Kogoj[1,2], Victor Blüml[2], Henriette Walter[2], Bilal Salem[3], Elie G. Karam[3] and Otto Lesch[2]

[1] VI. Psychiatric Department, Otto Wagner Spital, Vienna, Austria

[2] Department of Psychiatry and Psychotherapy, Medical University Vienna , Austria

[3] St. George Hospital University Medical Center, Beirut, Lebanon

Temperament has been shown to influence the psychopathology and the course of affective disorders (1,2) and somatoform disorders (3). Temperament has also been shown to be linked to suicidal ideation (4). With the briefTEMPS-M (5,6) a quick and valid assessment of temperament is possible. We have examined the impact of temperament in psychoactive substance use among college students (7) as well as the impact of temperamental traits on the psychopathology and course of alcoholism (8).

Patients with alcohol dependence were examined at the Department of Psychiatry and Psychotherapy, Medical University Vienna , Austria (8). The dimensions of alcohol dependence were assessed by means of a computerized structured interview, the Lesch Alcoholism Typology.

High scores in cyclothymic temperament were associated with a negative course of the disease and highly

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overlapped with the Lesch IV subtype of alcoholism.

In a parallel study 101 consecutive patients with opiate addiction treated at the Oum El Nour Rehabilitation Hospital in Lebanon were examined. The high overlap of the Lesch IV subtype and cyclothymic temperament was confirmed.

Therapeutic consequences of the findings are discussed.

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2 Perugi G et al. J Affect Disord. 2012; 136:e41–e49

3 Amann B et al. Psychosomatics. 2009; 50:605-12

4 Skala K et al. J Affect Disord 2012; doi:10.1016/j.jad.2012.03.010

5 Erfurth A et al. J Affect Disord. 2005; 85:53-69

6 Erfurth A et al. J Affect Disord. 2005; 85:71-6

7 Unseld M et al. J Affect Disord 2012; doi:10.1016/j.jad.2012.03.028

8 Vyssoki B et al. J Affect Disord. 2011; 135:177-83

Criminal conviction, impulsivity and course of illness in Bipolar Disorder

Prof A Swann (US)

Alan Swann is Professor and Vice Chair for Research at the Department of Psychiatry and Behavioral Sciences at the University of Texas Medical School in Houston, Texas, where he also serves as co-Director of the Center for Excellence in Mood Disorders.

He is directly involved in teaching, research, and patient care. He graduated from the University of Texas Southwestern Medical School in Dallas, Texas in 1972 and completed a medical internship at Columbia-Presbyterian Medical Center in New York. He completed a research fellowship at the National Institute of Neurological Disorders and Stroke and a Psychiatry residency at Yale University School of Medicine. Dr. Swann recently completed a term on the National Advisory Council on Alcoholism and Alcohol Abuse and has served on grant review boards for NIH and the Veterans Administration, where he was Chair of the Merit Review Board on Mental Health and Behavioral Sciences. He is a co-founder, and is president-elect, of the International Society for Research on Impulsivity. Dr. Swann is part of a group that integrates treatment with basic and clinical research in mood disorders. His research support has included the NIMH, NIAAA, and the American Heart Institute. Clinical research focuses on treatment of affective disorders, especially prediction of treatment response and development of more objective measures of disease severity, its underlying behavioral mechanisms, and its change during treatment. Preclinical human research concerns the neurobiology of behavior, such as impulsivity and motivation, which may be basic to bipolar disorder and its most severe complications. Basic research focuses on pharmacological and developmental aspects of behavioral sensitization to stimulants and other potential models for recurrence in affective disorders. His work has resulted in over 250 refereed publications, plus reviews and book chapters. He teaches medical students, residents, graduate students, and other trainees and has been awarded the Dean's Award for Teaching Excellence and Residents' teaching awards.

Abstract

Alan C. Swann*, Marijn Lijffijt, Scott D. Lane, Kimberly J. Kjome, Joel L. Steinberg, F. Gerard Moeller

Department of Psychiatry and Behavioral Sciences, The University of Texas Health Science Center at Houston, 1941 East Road, Houston TX 77054 USA, Alan.C.Swann@uth.tmc.edu

Objective: Bipolar disorder has a high incidence of criminal behavior. Contributing factors potentially include substance-use disorders, personality disorders, or other comorbidities related to impulsivity. We investigated impulsivity, symptoms of antisocial personality disorder (ASPD) or borderline personality disorder, substance-use disorder, age of onset, frequency of episodes, and history of criminal behavior in bipolar disorder.

Methods: There were 112 subjects with bipolar disorder, recruited from the community. Diagnoses were rendered by the Structured Clinical Interview for DSM-IV (SCID-I and –II), psychiatric symptom assessment used the Schedule for Affective Disorders and Schizophrenia, Change Version (SADS-C), severity of ASPD and borderline personality disorder by SCID-II symptoms, and impulsivity by questionnaire (Barratt Impulsiveness Scale (BIS-11)) and response inhibition measures. Logit analysis was used to determine relative contributions of continuous or categorical predictors identified in univariate analyses.

Results: Twenty-nine subjects had histories of criminal conviction. They did not differ from subjects without criminal histories in terms of current symptoms or treatment. Those with criminal convictions had more ASPD symptoms, less education, more substance-use disorder, more suicide attempt history, and a more recurrent course with propensity toward mania. Impulsivity, measured by impaired response-inhibition, was increased, but BIS-11 scores did not differ. Logit analysis showed that impaired response inhibition and ASPD symptoms, but not history of substance-use disorder, were significantly associated with criminal history. Subjects convicted for violent crimes were not more impulsive than those convicted for nonviolent crimes.

Conclusions: History of criminal behavior is related to ASPD symptoms, a recurrent and predominately manic course of illness, and impaired response inhibition in bipolar disorder, independent of current clinical state.

Supported by NIH grant MH069944

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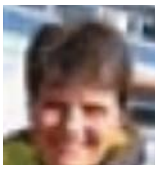
PARALLEL SESSION

Science Update 3: Risk and Bipolar Disorder

Chair: **Prof L Dell'Osso (I)**
Speaker: **Prof J Scott (UK)**

Risk and Bipolar Disorder

Professor Jan Scott



Jan Scott is Professor of Psychological Medicine at the University of Newcastle, an Honorary Professor at the Institute of Psychiatry and a Distinguished Founding Fellow of the Academy of Cognitive Therapy.

Professor Scott trained in psychiatry in Newcastle upon Tyne and was then a professor in Glasgow and the Institute of Psychiatry in London, before returning to Newcastle. Professor Scott also held visiting academic posts with Aaron Beck at the Penn State University in Philadelphia, Eugene Paykel at Cambridge University, and Eduard Vieta in Barcelona and was also awarded the RCPsych travelling scholarship to Johns Hopkins University, Baltimore. Jan Scott is an internationally renowned expert in the use of CBT in the treatment of depression and bipolar disorder and her research focuses on combined treatment strategies (using pharmacotherapy and psychotherapy) for individuals with difficult to treat mood disorders and treatment resistant psychosis, and the investigation of the role of psychosocial and cognitive factors in the onset and prognosis of severe mental disorders. Professor Scott is an internationally renowned author and has over 250 publications on these topics, including 'Overcoming Mood Swings'. Head of Glasgow University's Department of Psychiatry, she is a Fellow of the Royal College of Psychiatrists and the International Association of Cognitive Psychotherapists. She is also a trustee of the Mental Health Foundation.

Abstract

There has been an increasing focus on the need to improve the early identification of individuals at very high risk of, or in the first episode bipolar disorder. Several studies demonstrate that mood symptoms and episodes pre-date diagnosis and treatment by 6-10 years, which represents an unacceptable delay in case recognition and introduction of optimal treatments.

In psychosis research, two important strategies have helped inform the development of new service initiatives for young people - (a) careful delineation of prodromes and ultra high risk syndromes that identify cases likely to 'convert' in the imminent future and (b) the frequent estimation and reporting of duration of untreated psychosis. Using these findings has helped the introduction of indicated preventative strategies.

This paper will examine whether it is possible to use parallel concepts in bipolar disorder. First, the distal and proximal risk syndromes and putative prodromes will be discussed and 'at risk' syndromes for bipolar disorders that use a combination of state, trait and genetic markers will be outlined. Issues regarding the application of these models to clinical practice will be highlighted – such as the low specificity of childhood features, and the fact that the initial prodromal features may be for different for different types of mood episodes (rather than a single presentation of psychosis). The need to explore the best 'closing in' strategy (eg targeting help-seeking, impaired individuals in the peak age at onset age groups) will also be discussed. The lack of consistency in how researchers have defined the duration of untreated bipolar disorders will be outlines using data from a systematic review on the DUB. This also highlights the complexity of measuring the duration of untreated illness in bipolar disorder as there may be symptomatic and asymptomatic periods, but suggests the potential ways the DUB could be classified in order to monitor improvements in case detection in the future.

References:

Scott J, Hickie I, McGorry P (2011) Pre-emptive psychiatry: dreamland or a realistic outcome of the application of clinical staging models? In press.

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PARALLEL SESSION

Interactive 5: Bipolar IIB - The Beneficial B Form of Bipolar Disorder

The Case of Dominique Straus-Kahn and Mental Disorder

Chair: **Prof A Erfurth (At)**
Speaker: **Dr R Fieve (US)**

Dr. Fieve is Professor of Clinical Psychiatry at Columbia University Medical Center. He is an internationally renowned psychopharmacologist who pioneered the use of lithium in the United States to treat bipolar disorder. He has published close to 300 scientific papers and is the author of the bestselling book Moodswing (Bantam 1975, 1997), on Bipolar I disorder, and the books Prozac, Bipolar II (Rodale 2010) and Bipolar Breakthrough (Rodale 2006). His books Moodswing and Bipolar Breakthrough have been published in France under the titles Nous Sommes Tous des Maniaco-Depressives (Flammarion 1975) and Comment bien vivre avec de troubles bipolaires (2011). He is the Director of the Fieve Depression Center on Fifth Avenue and 76th Street in New York City where he maintains a private practice, a research foundation and a clinical trials site (FCS).

Every year Dr. Fieve spends two to three months in the South of France.

PRESENTATION ABSTRACTS

Abstract

Over the past four decades, I have treated many highly successful and charismatic New Yorkers whose bipolar lives have been marked by "accomplishment".

I coined the term "Bipolar II Beneficial" (Bipolar II B) for those individuals who may exhibit only mild to no depressions but also experience hypomanic, hyperthymic or cyclothymic behavior in which they are optimistic, highly energetic, visionary people, showing enormous accomplishment during their careers and, most often, hypersexuality. About 3- 5% of the Bipolar II individuals I have treated exhibit this Beneficial Bipolar Advantage. Although many of these people will never admit to depression or go for treatment, some will concede to periods of lack of optimism.

Recently, prominent political leaders have been described in the press as exhibiting suggestive Bipolar behavior manifesting at least 2 of the key features I have described in this proposed subtype, Bipolar IIB (beneficial), namely accomplishment and hypersexuality. The list includes President Bill Clinton, Governers Eliot Spitzer and Arnold Schwarzenegger, media magnate and politician Silvio Berlusconi, and former IMF head Dominique Strauss-Kahn (DSK). In my book "Moodswing", published in 1975, I described a number of Bipolar presidents and leaders including Winston Churchill, with his "black dog" depressions, incredible energy and lifetime accomplishments.

However the negative aspects of Bipolar IIB amidst a lifetime of accomplishment and leadership are also noteworthy and can include excessive risk taking, lack of good judgment, and extreme hypersexuality. The recent criminal charges against DSK have fueled a media frenzy of speculation. The aforementioned high-profile cases have led to our societie's misunderstanding that sexual acting out is simply a form of sexual addiction to be treated by counseling.

In contrast to having sexual addiction, do these politicians, including Dominique Strauss-Kahn, really have undiagnosed Bipolar B (Beneficial) psychiatric profiles? Are DSK's recent actions not the result of a brief psychotic break or momentary loss of touch with reality during a lifetime of outstanding accomplishment?

In my opinion, Dominique Strauss-Kahn has exhibited symptoms of a mental disorder. He has what I have described as a Bipolar Beneficial subtype condition not yet existing in our outdated DSM IV handbook of mental disorders.

In future elections, societies on both sides of the Atlantic may delve more deeply into the assets and liabilities of the hidden Bipolar IIB (beneficial) markers of our presidents and world leaders, before they cast their votes, as never before!

DEBATE FORUM

Lithium Use for Bipolar Disorder - does the LiTMUS trial change anything?

Discussant: Prof A Young (UK)
Speaker: Dr P Grof (Ca)

Paul Grof, M.D., Ph.D., F.R.C.P.C.(C

Since the fall of l968 Dr. Grof was a research psychiatrist and faculty member at McMaster University, Canada, and spent l977 - l978 as a Visiting Scientist at the NIMH in Bethesda, Maryland. Dr. Grof became Director of Research and Education at a teaching hospital of McMaster University, and l985 -2000 was active as Expert of the World Health Organization and as Visiting Professor at several European Universities. From l988 to 1993 Dr. Grof was Clinical Director of the Royal Ottawa Hospital and subsequently directed there clinical and research activities in mood disorders. Currently he is Director of Mood Disorders Center of Ottawa. He authored and co-authored over 450 papers and book chapters and 3 books.

Abstract

Nierenberg et al. found that adding lithium to the treatment of bipolar disorder (BD) as usual provides no demonstrable benefit. This may seem puzzling, considering lithium's abundantly proven efficacy as a mood stabilizer. However, the LITMUS study reflects persisting misperceptions about long-term lithium treatment

Lithium was proven to be an effective stabilizer already between 1967-1976, essentially for Kraepelinean manic-depression, fully remitting illness which did not include mood incongruent psychotic symptoms or elevated psychiatric comorbidity. And episodic course remains the strongest predictor of effective, lasting, replicable lithium stabilization. Lithium offers a similar benefit in other episodic conditions; for example cycloid psychoses, episodic schizophreniform psychoses, cluster headaches etc.; it has a variety of applications and not all are associated with BD.

Prospective studies reported that lithium responsive BD evolves in stages, often from non-mood childhood antecedent disorders, yet the episodic course and clinical profile remain present throughout development and the illness course Thus, stabilization on lithium appears to have little to do with bipolar symptoms per se and more to do with episodic dysregulation. Other types of therapeutic benefits of lithium, such as antisuicidal and antipsychotic, do not share these characteristics. For example the anti-suicidal effect has been demonstrated regardless of success or failure of lithium stabilization.

The broad concept of BD spectrum includes also other bipolar types and has good psychopathological justification; precision is important. To wit, in the past hypomanic activation had been greatly underestimated. However the spectrum approach has increased dramatically the prevalence, heterogeneity and the variety

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of treatment responses within the BD spectrum. The indication of lithium stabilization as the treatment of choice could not any longer be BD alone, but BD with a particular profile. This conclusion has been supported by both double-blind and large open long-term investigations.

The LITMUS study turned out to be the litmus test of the misperceptions. The findings indicate again that lithium stabilization should preferentially be administered to bipolar patients with clinical characteristics similar to those on whom the efficacy was originally proven. The studies using the broad BD approach have, on the other hand, found lithium maintenance either ineffective or reducing overactivity only. If BD patients with other clinical profiles receive a trial on lithium, it should be continued only if there are clearly demonstrable gains. If long-term lithium is maintained simply because the patient's symptoms fit BD, risks may distinctly outweigh dubious gains.

SYMPOSIUM: Sponsored by LUNDBECK

Bipolar I disorder: Early and accurate diagnosis and treatment

Chair: **Allan Young (UK)**

Clinically relevant subtypes of Mania (Giulio Perugi, Italy)

Bipolar I is a complex disorder manifesting itself through a broad spectrum of cyclical mood variations. Current research supports the prognostic and prescriptive validity of using inexpensive and practical strategies for better identifying subtypes of the disease. This can be of particular importance when treating manic episodes in order to provide optimal treatment, and to minimize the risks of over-diagnosis or unnecessary medication exposure. This presentation will aim at describing some "clinical pictures", which can be clinically relevant to recognize.

Taking a broader view: New perspectives on the functional outcome (Lars Häggström, Sweden)

Current clinical and health economic research support the need for an increased awareness of the progressive aspects of Bipolar I disorder. During the course of this chronic, often lifelong disease the recurrence of manic episodes constitute a "toxic" effect which fuels the progression of the disease to become even stronger. To achieve remission the ambition should be to individualize treatment based on best available practice including continuos evaluation of factors such as sleep, circadian rythm and cognitive disturbances. Evidence support that to prevent a malignant course, i.e optimise social and occupational functioning and prevent relapse, it is important as early as possible to identify, and utilize best possible treatment algorithms.

Asenapine, a multifunctional antipsychotic. From pharmacology to clinical benefits (Eduard Vieta, Spain)

The occurrence of mania is the basis for a diagnosis of bipolar I disorder, though depression has generally been the dominant mood state during the course of illness.

Asenapine is a new treatment option with some untypical properties. It is derived from a chemical class of tetracyclic antidepressants that is different from other antipsychotics, and has a unique sublingual mode of administration. The strong clinical efficacy of asenapine has been demonstrated in acute manic and mixed episodes. The efficacy is comparable to olanzapine over 12 weeks and is maintained up to 1 year. The multifunctional receptor profile of asenapine shows promise with regards to multisymptomatic efficacy.

Discussant: Allan Young, UK

PRESENTATION ABSTRACTS

PARALLEL SESSION

Plenary 6: Functional Remediation of Bipolar Disorder

Chair: **Prof E Vieta (Es)**

Speaker: **Dr A Martinez-Aran (Es)**

Anabel Martínez-Arán, PhD. Clinical psychologist, Doctor Cum Laude in Psychology and Master's degree in Diagnosis and psychological therapies by the University of Barcelona (Spain). She is a researcher of the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), and of the CIBER on Mental Health (CIBERSAM) as part of the Barcelona Bipolar Disorders Program (Hospital Clínic, University of Barcelona). She currently works at the Early Onset Psychosis Program of the Hospital Clinic of Barcelona. She has lectured and published several book chapters and articles on neuropsychological issues, and psychological interventions with regard to bipolar disorders. Her research work on neuropsychology has been funded by the Stanley Medical Research Institute (Bethesda, MD, USA) and currently by the CIBERSAM. She also serves as scientific consultant of the National Bipolar Disorders Association in Spain, is member of the Neurocognition Committee of the International Society of Bipolar Disorder, referee of several peer-review journals and teacher on the Master's course of Adult Psychopathology of the Universidad Autónoma de Barcelona and on the Master's course of Neurosciences of the University of Barcelona. In 2005, Dr Martinez-Aran received the highest award for her doctoral thesis on Neuropsychology of bipolar disorder by the University of Barcelona.

Bipolar Disorders Program, Clinical Institute of Neuroscience, Hospital Clinic of Barcelona, IDIBAPS, CIBERSAM, University of Barcelona, Barcelona, Spain

Abstract

Recent studies point to a significant degree of disability as well as persistent cognitive impairment in patients with bipolar disorder. These findings suggest that there is a gap between clinical and functional outcome in bipolar disorder that emerges at the very outset of the illness. Bipolar disorder can negatively impact the individual, reducing health-related quality of life, and functioning, including employment and work productivity. In this regard, cognitive impairment has been found to be a good predictor of functioning. One of the main concerns is that cognitive function has not been routinely examined in the studies of functioning in patients with bipolar disorder because clinical variables have been thought to impact function more than cognition. Moreover, findings from different studies also highlight the limitations of current treatment strategies regarding their capacity to improve the functioning and reduce the disability of bipolar patients. In this context, the Functional Remediation Program has been designed exclusively for bipolar patients. This therapy is based on a neurocognitive-behavioral model, involving neurocognitive techniques, psychoeducation on cognition-related issues and problem solving within an ecological framework. The results of a randomized controlled trial to test the functional remediation program versus the psychoeducation program versus a group following treatment as usual (TAU) will be shown. The primary outcome variable of the study is functional improvement measured blindly as the mean change in the Functioning Assessment Short Test (FAST) from baseline to endpoint, one year later. The Functional Remediation program, as a novel group intervention, has proven to be effective in improving functional outcome in a sample of euthymic bipolar patients as compared with TAU.

SYMPOSIUM: Sponsored by ASTRA ZENECA

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Bipolar disorder understanding: bridging evidence-based medicine and daily practice

Chair: **Prof Jean Michel Azorin (Fr)**

Bipolar understanding is more and more challenged to unify the recent findings in terms of Evidence Based Medicine, Real World Evidence and Daily Practice. The Wave Bd study is a great tribute to an increased understanding of bipolar disorder care in real life across countries. Moreover, these results raise questions on how to put into practice real world evidence and Evidence based medicine in bipolar disease care. Such question is of high interest when considering long term bipolar care where practitioners aim to limit relapse or recurrence thus allowing their patient to get back to a normal life.

Wave BD: a 360 degree real world evidence bipolar disorder perspective

Prof Eduard Vieta (Es)

Bipolar depressive polarity care: the challenge of translating EBM in clinical practice

Prof Philip Gorwood (Fr)

PARALLEL SESSION

Oral Platform Session I

Chair: **Prof A Swann (US)**

Temperaments as mediators of suicide risk, hopelessness and psychopathology in bipolar disorders

Maurizio Pompili Sant'Andrea Hospital, Roma, Italy

Objective: Completed suicide and suicide attempts are major issues in the management of bipolar disorders.

PRESENTATION ABSTRACTS

There is evidence that suicide rates among these patients are more than 20-fold higher than the general population and, furthermore, suicidal behavior is much more lethal in bipolar disorder than in the general population. Proper understanding of the psychosocial circumstances and the psychopathology of bipolar patients (including temperament) may help clinicians describe the clinical picture accurately and prevent suicidal behavior.

Method: The aims of the cross-sectional studies were to assess temperament and clinical differences between patients with BD-I and BD-II disorders, and to assess whether temperament traits are good predictors of hopelessness in bipolar patients, a variable highly associated with suicidal behavior and ideation. Patients completed the Temperament Evaluation of Memphis, Pisa, Paris and San Diego - Autoquestionnaire (TEMPS-A), the Beck Hopelessness Scale (BHS), the MINI (Mini International Neuropsychiatric Interview), and the Gotland Scale of Male Depression (GSMD). BD-II patients had higher scores on the BHS than BD-I patients.

Results: Patients with higher hopelessness (compared to those with lower levels of hopelessness) reported more frequently moderate to severe depression and higher MINI suicidal risk. Hopelessness was also associated with the individual pattern of temperament traits. A further investigation found that above 81% of the patients with prevailing cyclothymic-depressive-anxious temperament had mild to severe suicidal risk on the MINI Interview vs. only around 42% of the patients with prevailing hyperthymic temperament, and sixty-four percent of patients with prevailing cyclothymic-depressive-anxious temperament had BHS scores of 9 or higher versus only 13% of patients with prevailing hyperthymic temperament. Also, patients with prevailing cyclothymic-depressive-anxious temperament more likely had higher GSMD than patients with prevailing hyperthymic temperament.

Conclusion: Temperaments are important predictors both of suicide risk and psychopathology and may be used in clinical practice for better treat bipolar disorders patients.

The association between impulsivity and behaviour in individuals who screen positive on the Mood Disorders Questionnaire

Burden, J. Corcoran, R. Morris, R. Bristol, United Kingdom

Objective: Research has highlighted a clear association between the high levels of trait impulsivity found in individuals with bipolar disorder (BD) and certain behaviours common within this population (e.g. suicide, Swann et al 2005; substance use, Meade et al, 2008). This study aimed to extend these findings through the bipolar spectrum, by investigating the links between trait impulsivity and behaviour in a continuum sample of students who endorsed experiences of extreme mood.

Method: Participants completed a cross-sectional questionnaire online (using surveymonkey.com software). The questionnaire included a screening measure for the bipolar spectrum, the Mood Disorders Questionnaire (MDQ; Hirschfeld et al, 2000) and two scales used to measure trait impulsivity; the UPPS Impulsive Behaviour Scale (UPPS; Whiteside and Lynam, 2001) and the Positive Urgency Measure (PUM; Cyders et al, 2007). Participants also completed a novel questionnaire which asked about their engagement in 18 behaviours seen to be common in BD (including self harm, suicide and risky sex). Data was analysed using SPSS and R software.

Results: Participants who scored positive on the MDQ (MDQ+) were found to have elevated trait impulsivity compared to MDQ- participants (-24.786, $p < .001$). MDQ+ individuals also endorsed engaging in a wider range of behaviours than MDQ- participants (mean difference 2.54749, $p < .001$), and to engage in these behaviours with greater frequency (mean difference 0.18176, $p = .004$). Structural equation modelling indicated that the relationship between extreme mood and impulsive behaviour was moderated by trait affective impulsivity.

Conclusion: Impulsive and risky behaviour is common throughout the bipolar spectrum, including within non-clinical samples. Impulsivity may constitute an important moderator in the relationship between the experience of elevated mood and behaviour, and it is important to investigate further the role of impulsivity within the bipolar spectrum.

Objective versus Self-Report Measures of Impulsivity and History of Suicide Attempt in Youth with Bipolar Disorder

Sally M. Weinstein, Woo-Young Ahn, Amy E. West, Mani Pavuluri, Institute for Juvenile Research, Department of Psychiatry, University of Illinois-Chicago, Chicago, USA

Objective: Youth with bipolar disorder are at extremely high risk for suicidal behavior, with up to 50% of these youth attempting suicide by age 18 (Bhangoo et al., 2003). To understand the mechanisms linking bipolar disorder and suicidality, research must identify the factors that differentiate youth with suicidal behavior from those without such behavior. Theory and research highlight the role of impulsivity in models of suicidal behavior (e.g., Mann et al., 1999). Impulsivity may be particularly relevant to suicide risk in pediatric bipolar disorder (PBD) given the prominence of symptoms of impulsivity and behavioral disinhibition observed in PBD youth (Birmaher et al., 2002; Pavuluri et al., 2007), but few studies have examined these relationships. The present study seeks to focus on the role of impulsivity in accelerating suicide attempts among youth with PBD. We explored the relationship between impulsivity, assessed via an objective laboratory-based task (Stop Signal Task) as well as by self-report, and history of suicide attempt in youth with PBD. We hypothesized that PBD youth with a suicide attempt history would demonstrate greater impulsivity as compared to PBD non-attempters and healthy controls. Additionally, we expected that youth with more severe suicide attempt history (i.e., two or more attempts) would evidence greater impulsivity than single-attempt PBD youth.

Method: Data were collected as part of a cross-sectional, case-control study of suicidal youth ages 13 to 18 with

PRESENTATION ABSTRACTS

bipolar disorder (N = 99; mean age = 14.39, SD = 1.95). We recruited PBD suicide attempters (n=25), PBD non-attempters, with history of suicidal ideation (n=25), PBD youth with no suicide ideation/attempt history (n=24), and healthy controls (n=25). PBD patients included those diagnosed with narrow phenotype-bipolar disorder (Type I and II) during their first manic episode, and all youth were medication naïve. PBD non-attempters and healthy controls were age and IQ-matched with the PBD attempters, and groups did not significantly differ on age, race, gender, or IQ. Diagnosis of PBD was established via the Washington University Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS; Geller et al., 1996). Suicide history was assessed using the Columbia Suicide Severity Rating Scale (C-SSRS; Posner et al., 2007). Impulsivity was assessed via a behavioral paradigm, the Stop Signal Task (SST). In the SST task, motor response that is already 'on the way' from planning to execution, had to be voluntarily inhibited in response to a stop cue on some trials (Pavuluri et al., 2010). To index impulsivity, we calculated the Stop Signal Reaction Time (SSRT), or the latency of the inhibition process, via the integration method (Logan & Cowan, 1984). Impulsivity was also assessed via youth self-report (Barratt Impulsivity Scale; Barratt, 1985).

Results: Analyses of variance (ANOVAs) with Tukey post-hoc comparisons were conducted to examine group differences in impulsivity. Given our interest in severity of suicide attempt, we focused on the following groups: healthy controls (n=25), PBD non-attempters (including youth with history of ideation and no ideation/attempt history; n=49), PBD-single attempters (n=14), and PBD-multiple attempters (n=11). Findings partially supported hypotheses:

- Behavioral Task: Stop signal reaction times (SSRT) did not differ among healthy controls, PBD-non-attempters, and PBD-single attempters. However, multiple attempters had significantly greater impulsivity (M = 465.4, SD = 42.6) than healthy controls (M = 413.2, SD = 50.7), p = .01; additionally, differences between the SSRT for multiple- and single-attempters (M = 420.4, SD = 41.7) approached significance, p = .07.
- Self-Report: Healthy controls reported the lowest impulsivity (M = 60.7, SD = 9.5) as compared to PBD single-attempters (M = 70.2, SD = 11.8), multiple-attempters (M = 75.5, SD = 10.6), and non-attempters (M = 72.7, SD = 9.5), ps < .01. Impulsivity scores for single- or multiple-attempters did not significantly differ from PBD non-attempters.

Conclusion: In sum, youth with more severe attempt history (i.e., two or more suicide attempts) had significantly elevated levels of impulsive responding as examined by the computerized objective assessment. Findings revealed differential patterns for the self-report index relative to the behavioral measure, which is consistent with prior work with bipolar adults (e.g., Swann et al., 2005). Findings thus indicated that impulsivity may be a risk factor for suicidal behavior and future attempts among youth with PBD. Findings also suggest that such youth may reflect a qualitatively distinct subgroup with more specific pathogenetic processes, including impulsivity, at play. These findings must be interpreted cautiously, given the small size of the multiple attempter group, but warrant further study.

Additional Information: This work was supported by a grant from the American Foundation for Suicide Prevention (AFSP)

High nicotine dependence is a factor in the risk of suicide in Bipolar Disorder patients

Luis Gutiérrez-Rojas, Manuel Gurpegui, Francisco Soto, José María Martínez-Ortega, Lola Jurado. Avenida Federico García Lorca nº 31, Escalera 1, 2º C, Spain

Objective: To evaluate the intake of caffeine and tobacco in a group of Bipolar Disorder patients and relate it to social, demographic, clinical and evolutionary variables, and determine which of them is linked with a greater intake of caffeine and tobacco and high nicotine dependence.

Method: A cross sectional study was made with a group of 108 outpatients diagnosed with Bipolar Disorder, and these were interviewed.

Social and demographic data was gathered, clinical variables about the current situation of the patient, treatment sub-type, level of treatment compliance, and habits of caffeine and tobacco intake.

Results: The majority of the patients were feminine, married, with their own family and diagnosed with Type 1 Bipolar Disorder. 48% of them consumed caffeine regularly while 57% of them had at some time been a daily smoker, 44% of whom were currently active smokers; amongst the smoker group 50% had high nicotine dependence. High caffeine intake (>200 mg daily) has been linked to the elevated consumption of tobacco (OR 9.1; 95% CI: 2.2-37.7) and to a level of university studies (OR 1.6; 95% CI: 1.6-40.0). Furthermore, the start of Bipolar Disorder with a first manic attack is linked with daily smoking (OR 8.3; 95% CI: 2.5-33.3) and with high nicotine dependence (OR 4.1; 95% CI: 1.3-13.5). There is also a link between having a history of suicide attempts and the daily intake of tobacco (OR 5.4; 95% CI: 1.9-15.5) and with high nicotine dependence (OR 4.8; 95% CI: 1.6-15.0). Finally, high nicotine dependence is associated with an excessive intake of caffeine (OR 9.7; 95% CI: 2.3-40.5).

Conclusion: Among the patients with Bipolar Disorder, there is a tendency to consume tobacco and caffeine. A high daily intake of caffeine is linked with a high daily intake of tobacco and vice-versa. While the intake of caffeine doesn't appear to have clinical implications, the consumption of tobacco is linked both with the manic polarity of the illness and with having a history of suicide attempts, which can have significant evolutionary implications in this illness.

PRESENTATION ABSTRACTS

Bipolar affective disorders – investigations of the families

E. V. Gutkevich, E. D. Schastnyy, I. A. Zrazhevskaya
Mental Health Research Institute , Aleutskaya Street, 4, Tomsk, Russian Federation

Objective: to reveal peculiarities of family history (presence of mental or somatic diseases in first-degree relatives of proband) in patients with BAD, including quickly cycling course.

Materials and methods: we have investigated families of 279 patients with BAD (163 women and 116 men), from them 54 patients with quickly cycling course (42 women, 12 men). Average age at the moment of examination has constituted 45,65±0,34 years. Criteria for inclusion of patients: age at the moment of examination older than 18 years, meeting by diagnosis of BAD criteria of ICD-10.

Method: clinical-psychopathological, clinical-genealogical and mathematical ones. We observed basic ethical principles: informed consent and partnership.

Results: early onset of disease in patients - 25,02±0,74 years was revealed in absence of family history. Bipolar affective disorder in patients with family history began at earlier age if their first-degree relatives suffered from schizophrenia (18,00±1,00 years), oncological or cardiovascular pathology (21,17±1,70 years), anxiety (21,55±0,58 years) or depressive disorders (22,64±0,61 years), as compared with patients in whose family history epilepsy was present (36,±0,53 years), alcohol dependence (26,15±0,62 years) or BAD (24,82±1,35 years). In patients, BAD family history was determined by depressive disorders spectrum (37,28 %), alcohol dependence and anxiety disorders (13,26 % each, respectively). Variants of BAD and schizophrenia were represented in families of 9,32 and 7,89% of examined persons respectively, the rest pathology was documented only in single cases. The latest age of onset of BAD with quick cycles was noticed during sickness rate of relatives with epilepsy (36,00±0,00 years). We have revealed essential qualitative differences in family history of patients with quickly cycling character of bipolar affective disorder (in order of decrease of incidence rate): alcohol dependence – 16,67 %; BAD – 14,82 %; depressive disorders and schizophrenia – 12,96 % each; anxiety disorders – 9,26 %; somatic pathology and epilepsy – 1,85 % each. In patients with absence of course of BAD in quick cycles we revealed more often family history of anxiety disorders (14,23 %), than in patients with BAD with continual course (9,26 %). Family history of BAD and schizophrenia predominated in patients with quickly cycling course of BAD (14,82 and 12,96 %) during comparison with group of patients with BAD without frequent phases (8,00 and 6,67 %). In both groups family history of somatic pathology and epilepsy was represented by single cases.

Conclusion: BAD, including quickly cycling course, is characterized by high incidence of family history represented by mental disorders (depressive, anxiety disorders and alcohol dependence), somatic diseases (oncological and cardiovascular pathology) in first-degree relatives of proband.

How the nitrergic output to large brain vessels from the pterygo-palatine ganglion could matter in BPAD too.

Treviranus, Gottfried. M.D. Practice for Psychiatry and Psychotherapy FMH

Länggassstr. 30, CH 3012 Berne, Switzerland

Objective: To explore putative pathways from a.) germ signals acting on pattern recognition receptors (TLR e.g.) on macrophages/mast cells, causing b.) release of the amplificator NGF (Nicol 2007), which through peptides (CGRP e.g.) strongly stimulates c.) trigeminal afferents relaying d.) via bulk and synaptic transmission within the PPG. 2. To confront mostly recent knowledge of the very dense parasympathic nitroxidergic output of the PPG to major brain arteries (Taktakishvili 2010) with alternative functional and pathophysiological hypotheses (e.g. peroxynitrite) beyond the BBB-opening capacity (Yarnitzky 2004a,b), the slight vasodilation (Suzuki 1990) with its, evolutionarily scarcely relevant, emergency function (Goadsby 2002). These concern neurobiologically plausible (cluster headache, Henninger 2007; stroke, Torelli 2004; saccular aneurysm) or clinically since 90 years treated pathologies (facial and bodily pain; Piagkpou 2011), and migraine (Goadsby 2002). 3. As far as psychiatric disorders are concerned an large arterial supply framework - with consequences for intraparenchymal arteries is developed, whereby combined perivascular nervous and endothelial disturbances of the BBB (e.g. via mast cells, Mattila 2011; via gap junction, Eugenin 2012) ultimately lead to tissue deformation and function deficits. 4. As far as BAPD is concerned, the arterial supply to the very close striatal, pallidal, and thalamic stations of the three fronto-subcortical loops (Alexander 1994; Mega, Cummings 2001), which map the classic dimensions of action (ACC), thought (DLPFC), and feeling (LOFC), is reported. Mixed bipolar disorders could therefore mechanistically result from small areas of arterial dysfunction. Putative local arterial BBB disturbances then are put into correspondence with parallel disturbances of striatal shape reveiled by imaging studies of bipolar patients (Hwang 2006). Other deviations in vascular reactivity (Gómez-Carillo 2006), shape and WMHI (Kempton 2008) are considered along similar lines. 5. Immunomodulating properties of and resistance to lithium are discussed briefly.

Results: The above chain of argument is intended as a bold “real biologic” model, wherein signals transverse various systems in a conscious contrast to form-follows-function modelling (e.g. Yeh 2010).

Conclusion: The model at each step profits from the advancement in several fields, and the various constraints created at each interface.

Additional Information: www.biposuisse.ch/peripheral_causes_of_bipolarity_project (May 2012).

PRESENTATION ABSTRACTS

The dynamics of three-month bi-daily measures of global self-esteem functioning in bipolar disorder

Hugo Vachon, Julie Doron, Véronique Thomas-Ollivier, Marina Fortes-B ourbousson Laboratory "Movement, Interactions, Performance", UFR STAPS, Université de Nantes, Boulevard Guy Mollet, Nantes, France

Objective: Researches on depression emphasize that self-esteem is a main factor and that its regulation plays an important role in psychological functioning (DeHart & Plham, 2007). Most research has investigated the role of both the level and the variability of self-esteem as markers of vulnerability to depression. Although many researchers have theorized that low and unstable self-esteem can both lead to and result from clinical depression (Franck & DeRaedt, 2007; Kernis, 2006), recent studies on self-esteem suggest that historicity (i.e., time evolutionary properties) referred to the manner on how evolves self-esteem in daily life context (Fortes, Delignières, & Ninot, 2004) might be a more interesting way to understand depression. This perspective is particularly relevant for studies that would be conducted on chronic diseases (Fortes, Ninot, & Delignières, 2005).

Therefore, the aim of this study is to analyse the evolution of self-esteem during a three-month period in one patient with bipolar disorder. Our study was conducted within a methodological framework using ecological momentary assessment (Stone, 2007) with measures taken through a time-based process. To a more fully understanding, we used the association of quantitative approaches based on time series analysis and qualitative approaches based on audio records.

Method: After a medical ethics committee approved the study, John was included: a caucasian male, aged 39 unemployed, diagnosed bipolar II by a psychiatrist. This subject answered to one-item measure for global self-esteem (GSE) on a visual analog scale (10cm), twice a day (morning and evening) during a three-month period with a computerized device. This tool allowed recording audio messages after each evaluation. The GSE item is removed from the PSI-6b (Ninot et al., 2006), a French short version of the Fox and Corbin's PSPP (1989) including RSEI items (Rosenberg, 1965).

A time series of 180 observations was obtained. We calculated descriptive statistics such as mean and standard deviation to determine the level and stability of this psychological dimension. ARIMA procedures (Box & Jenkins, 1976) were performed to determine temporal dependencies and underlying processes. Audio messages have been recorded throughout this period.

Results: Descriptive statistics showed a low mean level and a great instability of GSE (M=5.03, SD=2,19). The ARIMA model that fitted well with GSE time series was an auto-regressive seasonal model which obeys to the following equation: Yt= μ + ðYt-1 + ðYt-2 + ő. Autoregressive models suggest two simultaneous processes: a first one implying short time dependencies and a second one involving a long term reference to past (trait-like). Qualitative data enabled to determine the life events which disrupted the subject's perception of GSE but also to point out an intrinsic dynamics independently of exogenous daily experiences.

Conclusion: This case-study first emphasizes explanatory process of GSE's fluctuations of a bipolar subject. Second, it shows the relevance of an idiographic protocol design to provide a potent means to more fully understand the functioning of psychological constructs such as the self.

Concept-matching, link-joy and bipolar disorders

Brian Bayly

Objective: The brain contains a system whose malfunction may be an important factor underlying the bipolar condition, a system at present hardly recognized. The objective is to draw attention to this system so as to promote research into its details and its immediate recognition in psychiatry.

The system in view is exemplified by two words that rhyme and so generate pleasure (a tiny momentary spasm). More generally, the system has as input two mental representations that match, fit well or overlap and has as output a hedonic spasm, jolt or blip. Single instances are sometimes recognizable, e.g. a single rhymed couplet or the fit of one piece into a jigsaw puzzle, but there are also streams of recognitions (hundreds per minute in reading or conversation), and the continuous positive hedonic tone of these pastimes is taken to be a merged aggregate effect from the stream of micro-events.

Sub-objectives are (1) to show the breadth of the field of instances i.e. the pervasiveness of the system's influence, and (2) to allow for readers' instinctive resistance. Any suggestion that might require adjustment of one's fundamental ideas tends to be unwelcome, but while the extent of the system's influence is speculative it is insisted that there is no room for doubt about its existence: subjective experience establishes the system's existence beyond any doubt.

Method: For brevity I will use the term link-joy (joy from a link between two representations). To see the extent to which link-joy pervades our lives one can note:

- repetitive visual patterns (wallpaper, friezes, colonnades)
- an intention and its result (using physical dexterity or skill)
- an expectation that is met (e.g. in music or other rhythmic activity)
- aesthetic experience (external object resonating with an agent's internal concept)
- puzzle-solutions and insights
- any recognition (e.g. a familiar object or scene, or a word heard or read)
- tidiness, matching how it is with how it should be.

In most of these instances other effects act simultaneously

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so that link-joy is partly obscured, but it is present nonetheless. In pervasiveness it is like the air we breathe: it escapes notice through being so constantly present.

Results: A normal person lives on the positive side of hedonically neutral (prefers seeing tomorrow to dying while asleep). When down, a bipolar person misses the pleasures of conversing, recognizing familiar things, completing household tasks, pursuing a hobby etc. When up, a bipolar person is unduly elated by everyday events and makes fanciful, far-fetched connections, hyper-linking. These behaviors are observable; their being at least in part the results of a normal, under-active or over-active link-joy system is a postulate that deserves exploration.

Conclusion: Once recognized, the link-joy system affords a wide-open opportunity. The possibility should be explored that fluctuations in the activity of the system contribute to the variations in mood of a bipolar subject. Several approaches --- psychiatric, pharmaceutical and neuroscience-experimental --- are available, with the prospect that improvements in treatment may be rapidly reached.

Clinical typology of atypical depression and its relation to bipolar disorder

A.S.Avedisova, M.P.Marachev, Moscow, Russia

Atypical depression (AD) is the common disorder in psychiatric and clinical practice (15,3-29%). According to the modern concepts AD is the 'transitional' syndrom or so called bridge between monopolar depression and bipolar II disorder.

Objective: To evaluate the influence of AD psychopatological structure on stereotype of affective disorder depending on the diagnostic criteria of bipolarity (DSM-IV, tight or more broader critieria).

Material and methods: Sixty patients with AD (DSM-IV) (average age 38.3±13.2 years, females – 87%) were enrolled in our study. We used ADDS scale and different diagnostic criteria of bipolarity (DSM-IV, tight or more broader criteria according to J.Angst et al., 2003).

Results: We differentiated three types of AD taking into account predominant clinical disorder and ADDS rating. The first type is characterized by predominant mood reactivity (26.6%) with partly or competely reversible hypothymia in response to actual or potential significant events. Normothymic state can be restored for variable time. Patients with the second (most common – 41.6%) type of AD show the triad of reversed vegetative symptoms: hypersomnia (excessive daytime sleepiness, attacks of sleepiness and prolonged awakening), hyperphagia (excessive hunger with frequent consumption of small quantities of food and episodes of abnormally large intake of food products, mainly carbohydrates; sometimes bulimia with weight gain of 3 to 12 kg) and leaden paralysis (the feeling on unusual heaviness in the extremities and paresthesia that may be spontaneous or induced by emotional stress). Patients with the third type of AD present with rejection sensitivity (31,6%) and combination of stable hypothymic state with interpersonal sensitivity/touchiness. Behavioral disorders include stereotyped histerical reactions, rejection reactions, dysphoric arousals associated with interpesonal conflicts, overt (agression, avoidance) or latent (hostility) emotional abandonment and social desadaptation.

The clinical typology of AD reflected the stereotype of affective disorder. According to DSM-IV criteria of bipolarity first type of AD was common in patients with recurrent depressive disorder (43.7%) and more rare in patients with bipolar disorder (12.5%). Second type of AD developed mainly in patients with bipolar disorder (36%) and extremely rarely in patients with recurrent depressive disorder (5.5%). Third type of AD was frequently present in patients with recurrent depressive disorder (31.5%) and uncommon in patients with bipolar disorder (5.2%).

The use of tight and broader criteria of bipolarity was associated with increase in rate of diagnosis of bipolar disorder to 18.7% and 62,5% in patients with type 1 AD, to 76% and 84% in patients with type 2 AD and to 10.5% and 31.5% in patients with type 3 AD.

Two-year catamnesis in 60 patients with primary AD showed with 62.5% specificity that type 2 AD was a predictor of bipolar II disorder.

Conclusion: We identified 3 types of AD that reflect the different stereotypes of affective disorders. AD with predominant reversed vegetative symptoms was reliable predictor of bipolar II disorder.

PARALLEL SESSION

Plenary 7: A 3-year, open label study of adjunctive Memantine in Treatment-resistant Bipolar Disorder

Chair: **Prof M Pompili (I)**
Speaker: **Prof G Serra (I)**

Gino Serra, M.D., is a psychiatrist and Professor of Pharmacology at the University of Sassari, Department of Biomedical Science. He had been a research pharmacologist at the Bernard Brodie Department of Neuroscience of the University of Cagliari until 1994. He has published a textbook on psychopharmacology [1], and more than 135 journal articles and book chapters on psychopharmacology, particularly pertaining to mechanisms of action of antidepressant and mood-stabilizing drugs, including studies of the role of dopamine in the actions of antidepressants and mood-stabilizers, as well as in the pathogenesis of mood desorders. In 1979 he first suggested that potentiation of dopaminergic transmission in neurons arising in the substantia nigra/ventral-tegmental-area induced by repeated treatment with antidepressants plays an important role in their therapeutic effects [2]. Recently he found that antidepressants, possibly by sensitizing dopamine D2 receptors, induce bipolar-like behavioral excitation in experimental animals.In fact, imipramine induces a sensitization of dopamine D2

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receptors (mania/hypomania), which is followed after 12, 33 and 40 days of imipramine withdrawal by a progressive desensitization of dopamine D2 receptors (depression) (3) associated with a depressive-like behaviour as assessed in the forced swimming test animal model of depression (4). Non-competitive NMDA glutamate receptor antagonists, including memantine, prevented dopamine D2 receptor sensitization in this experimental model. Accordingly, he suggested [5, 6] and he and his collaborators developed preliminary clinical support for the proposal that memantine may exert beneficial, mood-stabilizing effects. Indeed, they have recently observed in 3 naturalistic clinical studies that memantine, as an augmenting agent, was associated with clinically substantial antimanic and sustained mood-stabilizing effects in otherwise treatment-resistant bipolar disorder patients, with excellent tolerability and safety [7-10].

Abstract

Memantine is a non-competitive antagonist of glutamate NMDA receptors, currently used in the treatment of moderate to severe Alzheimer Disease, with excellent safety and tolerability profile.

We have recently reported that Memantine, as an augmenting agent, was associated with clinically substantial antimanic and sustained mood-stabilizing effects in treatment-resistant bipolar disorder patients (1, 2).

Here we present the results of a 3-year naturalistic trial on the antimanic and mood-stabilizing effect of Memantine in treatment-resistant bipolar disorders.

Patients [N= 22 (16 women and 6 men) mean age 43] were 16 BPI and 6 BPII. Ten were rapid cyclers, 6 continuous circular with long cycles, 6 had a course with free interval, 15 exhibited psychotic symptoms. All patients had been resistant to very intense standard treatments (Lithium, Anticonvulsants, Antidepressants, ECT, Typical and Atypical Antipsychotics). The severity of the patients condition and the change after memantine addition was evaluated on the Clinical Global Impression Bipolar (CGI-BP) Overall Bipolar Illness scale. Memantine (10-30 mg/day) was added to the previous (ineffective) treatment, which was left unmodified. All patients were monitored for 36 months. The average of CGI-BP score was 6.6 before the addition of memantine. The mean duration of illness was 22.4 years, and the duration of rapid cycling course 11 years. Patiens very much (scored 1) or much (scored 2) improved were 77.3%, 81.8%, 68.2%, 72.7%, 72.7% and 72.7%, at 6, 12, 18, 24, 30, and 36 months, respectively. Side effects: dizziness (N= 1), costipation (N= 1) and drowsiness (N= 1).

The results confirm that memantine was associated with a clinically substantial antimanic and sustained (3 years) mood-stabilizing effect in treatment-resistant bipolar disorder patients, with excellent safety and tolerability.

The possible mechanisms of the antimanic and mood-stabilizing effect of memantine will be discussed.

References:

Athanasios Koukopoulos, Daniela Reginaldi, Giulia Serra, Alexia E. Koukopoulos, Gabriele Sani, Gino Serra. Antimanic and mood-stabilizing effect of memantine as an augmenting agent in treatment-resistant bipolar disorder. Bipolar Disorders (2010). 12: 348-349.

Athanasios Koukopoulos, Giulia Serra, Alexia E. Koukopoulos, Daniela Reginaldi, Gino Serra. The sustained mood-stabilizing effect of memantine in the management of treatment-resistant bipolar disorders: Findings from a 12-months naturalistic trial. Journal of Affective Disorders (2012). 136: 163-166.

Plenary 8: Mixed states: diagnostic and therapeutic implications

Chair: Prof E Vieta (Es)

Speaker: Prof I Pacchiarotti (Es)

Isabella Pacchiarotti, MD, Phd, is graduated in Medicine at “La Sapienza” University of Rome. She is Doctor Cum Laude in Medicine. She is specialist in psychiatry and cognitive-behavioral psychotherapist. She has worked for four years in the Psychitric Unit of the Department of Neuroscience at Sant’Andrea Hospital, “La Sapienza” University of Rome, with a specific area of interest in bipolar disorders. She also has a broad background in neuropharmachology with specific training in neurobiology and treatment of bipolar disorder, with expertise in key research areas for this application. As a lecturer, she has taught several courses and lectures on bipolar disorder to medical students and residents in psychiatry at the University “La Sapienza” of Rome.

At present, she works as a researcher of CIBER Mental Health Program (CIBERSAM) in a tertiary care unit of the Bipolar Disorder Program of Hospital Clinic in Barcelona, Spain, headed by prof. Eduard Vieta. This unit stands at the forefront of research in the area of novel treatments in bipolar disorders, both pharmacological and psychological, including atypical antipsychotics, antidepressants, novel antiepileptic drugs and psycho-education. In particular, her areas of research experience are critical issues in bipolar disorder, such as the use of antidepressants and affective mixed states. She also works in the area of psychoeducation for bipolar disorders headed by Prof. Francesc Colom.

He has participated as a speaker in several international congresses and published more than 20 articles in peer-reviewed journals on topics related to the clinic and therapy of bipolar disorder.

Abstract

The issue of the diagnosis of mixed states occupies a central position in terms of diagnostic and therapeutic implications.

Current DSM-IV-TR criteria for mixed bipolar episode do not allow an adequate understanding of a vast majority of bipolar patients with mixed (hypo) manic-depressive features, keeping the qualification of “mixed episodes” for

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bipolar type I only.

The Task Force for the DSM-5 is oriented towards abolishing the mixed episode and shifting it to “mixed features specifier”. This would allow clinicians to consider mixed states in a less restrictive way, and extend them beyond the bipolar I subtype. Moreover, recent efforts have focused on establishing operational definitions of mixed states. Despite this, the definition and operationalization of mixed states remain still unsolved, leading to important limitations in the management of bipolar patients. Mixed states are associated with the evidence of a worse overall outcome: earlier age at first hospitalization and longer duration of illness, an increased relapse risk, a higher prevalence of substance use and other comorbidities, a higher risk of suicide, lower recovery rates in the long-term and lower response to antidepressant drugs.

Little evidence is available about how to treat mixed states other than dysphoric mania. Hence, the only controlled data available to date comes from subanalyses of randomized controlled trials in mania tha enrolled a variable number of mixed patients fulfilling criteria of mania, with no specific requirements with regards to the intensity of depressive symptoms. Unfortunately, there is no trial dealing specifically with the treatment of mixed states. Treatment options for mixed bipolar patients include anticonvulsants, lithium and antipsychotics. Although some anticonvulsants such as divalproate may be more effective than lithium in this patient population, there are few controlled data supporting the use of others (e.g. carbamazepine, and there is actually negative data with lamotrigine). The risk of switching to depression is high in mixed states. Conventional antipsychotics, such as haloperidol, may be less efficacious at protecting against a switch to depression than atypical antipsychotics.

Since ADs may reportedly worsen the outcome of manic or mixed episodes there is general consensus about discontinuing them during mania. Despite this, ADs are frequently prescribed at baseline and maintained in patients experiencing a manic/mixed episode. There are several studies that suggest that the prevalence of lifetime mixed episodes is associated with greater lifetime AD utilization. In this speech the main problems associated with diagnostic, clinical and therapeutic issues in mixed states will be discussed based on an update scientific evidence.

PARALLEL SESSION

Oral Platform Session II

Chair: **Prof A Erfurth (At)**

Deterministic dynamics of daily mood over 5 years in a patient with affective disorder

João Guilherme Ribeiro, Carlos Lourenço
Department of Psychiatry, Hospital Prof. Dr. Fernando Fonseca EPE. Portugal

Objective: From a dynamical systems perspective, affective disorders may be disturbances of the dynamics of affective systems. If the future behaviour of a system is determined by its previous states, then its dynamics is deterministic. The dynamics of a large time series of daily mood in a patient with affective disorder was analysed and tested for the presence of determinism.

Method: The analysis was performed on a published time series of daily mood records (N=1746) from a single patient (Groot, Journal of Mental Health 2010;19(4):352-362). He was diagnosed with dysthymia and a major depressive episode at the start of recording, and was put on venlafaxine. Mood was rated with a scale based on self-selected criteria. Spectral analysis was performed. Presence of dynamical determinism was assessed through correlation dimension (CD). This is a measure of the number of state variables needed to represent the dynamics of a system and hence its time-structural complexity. Random systems have higher CD than deterministic ones. CD for the original series was compared to that of 10 random series with the same linear properties, obtained from surrogate data generation via iterated Amplitude Adjusted Fourier Transform. Finally, two forecasting models were tested for predictability - a linear Autoregressive Moving Average (ARMA) model, and a nonlinear model of K-nearest neighbours (K-NN)-based local linear approximation of the dynamics in time-delay state-space. Model fit was computed such that 100% is a perfect fit.

Results: Spectral analysis showed no clear periodic cycles, and a power spectrum compatible with a noise-like 1/f^őpattern. Estimated ősignificantly was 0.83. Correlation dimension of the original series tended towards convergence and differed from those of surrogates for all embedding dimensions >1. For embedding dimension 10, CD from the original series was 5.72, inferior to CD from surrogates, p

Conclusion: Estimatedőfrom the power spectrum was similar to previous reports in patients with affective instability. A value closer to 0 would relate to behaviour more similar to white noise, and has been reported in healthy controls (Woyshville et al, Biol Psychiatry 1999;45:261-269). The loss of healthy “noisiness” may be a marker of affective disorder representing more rigid dynamics of mood. Mood variation for this patient was less complex (lower CD) than for a random linear system with similar behaviour, which is evidence of nonlinear determinism in the dynamics of mood. Convergence of CD suggests the possibility of modelling – and therefore predicting and controlling – the dynamics of mood in affective

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disorders, using a limited number of variables. However, measuring only one variable, it was not possible to achieve an operational model of mood variation at this stage.

Creativity and Bipolar Disorder: Family Study of 300,000 Patients

Mikael Landen, Gothenburg University, Section of psychiatry and neurochemistry, Sweden

Objective: Creativity has long been associated with mental disorder in general, and bipolar disorder in particular. The aim of the present study was to the alleged association between bipolar disorder and creativity, and to investigate whether an association is due to environmental or genetic factors.

Method: We performed a nested case-control study based on Swedish registries. The likelihood of holding a creative occupation in individuals, who had received inpatient treatment for schizophrenia, bipolar disorder, or unipolar depression between 1973 and 2003, was compared to controls. We also compared patients non-diagnosed relatives with relatives of controls.

Results: We identified 29,644 patients (11,910 males and 17,734 females) with bipolar disorder, 54,042 patients (29,479 males and 24,563 females) with schizophrenia, and 217,771 patients (84,352 males and 133,419 females) with unipolar depression. Patients with bipolar disorder as well as the healthy siblings of patients with bipolar disorder or schizophrenia were overrepresented in creative professions. Neither patients with unipolar depression nor their siblings differed from controls regarding creative professions.

Conclusion: This Swedish total population case-control study is several magnitudes larger than previous studies and demonstrates an increased likelihood for both patients with schizophrenia and bipolar disorder, as well as for their respective relatives, to hold a creative occupation, compared to controls. The absence of an association with depressed patients indicates that creative occupations are specifically linked to bipolar disorder and schizophrenia rather than to psychopathology per se. A familial cosegregation of both schizophrenia and bipolar disorder with creativity is suggested.

Prevention of Postpartum Psychosis in Women at High Risk

Veerle Bergink, Paul F. Bouvy, Jeroen S.P.Vervoort, Kathelijne M. Koorengevel, Eric A.P. Steegers, Steven A. Kushner Gravemdijkwal 230, 3000 CA, Rotterdam Netherlands

Objective: Women with a history of bipolar disorder or postpartum psychosis are at extremely high risk of relapse postpartum. Although lithium prophylaxis has demonstrated efficacy in reducing postpartum relapse, the timing of prophylaxis remains controversial given the balance of risks and benefits for the mother and fetus. Here we evaluate the use of lithium during pregnancy compared to its initiation postpartum in women at high risk for postpartum psychosis.

Method: In total, 70 pregnant women at high risk for postpartum psychosis were referred to our psychiatric outpatient clinic between January 2003 and December 2010. Women who were medication-free at the time of initial evaluation were advised to start lithium prophylaxis immediately postpartum. In contrast, women already on maintenance lithium during pregnancy were advised to continue this treatment.

Results: All women with a history of psychosis limited to the postpartum period (n=29) remained stable throughout pregnancy despite being medication-free. In contrast, 24.4 % of women with a history of bipolar disorder (n=41) relapsed during pregnancy, despite the majority using prophylaxis throughout pregnancy. During the postpartum period, relapse was highest in women with bipolar disorder who experienced mood episodes during pregnancy (60.0 %). Remarkably however, none of the 20 women with postpartum psychosis using postpartum prophylaxis relapsed, compared to 44.4% of postpartum psychosis patients who declined lithium prophylaxis.

Conclusion: We recommend initiating prophylactic treatment immediately postpartum in women with a history of psychosis limited to the postpartum period, offering an important clinical advantage by avoiding in utero fetal exposure to prophylactic medication.

Cognitive inhibition and affective priming effect in Major Depressive Disorder

B Gohier, D Denes, M Briere, CR Mesu, G Fournis, SA Surguladze, D le Gall, JB Garre, Department of Psychiatry, CHU, 4 rue Larrey, 49933 Angers Cedex, France

Objective: Automatic and controlled processes are required to complete and regulate the processing of emotional information. Patients suffering from Major Depressive Disorder (MDD) present both impairment in cognitive inhibition and a bias toward negative stimuli.

The aim of this study was to assess simultaneously automatic and controlled processes in emotional processing and to evaluate possible correlations.

Method: Twenty in-patients (14 women and 6 men) suffering from MDD (DSM-IV, MINI, BDI > 16) were compared to twenty healthy controls. To assess cognitive inhibition, we used the Prose Distraction Task (Connelly SL, 1991), Stroop test (1935) and Hayling Sentence Completion Test (Burgess and Shallice, 1997). Automatic process was evaluated with an affective priming task, which consisted of three subtests, differing in the modality of the prime (face, written word and sound. The targets were always written words.

Results: Individuals with MDD showed impairment in cognitive inhibition. In affective priming task, MDD showed a positive priming effect when both prime and target were with a negatively valence and an inverse effect when prime and target were with a positive valence.

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As we expected, we found a correlation between controlled and automatic processes in the way that priming effect and impairment in the second part of Hayling Sentence Completion Test were correlated, whatever the emotional condition (positive and negative).

Conclusion: These results confirm impairment in cognitive inhibition and bias toward negative stimuli in MDD, with a correlation between automatic and controlled process. This correlation in the two emotional conditions, positive and negative, should represent a trait-vulnerability in control processing of emotional information in MDD.

Additional Information: This communication should be presented in oral or poster session to the choice of scientific comitee

Mood Variability in Adult Women

Sarah Romans, David Kreindler, MD; Eriola Asllani MSc., Gillian Einstein, PhD; Sheila Laredo, MD; Anthony Levitt, MD; Brenda Toner, PhD; Donna Stewart, MD PO Box 7343, Wellington 6242 New Zealand

Objective: To compare mood variability between bipolar and non-bipolar adult women. Mood variability addresses the amplitude or score dispersion of mood items over time. The range is abnormally large during a bipolar episode but it is not known whether this also occurs for bipolar patients all the time including when they are not clinically depressed or manic.

Method: In the Mood in Daily Life (MiDL) study, Toronto, 76 women, randomly selected from the community gave daily mood ratings for six months using visual analogue scales at the same time each day.

The Mini-International Neuropsychiatric Interview generated research diagnostic classifications for each participant at the start of the project, including their lifelong experience of mania-hypomania. Means (& SDs) for two items, happiness and sad-blueness, from two MiDL groups, 1. n=17, with lifetime mania/hypomania, 2. the remainder, without mania/hypomania n=57, were compared using t-tests for the means of the standard deviation scatter for each woman over time.

Results: The means of the standard deviations for the two groups did not differ statistically for either happiness (with hypomania 18.00, without 16.5, df 29.0 t=-1.0 ns) or sad-blueness (with hypomania 19.13, without 18.27, df 29.8 t=-0.52 ns).

Conclusion: The two groups, probable bipolar and not bipolar, did not differ in their variation of mood. This suggests that women likely to have bipolar disorder do not have a consistently greater range of mood experience over time than women without bipolar disorder. There appears not to be an interepisodic 'forme fruste' excessive mood variation pattern in probable bipolar women.

Genome-wide study of CSF kynurenic acid in bipolar disorder implicates a molecular pathway underlying psychosis

C Sellgren[1], M Kegel[2], CJ Ekman[3], SK Olsson[2], Camilla I Svensson[2], C Hultman[1], P Lichtenstein1, SM Purcell[4,5,6], PF Sullivan[7], P Sklar[4,5,6], G Engberg[2], S Erhardt[2], M Landèn[1,8]

[1]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden. [2]Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. [3]Section of Psychiatry, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. [4]Psychiatric and Neurodevelopmental Genetics Unit, Center for Human Genetic Research, Massachusetts General Hospital, Boston, Massachusetts 02114, USA. [5]Stanley Center for Psychiatric Research, The Broad Institute of Harvard and MIT, Cambridge, Massachusetts 02142, USA. [6]The Broad Institute of Harvard and MIT, Cambridge, Massachusetts 02142, USA. [7]Departments of Genetics, Psychiatry and Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA. [8]The Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

Objective: N-metyl-D-aspartat-receptors (NMDARs) are implicated in psychosis, and elevated levels of the NMDAR antagonist kynurenic acid (KYNA) have been found in the cerebrospinal fluid (CSF) of bipolar disorder and schizophrenia patients. KYNA has also been suggested to play a role in cognitive functioning, and verbal working memory performance (WM) differs between schizophrenia and bipolar disorder with psychotic symptoms. In the present study, we first conducted a GWAS to evaluate genetic variability underlying elevated CSF KYNA in euthymic bipolar disorder. Second, we studied associations between the identified genetic trait and homovanillic acid (HVA), history of psychosis, functional measures of verbal working memory (WM), and brain structures implicated in WM. Third, we conducted an in vitro study to investigate molecular mechanisms underlying the association between CSF KYNA and the genetic trait.

Method: CSF and blood were collected from euthymic bipolar patients. Analysis of KYNA was performed using an isocratic reversed-phase high-performance liquid chromatography (HPLC) system. HVA levels were measured using mass fragmentography. Subjects were genotyped using the Affymetrix 6.0 array. To assess WM we used the Digit Span Test in WAIS-III. MRI images were acquired using a 1.5T scanner. Human astrocytes were stimulated with recombinant human IL-1β and KYNA levels were analyzed together with mRNA levels (PCR) and protein levels (Western Blotting) of the two upstream kynurenine pathway enzymes indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO).

Results: One SNP (rs10158645) in the GWAS reached genome-wide significance. rs10158645 was also associated with psychosis and CSF levels of HVA. Further, rs10158645 was associated with increased WM in euthymic bipolar disorder. Moreover, MRI scans of the brain

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revealed increased gray matter thickness in corresponding brain regions. The minor allele in rs10158645 is coupled to a decreased expression of sorting nexin 7 (SNX7). Down-regulation of SNX7 leads to an activation of caspase-8. Activation of caspase-8 results in the generation of IL-1β that is elevated in CSF of patients with bipolar disorder and schizophrenia. Using cultured human primary astrocytes, we found that IL-1β increases KYNA via induction of tryptophan 2,3-dioxygenase (TDO).

Conclusion: These multimodal data lend themselves to the formulation of a hypothesis regarding the molecular mechanisms underlying psychosis in bipolar disorder: Genetic variability that down-regulate SNX7 cause elevated IL-1β levels by activation of the c-FLIP/caspase 8 pathway. IL-1β induces TDO of the kynurenine pathway, which causes an elevation of KYNA that modulates dopamine neurotransmission and increases the vulnerability for psychosis. Even though we only studied bipolar disorder it is tempting to speculate that aberrations in these molecular mechanisms might be critical for psychosis in schizophrenia as well. In line with this, elevated CSF levels of IL-1β and KYNA, as well as increased TDO expression and activity, have been observed in schizophrenia. Finally, our concurrent neurocognitive and MRI data also suggest an association between our genetic finding and WM: a robust divergent trait marker of schizophrenia and bipolar disorder. Even though a conclusive interpretation of these results also requires similar analyses in schizophrenia, it raises the possibility that these molecular mechanisms underlie this observed phenotypic difference between schizophrenia and bipolar disorder.

PARALLEL SESSION

Clinical Practice 1: Selecting best treatment for the Bipolar Spectrum

Chair: **Prof A Erfurth (At)**

The Upcoming DSM-5 : Changes for Bipolar II Disorder and Minor Bipolar Disorder

Prof O Pinto (Br)

Olavo Pinto is a graduate of The Medical School of the Federal University of Rio de Janeiro, Brazil. He initially did his residency in Internal Medicine and worked as an internist for 10 years. In the late 80´s after finishing a residency program in Psychiatry at The Federal University of Rio de Janeiro he moved to the United States of America. In the USA he did his residency in Psychiatry at Georgetown University and University of California, San Diego programs. In San Diego he completed a 3 years Fellowship program in Mood/Bipolar Disorders under the supervision of Prof Hagop Akiskal. He was appointed Clinical Assistant Professor of Psychiatry till 2000 when he returned to his native city Rio, Brazil. From 2000 till now he is the head of the Neuropsychiatry/Bipolar Clinic in Rio. He has published original articles regarding new foundations for the diagnosis and treatment of bipolar illness mostly dealing with new concepts of the Bipolar Spectrum. He has lectured extensively around Brazil, South America, the United States and Europe.

Abstract

In the middle of next year it will be published the 5th edition of DSM. The main attention was geared towards the changes affecting hypomania criteria, because the increase in the prevalence of bipolar diagnosis needed a more realistic approach to this phase of the illness.

In regards of cyclothymia, it is certain that no changes will take place. This central temperament , crucial for the understanding of most Bipolar II or Spectrum diagnosis ,continues like it is today: totally forgotten and not being paid attention whatsoever.

Again, the central question remained the concept of true hypomania in regards to the importance of activation and energy , both crucial for the diagnosis, and also the number of days of duration of the episodes. Also very important are the recognition of mixed depressive episodes and mixed hypomanias.

Activation and energy will be added to the diagnosis of hypomania as part of the criteria A ,but in a useless way because it will be like this: Elevated or irritable mood AND Activation or increased energy. As everybody could see the word AND and not OR make the diagnosis even harder to be made because, in totally useless manner, is in the criterion A and is no longer belonging in the criterion B, In summation : energy and activation will be downplayed in importance as part of hypomanic episodes.

Changes for the number of minimal days necessary to make the diagnosis of hypomania are even more disappointing . with the support of studies like Jules Angst BRIDGE STUDY, clearly showing that even 1 day captures this phase of bipolar II, and others,the number of days of hypomania will stay the same, 4 days.

Mixed depression and mixed hypomanias will ,for the first time in the DSM system, appear in classification as specifiers in the NOS(not elsewhere specified)category.

Again, in a very non logical way, these specifiers will be allowed to be applied to Major Depression. To be quite clear: patients will be allowed to have hypomanic episodes and remain Unipolars.

Antidepressant resistant depression and suicidal behaviour: the role of underlying bipolarity

Prof X Gonda (Hu)

Xenia Gonda MA PharmD PhD is a clinical psychologist and pharmacist working as an assistant professor at the Department of Clinical and Theoretical Mental Health of Semmelweis University, Budapest and is also affiliated with the

PRESENTATION ABSTRACTS

Department of Pharmacodynamics. Her main research interests include personality genetics, neurobiology, pharmacology and psychosocial aspects of suicide and bipolar disorders, effects of seasonality and birth season, and mood fluctuations related to the reproductive cycle.

Abstract

The background of antidepressant nonresponse, as well as the complex relationship between antidepressants treatment and suicidal behaviour are among the hottest topics in contemporary psychiatry. Antidepressant-resistance, antidepressant-induced worsening of depression, antidepressant-associated (hypo)manic switches, mixed depressive episode and antidepressant-associated suicidality among depressed patients is relatively most frequent in bipolar/bipolar spectrum depression and in children and adolescents. As early age at onset of major depressive episode and mixed depression are powerful clinical markers of bipolarity, and the manic component of bipolar disorder (and possible its biological background) shows a declining tendency with age, antidepressant-resistance/worsening, antidepressant-induced (hypo)manic switches, and "suicide-inducing" potential of antidepressants seem to be related to the underlying bipolarity. There is no doubt that successful acute and long-term antidepressant pharmacotherapy of depressive patients significantly reduces the risk of suicidality in the vast majority of patients but antidepressant monotherapy (unprotected by mood stabilizers or atypical antipsychotics) is frequently ineffective and may rarely worsen bipolar depression and therefore increase suicide risk in a small, vulnerable subpopulation. Clinicians should identify persons who might be not helped or are even at risk by a given intervention. The formal recognition of subthreshold bipolar (bipolar spectrum) disorders, particularly of depressive mixed states, in our official diagnostic systems will help to identify those depressives who do not respond/worsen to antidepressant monotherapy and consequently are at increased risk of suicidal behaviour. Incorporating these new findings into everyday clinical practice is urgently needed.

Cognitive and temperamental correlates of lithium response

Prof J Rybakowski (PI)

Prof. Janusz K. Rybakowski graduated in 1969 at Medical Academy Poznan, Poland. In 1976-77 he was NIH Fogarty Research Fellow at Department of Psychiatry, University of Pennsylvania, Philadelphia. In 1985-1995 he was Chairman, Department of Psychiatry, Medical Academy, Bydgoszcz, and since 1994, the Head of Department of Adult Psychiatry, University of Medical Sciences, Poznan, Poland.

Prof. Rybakowski has authored or co-authored over 500 scientific articles, mostly published in international journals, on clinical psychiatry, as well as on neurobiology and psychopharmacology of psychiatric disorders. His main scientific achievements include the neurobiology of bipolar mood disorder and the mechanism of lithium action. He is also the author of the book "The Faces of Manic-Depressive Illness" (First edition, 2009). Prof. Rybakowski serves on editorial boards of Bipolar Disorders, Neuropsychobiology, Pharmacopsychiatry, International Journal of Psychiatry in Clinical Practice, Cardiovascular Psychiatry and Neurology, Depression Research and Treatment, Clinical Neuropsychiatry and Current Psychiatry Reports. Since 2009, he has been a Field Editor of the World Journal of Biological Psychiatry.

Abstract

Objectives: Lithium is still a cornerstone for a long-term treatment of bipolar mood disorder. A one third of bipolar patients treated longitudinally with lithium are "excellent lithium responders" in which lithium monotherapy can completely prevent further recurrences of manic and depressive episodes. Such patients are characterized by episodic clinical course with moderate frequency of episodes, good quality of remission periods, bipolar family history and low psychiatric comorbidity, closely reflecting Kraepelin's concept of "Manisch-depressives Irresein". The aim of this study is to assess the cognitive and temperamental correlates of quality of prophylactic lithium response.

Methods: For neurocognition study, the Wisconsin Card Sorting Test (WCST) was compared in 30 lithium treated-patients, among which 7 were lithium non-responders (NR), with 30 age-and gender matched healthy control subjects. Also, four tests from the CANTAB battery were compared between 60 lithium-treated patients, 13 of which were excellent lithium responders (ER) and 60 healthy control subjects. For the study of temperament, seventy patients receiving lithium for at least 5 years were assessed by two questionnaires: TEMPS-A (Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire) measuring depressive, cyclothymic, hyperthymic, irritable and anxious temperaments, and O-LIFE (The Oxford-Liverpool Inventory of Feelings and Experiences) measuring schizotypic traits such as unusual experiences, cognitive disorganization, introvertive anhedonia and impulsive nonconformity. The results of these were correlated with the quality of lithium prophylaxis assessed by Alda scale.

Results: Lithium non-responders performed worse on WCST compared to excellent and partial responders and matched healthy subjects. The performance on CANTAB tests was significantly worse in lithium-treated patients as a group, compared with matched healthy control subjects. However, the results of excellent responders were not different from those of the healthy persons. Using TEMPS-A scale, the response to lithium correlated positively with hypertymic temperament score ($r=0.31$, $p=0.009$), and negatively with anxiety ($r=-0.27$, $p=0.022$), cyclothymic ($r=-0.26$, $p=0.032$), and depressive ($r=-0.23$, $p=0.052$) temperaments scores. Using O-LIFE, the quality of lithium prophylaxis correlated negatively with cognitive disorganization score ($r=-0.24$, $p=0.049$).

Conclusions: Favorable response to lithium may be connected with preservation or even augmentation of cognitive functions. Excellent lithium responders

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may constitute a specific group of bipolar patients in which long-term lithium administration can produce complete normality. Out of affective temperaments, only hyperthymic one positively correlated with the quality of lithium prophylaxis while among schizotypic traits, cognitive disorganization showed negative correlation. Therefore, typical temperamental features of hypomania without cognitive disorganization may predict best lithium results.

PARALLEL SESSION

Interactive 6: Early Manifestations of Bipolarity: From Prodromes to Real Risk

Chair: **Prof E Youngstrom (US)**

Pediatric Bipolar Disorder- clinical picture and longitudinal course

Prof B Birmaher (US)

Endowed Chair in Early Onset Bipolar Disease, Professor of Psychiatry, University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, Pittsburgh, PA

Boris Birmaher, MD, is the Endowed Chair in Early Onset Bipolar Disease and Professor of Psychiatry at the University of Pittsburgh, School of Medicine. He has board certifications in both general psychiatry and child psychiatry. He received his medical degree from Valle University in Cali, Colombia and completed; training in general psychiatry at the Hebrew University, Hadassah Medical Center in Jerusalem, Israel; training in biological psychiatry at the Albert Einstein College of Medicine in New York; and training in child psychiatry at Columbia University, New York Psychiatric Institute in New York.

Dr. Birmaher has been involved in clinical work and research in pediatric mood and anxiety disorders for over 30 years. His research interests include areas of phenomenology, course and outcome, etiology and pharmacology, and psychosocial treatments. He is currently involved in several NIMH studies including: 1) "Course and Outcome for Adolescents with Bipolar Illness," aimed at describing the phenomenology, course, and associated factors in children and adolescents with bipolar spectrum disorder; 2) "Children of Bipolar Parents: A High Risk Follow-up Study," aimed at studying the longitudinal psychopathology of children of parents with bipolar disorder compared with children of community controls; and 3) "Longitudinal Assessment of Manic Symptoms," aimed at evaluating the predictive value of early-onset manic symptoms in a large sample of children ages 6-12 years old. Together with Dr. David Axelson, he is the Co-Director of the Child and Adolescent Bipolar Services (CABS) program, a program for the service, teaching and research of bipolar disorder in youth.

Abstract

There is controversy regarding the existence or the manifestations of bipolar disorder (BP) in children. Some clinicians often diagnose this disorder while others rarely see a child with BP. Since pediatric BP is accompanied by severe effects on the child's normal development and increases the risk for other psychiatric disorders and suicide, it is important to recognize and treat it early in life. The goal of this presentation is to critically review the symptoms of BP during childhood and adolescence and discuss the problems with its diagnosis at this age (e.g., variability in symptom presentation, effects of age on symptoms manifestation). In addition, the specific transmission of BP in families and the course and outcome of pediatric disorder will be reviewed.

In general, taking into account the developmental age of the child, the results of COBY are showing that symptoms of BP disorder in youth are similar to adults. However there are some developmental differences. Children and adolescents with BP have recurrent episodes, particularly subsyndromal symptoms of depression. However, there are important differences. For example, pediatric BP appears to be manifested by more rapid changes in mood, mixed episodes, time ill, behavior problems, and less severe manic and depressive symptoms than adult BP. Children have more comorbidity with ADHD and/or oppositional defiant disorders. Thus, it is not surprising that there are difficulties recognizing and treating children with BP.

Early intervention in bipolar disorders: recent elements of a new strategy

Prof P Conus (Ch)

Philippe Conus is Professor of psychiatry at the University of Lausanne. After training in internal medicine and psychiatry in Lausanne, he spent 3 years at the Early Psychosis Prevention and Intervention Center in Melbourne, Australia, where he developed with Prof Patrick McGorry and Prof Michael Berk, a specialized program for the treatment of first episode mania patients. In this context he ran a research program addressing various issues such as psychological approach and medication in first episode mania. One additional focus of the program was to explore the prodromal phase to first episode mania. Since returning to Switzerland, he developed an early intervention program for psychotic disorders (TIPP program) and took the head of the service of general psychiatry in September 2011.

Abstract

While early intervention in psychosis has become a major focus of research and treatment developments in the last 25 years, early intervention in bipolar disorders has only recently received some attention. Over the last decade, review and theoretical papers have shed a new light on elements that would justify the development of such specific treatment strategies. These elements suggest that the conceptualisation of a staging model for bipolar disorders may provide a valuable framework to

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guide diagnosis, prognosis and therapy from prodromal to highly resistant stages of the illness, and that it could also contribute to define clinically relevant targets for research. In this presentation, we will review elements supporting the development of early intervention strategies in bipolar disorders and describe potential targets for such developments. We will then present recent data on the identification of the prodromal phase of bipolar disorders and on treatment of first episode mania and will discuss some avenues for future research in this domain.

Advances in Assessment:

Fast and Frugal Methods of Detection Without Over Diagnosis

Prof E Youngstrom (US)
Psychology and Psychiatry, University of North Carolina at Chapel Hill, USA

Introduction: Bipolar spectrum disorder is not uncommon in youths. Epidemiological studies from around the world indicate that roughly 2% of youths meet criteria for bipolar spectrum disorders, with equal rates in the rest of the world as in the USA. This places bipolar disorder between the autistic spectrum and ADHD or depression in terms of prevalence. Based on the frequency, it is worth including in differential diagnoses. Typical clinical methods of evaluation often fail to detect bipolar disorder quickly or accurately.

Methods and Results: Adopting principles from Evidence Based Medicine and cognitive decision-making, it is possible to restructure the assessment sequence and methods to make more accurate diagnoses without adding significantly to the time and expense of evaluation. A dozen fast and frugal steps substantially improve detection of bipolar disorder based on vignette studies and a randomized trial training clinicians in some of the cognitive methods. Using parent checklists in combination with family history can rule bipolar out, and can raise the index of suspicion in cases where a semi-structured interview or mood charting methods would be justified (and often reimbursable). Some other sources of information have failed to show diagnostic utility, but still have a role in treatment planning.

Discussion: A combination of strategies is now available that can help improve detection of pediatric bipolar disorder while reducing false positive diagnoses. An algorithm that adds fewer than five minutes to most assessments and uses tools in the public domain would greatly increase the accuracy and consistency of clinical decisions around pediatric bipolar disorder. Methods would generalize well to bipolar disorder across the life cycle, which all too often goes misdiagnosed and managed sub-optimally in consequence.

Key Words: assessment, diagnosis, clinical decision-making

Selected References:

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EVENING LECTURE

The Portrayal of Bipolar Disorder, Mental Illness and Mental Health Professionals in Films

Chair: **Dr E Hantouche (Fr)**
Speaker: **Prof D Wedding (US)**

Danny Wedding was born in Rising Star, Texas and raised on a series of military bases around the country and in Germany and Panama. He has served as an Air Force medic and VISTA volunteer. Danny has traveled widely, and he has lived in Taiwan, Korea, Austria, and Thailand.

Danny was trained as a clinical psychologist at the University of Hawaii, and spent a postdoctoral year studying clinical neuropsychology and behavioral medicine at the University of Mississippi Medical Center. He later completed two years of postdoctoral training working first as a Robert Wood Johnson Health Policy Fellow and later as a AAAS Science Policy Fellow for the US Congress. The first year was spent working on the personal staff of Senator Tom Daschle; the second year was spent working for the Government Operations Committee in the House of Representatives.

Danny joined the University of Missouri-Columbia School of Medicine in 1991 as Professor of Psychiatry and Director of the Missouri Institute of Mental Health (MIMH). His primary responsibility is providing oversight and direction for MIMH, a university research and policy center serving the mental health community in Missouri. He would not have been qualified for this position had it not been for his rich policy experience as an RWJ Fellow.

Danny's research interests include international health, mental health policy, the portrayal of mental illness and addictions in films, and large scale community education projects designed to alter attitudes about mental illness and substance abuse. He has recently been collaborating with colleagues in the Department of Community and Family Medicine at Saint Louis University to develop a

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media campaign designed to reduce the incidence of Fetal Alcohol Syndrome in the Saint Louis region.

Danny is the author/editor of twelve books including Current Psychotherapies, Behavior and Medicine, the Neuropsychology Handbook, Screening for Brain Impairment and Movies and Mental Illness. His most recent book is the Handbook of International Psychology. The book on movies includes extensive discussion of the ways in which films perpetuate the stigma of mental illness. Danny also serves as the Editor for PsycCRITIQUES: Contemporary Psychology—APA Review of Books.

Abstract

This presentation will overview the ways in which psychopathology has been portrayed in both historic and contemporary films, based on the book Movies and Mental Illness (Wedding, Boyd and Niemiec, 2010). Five common myths that are frequently presented in films that portray a character with a mental illness will be discussed. These include the myth of traumatic etiology; the myth of the schizophrenogenic parents; the myth that mental illness merely represents harmless eccentricity; the myth that love alone is sufficient to overcome mental illness; and the belief that people with schizophrenia have split personalities.

Film clips will be used to illustrate these various myths. The presentation will pay particular attention to the presentation of bipolar disorder in films, using five primary exemplars:

- Splendor in the Grass (1961)
- A Woman Under the Influence (1974)
- Mr. Jones (1993)
- Michael Clayton (2007)
- Shine(1996)

Additional films will be introduced and reviewed during the presentation; some of the other films to be discussed include Blue Sky (1994), Lust for Life (1956), The Devil and Daniel Johnson (2005), Revolution #9 (2003), The Bell Jar (1979), Mad Love (1995), The Hours (2002), Girl Interrupted (1999), Bulworth (1998), Francis (1982), The Fisher King (1991) and Cobb (2003). The Patty Duke documentary Call Me Anna (1990), a biographical made for television movie depicting Ms. Duke's struggles with bipolar disorder, will also be discussed. Participants will be asked to share their thoughts about films they have seen that are good or bad portrayals of bipolar disorder and other psychiatric conditions.

Finally, this presentation will examine the portrayal of psychologists and other mental health professionals in movies, illustrating five recurring motifs: The psychologist as learned and authoritative; arrogant and ineffectual; seductive and unethical; omniscient and dangerous; or kindly and well intentioned. Films illustrating the core principles of positive psychology will be briefly discussed, and the use of films in the classroom and in therapy will be examined.

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Day 3: Wednesday, May 23, 2012

PLENARY SESSION

Plenary 9: Receptor targets for antidepressant therapy in bipolar disorder: an overview

Chair: **Dr J Cookson (UK)**
Speaker: **Prof K Fountoulakis (Gr)**

Konstantinos N. Fountoulakis, MD, PhD, is Assistant Professor of Psychiatry at Aristotle University of Thessaloniki, AHEPA University Hospital, in Thessaloniki, Greece.

Dr. Fountoulakis received his medical degree (1989), performed his residency in psychiatry (1998), and earned his PhD in psychiatry (1999) at the Aristotle University of Thessaloniki. He received a 3-year fellowship in psychosomatic medicine and a 1-year postdoctoral fellowship for research from the State Scholarships Foundation of Greece. Until 2003 he served as a medical officer in the Greek Armed forces retired with the rank of major. In 2005, Dr. Fountoulakis was a Research Fellow in the Department of Psychiatry, Division of Neuropsychiatry, at the University of Geneva in Switzerland.

Dr. Fountoulakis' areas of clinical and research interest are reflected in the topics that he teaches: general psychiatry, biological psychiatry, psychopharmacology, mood disorders, schizophrenia and personality disorders. He is an active member of a number of national and international professional organizations, including the EPA, APA, WPA, CINP, ECNP, ISAD, ISBD, EBF, the Cochrane Collaboration and others and was most recently a member of the Collegium Internationale Neuro-Psychopharmacologicum (CINP) Advisory Board to the Task Force on the Usefulness of Antidepressants and the Mental Health Economics Task Force of the International Psychogeriatric Association (IPA).

Abstract

The treatment of bipolar depression is one of the most challenging issues in contemporary psychiatry. Currently only quetiapine and the olanzapine-fluoxetine combination are officially approved by the FDA against this condition. The neurobiology of bipolar depression and the possible targets of bipolar antidepressant therapy remain relatively elusive. We performed a complete and systematic review to identify agents with definite positive or negative results concerning efficacy followed by a second systematic review to identify the pharmacodynamic properties of these agents. The comparison of properties suggests that the stronger predictors for antidepressant efficacy in bipolar depression were norepinephrine alpha-1, dopamine D1 and histamine antagonism, followed by 5-HT2A, muscarinic and dopamine D2 and D3 antagonism and eventually by norepinephrine reuptake inhibition and 5HT-1A agonism. Serotonin reuptake which constitutes the cornerstone in unipolar depression treatment does not seem to play a significant role for bipolar depression. Our exhaustive review is compatible with a complex model with multiple levels of interaction between the major neurotransmitter systems without a single target being either necessary or sufficient to elicit the antidepressant effect in bipolar depression.

Plenary 10: The Potential Clinical Benefits of the Glutamate Neuromodulator N-acetylecysteine in Bipolar Disorders and Associated Psychotic Conditions

Chair: **Dr J Cookson (UK)**
Speaker: **Dr R McCarthy (US)**

Richard H McCarthy MD PhD. I completed my PhD in Psychology from Fordham University while I was a first year student in the Faculty of Medicine of McGill University. After a year of medicine at the Montreal General Hospital, I completed Psychiatric Residency Training at The New York Presbyterian Hospital - Westchester Division. I am a recipient of the NAMI Exemplary Psychiatrist Award, a Distinguished Fellow of the American Psychiatric Association and am presently a Visiting Associate Professor of Clinical Psychiatry at SUNY Downstate Medical College. At present I work for the New York State Office of Mental Health as a Senior Statewide Consultant where I focus on the assessment and treatment of refractory, seriously mentally ill patients. I have published over 25 articles, and have lectured extensively throughout the Metropolitan New York area. In addition, I have an independent office practice for Psychiatric evaluations and treatments in White Plains, New York.

Abstract

N-acetylcysteine is an FDA approved medication, sold as Mucomyst, that is used to diminish secretion viscosity in pulmonary disorders such as COPD. N-acetylcysteine is also approved for use as an antidote to prevent hepatic toxicity in cases of acetaminophen overdose. N-acetylcysteine is a derivative of cysteine, a naturally occurring amino acid. As such it is available as an over the counter preparation and is commonly used by the general public for a wide variety of purposes. This is largely due to N-acetylcysteine's effect as an antioxidant.

Physiologically, n-acetylcysteine is a precursor to glutathione synthesis, the major antioxidant in the human body. Cysteine availability determines the rate-limiting step for glutathione synthesis. Cysteine transport into the cell is linked to glutamate exchange. Thus, in addition to reducing oxidative stress levels within the cell, cysteine also acts as a glutamate neuroregulator.

N-Acetylcysteine has been used to treat several major psychiatric disorders, including anxiety, depression, addiction, mania and psychosis. The levels of evidence supporting these uses varies considerably. This talk will present information about what is known about N-acetylcysteine's neurobiology and how It has been used to date in these psychiatric disorders. There will

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aslo be a brief discussion of the author's experience with N-acetylcysteine in the treatment of impulsivity and violence. Consideration will also be given to just what N-acetylcysteine may be doing that accounts for this broad array of effects.

PARALLEL SESSION

Interactive 6: Severe Bipolar Disorder - Pathology and Sequelae

Chair: **Prof Z Rihmer (Hu)**

Suicide and Bipolar Disorder

Prof P Courtet (Fr)

Philippe Courtet is Professor of psychiatry at the University of Montpellier, and Head of the Department of Emergencic Psychiatry at the Academic Hospital, Montpellier. He obtained his PhD in neurosciences and a Master degree in "genetic of suicidal behavior". Professor Courtet's areas of interest and expertise involve vulnerability to suicidal behaviour, genetics and brain imaging of suicidal behaviours, bipolar disorders and eating disorders. He is a member of the European Psychiatric Association, the European College of Neuropsychopharmacology, chairman of the task force "suicide" of the World Federation of Societies of Biological Psychiatry and of the Association Française de Psychiatrie Biologique et Neuropsychopharmacologie. He has published several articles, abstracts, reviews, and book chapters in several Peer-reviewed journals, including Archives of General Psychiatry, American Journal of Psychiatry, Molecular Psychiatry, Psychiatric Genetics, Biological Psychiatry, Brain Behavior. He is author of 7 book chapters and editor of the book "Suicides et tentatives de suicide", Flammarion, 2009.

Abstract

Suicidal behaviour represents a main public health issue, with 1,5 million deaths every year worldwide, and 10-20 times more suicide attempts. The risk of suicidal behaviour is particularly elevated in patients suffering a bipolar disorder. According to a stress vulnerability of suicidal behaviour, we will propose a review of risk factors in order to help clinicians in detecting high-risk patients. Indeed, some characteristics related to the bipolar disorder increase the suicidal risk (i.e. early age at onset, first years from illness-onset). We will discuss the suicidal risk during mood episodes focusing on mixed depression. Additionally, two kinds of events or conditions that are very frequent in bipolar disorder, aggravate the suicidal risk : comorbid psychiatric disorders and environmental stresses / social adversity. On the other hand, to identify high-risk patients it is probably more relevant to investigate the existence of a vulnerability to suicidal behaviour. The markers of such vulnerability are the following ones: a family history of suicidal behaviour, a personal history of suicidal behaviour, impulsive aggression, hopelessness, and a history of childhood abuse. Based on recent neuroscientific findings, we will challenge the conceptualization of a vulnerability stress model, and propose that a wide range of risk factors of suicidal behaviour are also associated with the bipolar disorder: impulsivity, decision making abnormalities, genetic polymorphisms, neuroanatomical patterns of emotional dysregulation. These vulnerability factors being shared by both suicidal behaviour and bipolar disorder, we suggest that by nature the bipolar disorder carry a high risk of suicidal behaviour. In this sense we will discuss the interest of lithium, which is interestingly a common treatment. These considerations may lead us to change our paradigm, and move from the identification of bipolar patients at risk for suicide to systematically implement prevention strategies, as we consider that every bipolar patient is at risk. This view may also promote the search of protective factors, which may represent future target of potential treatments.

Smoking, suicide and BP-II

Prof Z Rihmer (Hu)

Abstract

Smoking and its health consequences are very prevalent among psychiatric patients. Major depression, schizophrenia and particularly bipolar mood disorder is associated with much higher rate of cigarette smoking than that of the control population. Clinical and epidemiological studies also have reported on a significant association between cigarette smoking and suicidal behaviour, and cigarette smoking seems to be an independent risk factor for suicide. The cause of the strong association of smoking with suicidal behaviour is not exactly known. It has been suggested that lifetime smoking and lifetime depression are genetically related, and that smoking, impulsive-aggressive personality features, in psychiatric patients were significantly associated with subsequent completed suicide. Findings also indicate that cigarette smoking, impulsive-aggressive personality traits and suicidal behaviour might be related to lower brain serotonin function, particularly in patients with bipolar disorder. In addition to decreased cental serotonin function, low platelet MAO activity and some personality traits such as high impulsivity, sensatioin seeking, extroversion, and specific affective temperaments has been also reported to be related both with smoking and with suicidal behaviour. Studies - investigating the relationship between smoking, mood disorders and the suicidal behavior both at individual and group level – indicate that 1/ cigarette smoking is significantly more frequent among bipolar (bipolar II) disorder patients than in the general population, 2/ the prevalence of mood disorders are markedly elevated among smokers, and 3/ cigatette smoking and suicidal behaviour are strongly related. Smoking is one of the clinically easily explorable suicide risk factors in patients with mood disorders, and in the case of other risk factors it can be considered as an alarming sign.

PRESENTATION ABSTRACTS

The severe part of BP-II Spectrum

Dr J Deltito (US)

Joseph Deltito MD is currently a Professor on the Clinical Faculty of New York Medical College. He also has recently transferred his clinical practice to Pound Ridge, New York. He is a recognized expert in all aspects of Anxiety and Mood Disorders recognition and treatment. He has worked as an assistant to Professors David Sheehan, Gerald Klerman, and Giovanni Cassano who have served as his main mentors. An expert in Psychopharmacology and research methodology he is currently a Senior consultant at the Gianfranco DeLisio Institute for Behavioral Research (Pisa, Italy) and is well recognized in the USA through his frequent commentary on Psychiatric and Socio-Cultural issues on National TV.

Abstract

More than 20 years ago the word “Borderline”, as used in Borderline Personality Disorder, was eloquently described as an “Adjective in search of a Noun” by Hagop Akiskal. Despite, that at the time, there was a lack of a universal agreement as to which noun would best fit this adjective, growing empirical research over the years suggests the answer is “Affective Disorders” in general, and in particular, Bipolar Spectrum Disorders. Although the relationship of Borderline Personality Disorder and other Cluster B Personality Disorders remains somewhat obscure and controversial, one may conceptualize these disorders as representing the more severe end of the Bipolar II Spectrum. The impulsivity, chaotic and exploitive interpersonal relationships, risk taking behaviors, and mood liability associated with Borderline, Sociopathic, Narcissitic and Histrionic Personality Disorders in themselves is strongly suggestive of Bipolar Disorder. The efficacy of Mood Stabilizing and Atypical Antipsychotic medications in these Personality Disorders tends to reinforce a conceptualization of a relationship to Bipolar Disorder, perhaps not in all , but nevertheless in many patients with these disorders. Growing evidence in the realm of Borderline Personality Disorder shows this constellation of symptoms both naturally and while under treatment to be more waxing and waning in their overt presentations than previously thought. Distress and Disability seem to vary more widely over a lifetime than previously thought and this finding may be more consistent with an underlying Bipolar II Substrate.

Data will be presented from a study that examines clinical indicators for Bipolarity in a cohort of patients with Borderline Personality Disorders. A reasonable argument can be made that the majority of these patients belong to a Bipolar Spectrum. Clinical and Epidemiological factors will be examined as they refer to the accumulated clinical experience of the attendees of this lecture. An intriguing apparent enigma will be examined interactively with the attendees: Why is it that Borderline patients, most of whom are seen in clinical practice while in their 20s and 30s are rarely seen clinically while in their 40s and 50s?

PARALLEL SESSION

Clinical Practice 2: Unmet Needs in Treating BP-II Spectrum

Chair: **Dr E Hantouche (Fr)**

Think Effectively About Mood Swings (TEAMS): the science and practice of novel CBT in BDs

Dr W Mansell (UK)

Warren Mansell is a Reader in Psychology, Accredited Cognitive Behavioural Therapist, and Chartered Clinical Psychologist. He has authored over 100 publications on CBT and in 2011 received the May Davidson Award from the British Psychological Society for an outstanding contribution to the field of clinical psychology in the first ten years since qualifying.

Abstract

The theory, evidence and practice of Think Effectively About Mood Swings (TEAMS) will be described. TEAMS is based on an integrative cognitive model of mood swings and bipolar disorders that identifies extreme positive (e.g. “When I am full of energy, all my problems disappear”) and extreme negative (e.g. “When I am agitated I always end up making a fool of myself”) appraisals of internal states - these are the client’s perceived changes in mood, arousal, affect and behaviour. The conflicting positive and negative appraisals are seen to maintain and escalate symptoms and disrupt functioning (Mansell et al., 2007). The model is maybe unique in that it can be utilised across different therapeutic approaches. Cognitive therapists can help clients to identify and challenge their appraisals; behaviour therapists can help clients engage in exposure to previously avoided internal states; cognitive behaviour therapists can formulate cycles of internal states, appraisals and behaviours to devise experiments to test longstanding beliefs; ‘third wave’ therapists can help clients to mindfully face their internal states, and associated self-states, in ways that are accepting and in tune with their deeply held values. How can one model lend itself to multiple approaches? The answer is through utilising a more fundamental integrative framework - Perceptual Control Theory (PCT; Powers et al., 1960; Powers, 1973). The empirical groundings of PCT have been in development since the 1950s, yet it could be considered to be informing a ‘future wave’ of CBT. PCT explains how varied and ‘complex’ behaviour that we witness in other people can be rooted in a more tightly focused attempt to achieve biological homeostasis of key variables, including internal states. PCT also emphasises the role of control in well-being, and conflict in psychological distress. Several prospective studies illustrate that it is the conflict between appraisals, and therefore the opposing attempts to try to stabilise internal states, that is characteristic of bipolar vulnerability. Implications for research, including computer modelling,

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interviews with patients, and an ongoing NIHR-supported randomised controlled trial of TEAMS will be discussed.

Current role of psychodynamic treatment in Bipolar Disorder

Dr R Bush (US)

Dr. Rachel W. Bush received her Ph.D. in Clinical Psychology from the University of Massachusetts at Amherst in 1989. Following completion of her degree, she served as a Psychology Fellow at The New York Hospital-Cornell Medical Center, Westchester. The fellowship was intensive research and clinical work on severe personality disorders within the inpatient units. Upon completion of the fellowship she remained on the faculty as a Professional Associate and currently is a Professional Associate at The New York Presbyterian Hospiital, Weill Cornell Medical teaching and supervising medical students, residents, interns and fellows. In addition she is in private practice in Pound Ridge, New York and licensed in both New York and Connecticut as a clinical psychologist.

Abstract

Contemporary psychodynamic psychotherapy can be one particularly important integrative approach for enhancing treatment outcome for bipolar illness in clinical practice today. This talk will be on the interface between theory and practice. Dr. Bush will be utilizing numerous clinical vignettes to demonstrate strategies for improving the therapeutic alliance, the treatment frame, as well as establishing a therapeutic contract in order to facilitate emotional regulation and stabilization. We will explore the power of insight, corrective emotional experiences, the management of aggression, and patterns of emotional dysregulation as therapeutic themes.

It is clear that transference/countertransference dynamics, medication compliance, psycho-education, daily routines around sleep/wake cycles, ongoing improvement of interpersonal relationships and the reduction of negative self-destructive behaviors become central therapeutic issues. We will also explore strategies for minimizing regression and resistance as well as facilitating reality testing and treatment compliance. Predictors for bipolar relapse including alcohol and drug abuse, familial distress and trauma will be examined through the perspectives of the ways in which an individuals behavior can be affected by unconscious past experiences.

The determination of effectively "working through" central dynamic themes will be emphasized within the context of a multi-modal treatment approach that frequently will include, individual psychotherapy, couples treatment, pharmacotherapy and group psychotherapy as powerful tools for guiding patients through the periods of emotional instability leading to derailments. The utility of an outpatient dynamic treatment team will be framed as one strategy for effectively diluting the transference and preventing negative therapeutic reactions. We will also explore strategies for facilitating reality testing, treatment compliance and addressing themes around abandonment, object constancy, The development of a secure attachment paradigm and increased self reliance, independence, and autonomy (Stern, Ainsworth, Trevarthen, Bowlby). The use of humor and play throughout the treatment process as an essential shared creation and test of prognosis (Winnicott, Fairbairn, Sullivan) and therapeutic scaffolding will be defined. Relevant developmental themes will be explored by focusing on the literature on emotional dysregulation and affective attunement. We will utilize a developmental-life cycle perspective in examining how self reflection and the development of mindfulness can lead to the containment of experiences that previously were not readily tolerated. We will conclude with strategies for the psychotherapist's ability to cope effectively with the unexpected, the role of consultation and effective discharge planning with thoughts about resiliency, internalization of the therapeutic experience and generalizability.

ROUND TABLE

Clinical Neurobiology of Bipolar Disorder

Chair: **Prof K Fountoulakis (Gr)**

Relationship of body mass index, symptoms and cognition in mood disorders and schizophrenia

Dr M Siamouli (Gr)

Melina Siamouli, MD, is a psychiatrist and a research associate in the 3rd Department of Psychiatry at Aristotle University of Thessaloniki, Greece. Dr. Siamouli received her medical degree at Aristotle University of Thessaloniki, Greece in 1998. She performed her residency in psychiatry and received her license in 2006. After that she worked as a psychiatrist in a private mental clinic (2008-2011) and in her private practice (2006-today). Dr Siamouli is a research associate in the 3rd Department of Psychiatry of the Aristotle University of Thessaloniki (2006-2008 and 2010-today). Her areas of clinical and research interest are biological psychiatry, psychopharmacology and mood disorders. She has co-authored more than 100 papers delivered to Greek and international congresses, and participated as a speaker in 7 symposiums. She is also the co-author of 28 papers published in international journals such as the Journal of Affective Disorders, Schizophrenia Research, Psychiatry Research, Annals of General Hospital Psychiatry, British Journal of Psychiatry and the Lancet, among others, with 170 citations and h=8. Dr Siamouli served as an invited reviewer for several peer-reviewed international journals and was an invited author for the Current Opinion in Psychiatry. She is also the lead editor of a forthcoming special issue of Depression Research and Treatment. Since 2012 she serves as Secretary of the Private Practice Section, of the World Psychiatric Association.

PRESENTATION ABSTRACTS

Abstract

Over the past decades there is a growing interest concerning the neurocognitive function of mental patients mainly due to its association to several aspects of outcome like social functioning and psychosocial rehabilitation. Patients with schizophrenia exhibit deficits in all domains of neurocognitive functioning, not only during the acute phase but also in remission. Unlike the traditional Kraepelinian concept, contemporary research has revealed the presence of neurocognitive dysfunction also in bipolar disorder, where just like in schizophrenia, cognitive deficits are present not only during mood episodes but also during euthymia. The comparison between these two patient groups yielded controversial results, with some researchers reporting a significantly better performance of the bipolar group while other support the idea of a similar deficit profile. On the other hand, medical conditions precipitated by obesity but also obesity in itself are associated with poor neurocognitive performance. Data concerning the effect of obesity on the neurocognitive function of psychiatric patients is rather limited. Our research data indicate the lack of an association between overweight/obesity and neurocognitive function in patients with schizophrenia and mood disorders, while normal controls are significantly affected by the deteriorating effect of obesity. This may be suggestive of a “floor effect” in both patient groups, however further investigation is needed.

Neurobiology of disability in bipolar disorder

Dr M Magiria (Gr)

Dr Stamatia Magiria received her medical degree at Aristotle University of Thessaloniki, Greece in 2000. She performed her residency in psychiatry and received her license in 2009.From then she is working as a psychiatrist in her private practice. She is about to complete her PhD at Aristotle University of Thessaloniki. Her areas of clinical and research interest is psychopharmacology, biological psychiatry, mood disorders and trans-cultural psychiatry. She has co-authored more than 30 papers delivered to Greek and international congresses and 11 of them are published in International Journals such as Schizophrenia Research, Annals of General Psychiatry, Psychiatry Research, Cognitive and Behavioral Neurology among others, with 37 citations and h=3.

Abstract

Bipolar disorder (BD) is one of the most severely debilitating of all medical illnesses. It can lead to significant suffering for patients and their families. Bipolar patients manifest lower level of work productivity, work reduced hours and they are more likely to miss work. They experience high rates of relapse, a chronic recurrent course, functional impairment and psychosocial disability. For a large number of patients outcomes are poor. Previous research on functional outcome in BD has unconverted various factors that exacerbate psychosocial disability over the course of illness, including genetics, illness severity, stress, anxiety and cognitive impairment. Little is known about the specific pathophysiology of BD. A better understanding of the neurobiological underpinnings of this condition will be essential for the future development of specific targeted therapies that are more effective than currently available treatments.

Bipolar disorder in the frame of dementia

Dr D Kontis (Gr)

Dimitrios Kontis, MD, PhD

I am currently working as a consultant clinical psychiatrist at the 1st Psychiatric Department of the Psychiatric Hospital of Attica. I am the founder and director of the Unit for the Study of Cognition in Psychosis at the same hospital. I studied medicine at the University of Athens Medical School (1990-1996). During 1998-2003 I was trained in adult psychiatry at the Psychiatric Hospital of Attica. I received my PhD degree in 2005. The subject of my PhD research was the investigation of serotonergic and dopaminergic mechanisms in animal models of obsessive-compulsive disorder and schizophrenia. It was conducted at the Laboratory of Experimental Psychology, Department of Psychiatry, Athens University Medical School. I am a visiting research fellow at the Department of Psychology, Institute of Psychiatry, King’s College, London. During 2006-2007 and 2010-2011 I completed two research fellowships at the Institute of Psychiatry, under Professors Robin Murray and Til Wykes, respectively. During these fellowships I was trained and participated in research in the areas of Neuroimaging in Psychiatry and Cognitive Remediation of Schizophrenia. I am co-author of 16 papers in peer-reviewed psychiatric journals, which have already received more than 100 citations. I have also contributed in more than 100 papers which have been published in international and Greek conferences. I have made 20 talks as an invited speaker in Greek and international conferences. The John S. Latsis Public Benefit Foundation has supported my work on cognition in schizophrenia. My main research interests are cognition in schizophrenia, psychogeriatrics and mood disorders.

Abstract

Dementia and bipolar disorder have been traditionally considered two separate clinical entities. However, recent data support that they are related. Several theories have been put forward to interpret this relationship. One theory proposes that symptoms of bipolar disorder in the elderly could be secondary to a dementia process. An alternative one includes cases of pseudodementia in elderly patients with bipolar disorder who exhibit cognitive deficits which resemble dementia and are reversible through treatment optimization. On the other hand, bipolar disorder could indeed increase the risk for developing of dementia at old age. Finally, dementia could unmask a latent bipolar disorder in elderly people. The two disorders demonstrate similarities supporting their possible relationship. These similarities can be identified in the domains of clinical expression, neurochemistry (alterations in the activity of brain monoaminergic neurotransmitter systems and hyperactivity in the hypothalamus-pituitary-adrenal axis) and structural brain neuroimaging (MRI: lateral

PRESENTATION ABSTRACTS

ventriculomegaly and white matter hyperintensities). Despite the above similarities, the two disorders also demonstrate important differences. Cognitive symptoms prevail in dementia and mood symptoms in bipolar disorder, while amyloid depositions are consistently found in brain areas in dementia but are usually absent in bipolar disorder. In dementia but not in bipolar disorder there is consistent evidence for diffuse brain structural abnormalities and lower hippocampal volumes. Dementia and bipolar disorder present different abnormalities in functional brain neuroimaging. With respect to their treatment, acetylcholinesterase inhibitors and memantine are indicated against cognitive symptoms in dementia and also improve behavioural and psychological symptoms. Lithium, anticonvulsants, antipsychotics and antidepressants are effective in bipolar disorder but their use in dementia is controversial. The study of bipolar disorder in the elderly and of the role of lithium in dementia could help clarify the relationship of the two disorders. Bipolar disorder in the elderly is heterogenous and could be of an earlier or later-onset. There are not yet evidence-based data on its therapeutic management. A subgroup of elderly bipolar patients suffer from type VI bipolar disorder which combines bipolar and dementia-like symptoms. However, the validity and treatment of this bipolar subtype remain to be delineated. Similarly, future studies should also clarify the emerging role of lithium in elderly bipolar disorder and the prevention of dementia. In conclusion, bipolar disorder in the frame of dementia can be used as a useful paradigm for the delineation of the pathogenesis and treatment of both disorders which encompasses the traditional categorical approach in psychiatric diagnosis and treatment.

Dopamine pathways in Bipolar disorder and Schizophrenia

Dr E Tsapakis (Gr)

Dr EM Tsapakis, BSc(Hons), MBBS, MSc, MRCPsych, PhD(London) Dr Tsapakis studied pharmacology at King's College London and medicine at St. George's Hospital Medical School, University of London. Having earned the first prize in psychological medicine (the Arthur Crisp Prize), she went on to train in psychiatry at the Maudsley Hospital. She has worked under Ross Baldessarini's mentorship at Harvard Medical School whilst on a traveling fellowship awarded by the Royal College of Psychiatrists. In 2007, she earned a Masters in Affective Neuroscience from the University of Maastricht. In 2009, she earned a PhD in pharmacogenetics (on the role of metabolic enzyme variants in response to treatment with psychotropic agents) and pharmacogenomics (on the differential gene expression induced by antidepressants in juveniles) from the Institute of Psychiatry, King's College London. Dr Tsapakis' awards include a Young Scientist Award at the 11th Biennial Winter Workshop on Schizophrenia (2002), a Research Award at the 5th International Neuropsychiatry Congress (2004), a Young Investigator Award for the 20th International Congress in Schizophrenia Research (2005), and a Poster Prize at the 3rd International Congress on Brain and Behaviour (2007). Dr Tsapakis is a visiting research associate at the Institute of Psychiatry, King's College London and at Harvard Medical School, Boston, MA. She obtained her CCT in General Adult Psychiatry from the General Medical Council in the UK in 2010 and has since worked as a Consultant psychiatrist on Crete, Greece, directing a private mental health unit.

Abstract

For the past hundred years most clinical work and research in psychiatry has proceeded under the assumption that schizophrenia and bipolar affective disorder are distinct entities with separate underlying disease processes. However, many individuals with severe psychiatric illness have both prominent mood and psychotic symptoms – raising the possibility, indeed the likelihood, that there is not a neat biological distinction between schizophrenia and bipolar affective disorder (BD), especially as treatment for both largely relies on dopamine (DA) D2 receptor antagonism. Furthermore, while dopamine systems have been implicated in the pathophysiology of schizophrenia and psychosis for many years, how dopamine dysfunction generates psychotic symptoms remains unknown. Evidence linking abnormal mesolimbic activity, reward learning and psychosis will be presented, in addition to results showing genetically influenced variations in dopamine transmission modulating the response of brain regions involved in anticipation and reception of rewards. These responses may thus contribute to individual differences in predisposition to neuropsychiatric disorders. It has also been demonstrated that catechol-O-methyl transferase (COMT) inhibition modulates dopamine levels in the prefrontal cortex (PFC) and improves performance on a PFC-dependent task of the type impaired in patients with schizophrenia, suggesting that COMT might be a useful therapeutic target for ameliorating cognitive dysfunction in schizophrenia. Moreover, a heritable dysfunction in the dorsolateral PFC (DLPFC) of patients with schizophrenia has been demonstrated, and prefrontal dysfunction in schizophrenia is coupled to striatal dopamine disinhibition. Furthermore, a dysfunction in the lateral FPC has been shown in bipolar disorder patients. It, therefore, appears that changes in DA neurotrasmission are associated with schizophrenia and BD. In addition, the effect of drugs such as cannabis, which are known to induce psychotic symptoms, anxiety and to impair memory and psychomotor control in healthy and psychotic individuals, seem to act in a way that exacerbates DA dysregulation within the dopaminergic system. These and other studies on other neurotransmitter systems have begun to challenge and may soon overturn the traditional dichotomous view between schizophrenia and bipolar disorder.

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- **AETIOLOGY, PATHOLOGY & SEQUELAE**
- **CHILDHOOD AND ADOLESCENCE**
- **CLINICAL TREATMENT/MANAGEMENT**
- **DIAGNOSIS AND DEFINITIONS**
- **EPIDEMIOLOGY**
- **PSYCHOLOGICAL ASPECTS**

*By 1st author surname alphabetical order

AETIOLOGY, PATHOLOGY & SEQUELAE

Regulation of IGF-1 expression in the hippocampus by acute peripheral lipopolysaccharide administration in prenatally stressed animals

Author: Agnieszka Basta-Kaim1, M. Leśkiewicz1, A. Zelek-Molik2, K. Rafa-Zabłocka2, E. Szczęsny1, K. Głombik1, B. Budziszewska1, M. Kubera1, I. Nalepa2, W. Lasoń1
Department of Experimental Neuroendocrinology
Institute of Pharmacology PAS
Poland basta@if-pan.krakow.pl

Objective

Recent data suggest that a disturbed interaction between the endocrine, immune and nervous systems play an important role in pathogenesis of this disorder. Changes in the pro-inflammatory cytokine levels and increased glucocorticoid action can cause disturbances observed in this disease, especially affecting the synaptic plasticity and neurogenesis. It has been also suggested that the weaker activity of growth factors, such as brain-derived growth factor and insulin-like growth factor (IGF), plays a key role in pathogenesis of depression. In peripheral tissues, pro-inflammatory cytokines and glucocorticoids are the main factors reducing IGF transmission, however, IGF regulation in the central nervous system is little known. IGF exerts multidirectional effects: intensifies cell proliferation and differentiation, enhances neurogenesis in the hippocampus in adult animals and exerts the antidepressant activity. The aim of the present study was to find out whether in the animal model of depression there are changes in IGF-1 levels in the frontal cortex and/or in the hippocampus, i.e. in the regions in which the synaptic plasticity is particularly disturbed in depression.

Method

Pregnant Sprague-Dawley rats were subjected daily to three stress sessions from day 14 of pregnancy until delivery. After weaning, male rats from each experimental group were collectively housed. At 3 months of age the control and prenatally stressed male rats were tested for behavioral changes in the Porsolt test and in the elevated plus-maze test. Two days after behavioral test the animals were divided in four groups: control, control +LPS, prenatally stressed, prenatally stressed +LPS. Lipopolysaccharide (LPS) was injected once intraperitoneally and 4 hours later animals were killed by rapid decapitation and the hippocampi were dissected out and stored at –80oCfor ELISA study. Fresh isolated tissue samples were placed in the RNAlater solution and stored at 40C to total RNA extraction. The expression of mRNA were measured by RT-PCR methods.

Results

It was found that prenatally stressed rats displayed increased immobility time and decreased climbing behaviour in the forced swimming test, so they showed depression-like behavior. There were no significant changes in the elevated plus-maze test, however, the prenatally stressed rats spent less time in the open arm. ELISA study showed that the level of IGF-1 in the hippocampus of prenatally stressed animals was decreased. LPS administration suppressed IGF-1 level in control animals. Moreover, in prenatally stressed rats after LPS treatment, the level of IGF-1 was significantly decreased in comparison with stressed animals. On the other hand, the IGF-1 mRNA expression was decreased only after acute LPS administration in control animals.

Conclusion

The obtained data showed that prenatal stress evoked a long-term elevation of immobility behavior in the forced swim test. In the used animal, the level of IGF-1 in the hippocampus was lowered and regulated by proinflammatory cytokines (LPS).

In summary, there is an important negative feedback between cytokines and IGF -1 systems. An appropriate balance between the immune and IGF systems is necessary for normal behavior, development and quality of life.

Additional Information

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Neuroactive steroids, Steroid metabolism and Schizophrenia

Author: Marie Bicikova, M. Hill, L. Sosvorova, *D.Ripova, *P. Mohr
Institute of Endocrinology, Department of Steroids and Proteofactors
Národní 8, 11694 Prague , Czech Republic
mbicikova@endo.cz

Objective

The role of neuroactive steroids (NAS) in the brain physiology and patholophysiology consists in modulation of ligand-gated ion channels as the type A ő aminobutyric-acid receptor (GABAA-R) or glutamate, especially N-methyl D-aspartate receptors (NMDA-R), and also ő l receptor. Schizophrenia is associated with biochemical alterations and impaired neurotransmission. Recent studies brought evidence that alterations in circulating levels of neuroactive steroids are associated with pathological processes in the central nervous system (CNS). The neuroactive steroids and their peripheral precursors probably penetrate into the CNS influencing thus a course of the disease. Some

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evidences suggest their possible use as therapeutic agents mainly for their neuroprotective activities in therapy of neurodegenerative and psychiatric disorders.

On the other hand the spectrum of steroids investigated in patients with schizophrenia is limited. Therefore, the information concerning alterations of the steroid metabolome associated with the disease and/or its treatment is of interest as regards the pathophysiology of the disease.

Method

We assessed 48 serum steroids and steroid polar conjugates in a groups of drug-naive patients (13 adult men and 9 women) and after 6-months therapy by atypical antipsychotics and age-matched healthy controls (22 males, 25 females) using the GC-MS.

The differences between the groups of healthy controls, untreated patients and patients after treatment with atypical antipsychotics were evaluated separately for each gender using the age-adjusted ANCOVA followed by Least Significant Difference multiple comparisons (p=0.05). Further, the multivariate regression with reduction of dimensionality (the method of orthogonal projections to latent structures, OPLS) was applied.

Results

The most abundant GABA-ergic steroid in males, unconjugated androsterone, was lower in the drug-naive patients but reached the levels common in healthy controls after treatment with atypical antipsychotics. We observed depressed levels of pregnenolone, (PREG) in drug-naive patients of both sexes than in controls while the levels of its sulfate were higher. Pregnenolone serves as a precursor of all neuroactive steroids and its low levels limit the synthesis of endogenous neuroactive steroids in the periphery, including brain.

Pregnenolone sulfate is known as a positive modulator of NMDA-receptors and, along with elevated cortisol, may contribute to the hyperactivity and chaotic thoughts in the patients. Increased levels of pregnenolone sulfate are giving evidence of basal pituitary-adrenal overactivity in the first episode patients with schizophrenia. Its levels tended to reduction after antipsychotic therapy (reaching significance in women) but remained still elevated when compared with controls. This phenomenon could play a role in patients with negative symptoms and failed cognitive functions. In addition, their 7alpha/beta-hydroxy-metabolites were depressed as well.

The multivariate regression model that was based on the steroid metabolome predicted schizophrenia status from the serum steroids was with 100% efficiency in women and 95% in men. The treatment with atypical antipsychotics, particularly with olanzapine, leads to reinstatement of steroid metabolism in schizophrenic patients.

Conclusion

The steroid metabolome model may be used as an efficient diagnostic tool for further studies with other diagnosis than schizophrenia.

Additional Information

The work was supported by the grant MHCZ NS-9835-4 and by project “Advanced education of own staff in clinical and molecular endocrinology” (CZ.2.17/1.1.00/32386).

Bipolar Disorder and disreactive disorders: a complex relationship

Name: Francesca Casalini, N.Mosti, S.Belletti, V.Mastria, S.Rizzato, A.Del Carlo, M.Fornaro, L.Dell’Osso, G.Perugi
Department of Psychiatry of University of Pisa, via dell’omodarme, 38, Pisa (Italy)
casalinifrancesca@gmail.com

Objective

Scientific literature and clinical practice reported frequent association between Bipolar Disorder and medical conditions. Few resarch explored the possible relationships between clinical and course characteristics of mood disorder and specific physical illnesses.

Method

We reported data derived from a sample of 244 bipolar patients consecutively referred to outpatients and inpatients units of the Department of Psychiatry of the University of Pise, Italy. All patients have been selected on the basis of DSM IV criteria for Bipolar I, II and NOS and have been evaluated by means of structured and semi-structured interviews, exploring diagnostic criteria (Structured Clinical Interview for diagnosis-SCID) and familial, clinical, course, comorbidity and treatment characteristics of the mood disorder (Structured Interview for Mood Disorders-SIMD). CGI for severity of the illness, GAF score for functional adjustement and TEMPS-35 for affective temperaments have been also administred. Finally, all patients have been carefully screened for physical illnesses by anamnestic interview and physical examination.

Results

In our sample, more than 40% of the patients reported disreactive disorders (autoimmune-allergic diseases). Such a prevalence was about 5 times the general population and was similar in males and females. There was no relationship with bipolar subtype, severity of the illness and age. Bipolar patients with immuno-allergic diseases reported higher scores for anxiety and excitement at BPRS scale and higher scores for cyclothymic and anxious temperaments.

Conclusion

Our results suggest the existence of specific bipolar subtype on the basis of comorbidity with immuno-allergic diseases. Further research is necessary in order to better define this association.

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Substance Use disorder with adult Attention Deficit Hyperactivity Disorder and Bipolar Disorder; a distinct clinical phenotype?

Authors: 1Ceraudo G., 2Toni C., 1Vannucchi G., 1Rizzato S., 1Casalini F., 1Benvenuti M., 1Del Carlo A., 1Mosti N., 1Dell'Osso L., 1,2Maremmani I, 1,2Perugi G.

1Department of Psychiatry, Pharmacology, Neurobiology and Biotechnology, University of Pis, a2Institute of behavioural Sciences "G.DeLisio", Pisa, Salvatore Rizzato, via liguria 1 Pis, Italy

salvorizzato@gmail.com

Authors

1Ceraudo G., 2Toni C., 1Vannucchi G., 1Rizzato S., 1Casalini F., 1Benvenuti M., 1Del Carlo A., 1Mosti N., 1Dell'Osso L., 1,2Maremmani I, 1,2Perugi G.

1Department of Psychiatry, Pharmacology, Neurobiology and Biotechnology, University of Pisa

2Institute of behavioural Sciences "G.DeLisio", Pisa

Objective

Comorbidity between substance use disorder (SUD) and attention deficit hyperactivity disorder (ADHD) in adulthood has been reported in epidemiological and clinical sample. In order to assess the impact of comorbid ADHD, we investigated the prevalence, clinical and epidemiological features associated with such comorbidity in a sample of adult patients diagnosed with SUD.

Method

109 outpatients (aged 18-65 years) with SUD were included. All patients were screened using the Adult ADHD Self-report Scale (ASRS) v. 1.1 and the Diagnostic, Clinical and Therapeutic Checklist (DCTC), a semi-structured interview developed for the exploration of the criteria of major Axis I and Axis II diagnoses according to DSM-IV criteria, the Clinical Global Impression Bipolar (CGI-BP) scale, Global Assessment of Functioning (GAF) scale and the Sheehan Disability Scale (SDS).

Results

Twenty patients out 109 (18.35%) fulfilled both DSM-IV and ASRS v 1.1 criteria for ADHD. ADHD patients showed a higher prevalence of Bipolar Disorder (80% vs 43.2%, chi-square = 8.84, p=.003) and current manic or mixed episode at the time of observation (40% vs 16.9%, chi-square=3.29, p=.027) than No-ADHD patients. "Treatment resistance" (15% vs 3.4%, chi-square= 4.25, p=.039) and "irritability" (35% vs 15.7%, chi-square=3.90, p=.048) in response to previous treatment with antidepressants were more frequently reported by ADHD compared to No-ADHD patients. No significant difference between ADHD and No-ADHD patients were observed in terms of prevalence of comorbid Anxiety Disorders and Impulse Control Disorders.

Conclusion

In patients with SUD the presence of comorbid adult ADHD influences the course, prognosis and therapeutic management. Patients with SUD and adult ADHD present high rates of comorbid BD. Patients with ADHD, SUD and BD seems to be a distinct phenotype characterized by early onset and mood instability. Some limitations of this study are retrospective design and sampling bias due to the fact that most of the patients had an history of severe opioid addiction. Further research is needed to confirm our findings and the clinical and therapeutic implications of SUD-ADHD-BD comorbidity.

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C-reactive protein levels and its relationships with suicide risk and alexithymia among newly diagnosed, drug-naive patients with non affective psychosis

Author: Domenico De Berardis 1-2, Nicola Serroni 1, Daniela Campanella 1, Luigi Olivieri 1, Francesca Ferri 1, Stefano Marini 1-2, Luisa Del Nibletto 1, Carla Ranalli 1, Alessandro Carano 2-3, Marilde Cavuto 4, Giovanni Martinotti 2, Francesco Saverio Moschetta 1 and Massimo Di Giannantonio 2

1 NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "G. Mazzini", Asl 4 Teramo, Italy

2 Department of Neurosciences and Imaging, Chair of Psychiatry, University "G. d'Annunzio" of Chieti, Italy

3 NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "C. G. Mazzoni" Ascoli Piceno, Italy

4 IASM, L'Aquila, Italy

National Health Service, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, "G. Mazzini" Hospital, p.zza Italia 1, 64100 Teramo, Italy.

dodebera@aliceposta.it

Objective

The aim of present study was to evaluate C-Reactive Protein (CRP) levels in patients with newly diagnosed, drug-naïve patients with non affective psychosis, testing the hypotheses that in such patients serum CRP levels would be higher than in healthy controls and related to more severe psychopathology, suicide risk and alexithymia.

Method

CRP levels of 30 adult patients and 30 sex- and age-matched healthy controls were evaluated. Patients were tested with the Scale of Suicide Ideation (SSI), the Toronto Alexithymia Scale (TAS-20), the Scale for the Assessment of Positive and Negative Symptoms (SAPS and SANS) and the Calgary Depression Scale for Schizophrenia (CDSS).

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Results

Higher suicide risk patients showed higher CRP levels than lower suicide risk patients and healthy controls. Moreover such patients showed higher SAPS, SANS and CDSS scores than lower suicide risk patients. In linear regression model, CRP was significantly associated with higher SSI and TAS-20 scores. In linear regression model, CRP was significantly associated with higher SSI and TAS-20 scores.

Conclusion

The results of the present study support the notion that CRP, suicide risk and alexithymia are strictly linked among newly diagnosed, drug-naïve patients with non affective psychosis, independently by depressive symptoms or general psychopathology. Limitations are discussed.

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A nested population-based case-control study on inflammation markers in early-stage mood disorders

Authors: Alexandre Silva de Mello, Gabriele Ghislani, Jean Pierre Oses, Manuella Kaster, Karen Jansen, Carolina David Wiener, Flávio Kapczinski, Pedro Magalhães, Jerônimo Branco, Ricardo Pinheiro, Ricardo Azevedo da Silva Rua: Gonçalves Chaves, 373, Sala: 411 - Prédio C, Pelotas - Rio Grande do Sul, CEP: 96015-560, Brazil

melloas@gmail.com

Objective

Previous studies in clinical samples suggest that bipolar disorder is associated with a high inflammation set point, even in the early stages. Here, we sought to confirm these findings in a case-control study nested in a population based sample of young adults aged 18-24 years old.

Method

Individuals from the general population with a positive screen for bipolar disorder were recruited, as well as two groups of controls. One had only depressive episodes and the other had no history of mood episodes. This yielded a sample of 231 participants. Two pro-inflammatory cytokines, interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) and an anti-inflammatory cytokine, interleukin-10 (IL-10), were measured.

Results

IL-6 levels were not associated with any of the predictors and IL-10 levels were associated only with social class. TNF-α levels were higher in those who used illicit drugs and lower in those who used any psychiatric medications. Sensitivity analyses restricting to those who did not use any illicit drugs of medications revealed higher TNF-α serum levels in bipolar disorder. Excluding extreme results, TNF-α serum levels were also higher in bipolar disorder than in major depression.

Conclusion

This study confirms an early, if subtle, pro-inflammatory state in bipolar disorder.

Memantine prevents the "bipolar-like behaviour" induced by chronic treatment with imipramine in rats.

Authors: Francesca Demontis, Adriana Cubeddu and Gino Serra

Largo Cavallotti 28 Sassari, Italy

fra.demo@hotmail.it

Objective

We recently found that chronic treatment with imipramine induced a 'bipolar-like behaviour' (i.e. a cycle of mania-depression) in rats (D'Aquila et al, 2003; D'Aquila et al, 2004). In fact, as expected, imipramine induces a sensitization of dopamine D2 receptors (mania/hypomania), which is followed after 12, 33 and 40 days of imipramine withdrawal by a progressive desensitization of dopamine D2 receptors (depression) (D'Aquila et al, 2003) associated with a depressive-like behaviour as assessed in the forced swimming test animal model of depression (D'Aquila et al, 2004). The stimulation of NMDA receptors is required for the development of dopamine receptor sensitization induced by antidepressants. Indeed, we found that the administration of MK-801, a selective non-competitive NMDA receptor blocker, completely prevents the dopamine receptor sensitization induced by imipramine (D'Aquila et al, 1992) and by electroconvulsive shock (D'Aquila et al, 1997).

The aim of the present work is to evaluate the effect of Memantine, a non-competitive NMDA receptor antagonist, on bipolar-like behaviour induced by chronic treatment with imipramine.

Method

Sprague-Dawley male rats (Harlan, Italian) were used as subjects, divided in four different groups and treated for 21 days with Vehicle, Imipramine (20 mg/Kg I.p.), Memantine (10mg/Kg I.p.) and Memantine+Imipramine.

The four groups were tested for motor activity (see D'Aquila et al 2003) induced by Quinpirole (0.15 mg/Kg s.c.) 24 h and 15 days after the end of Imipramine treatment. Moreover, after 15 days Imipramine discontinuation animal were tested in the forced swimming test (FST) animal model of depression (see D'Aquila et al. 2004).

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Results

As expected, imipramine potentiated the locomotor activity induced by quinpirole after 24 h of the end of imipramine administration, but reduced the quinpirole effect after 15 days. Moreover, animals treated with imipramine, after 15 days of drug discontinuation showed a depressive-like behaviour in the FST.

Memantine prevented both the behavioural supersensitivity and subsensitivity to quinpirole induced by imipramine. Moreover animals treated with the combination of memantine and imipramine did not show the depressive-like behaviour in the FST.

Conclusion

The results show that memantine prevents both the up-regulation induced by chronic imipramine and the down-regulation of dopamine D2 receptors associated with a depressive-like behaviour observed after imipramine withdrawal.

These observations provide strong experimental evidence supporting the hypothesis (Serra, 2010) of the antimanic and prophylactic effect of memantine in bipolar disorders, and provided a robust pharmacological rationale to the clinical observations of Koukopoulos et al (2010. 2012).

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Bipolar disorder with seasonal pattern:clinical implications in 452 patients.

Authors: Pierre Alexis Geoffroy1,3,4,5 , Bruno Etain1,3,5 , Carole Boudebesse1,3 , Mohamed Lajnef1 , Frank Bellivier 1,2,3,5, Marion Leboyer1,2,3,5.

Remerciements (à mettre sur le poster) : S. Gard et JP. Kahn

1) Inserm, U955, Psychiatrie génétique, Créteil, 94000, France ;

2) Université Paris Est, Faculté de médecine, Créteil, 94000, France ;

3) AP-HP, Hôpital H. Mondor - A. Chenevier, Pôle de Psychiatrie, Créteil, 94000, France ;

4) Pôle de psychiatrie, Univ Lille Nord de France, CHRU de Lille, F-59000 Lille, France ;

5) Fondation Fondamental, Créteil, 94000, France.

pierre.a.geoffroy@gmail.com

Objective

Bipolar affective disorder (BD) is a multifactorial disorder with heterogeneous clinical presentations. More than 25% of bipolar patients may present seasonal pattern (SP). To the best of our knowledge, only one study has been performed on SP and its clinical characteristics in bipolar patients (Goikolea et al., 2007). We propose a new study of a larger sample of 452 bipolar patients to compare clinical and demographic features of bipolar patients with and without SP.

Method

Four hundred and fifty-two bipolar I and II patients were recruited at three university-affiliated psychiatric departments in France (Paris Est, Bordeaux, and Nancy). SP was defined according to DSM-IV criteria. Clinical and socio-demographic variables were obtained from structured interviews with the patients and their relatives.

Results

Four hundred and fifty-two bipolar patients (n=452) in euthymic state were included in the study, 102 of them (22.57%) were considered as having SP according to DSM-IV criteria. Bipolar patients with SP presented bipolar II disorder predominantly (p=0.0064), were more likely to display rapid cycling (p

<0.0001) and eating disorder comorbidity (p=0.0039). Patients with SP showed significantly more mood episodes (p=0.00047) (including manic, hypomanic, mixed and depressive episodes) and more depressive episodes (p><0.0001). Moreover, patients with SP presented a significantly younger age of onset of the mood disorder than patients with no SP (p=0.028). Patients with SP did not show a longer course of illness that could explain those outcomes. Multivariate analysis showed a significant association of BD patients with SP for bipolar II subtype (OR=1.99, p=0.013), rapid cycling (OR=2.04, p=0.018), eating disorder (OR=2.93, p=0.0033) and the total number of depressive episodes (OR=1.12, p=0.0017). >

Conclusion

Due to its severe clinical characteristics, its high prevalence and its clinical and prognostic implications, SP constitutes a potentially important specifier of BD that could be usefully integrated into future nosographical classifications such as DSM-V. The results imply that seasonality may reflect increased severity and need for specific treatment. A key challenge is posed by the use of SP in treatment decision algorithms, but further research in this area would aid clinicians in developing focused treatment strategies.

Lability of mood and stressors in the internal and external environment

Authors: Dr Sunjai Gupta OBE.

Department of Health, England, and Visiting Senior Lecturer, Institute of Psychiatry.

Wellington House, 133-155, Waterloo Road, London SE1, United Kingdom

sunjai.gupta@dh.gsi.gov.uk

Objective

In his seminal work, Cannon refers to the "stresses and strains of homeostasis " associated, for example, with low blood sugar levels.

Method

Analysis of data from the 2003 Health Survey shows that lability of affect (particularly positive affect), as assessed

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using the GHQ12, shows a significant negative association with fasting blood glucose even after the background level of glucose as assessed by glycosylated haemoglobin,was controlled for. This suggests that lability was related to the subsequent degree of physiological "stress" produced by the fall in blood glucose produced by the fasting state.

Results

The present study analysed the relationship between lability and other measures of stress (including perceived stress and social support) derived from the Health Survey.

Conclusion

Implications for the aetiology of illnesses such as bipolar disorder are discussed.

Additional Information

The above abstract is necessarily very general. This is because I am shortly expecting to receive new data from the Health Survey and the poster (or posters) will be based on analysis of these as well as on new analyses of existing data. Depending on what the analyses show I may be interested to give an oral presentation (if this could still be considered) but for the present I am submitting an application for a poster presentation only.

The Impact of Mood and Anxiety Disorders on Visual Rivalry; A Review

Author: Miss Alexia Haysom, Dr Georgina Hosang
12 Victoria Chambers, Paul Street, London, EC2A 4ED, United Kingdom
alexia.haysom@kcl.ac.uk

Objective

The aim of this review is to investigate the impact of mood and anxiety disorders on visual rivalry. Recent research on bipolar disorder (BD) has revealed a difference in rivalry rate that could implicate certain neural circuitry in the pathophysiology of the disorder. This suggests a potential for visual rivalry in understanding other mood disorders as well as anxiety disorders, which have a high rate of comorbidity.

Method

A keyword search of English language and non-paediatric studies in PubMed, MEDLINE and EMBASE was carried out. Reference lists of selected papers were then used to perform a manual search. Due to the small body of literature pertaining to this field, no quality assessment was imposed on the studies included.

Results

Eleven studies were selected for the review. Patients with major depression were not found to differ from controls during rivalry tasks. Of the five studies examining bipolar disorder (BD) and visual rivalry, four of them demonstrated a slower rate of alternation. Results from studies examining anxiety were more heterogeneous, although differences in diagnostic criteria hinder comparison.

Conclusion

The slow rate of alternation associated with BD could represent an endophenotype which would facilitate genetic research. It also underpins a pathophysiological theory of BD of a slow interhemispheric switch mediated by an oscillator in the midbrain. The small body of literature, coupled with methodological and diagnostic inconsistencies weakens any conclusions drawn. There is a strong case for further research into this area.

Dextromethorphan induced bipolar disorder

Author: Dr Rajesh Jacob, Consultant Psychiatrist, Institute of Mental Health, SingaporeDr Jerome Nicholas Nicholapillai, Post graduate resident in Psychiatry Institute of Mental Health
Singapore rajeshjacob28@hotmail.com

Objective

There are very few case reports in the existing literature linking Dextromethorphan and bipolar disorder. We describe a patient who developed recurrent episodes of mania following sustained dextromethorphan use and which resolved after cessation of its use.

Method

The patient is a 42 year old male who has a history of heroin, Subutex and Midazolam use in the past but completely stopped its use in 2008.He started consuming dextromethorphan tablets about 30 a day (450 mg daily) since May 2011 about two to three times a week.He did not consume any other illicit drugs or alcohol. He started exhibiting symptoms of mania 2 to 3 weeks after starting Dextromethorphan which required inpatient admission for a week. Symptoms resolved after a few days of admission. He had a second admission on 17th June 2011 after he restarted the use of Detromethorphan after discharge. He exhibited short lived manic symptoms which settled 1 week after admission.This was followed again by a 3rd episode of mania which occured in September 2011 which lasted for 2 weeks and required inpatient admission. There was no past history of either manic or depressive episodes prior to onset of use of dextromethorphan or any significant family history

Results

All these 3 episodes of mania occured after heavy consumption of dextromethorphan and resolved with cessation of use.

Conclusion

This report adds to the existing sparse literature about dextromethorphan inducing manic episodes.

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Exploring biomarkers for neurodegenerative processes in the cerebrospinal fluid from bipolar patients

Author: Joel Jakobsson, Henrik Zetterberg, Kaj Blennow, Carl-Johan Ekman, Anette GM Johansson, and Mikael Landén.

Sahlgrenska universitetssjukhuset, Blå Stråket 15, floor 3, 413 45 Göteborg, Sweden

joel.jakobsson@neuro.gu.se

Objective

Bipolar disorder is a common psychiatric disorder characterized by recurrent episodes of mania/hypomania and depression. Cognitive dysfunction is common in euthymic bipolar patients indicating a neurodegenerative component in the pathophysiology of bipolar disorder. Thus, we set out to investigate a panel of biomarkers, known to be altered in Alzheimer's disease, in the cerebrospinal fluid from bipolar disorder patients and healthy controls.

Method

The cerebrospinal fluid concentrations of T-tau/P-tau/Aβ1-42 (Inno-Bia AlzBio3 kit), Aβ38/Aβ40/Aβ42 (MSD®Human/Rodent (4G8) Abeta-Triplex Assay), and sAPP-α/sAPP-β (MSD® sAPP-α/sAPP-β Multiplex Assay), were measured in a well-defined bipolar disorder patient-control material including 139 patients and 71 healthy controls.

Results

The cerebrospinal fluid concentrations of sAPP-α and sAPP-β were significantly lower in bipolar patients compared to controls. Moreover, the Aβ42/Aβ38 and the Aβ42/Aβ40 ratios were higher in bipolar patients than controls, but there were no discernible differences in the concentration of T-tau, P-tau, Aβ1-42, Aβ38, Aβ40, or Aβ42. With respect to diagnostic subgroups, the concentration of Aβ was lower among bipolar type I patients than bipolar type II patients. Furthermore, both Aβ and tau were negatively associated with disease severity (as estimated by CGI-score) in bipolar type I patients. Lithium treatment was associated with lower Aβ42/Aβ38 ratio and higher tau concentrations.

Conclusion

The findings suggest that the APP metabolism is altered in bipolar disorder and that the Aβ and tau metabolism is sensitive to lithium treatment and associated with disease severity. There were no signs of an Alzheimer-like neurodegenerative process among bipolar patients.

Incidence of metabolic syndrome in bipolar I disorder patients after 12 and 52 weeks of exposure to asenapine or olanzapine

Authors: R.S. McIntyre and C. Sapin

Associate Professor of Psychiatry and Pharmacology, University of Toronto, Head, Mood Disorders Psychopharmacology Unit, University Health Network, 399 Bathurst Street, MP 9-325, Toronto, ON M5T 2S8, Canada roger.mcintyre@uhn.ca

Objective

Atypical antipsychotics are widely prescribed to treat bipolar disorder patients. However, reports of significant weight gain, dyslipidemia and hyperglycemia have raised considerable concern. These adverse effects can potentially lead to the development of metabolic syndrome (MetS) which is characterized by a confluence of biochemical and clinical risk factors for cardiovascular disease e.g. hypertension, abdominal obesity, impaired lipid metabolism (blood triglycerides, cholesterol) and/or impaired blood glucose regulations.(1) Amongst the atypical antipsychotic drugs, olanzapine has the most reports of metabolic hazard with, clinically significant weight increase and metabolic syndrome. The awareness of patients' risk of developing MetS resulted in treatment guidelines to regularly monitor relevant physical and laboratory parameters in patients receiving atypical agents notably metabolically hazardous agents.

The aim of these analyses was to estimate the incidence of MetS in bipolar I disorder patients with manic or mixed episodes after 12 and 52 weeks of exposure to asenapine or olanzapine.

Method

In this post-hoc analysis, data from patients completing a 9-week double-blind, extension study(2) (of 3-week efficacy trials(3,4)) were included. In addition data from patients who completed a further 40-week double-blind, extension study5 are included. Patients were treated with asenapine (10 or 5 mg twice daily), or oral olanzapine (5-20mg once daily). The National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) definition of MetS was used, whereby a person has MetS if he/she has 3 or more of the following risk determinants: waist circumference >102 cm for men and >88 cm for women, triglycerides ≥150 mg/dL, HDL cholesterol

<40 mg/dL for males and ><50 mg/dL for females, sitting blood pressure ≥130/85 mm Hg, or fasting glucose ≥110 mg/dL.(6) Prevalence of MetS was calculated at baseline. Incidence (i.e. in patients without MetS at baseline) was calculated after 12 weeks and 52 weeks of treatment. Chi-square tests were used to compare the prevalence and incidence between treatments. >

Results

Following the 3-week efficacy trials, 407 patients were included in the 9-week extension study (asenapine 180, olanzapine 227), 328 completed (asenapine 143, olanzapine 185). The prevalence of MetS at baseline of the extension study was 20.6% (n=37) in the asenapine group and 18.5% (n=42) in the olanzapine group (p=0.603).

After 12 weeks of treatment exposure, the incidence of MetS was significantly higher in the olanzapine [19.5% (n=36)] group than in the asenapine group (7.8% [n=11]) (p=0.003).

Of the 183 patients included in the 40-week extension study (78 asenapine, 105 olanzapine), 143 completed (59 asenapine, 84 olanzapine). The prevalence of MetS at baseline of this extension study was 24.4% (n=19) in the asenapine group and 20% (n=21) in the olanzapine group (p=0.48).

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After 52 weeks of treatment exposure, the incidence of MetS was numerically higher in the olanzapine (21.4% [n=18]) group than in the asenapine group (10.2% [n=6]) (p=0.076).

Conclusion

These post-hoc analyses illustrate the high risk of developing a MetS with olanzapine, already after 12 weeks of treatment. The incidence of MetS after 12 or 52 weeks of treatment with asenapine was found to be considerably lower.

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Characteristics of suicidal attempts in bipolar disorder : differences between subtypes 1 and 2

Authors: Emilie Oliéa,b,c,d*, Fanny Molièreb,d*, Isabelle Jaussenta,c, Séverine Beziat a,c, Sébastien Guillaumea,b,c Philippe Courteta,b,c,d

a Université Montpellier 1, Montpellier, France

b CHU Montpellier, France

c Inserm, U1061, Montpellier, France

d Fondation Fondamental, France

* These authors equally contributed to this abstract.

Département Urgences Post Urgences psychiatriques, Hopital Lapeyronie , CHU Montpellier

191 avenue du Doyen GGiraud , 34295 Montpellier cedex 5, France

e-olie@chu-montpellier.Fr

Objective

To investigate whether bipolar II disorder (BP-II) has different characteristics from bipolar I disorder (BP-I) among suicide attempters.

Method

311 patients suffering from bipolar disorder (165 BP-I and 146 BP-II), hospitalized after a suicide attempt, were interviewed by semi-structured interview and validated questionnaires about DSM-IV axis I disorders, suicide attempt characteristics and a wide range of personality traits relevant to suicidal vulnerability. Logistic regression analysis was performed to determine differences between BP-I and BP-II attempters.

Results

There was no significant difference between BP-I and BP-II suicide attempters according to sociodemographic variables. BP-I and BP-II patients did not differ for suicide intent assessed using the underscore expectation and intention of attempt measured on the Suicidal Intent Scale [44% versus 46% for a score above 11, OR = 0.83, 95% CI = (0.46-1.49) and lethality of suicide attempt as measured by the risk score of the Risk Rescue Rating Scale [OR=1.06 for 1 point increased 95% CI[0.97;1.15]]. There was no significant difference for other characteristics of suicide behavior such as number of previous attempts, age at first suicide attempt, use of violent mean. Personality traits such as impulsivity (Barrat Impulsivity Scale), aggression (Buss-Durkee Hostility Inventory), emotional lability (Affective Lability Scale), and hopelessness were similar between BP-I and BP-II patients. There was no significant difference between the two groups in rates of comorbid substance abuse, anxious disorder or eating disorder.

Conclusion

BP-I and BP-II subtypes have similar features of suicide attempt and personality traits relevant to suicidal risk.

The effectiveness of sleep regulation on the “therapeutic milieu” in bipolar depression by aripiprazole adjunctive therapy

Author: Kentaro Ooga, T. Okudaira , E. Shiba , Y. Furukawa , N.Watanabe

Nihon University, School of Medicine, Department of Psychiatry, 1-8-13, Kandasurugadai, Chiyoda-ku, Surugadai Nihon University Hospital, 101-8309 Tokyo, Japan

1Nihon University School of Medicine, Department of Psychiatry, Tokyo, Japan.

2Nihon University School of Medicine, Department of Medicine Division of Integrated Herbal Medicine, Tokyo, Japan. 3Department of Psychiatry, Yamaguchi Hospital, Japan.

4Department of Psychology, California State University, Fullerton, United States of America ooga.kentarou@nihon-u.ac.jp

Objective

Bipolar depression tends to be refractory to treatment and takes a prolonged course. Its atypical symptoms, such as hypersomnia, leaden paralysis, bulimia, and hypersensitivity to rejection, make it difficult for patients to go out, preventing their rework. We have already reported the course of treatment, which improved irregular sleep-wake patterns, followed by the augmentation of aripiprazole in a case of bipolar depression comorbid with AD/HD.

Moreover, we are going to report the course of aripiprazole augmentation therapy in five cases of bipolar depression.

Method

The subjects were five adults with bipolar depression (age19-43, Female n=5). They tended to show sleep-wake rhythm disturbances, corresponding to episodes which were induced by interpersonal stress or the loss of s daily routine. They had more episodes of irritability, impulsiveness, dissociative symptoms, personality changes, and criminal behaviors during the periods of manic-depressive mixed states. Combined administration of mood stabilizers relieved these symptoms. The subjects were instructed to keep sleep logs (Social Rhythm Metrics-5) to monitor their daily sleep-wake rhythm. We gave them some advice to ensure time for each meal and sleep and regulate their everyday life through a fixed schedule, such as doing regular housework. Aripiprazole was administered variably between 3-18mg/daily based on tolerability and efficacy.

Results

Prior to aripiprazole prescription, the patients could not wake up in the morning and irregular circadian rhythm had been continued. After aripiprazole administration, the patients were able to get up at a fixed time, do daily routines efficiently, and improve depressive moods, malaise, and atypical symptoms. Their euthymic mood state was maintained for a long time.

Conclusion

In the Bellevue Sanatorium of the middle of the 19th century, the patients with affective psychosis had been treated by integrative therapeutic approaches, which included creating a structured environment on “Moral Treatment” and regulating life rhythm with physical therapy, such as balneotherapy, hydrotherapy, and electrotherapy. The “somatist,” Binswanger put higher emphasis on the effectiveness of the “therapeutic milieu.” He prescribed a small amount of “psychotropic” drugs, not merely for eliminating psychotic symptoms from patients, but also for activating their physical function. In the aripiprazole adjunctive therapy, the physiological functions (sleep-wake rhythm) have been adjusted in patients with bipolar depression. Regular life is maintained as a result; it has resulted in long normal mood state. This is similar to the “therapeutic milieu” aimed at by Binswanger. We can expect the same effect on the recovery of depression by herbal medicine and Morita therapy.

Neurocognitive function in bipolar disorder: a comparison between bipolar I and II disorder and matched controls

Author: Erik Pålsson, Clara Figueras, Anette GM Johansson, Carl-Johan Ekman, Björn Hultman, Josefin Östlind and Mikael Landén

Department of Psychiatry and Neurochemistry Sahlgrenska University hospital, Bla straket 15, 413 45 Göteborg, Sweden

erik.palsson@neuro.gu.se

Objective

It has been suggested that the degree and type of cognitive impairment differ between bipolar I and bipolar II disorder, but data is conflicting and remains inconclusive.

Method

67 patients with bipolar I disorder, 43 with bipolar II disorder, and 86 randomly selected population-based healthy controls were compared. An extensive battery of neuropsychological tests was administered assessing estimated premorbid IQ, attention, processing speed, verbal and visual memory, and executive functions. Patients were tested during a euthymic phase of the disorder.

Results

Patients with bipolar type I and type II were cognitively impaired compared to healthy controls, particularly on tasks measuring aspects of executive function. However, there were no statistically significant differences between the two diagnostic subtypes. The strongest predictors of cognitive impairment within the patient group were current antipsychotic treatment and duration of illness.

Conclusion

The present study suggests that the type and degree of cognitive dysfunction is similar in bipolar I and II patients. Notably, treatment with antipsychotics - but not a history of psychosis - was associated with more severe cognitive impairment. Given that patients with bipolar I disorder are more likely to be on antipsychotic drugs, this might explain why some previous studies have found that patients with type I bipolar disorder are more cognitively impaired than those with type II.

Effects of repeated co-treatment with fluoxetine and risperidone on the behavioral effects and serum corticosterone level in rats subjected to the forced swimming test

Authors: Zofia Rogóż, Anna Gądek-Michalska

Department of Pharmacology, Department of Physiology, Institute of Pharmacology Polish Academy of Sciences, 12 Smetna Street, 31-343 Krakow, Poland

rogoz@if-pan.krakow.pl

Objective

Several clinical reports have suggested a beneficial effect of the addition of a low dose of an atypical antipsychotic drug (e.g., risperidone) to the ongoing treatment with antidepressant drugs (ADs), especially with selective serotonin reuptake inhibitors (e.g., fluoxetine, fluvoxamine or poroxetine) in the treatment of drug-resistant depression. Risperidone, whose low doses block mainly 5-HT2A serotonin receptors and higher ones dopamine D2 receptors, is known to produce minimal extrapyramidal side-effects compared to classical antipsychotics. To understand the mechanism of the clinical efficacy of a combination therapy with an AD and an atypical antipsychotic in treatment-resistant depression, in the present study we examined the effect of joint administration of fluoxetine and a low dose of risperidone, given separately or jointly, on the behavioral reactivity of the central 5-HT1A- and 5-HT2A - or dopamine systems and

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in the forced swimming test (an animal test of depression), as well as on serum corticosterone level of male Wistar rats.

Method

Fluoxetine (5 or 10 mg/kg ip) was given once or repeatedly (for 14 days), separately or jointly with risperidone (0.05 or 0.1 mg/kg ip). All the experiments, i.e. the behavioral syndrome (body posture and forepaw treading) evoked by the 5-HT1A receptor agonist 8-OH-DPAT (5 mg/kg ip) and the head twitches reaction induced by the 5-HT2A receptor agonists DOI (2.5 mg/kg ip), or the hyperactivity induced by D-amphetamine (5 mg/kg sc) or immobility time in the forced swimming test, or serum corticosterone level were carried out 24 hours after a single (acute treatment) or the last dose (repeated treatment) of fluoxetine or risperidone.

Results

The obtained results showed that acute co-treatment with fluoxetine (5 or 10 mg/kg) and risperidone (0.05 or 0.1 mg/kg) did not change the behavioral syndrome evoked by 5-HT1A or 5-HT2A receptor agonists or the hyperactivity induced by D-amphetamine in rats. Moreover, repeated co-treatment with fluoxetine and risperidone induced more potent inhibition of the body posture and forepaw treading evoked by 5-HT1A receptor agonist (8-OH-DPAT), but changed neither the head twitches reaction evoked by the 5-HT2A receptor agonist (DOI) nor the action of D-amphetamine, a dopamine agent, compared to treatment with either drug alone. In addition, fluoxetine evoked an antidepressant-like effect in the forced swimming test (i.e. it decreased the immobility time) and also decreased serum corticosterone level in stressed rats subjected to the forced swimming test. Co-treatment with fluoxetine and risperidone produced a more pronounced antidepressant-like effect than did either of the drugs alone, while serum corticosterone level in those animals did not differ from that found in fluoxetine-treatment rats.

Conclusion

The obtained results indicate that a low dose risperidone enhances the antidepressant-like effect of fluoxetine and that among other mechanisms, 5-HT1A receptors may play some role in this effect. Furthermore, they may be of particular importance to the pharmacotherapy of drug-resistant depression.

Additional Information

Acknowledged: This study was financially supported by grant POIG. 01.01.02-12-004/09-00 from European Regional Development Fund.

Cerebrospinal fluid neuropeptide Y level associated with anxiety and suicide attempts in bipolar disorder

Author: Johan Sandberg, Aleksander A. Mathé, Mikael Landén

Gibraltargatan 92, Apartment 0966, 41279, Gothenburg, SWEDEN

johan.sandberg@neuro.gu.se

Objective

Neuropeptide Y (NPY) is a neurotransmitter found in the central and peripheral nervous system. It is associated with a variety of behavioral and physiologic functions including anxiety, learning and memory processes, energy balance, seizure activity and alcohol consumption. Additionally, cumulative evidence from preclinical and clinical studies implicates NPY in the pathophysiology depression and anxiety disorders. Findings of reduced expression of NPY mRNA in the prefrontal and frontal cortex of bipolar subjects suggest that NPY is also implicated in the pathophysiology of bipolar disorder. In the present study we set out to further investigate the role of NPY in bipolar disorder.

Method

Cerebrospinal fluid (CSF) concentrations of NPY-like immunoreactivity (NPY-LI) were determined in 122 patients with bipolar disorder. Assessments included a meticulous diagnostic interview by means of the Affective Disorder Evaluation (ADE) and personality tests including the Swedish Universities Scales of Personality (SSP).

Results

Accounted suicide attempts were found to be associated with reduced NPY-LI in CSF. Further, there was a negative correlation between NPY-LI in CSF and psychic and somatic trait anxiety. Interestingly, treatment with the anticonvulsant lamotrigine was significantly associated with increased NPY levels in CSF. Lithium treatment, which previously has been shown to raise NPY protein and mRNA levels in several brain regions in rats, was related to reduced NPY levels in CSF at a trend level.

Conclusion

The present results are in line with previous studies and indicate that neuropeptide Y might modulate anxiety and suicidal behavior in bipolar disorder. The positive correlation between NPY-LI and lamotrigine treatment raises the possibility that the lamotrigine mechanism of action might involve the NPY-ergic system.

Additional Information

Institution: University of Gothenburg, Institute of Neuroscience and Physiology

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The kynurenine pathway and cognitive performance in euthymic bipolar disorder

Authors: C Sellgren1, SK Olsson2, S Erhardt2, G Engberg2, P Lichtenstein1, M Landèn1,3

1Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden. 2Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. 3The Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden.

Objective

Kynurenic acid (KYNA) is a neuroactive metabolite produced in the kynurenine pathway. Increased KYNA concentrations have been found in the cerebrospinal fluid (CSF) of patients with euthymic bipolar disorder. KYNA as well as other metabolites in this pathway are implicated in cognitive processing. In the past years, it has become evident that bipolar disorder patients exhibit less pronounced cognitive symptoms also in the euthymic state. In this study, we analyze the association between CSF KYNA and cognitive performance in euthymic bipolar disorder.

Methods

CSF KYNA from 53 euthymic bipolar patients were analyzed utilizing high performance liquid chromatography (HPLC). The neuropsychological assessment was carried out using WAIS-III. First, we studied CSF KYNA and Full-Scale IQ. CSF KYNA was then evaluated against the Verbal Comprehension Index (VCI), the Working Memory Index (WMI), the Processing Speed Index (PSI), and the Perceptual Organization Index (POI).

Results: There was a significant association between CSF KYNA and Full-Scale IQ (n=53, unstandardized β=8.2, 95%CI:3.5–13.0). Adjustment for age, gender, type of bipolar disorder (1,2 or NOS), life-time number of mania and depression, life-time history of psychosis, MADRS score, YMRS score and type of medication (lithium, antipsychotics, valproic acid, lamotrigin, propiomazine) did not have a substantive effect on the results (n=53, unstandardized β=10.0, 95%CI: 3.0–17.0). CSF KYNA was then analyzed against VCI (n=53, unstandardized β=5.9, 95%CI:1.8–10), WMI (n=53, unstandardized β=6.6, 95%CI:1.3–11.8), POI (n=53, unstandardized β=6.8, 95%CI:1.5–12.2, P=0.015), and PSI (n=53, unstandardized β=6.6, 95%CI: 1.9–11.3). All analyses against these subindex remained significant after adjusting for potential confounders.

Conclusions

In the observed range a remarkably strong positive net effect of CSF KYNA on Full-Scale IQ was observed. Several mechanisms of actions are possible and studies of causality are needed. Further analyses using the secondary subindices gave no conclusive results regarding KYNAs relative effect on different cognitive domains. Most likely, more demarked neurocognitive tests are needed to reveal such effects.

Working memory performance in bipolar disorder: the role of dopamine transmission in the prefrontal cortex

Authors: C Sellgren1, G Engberg2, S Erhardt2, P Lichtenstein1, M Landèn1,3

1Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden. 2 Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. 3The Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden.

Objective: Cerebrospinal fluid (CSF) concentrations of the major dopamine metabolite homovanillic acid (HVA), and the major serotonin metabolite 5-hydroxy-3-indoleacetic acid (5HIAA) have been found to be significantly higher in manic than in depressive episodes in bipolar disorder. Working memory can be improved or worsened by manipulating dopamine in the prefrontal cortex (PFC). In bipolar disorder, working memory foremost appears to be a state dependent deficit contingent on the presence of affective symptoms. In primates, PFC concentrations of HVA have been shown to correlate with HVA concentrations in CSF. In this study of euthymic bipolar disorder patients we investigate the associations between these monoamine metabolites in CSF and working memory performance.

Methods: CSF was collected from euthymic bipolar type 1,2 or NOS patients enrolled in a long-term follow-up program at a bipolar outpatient unit at the Northern Stockholm psychiatric clinic, Stockholm, Sweden. CSF HVA and CSF 5HIAA concentrations were analyzed utilizing mass fragmentography. A trained psychologist carried out the neuropsychological assessments. To assess working memory we used total scores from the Digit Span Test in the Swedish version of Wechsler Adult Intelligence Scale, Third Edition (WAIS-III). Manic symptoms were evaluated using Young Mania Rating Scale (YMRS), and depressive symptoms using Montgomery-Åsberg Depression Rating Scale (MADRS).

Results: In our sample of euthymic bipolar disorder type 1 or 2 (YMRS mean = 1.7, SD = 2.6, MADRS mean = 4.8, SD = 5.8) CSF-HVA was associated with increased score in DST adjusted for age, sex, type of bipolar disorder, YMRS and MADRS score (n = 87, standardized β = 0.27, P = 0.009). No association was seen between CSF 5HIAA and DST score (n = 87, standardized β = 0.16, P = 0.2). Mean total score in the Digit Span Test was 15.8 (SD = 4.1). No significant differences were seen between the bipolar type 1 and type 2 groups regarding CSF HVA or total score in the Digit Span test. Use of an anitipsychotic did not significantly influence CSF HVA.

Conclusions: In euthymic bipolar disorder, increased CSF concentration of HVA was associated with improved performance in a verbal working memory task. Excessive dopamine transmission - as well as dopamine depletion - in the PFC is known to cause working memory impairment. As working memory appears to be a state dependent deficit - contingent on the presence of affective symptoms

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in bipolar disorder – one possibility is that fluctuations in verbal working memory during the course of bipolar disorder follow the inverted 'U-shaped dose/response curve of dopamine actions in PFC. That would explain why the working memory deficit is restricted to affective episodes in bipolar disorder. In patients with persistent working memory deficits in euthymia, dopamine levels in PFC may be a potential target for the development of neuroprotective drugs.

Dementia progress and prediction of disease development in patients with hydrocephalus

Author: Lucie Sosvorová 1), Marie Bičíková 1), Milan Mohapl 2) and Richard Hampl 1)

1) Institute of Endocrinology, Department of Steroids and Proteofactors, Národní 8, 11694, Prague 1, Czech Republic

2) Central Military Hospital, Department of Neurosurgery, U Vojenské nemocnice, 1200, 169 02, Prague 169 02 Prague 6, Czech Republic, Institute of Endocrinology, Department of Steroids and Proteofactors, Národní 8, 11694 Prague 1, Czech Republic

lsosvorova@endo.cz

Objective

Dementia is together with gait disturbance and urinary incontinence the most characterise consequence of hydrocephalus. It is generally classified as an elevation of the cerebrospinal fluid (CSF) pressure within the brain, which distorts soft brain tissues. On the basis of these clinical features, it is usually difficult to distinguish hydrocephalus symptoms from that of Alzheimer's dementia, vascular dementia and Parkinson's disease. The diagnosis is difficult, mainly based on expensive imaging studies as computed tomography, ultrasound and magnetic resonance.

Our research concerns the patients suffering from hydrocephalus, the neurosurgical treatment of which consists in decrease of the intracranial pressure by sucking off the excessive CSF, which is channelled by introduced drainage system (shunt) into the abdominal cavity. We attempt to find out hormonal markers in CSF, which would enable us prediction and consequent targeted treatment of dementia, which, after initiatory relief, appears in most of the patients (in ½ as early after 3 months-, and in almost ¾ after 3 years from operation).

In these and other patients with CSF disorders, hypercortisolemia was found repeatedly. Strong mineralocorticoid active hormone cortisol is formed from cortisone stored within the cells through the activity of 11β-HSD. To determine the results of hydrocephalus improvement, we calculated the cortisone/cortisol ratio. Based on previous experience, the levels of neurosteroids DHEA, DHEA-sulphate and homocysteine were measured.

Method

The HPLC-DAD method was used for the evaluation of cortisol and cortisone levels in CSF. The values of LOD and LOQ for cortisol and cortisone were in the range of 0.5 – 1 nmol/L and 2.0 – 2.5 nmol/L. The recoveries of cortisol and cortisone in CSF ranged from 88% to 109%, for the repeatability of the study, corresponding values 3.7 % to 7.6% were found. GC-FID method developed in our department was used for the determination of homocysteine levels. For the assessment of DHEA and DHEA-sulphate levels, the commercial available RIA was used.

Results

In our group of patients after 1 month from operation the cortisone/cortisol ratio in 80% of patients increased considerably and this shows the improvement of hydrocephalus state. The CSF cortisol and cortisone levels ranged around 10 - 30 nmol/L and 1 – 15 nmol/L respectively. The DHEA and DHEA-sulphate levels ranged from 0.07 to 0.91 nmol/L and 0 to 33.3 nmol/L. The levels of homocysteine were in order of μmol/L.

We are at the beginning of our study. It will be of interest to see the changes of cortisone/cortisol ratio in comparison to clinical state in several next years.

Conclusion

Our preliminary results show remarkable changes in cortisol and cortisone CSF levels in patients after the surgical treatment by shunt. The finding of increased cortisol/cortisone ratio 1 month after operation supported our theory on the 11β-HSD importance.

Our results should sort out the laboratory changes which would be helpful in an objective evaluation of the disease stage. An early and accurate diagnosis would help in the therapeutic strategy, which would suppress or attenuate progression of the disease leading to some type of dementia.

Additional Information

Acknowledgement: IGA MZCR NT/12349-4

Neurocognitive functioning in patients recently diagnosed with bipolar disorder

Author: Kjetil Sundet, Hellvin T, & Melle I

Department of Psychology, University of Oslo, P.O.Box 1094 Blindern NO-0317 Oslo

Norway, k.s.sundet@psykologi.uio.no

Objective

Although cognitive dysfunction is well established in bipolar disorder, less is known about impairments early in the course of illness. The present report compares neurocognitive function in a group of patients recently diagnosed with BD to an age, gender and education matched sample of healthy controls.

Method

Patients with first episode mania (n=34) and previously untreated mania (n=21) were neuropsychologically tested after their first treated manic episode, along with 110 healthy control subjects. Cognitive domains evaluated included verbal and visual memory, attention, processing speed, executive functioning, and IQ. Results were

corrected for speed of processing differences, and compared to previously reported results for multi-episode bipolar disorder patients.

Results

Differences were found within all cognitive domains with largest effect size difference for psychomotor speed. When controlling for psychomotor speed, two measures remained statistically significant. Mean proportion of patients with clinically impairments was 16 % within both groups.

Conclusion

Neurocognitive dysfunctions are present early in the course of bipolar disorder and reach the level of clinical significance for a subgroup of individuals. Our findings suggest that the neurocognitive dysfunction may increase with illness progression.

Additional Information

The abstract is based on a paper accepted for publication in Bipolar Disorders.

Influence of the drug exposure definition on the assessment of the antipsychotic metabolic impact in patients treated with mood stabilizers

Authors: Marie Tournier1, 2, 3, Bernard Bégaud1, 2, 4, Audrey Cougnard2, Guy-Robert Auleley5, 6, Jean Deligne5, Claudine Blum-Boisgard5, Anne CM Thiébaut2, 7, Hélène Verdoux1, 2, 3

Hôpital Charles Perrens, 121 rue de la Béchade, 33076 Bordeaux cedex, France

1) Univ. de Bordeaux, U657, F-33000 Bordeaux, France

2) INSERM, U657, F-33000 Bordeaux, France

3) Centre Hospitalier Charles Perrens, F-33000 Bordeaux, France

4) Centre Hospitalier Universitaire de Bordeaux, F-33000 Bordeaux, France

5) Caisse Nationale du Régime Social des Indépendants, National Medical Department, Paris, France

6) National Cancer Institute, Clinical Research Department, Boulogne-Billancourt, France

7) Institut Pasteur, Unité de Pharmaco-Epidémiologie et Maladies Infectieuses (PhEMI), Paris, France

mtournier@ch-perrens.fr

Objective

To assess the influence of the antipsychotic exposure definition on the comparison between first-generation (FGAP) and second-generation (SGAP) antipsychotics and mood-stabilizers using: (i) a dichotomous measure (exposed/non-exposed over the follow-up); (ii) a categorical measure taking into account the chronology of exposure at the time of the metabolic event (current, recent, and no use); and (iii) a continuous measure (cumulative duration).

Method

A historical fixed cohort was identified from the 2004-2006 claims database of the French health insurance programme for self-employed workers, including 3,172 patients aged 18 years and over who used conventional mood-stabilizers over a three-month period. A metabolic event was defined as an incident dispensing of anti-diabetic or lipid-lowering drug.

Results

A metabolic event occurred in 367 patients (11.6%). Compared with conventional mood-stabilizers, the risk of metabolic event was negatively associated with exposure to SGAPs over the follow-up [HR 0.53 (CI95% 0.34-0.82) p=0.004], positively associated with recent, but not current, exposure to SGAPs [HR 2.1 (95%CI 1.2-3.7) p=0.006] and not associated with cumulative duration of SGAPs [HR 1.001 (CI95% 0.999-1.003) p=0.20].

Conclusion

The definition of exposure to antipsychotics in studies exploring their metabolic impact is of paramount importance in understanding this association. Different definitions can lead to opposite results. Not taking into account past exposure, in order to minimize the depletion of susceptibles effect, may lead to absurd results.

Assessing of cognitive function in patients with bipolar affective disorder during manic episodes

Authors: Madalina Vrabie 1, I. Miclutia 23, V. Marinescu 14, C. Popescu 3

1 Clinical Hospital of Psychiatry “Al. Obregia” Bucharest, Romania, 2 Department of Psychiatry, University of Medicine & Pharmacy “Iuliu Hatieganu” Cluj-Napoca,Romania, 3 Second Psychiatric Clinic, Emergency County Hospital Cluj-Napoca, Romania, 4 Department of Psychiatry, University of Medicine & Pharmacy “Carol Davila”, Bucharest, Romania str. Bogdan Gh. Tudor, nr.4, bl.20A, sc.1, et.5, ap.23, sector 3, Bucharest

Romania, madalina.vrabie@yahoo.com

Objective

The objective of this study is identifying specific domains of cognitive dysfunction for manic episodes in bipolar affective disorder.

Method

We examined 60 bipolar (depressive: Hamilton Depression Rating Scale HAMD score >= 17, manic/hippomanic: Young Mania Rating Scale YMRS score >= 12, euthymic: 6 month of remission, HAMD score <= 8, YMRS score <= 6) patients (according to DSM IV TR). All the patients were free of psychotic symptoms (defined by the present of either hallucinations or delusions) at the moment of neurocognitive evaluation. The comparison group consisted of 20 healthy subjects without history of neurological and/or psychiatric disorder. The cognitive battery included standardized test of IQ, attention, working memory, visual memory, verbal memory and executive functioning. Demographic data were systematically obtained and included gender, age, years of education, socioeconomic status and current employment. Data about family history and information about psychiatric history, past and current treatment, history of psychosis, duration of illness and age of onset (defined as the age when subjects first experienced an episode of

either polarity) were collected. We analyzed statistically these data and identified specific domains of cognitive dysfunction for manic episode of bipolar affective disorder.

Results

Stable and lasting cognitive impairments involving executive functioning (working memory, executive control, verbal fluency, mental manipulation and cognitive flexibility), verbal learning and memory and attention are evident across all phases of illness. Sustained attention (vigilance) is impaired in bipolar patients regardless of whether they are studied during periods of mania or depression. Performances on task that tapes domains of verbal learning and memory, and sustained attention were particularly impaired in manic patients.

Cognitive deficits are more frequent in manic patients with more severe course of illness, as indicated by: longer durations of mood disturbance (negatively correlated with executive function, psychomotor speed, attention, concentration and verbal memory-associated with a higher number of past manic episodes too), younger age at onset, history of multiple and frequent episodes (with manic episodes impacting neuropsychological impairment most extensively; attention and executive function deteriorated by the recurrence of episodes) and higher number of hospitalization (negatively correlated with visual and verbal memory, verbal fluency, spatial memory, psychomotor speed and executive function). There's as well a specific relationship between executive functioning and admission for mania.

Conclusion

The recurrence of episodes of mania and/or depression is a feature of bipolar affective disorder and it interferes with neurocognitive performance. There are persistent cognitive deficits over the course of bipolar affective disorder and specific cognitive impairment of each phase of the illness, like mania. This study identified several important risk factors that may moderate these cognitive deficits in manic patients.

Assessing of cognitive function in patients with bipolar affective disorder during manic episodes

Authors: M. Vrabie, I. Miclutia, V. Marinescu, C. Popescu
Str. Bogdan Gh. Tudor, nr.4, bl.20A, sc.1, et.5, ap.23, sector 3, Bucharest, Romania
madalina.vrabie@yahoo.com

Objective

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Results

Stable and lasting cognitive impairments involving executive functioning (working memory, executive control, verbal fluency, mental manipulation and cognitive flexibility), verbal learning and memory and attention are evident across all phases of illness. Sustained attention (vigilance) is impaired in bipolar patients regardless of whether they are studied during periods of mania or depression. Performances on task that tapes domains of verbal learning and memory, and sustained attention were particularly impaired in manic patients.

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The recurrence of episodes of mania and/or depression is a feature of bipolar affective disorder and it interferes with neurocognitive performance.There are persistent cognitive deficits over the course of bipolar affective disorder and specific cognitive impairment of each phase of the illness, like mania. This study identified several important risk factors that may moderate these cognitive deficits in manic patients.

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CHILDHOOD AND ADOLESCENCE

An Adolescent With Asperger's Disorder And Comorbid Bipolar Disorder: A Case Report

Author: Tezan Bildik, B. Ozbaran, S. Gokcen, S. Korkmaz-Cetin, S. Erermis
Ege University Medical School, Department of Child Psychiatry, Izmir,Turkey
tezanbildik@yahoo.com

Objective

Adolescents with Asperger's disorder often are seen by child psychiatrists, as having a variety of behavioral and emotional disturbances. Aggression and self-injury are among the most common problematic behaviors. In some adolescents, these disturbing behaviors are symptoms of a comorbid psychiatric condition. However, many clinicians continue to accept these disturbing behaviors as part of the underlying pervasive developmental disorder. Hence, it is particularly important to recognize and treat comorbid psychiatric conditions in these patients, which can considerably improve functioning.

Method

Retrospectice chart review for in a outpatient adolescent.

Results

The case report describe information about the occurrence of psychiatric disorders among developmentally disabled children, with an emphasis on those with pervasive developmental disorders. It also serves as an illustration of how disturbing behaviors can be symptoms of comorbid psychiatric disorders and emphasizes the necessity of accurate diagnostic formulation in these patients.

Conclusion

For this adolescent, once he was diagnosed with comorbid bipolar disorder, appropriate treatment led to a decrease in disturbing behaviors, an improvement in quality of life for the adolescent, and a decrease in family burden.

Bipolar Disorder and ADHD. Different aspects of the same psychopathological entity or just comorbidities? An interesting case report.

Authors: K. Bonotis, A. Zerdelis
Department of Psychiatry, University Hospital of Larisa, University of Thessaly, Larisa, Greece

Background: Comorbidity between BD and ADHD has been estimated as high while this correlation remains unclear (Faraone et al., 1997; Youngstrom et al, 2010; Zepf, 2009) In this case report we are discussing a case of a 33 years old male with an interesting psychiatric history tracing back to his juvenile times.

Main clinical features: He was born with the help of forceps. Through his first decade of life failed to develop proper social activities and create interpersonal relationships effectively. It was also noted that he was very inattentive in school activities.

At the age of 11, following a head injury with a ball, he presented dizziness, gait disturbance and irritability as he was crying and worrying about past events and experiencing negativism. It is noted that he was unable to distinguish real events of life from his dreams. In these terms he was admitted to the hospital and acute brain infection/inflammation was ruled out which was negative. The EEG was also normal. He was treated with antidepressants with poor response and later on he developed generalized fear and coprolalia. Gilles de la Tourette was suspected and he was started on haloperidol which was not well tolerated. After those events he was transferred to pediatric psychiatry department and there he manifested two-week long mutism.

After careful history-taking and observation the diagnosis of bipolar disorder was established. He was started on mood stabilizers and he responded very well. By this time, symptoms of attention deficit and extreme hyperactivity/ impulsivity were observed and the diagnosis of ADHD was also made.

Since then he has been hospitalized many times for exacerbations of bipolar disorder, either manic or depressive ones. During the later, he states that he is somnolent and experiences psychomotor retardation. During the manic diversion and milder during his normothymic state, his main symptomatology stems from his impulsivity and inattentiveness. As a result, he is generally unable to sustain viable interpersonal relationships and this is an additive cause of anxiety to his baseline psychopathology. A recent psychometric evaluation revealed a borderline intelligence (I.Q = 80) with deviation between verbal and practical intelligence (V.I. > P.I.). During the last 7 years he is experiencing frequent episodes of syncope without objective etiology being identified.

The psychopharmacological approaches are summarized in his current treatment which consists of: valproate (1500mg), olanzapine (20mg), quetiapine (400mg), lorazepam (2,5mg), lamotrigine (100mg), thyroxine (100μg history of hypothyroidism).

It should be noted that there is no psychiatric history in his family which is very supportive to him whatsoever.

Conclusion: The overlapping symptoms in this patient complicate both the diagnosis and treatment. This case indicates the need for further investigation.

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Childhood Attachment and Parental Bonding in Bipolar Disorder: A Review

Authors: Kevin Clarkson and Dr. Georgina Hosang
MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London

Background

The aetiology of bipolar disorder (BD) cannot be explained by genetic factors alone. Research into early attachment style and parental attributes of warmth, acceptance and control has identified differences in the early relationships of bipolar individuals that may indicate a role in the development of the illness.

Objectives:

This paper presents a systematic review of empirical research into the predictive or correlating relationships between childhood attachment style, parental bonding and BD.

Method: A search was conducted in Medline (1948-2012) and PsychInfo (1806-2012) and studies selected based on their capacity to identify correlations, or advance theoretical thinking in this field. Quality criteria were applied and results consolidated using a best evidence synthesis approach. Results: Thirteen studies observed early parental bonding in a bipolar cohort, while five studies explored childhood attachment. Attachment: Evidence supports a significant relationship between early attachment insecurity and later psychopathology. Parental bonding: There is strong evidence that parental control is unrelated to future BD in offspring. While evidence for the influence of father-child relationships is inconclusive, individuals who develop BD are more likely to experience low maternal warmth and increased rejection during childhood.

Conclusion

Insecure attachment, low maternal warmth and increased rejection in childhood have a small but significant correlation with future bipolar diagnoses. Results are discussed in the context of two theories of BD aetiology – Behavioural Activation System Dysregulation and the Manic Defence – supporting the view that early parent-child relationships modulate the influence of other developmental, environmental and genetic factors in at-risk children.

Alexithymia, somatic complaints and depressive symptoms in adolescence: a one-year longitudinal study

Authors: Domenico De Berardis 1-2, Nicola Serroni 1, Daniela Campanella 1, Luigi Olivieri 1, Francesca Ferri 1, Stefano Marini 1-2, Luisa Del Nibletto 1, Carla Ranalli 1, Alessandro Carano 2-3, Marilde Cavuto 4, Giovanni Martinotti 2, Francesco Saverio Moschetta 1 and Massimo Di Giannantonio 2

1 NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "G. Mazzini", Asl 4 Teramo, Italy

2 Department of Neurosciences and Imaging, Chair of Psychiatry, University "G. d'Annunzio" of Chieti, Italy

3 NHS, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "C. G. Mazzoni" Ascoli Piceno, Italy

4 IASM, L'Aquila, Italy

National Health Service, Department of Mental Health, ASL 4, Psychiatric Service of Diagnosis and Treatment, "G. Mazzini" Hospital, p.zza Italia 1, 64100 Teramo, Italy.

dodebera@aliceposta.it

Objective

To evaluate relationships between alexithymia, somatic complaints and depressive symptoms in a non-clinical sample of school-aged Italian adolescents.

Method

A mixed male–female sample of 155 school-aged adolescents (75 Females and 80 Males with a mean age of 15.8 years), living in an urban district of Central Italy, was investigated with self-reported

rating scales. Scales were: Toronto Alexithymia Scale (TAS-20), Beck Depression Inventory (BDI), Symptom Checklist 90 – Somatization Subscale (SCL-90-SOM), State-Trait Anxiety Inventory (STAI),

Rosemberg Self Esteem Scale (RSES) e Barratt Impulsiveness Scale (BIS-11). Subjects were evaluated at three times: at the beginning (T0), at the middle (T1) and at the end (T2) of the scholastic year.

Results

25 subjects (16.1%) were categorized as alexithymics and, overall, showed greater psychological distress than non-alexithymics. Alexithymia levels remained stable during the time as well as the number of alexithymics. Alexithymics were more suitable to develop more severe depressive symptoms. Partial correlations controlling for age and gender, showed that TAS-20 total score and DIF/DDF subscales correlated with all study variables both at the beginning and at the end of the study, whereas EOT correlated slightly only with SCL-90-SOM at both times. Results of a linear regression supported the notion that depressive symptoms at endpoint were signifi cantly associated with female sex, DIF subscale of TAS-20 and higher SCL- 90-SOM scores.

Conclusion

Alexithymia, depressive symptoms and somatic complaints appeared to be highly correlated in adolescence. Findings of the present study substantially confi rm those of other study in adult general population. However, further longitudinal studies on larger samples and/or clinical samples of adolescents are needed to defi nitely clarify this topic.

Additional Information

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Parental reports of early psychopathology in children and adolescent with Bipolar Disorder

Author: Mariely Hernandez,M.A., Marie C. Grant, M.A., George Nitzburg, M. Phil, Argelinda Baroni, M.D., Jezelle Estrado, M.A., Gianni L. Faedda, M.D.

235 East 50th Street, #35, New York, NY 10022, United States

marielyh@gmail.com

Objective

Early psychopathology in children diagnosed with Bipolar Disorder (BD) remains poorly characterized. Parental retrospective reports provide helpful details on the earliest manifestations and their evolution over time, occurring early in the course of BD and often before a formal diagnosis is made and/or treatment is implemented.

Method

Retrospective ratings of 35 activation/withdrawal symptoms were obtained from the parents of children diagnosed with BD attending an outpatient specialty clinic. Diagnoses were established using DSM-IV criteria following K-SADS-PL interviews. Demographic, socio-economic and adoption status, comorbid lifetime diagnoses and family history of mood Disorder were assessed. Previously reported early symptoms of BD were only rated in each subject for the earliest occurrence causing impairment.

Results

Consistent with the findings of previous reports, three symptoms, decreased sleep, irritability and temper tantrums were found frequently (>20%) and from a very early age (>3 y/o) in children who later developed BD. Five additional symptoms, increased crying, anxiety, short frustration tolerance, hyperactivity and aggression were found in more than 10% before the age of 3 years of age, and represent further early psychopathology in children with BD. Before age 7, parents reported high rates of temper tantrums (56%), aggression (52%), anxiety (47%), decreased attention span (45%), hyperactivity and irritability (43%), or decreased sleep (41%); somewhat less common, but perhaps more specific for BD were poor frustration tolerance (31%), brief elevated mood (28%), pressured speech (25%), hypersexual behavior (16%), grandiosity and racing thoughts (12%); bedwetting and somatic complaints occurred in 17% and 16 % respectively. The mean age of onset of psychiatric symptoms was significantly lower in bipolar children with comorbid ADHD compared to children without comorbid ADHD ($F=5.04$, $p<0.05$), indicating that attention symptoms precede mood symptoms in cases with comorbid ADHD. We found no significant differences between groups when most severe manic or depressive episodes were compared ($F=1.67$, $p>0.05$), suggesting that bipolar patients with and without comorbid ADHD may present with similar symptoms' severity profiles during episodes.

Conclusion

Retrospective reports of early psychopathology in children with BD revealed a very early onset of symptoms of sleep disturbances, irritability and temper tantrums preceding sometimes by several years the syndromal onset of BD. These results are consistent with previous reports a progression of symptoms from atypical and non-specific psychopathology towards syndromal BD.

Early functional impairment in bipolar youth

Authors: Jansen K, Magalhaes PVS, Quevedo LA, Souza L, DMPinheiro RT, Kapczinski F, da Silva RA , 373 Gonçalves Chaves Street, office 416C, postal code 96015-560 - Pelotas/RS,Brazil

jansen@ucpel.tche.br

Objective

To assess at specific functioning effects of people without any mood disorders and people with depression or bipolar disorder.

Method

This is a case-control study nested in a population-based cross-section of young adults. The Structured Clinical Interview for DSM-IV (SCID) was used for diagnostic of depression and bipolar disorder while the Functioning Assessment Short Test (FAST) was employed to assess functioning.

Results

The sample for the case-control study consisted of 231 subjects. Of these, 95 were control subjects, 82 had major depression and 54 had bipolar disorder. Of the clinical variables, misuse of illicit drugs (p

<0.001), current depressive symptoms (p=0.001), a diagnosis of major depression (p=0.002) or bipolar disorder (p><0.001) independently predicted worse functioning in the multivariate model. Finally, the overall prevalence of significant functional impairment was 76% in the bipolar disorder group, 65% in the depression group and 25% in the control group (p><0.001). >

Conclusion

Understanding the functional impairment associated with bipolar disorder only in terms of "residual" symptoms is likely to be hindering the development of interventions aimed specifically at the functional impairment.

POSTERS

Prodromal symptoms of bipolar disorder

Authors: Rabaa Jomli, U Ouali, A Ouertani, I Farhat, Y Zgueb, F Nacef

Psychiatric hospital, Manouba 2010, Tunisia

rabaa.jomli@yahoo.fr

Objective

The aim of our study was to determine the different prodromal manifestations of bipolar disorder in a sample of young patients admitted for the first time for a mood episode

Method

We conducted a retrospective study from clinical files of all patients aged 20 years or less at the time of their first admission to our psychiatric department. Included were all patients admitted between January 2009 and December 2011 and who received a diagnosis of Bipolar I disorder according to DSM IV. We defined sociodemographic, clinical and therapeutic characteristics of these patients. Particular attention was paid to manifestations during the premorbid and the prodromal period which were reconstituted with the help of members of the family.

Results

A total number of 36 patients were admitted during the period of the study, 14 female and 22 male patients. 35% of patients had a family history of mood disorders. Mean age at first contact with mental health service providers was 20 years, and mean age of onset of bipolar disorder was 18 years. The main prodromal signs and symptoms in our sample were: a decline in academic performance (55.6%), substance abuse (36.1%), conduct disorders (33.3%), anxiety disorders (25%) and somatic complaints (13.9%). The first mood episode was of manic polarity in 75% of our patients and required admission to a psychiatric department in 91% of our patients. The high percentage of hospital admissions for a manic episode might be explained by the frequency of disruptive behavior associated to this condition whereas depressive episodes seem to be more tolerated by family members.

Conclusion

Prodromal symptoms of Bipolar disorder seem to be non specific. However, they might be an indication to treatment, often Psychotherapy. In individuals with high genetic risk of Bipolar disorder, in addition to punctual treatment, a more structured follow-up should be proposed.

Rates and predictors of rehospitalization after the first lifetime hospitalizations for manic or mixed episode . A naturalistic study in Spanish sample of Bipolar I inpatients

Management of resistant paediatric bipolar disorder: a case report

Authors: Sami Othman, Fatma Charfi, Zeineb Abbes, Soumya Halayem, Asma Bouden, Ahlem Belhadj, Mohamed Bechir Halayem

Private adress : Residence les orangers, Immeuble Dalia 4, appart 121, PB 2010,La Manouba Tunisia

Professional adress : service de pédopsychiatrie, RAZI Hospital, PB 2010, La Manouba, Tunisia

sami.othman1@yahoo.fr

Objective

Describe the management of a case of resistant bipolar disorder in a adolescent aged 14 years

Method

A case report of a resistant biolar disorder added to a literature review conducted using medline and the following keywords: bipolar disorder, guidelines, evidence based, practice parameters, recommendation, consensus, assessement, diagnosis, treatement, paediatric, child, adolescent

Results

We report the case of an adolescent aged 14years followed at the department of child and adolescent psychiatry at razi hospital in tunis since the age of 11. In three years she was hospitalized 12 times and received - different associations of antipsychotics (risperidone, olanzapine, quetiapine, and haloperidol) and mood stabilizers (lithium, valroique acid, and carbamazepine). The diagnosis of resistant bipolar disorder was retained and the patient is receiving 400mg of clozapine daily. During the last 6 months we noted an amelioration of psychotic symptoms and a stabilisation of her mood.

Conclusion

This presntation confirms the difficulties of diagosis of the early onset bipolar disorder which seems to be a resistant disorder requiring specific management

Early onset biolar disorder: about a Tunisian sample

Authors: Sami Othman, Fatma Charfi, Soumya Halayem, Zeineb Abbes, Ahlem Belhadj,Asma Bouden, Mohamed Bechir Halayem

Private adress: Residence les orangers, Immeuble Dalia 4, appart 121, PB 2010,La Manouba Tunisia

Professional adress : service de pédopsychiatrie, RAZI Hospital, PB 2010, La Manouba, Tunisia

sami.othman1@yahoo.fr

Objective

The purpose of this work is to try to specify the clinical, evolutionary and therapeutic characteristics of early onset bipolar disorder in a Tunisian sample of young people hospitalized at Razi Hospital in Tunis, Tunisia

Method

It is about a cross-sectional study realised in the department of child and the adolescent psychiatry at the Razi hospital in Tunis during the period from 2003 to 2009. 27 patients were included in this study. They were aged between 12 and 16 years. To assess the bipolar condition, we used the DSM-IV criteria and the KSADS.

Results

13 girls and 14 boys were included in this study. The mean

age of these subjects at their first hospitalization was 14.33 years. The mean duration of their follow-up was 28 months (6 to 72 months). 26 was diagnosed bipolar I subtype and only one case was diagnosed bipolar II subtype. First episodes had an acute onset characterized by psychotic features, irritability, hyperactivity, substance abuse. The diagnoses at their first hospitalization were very heterogeneous: 74 % manic episode, 22% major depression and 4% schizophreniform disorder. A family history of mood disorder was found in 37% and family and a history of schizophrenia was found in 22% of cases

Conclusion

Many authors underline the frequency of atypical or "erroneous initial diagnoses" such as schizophrenia, ADHD, borderline disorder and conduct disorder. Vigilance is still required in atypical affective manifestations in children because some recent longitudinal studies have noted the trend towards narrow spectrum of bipolar disorder with initially a table of non specified bipolar disorder. We underlined the need to properly evaluate mood in children and adolescents, particularly during psychotic episodes.

Atypical prodromal onset in affective disorders

Authors: Giulia Serra1, Giovanni Manfredi1,2, Gianni Faedda3, Lavinia De Chiara1, Gabriele Sani1,2, Alexia Koukopoulos1,2, Athanasios Koukopoulos2, Paolo Girardi1,2

1NESMOS Department, La Sapienza University, Rome, 2Centro Lucio Bini, Roma

3Centro Lucio Bini, New York , Viale Pinturicchio, 79 Roma, Italy

giuliaserra@gmail.com

Objective

Often the onset of affective disorders is not an affective episode but a different psychopathological manifestation. It has been shown that it takes on average 12 years from the first psychopathological manifestation to the first diagnosis of bipolar disorder (1). Early detection of recurrent mood disorders is an important issue to avoid ineffective and harmful treatment and to early commence prophylaxis in order to ensure a better prognosis (2). The goal of our study is to evaluate these atypical prodromal manifestations.

Method

We reviewed the clinical history of 304 outpatients diagnosed with an affective disorder (138 men and 166 women), followed at the Centro Lucio Bini in Rome. Our sample was constituted by 82 BPI, 96 BPII, 34 cyclothymic and 92 unipolar depressive patients. We investigated how many of these patients had an onset other than affective in their clinical history and we measured the interval between the atypical onset and the first affective episode.

Results

Among BPI patients, 26 of 82 (32%) had an atypical onset: 6 patients suffered from anxiety disorder at onset, 6 from substance abuse, 4 from eating disorder, 3 from obsessive compulsive disorder, 2 from panic disorder and the remaining had non-specific psychopathological traits such as insomnia, aggressiveness, cognitive disorders, hyperkinesias or fainting.

Among the BPII patients, 48 of 96 (50%) had an atypical onset: 11 patients suffered from panic disorder at their onset, 8 from eating disorder, 7 from substance abuse, 5 from anxiety disorder, 5 from obsessive compulsive disorder, 2 from social phobia, 2 from impulse dyscontrol syndrome (kleptomania or gambling), 2 had accentuated cyclothymic and irritable temperamental traits, others showed non-specific psychopathological features such as jealousy, dysphoria, flights, school difficulties.

Among cyclothymic patients, the majority (25 of 34, 73%) had a non-affective syndrome at their psychopathological onset. Five suffered from panic disorder at onset, 3 from eating disorder, 2 from obsessive-compulsive disorder, 2 from insomnia, 2 from nausea, 2 from neurovegetative symptoms (sweating), 1 from irritability and 1 from premenstrual syndrome.

Among unipolar patients, 46 of 96 (50%) had an atypical onset. Twelve patients suffered from anxiety disorder, 8 from panic disorder, 7 from substance abuse, 6 from obsessive compulsive disorder, 3 from insomnia, 2 from nausea, 1 from headache, 1 from stutter and 1 from jealousy.

The time interval between the atypical onset and the first affective episode is on average 6.35 years for BPI patients, 11.25 years for BPII patients, 9.9 years for cyclothymic patients and 13.76 for unipolar patients, respectively.

Conclusion

About 49% (145 of 304) of patients had an atypical syndrome at their onset (53% of men and 47% of women). Our results strongly suggest that diagnosis based only on a cross-sectional evaluation of onset symptoms appears to be insufficient for early detection of bipolar disorder and it must be supplied by further evaluation. A biographic approach to the patient, a thorough anamnesis of the pre-morbid temperament (3,4), personality and associated antecedents (5), family history, longitudinal observation of the course of illness, should be considered in order to make a correct diagnosis.

POSTERS

CLINICAL TREATMENT/MANAGEMENT

Changes in treatment patterns of bipolar disorder with mood stabilisers

Authors: Karanti Alina, Kardell M, Lundberg U and Landén M

Sahlgrenska Academy at Gothenburg University, Institute for Neuroscience and Physiology, Section of Psychiatry and Neurochemistry, Sweden, alina.karanti@vgregion.se

Objective

Most of the guidelines for bipolar disorder suggest first-line treatment with the mood stabiliser lithium. Among other options are valproate, olanzapine, quetiapine and lamotrigine. Little is known about the adherence to these guidelines in the clinical setting. Also, it is not known whether changes in prescription pattern might occur that are not related to changes in guidelines. To shed light on these issues, we analysed recent prescription trends in mood stabilisers for the treatment of bipolar disorder in Sweden.

Method

Sweden holds a national Quality Assurance register for the treatment of bipolar syndrome: BipoläR. The registration in BipoläR is voluntary and the QA-register includes patients with bipolar disorder type I, II, NOS and schizoaffective disorder of manic type. The baseline registration contains a detailed description of patient profile including, e.g., diagnostic subtype, age of onset, family history. The annual follow-ups contain treatment, adverse effects, several outcome variables and information on somatic comorbidity. By 2011, there were 7358 baseline registrations of patients with bipolar disorder who were analysed to examine the patterns in prescription of mood stabilisers.

Results

In 2007, 63% of women with bipolar disorder were prescribed lithium and 17% lamotrigine, while in 2011 39% of women had lithium and 37% lamotrigine. In men, lithium went from 71% to 50% and lamotrigine increased from 15% to 23% during the same period. About 10 percent more men than women are prescribed lithium. The prescription of other mood stabilisers including valproate as well as combination treatment with mood stabilisers did not change during these years. When only patients with Bipolar disorder type I are considered, the prescription of lithium has decreased significantly from 74% to 61% between 2007 and 2011. With respect to lamotrigine prescriptions, there has been no change for bipolar I subtype, but in the bipolar II group lamotrigine has increased significantly from 26% in 2007 to 47% in 2011.

Conclusion

Between 2007 and 2011, the lithium prescriptions have decreased whereas the lamotrigine prescriptions have increased in Sweden. No substantial changes in relevant treatment guidelines during the years 2007 to 2011 have been made to justify these changes in prescription patterns. However, both American Psychiatric Association Guidelines (APA) in 2002 and Texas Medical Algorithms Project (TMAP) in 2005, suggest lamotrigine as first line treatment of bipolar depression, which might have contributed to the increased prescription of lamotrigine. There has been much discussion in Sweden about the role of lamotrigine in treating affect lability in a broader meaning including conditions with "soft" bipolar spectrum signs, which can eventually explain the clinicians' increasing tendency to prescribe lamotrigine. The role of marketing promotion by the pharmaceutical companies and influence on the clinicians should also be considered. Lithium is not promoted nowadays of pharmaceutical companies and therefore there is a less exposure of clinicians to data and evidence that support the use of lithium; that fact can be a risk for altered prescription patterns and attitude concerning lithium.

Efficacy and tolerability of Quetiapine XR in Bipolar affective disorder

Name: Roxana Andrei Str. Anastasie Panu, Nr. 15, Bl. Ghica-Voda, Sc. 2C, Etj. 7, Ap. 28, Iasi, Romania, cod 700021, Romania, roxana_cam_17@yahoo.com

Objective

The present study evaluated the efficacy and tolerability of quetiapine monotherapy in patients with bipolar disorder in a clinical practice setting.

Method

This 12 week, prospective, open clinical study in 80 adults with bipolar disorder treated in a psychiatric hospital compared outcomes in patients treated with quetiapine extended release (XR) 300 mg/day or 600 mg/day (N=40), evening dosing, once daily. Primary efficacy was based on the Montgomery Åsberg Depression Rating Scale (MADRS) and the Young Mania Rating Scale (YMRS). Tolerability was assessed using the Udvalg for Kliniske Undersogelser (UKU) side-effects scale.

Results

MADRS total score decreased from 34 at baseline to 19 at week 4 in the 600 mg/day group (P

<0.001) and from 33 to 22 in the 300 mg/day group (P><0.001) and decreased further to 4 vs. 7 points at week 12. Similar results were found for the YMRS. Remission rate (MADRS ><10, respectively YMRS ><12) was significantly greater (P = 0.011, respectively P = 0.010) with quetiapine XR 600 mg/day than with 300 mg/day at week 12. Quetiapine XR was generally well tolerated with 10% of the patients in the 600 mg/day group and 7.5% of the patients in the 300 mg/day group reporting adverse events on the UKU scale. >

Conclusion

Both doses of quetiapine XR were efficacious and well tolerated with a stronger improvement in MADRS and YMRS for patients receiving 600 mg/day starting at week 4 of treatment.

POSTERS

Effects of asenapine on manic and depressive symptoms in bipolar I patients with mixed episodes: results from post-hoc analyses

Author: Jean Azorin JM, Sapin C, Weiller E and Hansen K
Hospital Ste Marguerite, Marseille, France
Jean-michelRoch.AZORIN@ap-hm.fr

Objective

Asenapine demonstrated superiority over placebo in bipolar I disorder patients experiencing acute manic or mixed episodes in two 3-week, randomised, placebo- and olanzapine-controlled trials (1, 2), and comparable efficacy to olanzapine in a 9-week non-inferiority extension trial (3). We assessed the effects of asenapine on manic and depressive symptoms in patients experiencing manic episodes with depressive symptoms

Method

Post-hoc analyses on pooled data were conducted. A total of 977 patients were randomised in the original trials to flexible-dose asenapine (10 or 5mg twice daily), placebo, or oral olanzapine (5-20mg once daily) for 3 weeks. In the intent-to-treat population, 295 patients had a DSM-IV-TR mixed episode (placebo: 66, olanzapine: 122 and asenapine: 107). Of these, 102 patients (olanzapine: 56; asenapine: 46) entered the 9-week extension study. Changes from baseline in Young Mania Rating Scale (YMRS) and Montgomery-Åsberg Depression Rating Scale (MADRS) total and individual item scores were analysed through analysis of covariance models with treatment and centre as factors and baseline value as covariate on observed cases.

Results

Decreases in YMRS and MADRS total scores were significantly greater with asenapine (YMRS: -15.0; MADRS: -8.2) versus placebo (YMRS: -11.5; MADRS: -4.5) at week 3; differences between olanzapine (YMRS: -13.3; MADRS: -6.5) and placebo were not statistically different. The effect of asenapine on manic and depressive symptoms was maintained over the extension trial (week 12, YMRS: -22.4; MADRS: -11.9); non-statistically different from olanzapine (YMRS: -20.2; MADRS: -7.9). At week 3, asenapine was significantly superior to placebo in improving the individual item scores for 'inability to feel', 'elevated mood', 'sexual interest', 'language/ thought disorders','reduced appetite' and 'inner tension'; asenapine was significantly superior to olanzapine in improving 'inner tension'. At week 12, asenapine was significantly superior to olanzapine in improving the individual item scores for 'disruptive/ aggressive behaviour', 'appearance' and 'inability to feel'.

Conclusion

In these post-hoc analyses asenapine had significantly better treatment effects for both manic and depressive symptoms than placebo, and more pronounced effects than olanzapine in some symptom domains.

Additional Information

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Current status and management of patients with bipolar disorder in France in 2011

Author: Sylvie Coulomb5, Vincent Camus1, Philippe Courtet2, David Gourion3, Pierre Michel Llorca4, Michael Lukaziewicz5

Affiliations:

1 - Clinique psychiatrique universitaire, CHRU de Tours, INSERM U930 & Université François Rabelais de Tours, boulevard Tonnelé, 37044 Tours Cedex 01, France

2 - Département d'Urgence & Post Urgence Psychiatrique, CHU de Montpellier, Hôpital Lapeyronie, 34295 Montpellier cedex 5, France

3 - 17 rue des Marronniers, 75016 Paris, France

4 - Service de psychiatrie, CHU de Clermont-Ferrand, 63000 Clermont-Ferrand, France

5 - Laboratoire AstraZeneca, 1 place Louis Renault, 92844 Rueil-Malmaison cedex

AstraZeneca, 1 place Louis Renault, 92844 Rueil-Malmaison Cedex, France
sylvie.coulomb@astrazeneca.com

Objective

To assess the characteristics of patients suffering from bipolar disorder (BD) in different types of care settings and to compare care procedures.

Method

Quantitative survey conducted between December 2010 and February 2011, among 439 psychiatrists, on 2529 patients (inpatients, n=319; outpatients from community mental health team, n=1090; outpatients from psychiatrist in private practice, n=1020).

Results

Among the studied patients population (mean age: 47 years; women, 58%), BD is distributed as follows: type I BD, 56%; type II, 40% BD; other types of BD, 4%. Rapid cycing subtype is, 10% of the population. The prevalence of somatic and psychiatric comorbidities is high (anxiety disorders, 48%; abuse and dependence on toxic substances, 17 and 10% respectively). The risk of suicide, when assessed, is 6%. In about half of the patients (48%), the polarity of the initial bipolar episode was found to be of depressive type (versus 39% for the manic/hypomanic type). Outpatients are globally less dependent in AVQ and show better ability in self-management of their disease's symptoms and treatment, whereas the social and professional consequences and impact is higher in inpatients.

Based on the psychiatrist's declarations, 39% of the patients are symptom-free at the time of the last consultation, 38% are in a stabilized phase but with residual symptoms, 19% present either a manic or depressive acute BP episode, and 4% are in a mixed-state. The symptomatic patients (61%) show mostly to suffer from depressive symptoms that are considered either acute symptoms (in patients with a depressive episode) or residual symptoms (in patients in the intercurrent phase). The predominant depressive polarity is equally observed in both hospitalized and outpatients.

POSTERS

The pharmacological treatment of BD includes polytherapy in 73% of the patients. In the manic episodes (n=126), patients are treated with a Mood Stabilizer (MS, 56%) alone or in association with atypical antipsychotic (AAP, 52%). Patients in depressive episodes (n=342), receive an antidepressant drug associated with a MS or an AAP (70%). In symptom-free or symptomatic intercurrent periods (n=1943), patients are treated with MS (49-58%) or AAP (37-49%), alone or in association.

Conclusion

The BD patients evaluated in our survey are in majority diagnosed with type I BD, associated with high rate of comorbidity. Among the symptomatic patients, the most prevalent symptoms, either acute or residual, are of the depressive type. In a vast majority of cases, whatever their clinical status, patients with BD receive polytherapy.

Treatment adherence is improved in patients affected by schizophrenia or bipolar disorder switching from quetiapine IR to quetiapine XR

Author: Luca Degli Esposti, Flore La Tour, Claudio Mencacci, Gino Montagnani, Carlotta Pasina, Diego Sangiorgi, Edoardo Spina. Health, Economics, and Outcomes Research, CliCon Srl, Via Salara 36, Ravenna I-48121, Italy susan.parker@fishawack.com

Objective

Schizophrenia and bipolar disorder (BD) are serious psychiatric conditions that are commonly treated with antipsychotic medications. Non-adherence to treatment can increase the risk of relapse; therefore, improving this aspect may allow a more efficient use of healthcare resources for these patients. The Italian Burden of Illness in Schizophrenia and BD (IBIS) study aimed to describe pharmaco-utilisation of antipsychotic treatment in schizophrenia and BD patients. A secondary study objective was to assess levels of treatment adherence for patients switching from quetiapine immediate release (QTP-IR) to quetiapine extended release (QTP-XR). Here we present interim analyses on treatment adherence from administrative databases in 6 of 20 Italian Local Health Units included in the study.

Method

This was a multicentre, retrospective, observational cohort study (NCT01392482). All patients were aged ≥18 years and had been diagnosed with schizophrenia or BD according to ICD9-10 codes. A subgroup of patients was included for analysis of treatment adherence levels when they switched from the antipsychotic medication QTP-IR to QTP-XR during the adherence enrolment period of 1 January 2009 to 30 June 2010. Data were collected for 6 months before the switch (IR period) and 6 months after the switch (XR period). A control group that received QTP-IR was matched to the switching group based on diagnosis, gender and age, for analysis. Treatment adherence ±SD was estimated using the Catalan method[1], which calculated the total number of days' supply of medication dispensed within each episode divided by the total length of the interval, multiplied by 100.

Results

Of the 6817 patients in the study population, 213 switched medication from QTP-IR to QTP-XR (86 with schizophrenia, 127 with BD). The mean ±SD dose of QTP-IR received was 488 ±297 mg in patients with schizophrenia, and 425 ±234 mg in patients with BD.

Upon switching to QTP-XR, the mean ±SD dose was 454 ±255 mg in patients with schizophrenia, and 462 ±272 mg in BD patients. Overall, there was an increase in treatment adherence after switching (from 44.2 ±24.7% to 62.6 ±26.5% [p=0.009]). For patients with schizophrenia, adherence increased from 48.3 ±23.5% to 56.5 ±27.0% (p=0.125), and for patients with BD adherence increased from 41.5 ±25.3% to 66.7 ±25.4% (p=0.036). In the matched control group, smaller increases in adherence were observed both in the overall population (51.8 ±22.5% to 53.4 ±26.4% [p=0.493]) and when stratified by disease (55.7 ±22.2% to 56.6 ±25.7% [p=0.816] in patients with schizophrenia and 49.2 ±22.4% to 51.3 ±26.8% [p=0.479] in patients with BD).

Conclusion

These interim analyses suggest that treatment adherence improved in patients with schizophrenia and BD after switching from QTP-IR to QTP-XR.

Additional Information

Study funded by AstraZeneca; Clinical Trials Registry: NCT01392482.

Catalan VS, Lelorier J. Predictors of long-term persistence on statins in a subsidized clinical population. Value in Health 2000; 3: 417–25.

There is a high level of variability in antipsychotic treatment for patients affected by schizophrenia or bipolar disorder

Author: Luca Degli Esposti, Flore La Tour, Claudio Mencacci, Gino Montagnani, Carlotta Pasina, Diego Sangiorgi, Edoardo Spina. Health, Economics, and Outcomes Research, CliCon Srl, Via Salara 36, I-48121, Ravenna. Italy, susan.parker@fishawack.com

Objective

Schizophrenia and bipolar disorder (BD) are serious psychiatric disorders that are commonly treated with antipsychotic medications, either alone or in combination. Little is known about which combinations of antipsychotics are frequently used in clinical practice and whether standardised treatment guidelines may be appropriate. The Italian Burden of Illness in Schizophrenia and BD (IBIS) study aims to describe the pharmaco-utilisation of antipsychotic and concomitant medications for patients affected by schizophrenia and BD in order to evaluate the level of treatment variability.

Method

This was a multicentre, retrospective, observational cohort study (NCT01392482). The preliminary analyses shown are based on data from administrative databases of 6 of 20 Italian Local Health Units included in the study, collected

between 1 January 2008 and 31 December 2010. All patients were ≥18 years old, had been diagnosed with schizophrenia or BD according to ICD9-10 codes and were prescribed antipsychotics during the study period. Patients were retrospectively followed for 1 year from index date (first prescription of antipsychotics).

Results

In total, 6817 patients (4097 with schizophrenia, 2720 with BD) were included in the study population. In patients with schizophrenia, 65.5% were treated with a single antipsychotic, and 34.5% were prescribed more than one antipsychotic during the study period. A notable number of patients with schizophrenia, receiving either single or multiple antipsychotics, respectively, also received mood stabilisers (13.5%, 21.3%), antidepressants (15.9%, 17.5%) or both (5.5%, 15.2%). In patients with BD, 66.7% were prescribed a single antipsychotic and 33.3% multiple antipsychotics. Concomitant medications were more frequently prescribed in patients with BD than in those with schizophrenia; BD patients receiving single and multiple antipsychotics, respectively, also received mood stabilisers (31.0%, 27.0%), antidepressants (14.8%, 13.6%) or both (34.9%, 48.5%). Among patients receiving a single antipsychotic, more than 20 different antipsychotics were used. The most frequently prescribed medications in patients receiving a single antipsychotic were: olanzapine (26.3%), risperidone (18.2%) and clozapine (17.1%) in patients with schizophrenia; and olanzapine (37.9%), quetiapine (20.2%) and risperidone (10.5%) in patients with BD. In patients receiving multiple antipsychotics, 333 different combinations were used. The five most frequently used antipsychotic combinations for schizophrenia were: haloperidol + olanzapine (9.0%); haloperidol + quetiapine (4.5%); clozapine + haloperidol (4.2%); olanzapine + risperidone (2.7%); and aripiprazole + clozapine (2.3%). The five most common antipsychotic combinations for BD were: olanzapine + quetiapine (6.9%); haloperidol + olanzapine (5.3%); aripiprazole + olanzapine (5.0%); haloperidol + quetiapine (4.2%); and chlorpromazine + olanzapine (4.1%).

Conclusion

These interim results show a high level of treatment variability in schizophrenia and BD patients, confirming the need for personalised treatment pathways based on patient characteristics in the management of patients with schizophrenia and BD.

Additional Information

Study funded by AstraZeneca; Clinical Trials Registry: NCT01392482.

Impulsivity in Anxiety Disorders: the role of affective temperaments and current comorbid mood symptomatology

Author: Alessandra Del Carlo1, Marzia Benvenuti1, Federica Dima1, Daniela Cesari1, Salvatore Rizzato1, Francesca Casalini1, Liliana Dell'Osso1, Giulio Perugi1,2
Department of Psychiatry, Neurobiology, Pharmacology, Biotechnology, University of Pisa, Pisa, Italy - via Roma 67, Italy, 1 Department of Psychiatry University of Pisa, Pisa, Italy;
2 Institute of Behavioural Sciences G. De Lisio, Pisa, Italy, alessandra.delcarlo@gmail.com

Objective

Higher level of impulsivity has been reported in patients with anxiety disorders than in healthy controls. The presence of both trait and state impulsivity was associated with the presence of comorbid cyclothymic disorder. In the present study we explore the relationship among impulsivity and co-morbid cyclothymia, affective temperaments and current mood symptomatology in patients with anxiety disorders.

Method

A sample including 78 subjects with anxiety disorder(s) underwent a diagnostic and clinical evaluation by the Mini Neuropsychiatric Interview (M.I.N.I), Bach-Raephelsen Depression and Mania Scale (BRDMS), the State-Trait Anxiety Inventory (STAI), the Hypomania Check List (HCL-32), the Clinical Global Impression (CGI), the Brief Questionnaire for the Affective and Anxious Temperament Evaluation of Memphis, Pisa, Paris and San Diego-35 items (Brief-TEMPS-35). A psychometric and a neuro-cognitive evaluation of impulsivity were conducted by the Barratt Impulsiveness Scale (BIS) and the Immediate and Delayed Memory Task (IMT\DMT). The initial sample of patients with anxiety disorders was then subdivided into two subgroups depending on the presence of comorbid cyclothymia (Cyclo+, n=26 and Cyclo-, n=52). We compared symptomatological, temperamental, personological and impulsivity measures in Cyclo+ and Cyclo-. We also correlate BIS, IMT and DMT scores with Brief-TEMPS-35 subscales and BRDMS scores.

Results

The comparison between Cyclo+, Cyclo- showed that Cyclo+ are the most impulsive subjects in all the investigated measures. Correlational analyses showed that cyclothymic and irritable temperaments were significantly related to trait impulsivity (measured by BIS), while severity of (hypo)manic symptomatology was significantly related to state impulsivity (measured by IMT/DMT).

Conclusion

In our sample of cyclothymic anxious patients, trait impulsivity could be attributed to the temperamental disposition, while state impulsivity seems to be related to the presence of current hypomanic symptomatology.

POSTERS

Rabbit syndrome due to olanzapine in a patient with Bipolar disorder

Author: Dr.Ganesh Kunjithapatham, Dr.Chieh-his Jessie Chiu

Consultant Psychiatrist , Institute of mental health, 10 BUANGKOK VIEW

SINGAPORE, 539747, Singapore, ganesh1970@gmail.com

Objective

There are very few case reports in the literature on rabbit syndrome due to olanzapine and other atypical antipsychotic agents.we describe a patient who developed this syndrome with olanzapine and it improved with reduction of dose and with introduction of antcholinergics (benzhexol).

Method

32 year old lady with learning disablity and bipolar depression(Severe Depressive disorder with psychotic symptoms). She developed rabbit syndrome after the dose of olanzapine was increased to 15mg.Symptoms improved after the reduction of dosage to 5mg and with the introduction of anticholinergic agents

Results

Patient is currently receiving Olanzapine 5mg/day and Mirtazepine 30mg/day and the extrapyramidal symptoms have abated.

Conclusion

This case adds on to the existing literature of rabbit syndrome secondary to use of atypical antipsychotic drugs.

Additional Information

There is no financial conflict of interest.

Comparing second generation antipsychotics metabolic side effects in bipolar disorders and schizophrenia: a meta-analysis

Authors: Hoda Moteshafi, Emmanuel Stip

7331, rue Hochelaga, Montréal (Québec) H1N 3V2, Canada, h.moteshafi@gmail.com

Objective

Second generation antipsychotics (SGAs) are extensively prescribed for a number of psychiatric disorders including schizophrenia, bipolar mania, and unipolar and bipolar depression. Second generation antipsychotics have been linked to several forms of morbidity, including obesity, hyperlipidemia, and type-2 diabetes mellitus, which predict metabolic syndrome, cardiovascular morbidity, and malignancy. The expanded use of SGAs in psychiatry suggests a need to investigate whether there is a difference in the incidence and severity of side effects related to diagnosis. The aim of the present meta-analysis is to separately examine SGA-induced metabolic side effects in patients with schizophrenia and bipolar disorders.

Method

A comprehensive literature search was conducted to identify studies reporting side effects of the five most commonly prescribed SGAs (aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone) in the treatment of schizophrenia or bipolar disorders. A search of computerized literature databases (PubMed, PsycINFO, EMBASE, and clinicaltrials.gov) was conducted. 113 studies (19150 patients) that contain metabolic side effects and address the SGAs monotherapy treatment of adults were included in the analysis. Effect size estimates were calculated from sample size, mean, and standard deviations for each group of patients. Tolerability outcomes were separately calculated for schizophrenia and bipolar disorders patients and were compared together. Meta-regression and sub-analyses were used to assess the influence of treatment duration, dose, age, and sex ratio on tolerability outcome.

Results

Tolerability outcomes show that olanzapine and quetiapine were associated with weight gain, increase in blood triglyceride, LDL, glucose, and total cholesterol levels in both schizophrenia and bipolar disorders patients. Moreover, all metabolic changes were higher in the schizophrenia group compared to the bipolar disorder group, even though some of these differences were not statistically significant. Olanzapine treatment led to significantly higher weight gain in schizophrenia patients than in bipolar disorders patients (p=0.020). In addition, by quetiapine treatment blood cholesterol and LDL levels were significantly higher in the schizophrenia group, relative to the bipolar disorders group (p=0.000).

Conclusion

Our results suggest that schizophrenia patients may be more vulnerable to some SGA-induced metabolic disturbances. The findings may be explained by considering the fact that in addition to genetic disposition for metabolic syndrome in schizophrenia patients, they have an especially high incidence of lifestyle risk factors for cardiovascular diseases such as poor diet, lack of exercise, stress and smoking. It might be that an antipsychotic induces severity of side effect according to the phenotype.

Clozapine in treatment-resistant bipolar disorder: a case series

Author: U. Ouali (1) , R. Jomli (2) , A. Ouertani (2) , J. Masmoudi (1), F. Nacef (2), A. Jaoua

(1): Hedi-Chaker Hospital, Department Psychiatry A, Sfax (Tunisia)

(2): Razi Hospital, Department Psychiatry A, Manouba (Tunisia)5 rue Astarte, 2016 Carthage, Tunisia

uta.ouali@gmail.com

Objective

Numerous studies suggest Clozapine to be effective in treatment-resistant manic and mixed episodes. For this indication, Clozapine has been introduced into major treatment guidelines of bipolar disorder. We report a series of eight patients with Bipolar I disorder receiving Clozapine (add-on therapy) for treatment resistance. The aim of this study is to define the demographic and clinical parameters of the sample, to evaluate treatment-response and adverse effects of Clozapine and to describe compliance with treatment after the introduction of Clozapine.

POSTERS

Method

We conducted a retrospective, observational study of eight patients with Bipolar I disorder as defined by DSM IV criteria who received Clozapine for treatment-resistant manic or mixed states. All of the described patients were male. Average duration of bipolar illness before introduction of Clozapine was 11.9 years, and average duration of follow up after introduction of Clozapine was 3.6 years. Seven out of eight patients had been hospitalized during instauration of Clozapine therapy. Clinical response was measured through continued clinical assessment.

Results

The patients of our sample had a predominance of manic or mixed episodes, four out of eight patients presenting with unipolar mania. Five patients suffered from psychotic mood episodes. Number and severity of manic and mixed episodes decreased significantly for all patients after introduction of Clozapine. Three patients showed important overall improvement with return to previous levels of functioning. Four patients demonstrated moderate improvement and one patient had minimal improvement in mood stabilization and functioning. Mean effective Clozapine-dose was 284.4 mg/day. Most frequently observed adverse effects were weight gain (five patients) and sedation (three patients). One patient developed type II diabetes, and one presented with transient thrombopenia. Difficulties with compliance to treatment were encountered in three patients. Non-adherence to treatment was not only due to adverse effects of treatment but also to a lack in insight.

Conclusion

This case series underlines the efficacy of Clozapine as add-on medication in treatment resistant bipolar disorder. It shows that Clozapine can be effective at relatively low doses even in patients with psychotic bipolar disorder and for a significant period of time. However, patients should be closely monitored for adverse effects, particularly weight gain which was frequent in our sample.

Management of Metabolic effects of antipsychotics during pregnancy

Authors: Maria Rocha, Odete Santos (1); Isabel Rocha (2)

Rua do Passal 114, 4430-875, Avintes, Vila Nova de Gaia, Portugal

(1) Nutricionist in Magalhães Lemos Hospital

(2) Psychiatrist in Póvoa do Varzim/ Vila do Conde Hospital Center and Magalhães Lemos Hospital

mroca@sapo.pt

Objective

Based on a case report of a psychotic 26 year old childbearing patient, the authors propose to review the use of medication during pregnancy in bipolar and psychotic disorders, and also, the nutricional aproach needed to face metabolic side effects of atypical antipsychotics, since it lacks data concerning this issue.

Method

A literature research and review was undertaken for the use of mood stabilizers and antipsychotics during pregancy, trough Medline database until current data. Clinical data were reported based on clinical charts and clinical interview.

Results

Mood stabilizers and antipsychotics are estabilished and effective treatments that assist in the prevention of relapse in bipolar and schizophrenic patients, and may also be used in the prevention of puerperal psychosis. Optimal antenatal management of women envolves close liaision between the treating Psychiatrist, Obstectrics, maternal child health nurses and neonatal Pediatricians. Unfortunately it is estimated that more than 50% of pregancies are not planned and many women do not realise they are pregnant until the end of the first trimester.The metabolic side effects from atypical antipsychotics points out the need for a nutricional aproach and consultation troughout the pregnancy due to the increased risk of diabetogenic pregnants and large-for-date babies. In the case of this patient, with a Schizoafective disorder, treatment was mantained with Olanzapine. The patient was engaged in dietary measures and exercise and followed in nuticional consultation in a colaborative care with Psychiatry. The outcome was favourable and no metabolic sindrome was found during pregnancy and patient delivered a normal weight baby.

Conclusion

Decision regarding psychotropic treatment of pregnant women with bipolar and psychotic disorders requires thorough knowlegde of available reproductive safety of drugs, awarness of the dangers of maternal relapse, and acceptance of the fact that no decision is risk free.

This patient was mantained on Olanzapine due to high risk of relapse. Metabolic side effects were minimised trough nutricional colaborative care. More case reports/ investigation are needed relating approach of the metabolic side effects of atypical antipsychotics during pregnancy.

Asenapine: the first tetracyclic antipsychotic for the treatment of schizophrenia and bipolar i disorder

Authors: Mohammed Shahid PRECLIN-2D Ltd. 36 Torridon Avenue. Dumbreck. Glasgow

United Kingdom, mo.shahid@preclin-2d.com

Objective

The development of second generation antipsychotics (SGAs) was an important milestone in the treatment of psychiatric disorders. SGAs were originally defined by a reduced risk of extra-pyramidal symptoms. However, with the recent introduction of new drugs the SGAs have become a heterogeneous and perhaps poorly defined group. New compounds show significant differences in chemistry and pharmacology as well as clinical properties, prompting the need for a re-appraisal. One such new compound is asenapine, an antipsychotic indicated for the treatment of schizophrenia and manic/mixed episodes of bipolar I disorder in adults in the US; in the EU it is approved for the treatment of moderate to severe manic episodes associated with bipolar I disorder in adults. We will present an evaluation of the preclinical profile of asenapine to assess its position within the current group of antipsychotics.

Method

The preclinical properties of asenapine have been reviewed and compared to other antipsychotics. This includes data

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from studies on receptor binding affinities and functional characteristics, in vivo electrophysiological and neurochemical effects, and potential clinical activity in animal models.

Results

Asenapine is the only tetracyclic antipsychotic drug. It has a unique human receptor signature, and a functional activity profile that differs from other antipsychotics (Shahid et al., 2009). Receptor-binding and functional assays show that, in addition to a strong 5-HT2A/D2 receptor activity, asenapine has a unique combination of potent 5HT2C, 5HT6, 5HT7 serotonergic and α2 adrenergic receptor antagonist properties that may confer potential therapeutic advantages including improvements in depressive, cognitive and negative symptoms. Moreover, its modest histamine H1 receptor affinity and no appreciable activity at muscarinic receptors, suggests low potential for weight gain and metabolic deregulation, and of anticholinergic adverse effects, respectively. The electrophysiological and neurochemical effects of asenapine in rat brain are consistent with a mode of action reflecting its core receptor pharmacology (Ghanbari et al., 2009). Thus in vivo, asenapine has a broad impact on multiple neurotransmitter systems (serotonin, noradrenaline, dopamine, glutamate, and acetylcholine) at therapeutically relevant dose levels (Frɛnberg et al., 2009). Furthermore, receptor pharmacology based hypotheses for potential clinical activity were evaluated and validated in a variety of animal disease models (Marston et al., 2011; Elsworth et al., 2012). The data from these behavioural models demonstrated that asenapine has antipsychotic/antimanic, antidepressant and cognition improving properties. The antipsychotic/antimanic efficacy of asenapine has been established by clinical trials in patients (McIntyre et al., 2012). Furthermore, preliminary data from post hoc analysis of trials in mixed manic subjects has provided evidence for efficacy against depressive symptoms (Szegedi et al., 2011).

Conclusion

Asenapine is the first tetracyclic antipsychotic. It has a unique human receptor binding profile and a distinctive mechanism of action compared to other antipsychotics. These properties may confer beneficial impact in the treatment of both schizophrenia and bipolar I disorder.

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Drug treatment of bipolar II depression during and after pregnancy

Author: Verinder Sharma, Christina Sommerdyk, Bin Xie, Karen Campbell

Regional Mental Health Care- London, Mood Disorders, 850 Highbury Ave.

London ON N6A 4H1, Canada

vsharma@uwo.ca

Objective

The objective of this study was to evaluate the pharmacotherapy of bipolar II disorder during pregnancy and the postpartum period.

Method

The use of psychotropic drugs and recurrence risk during and after pregnancy was studied in a prospective, observational study of 37 women with bipolar II disorder.

Results

During pregnancy the majority of participants (54.0%) were not on any psychotropic medication, approximately one third (32%) received monotherapy, and the rest were on combination therapy. In comparison, during the postpartum period only 14% of participants were not on any psychotropic medication, approximately 35% received monotherapy, and over 50% were on combination therapy. While only 13.5% of participants were on 3 or more psychotropic drugs during pregnancy, 21.6% required 3 or more psychotropic drugs after childbirth.

Conclusion

The findings of this prospective, observational study indicate that the recurrence risk is much higher after childbirth than during pregnancy in spite of higher utilization of psychotropic drugs in the postpartum period.

Have modern treatment routines eliminated the risk of lithium uremia?

Authors: Jan Svedlund, Harald Aiff,Per-Ola Attman, Mattias Aurell, Hans Bendz, Staffan Schön

Departments of Psychiatry and Nephrology, Sahlgrenska University Hospital, Department of Clinical Sciences, Psychiatry, Lund University, Department of Internal Medicine, Ryhov County Hospital, Gothenburg, Sweden, Sahlgrenska University Hospital,

Blå Stråket 15, SE 413 45 Gothenburg, Sweden, jan.svedlund@vgregion.se

Objective

The discovery of lithium nephropathy in 1977 resulted in considerable changes of the prevailing treatment routines in order to diminish or eliminate the risk of this serious lithium treatment side effect. We can safely state that by 1980 the modern treatment principles had become widely spread all over Sweden. Therefore we chosed 1980 as a breakpoint for “old” versus “modern” lithium treatment. Our own previous studies of lithium nephropathy have shown that the risk of end-stage renal disease (ESRD) is increased sixfold among lithium patients compared to the general population (Bendz et al.2010). The increased prevalence of

ESRD was limited to patients who had started their lithium treatment in 1980 or earlier i.e. during the earlier lithium era when dosages were high and the security measures were undeveloped or even nonexistent. The purpose of the present study was to investigate whether the modern treatment principles of lithium have eliminated or reduced the risk and thus the prevalence of ESRD among lithium-treated patients.

Method

The present study covers the same two regions as our previous study. The prevalence date was December 31, 2010 and the lithium-treated population was estimated to 4,135 patients. All patients with renal replacement therapy (RRT) i.e. on dialysis or with a kidney transplant in the area who did not participate in the earlier study were asked about lithium treatment, present or past. Those who answered affirmatively were then asked for permission to review their somatic and psychiatric charts. The charts were reviewed in detail.

Results

Twenty-one patients on RRT answered affirmatively about current or past lithium treatment. We got written consent to review their charts in 19 cases. Out of these 19 patients, 17 had a history of lithium treatment according to their medical records. The role of lithium as an etiological factor for ESRD was classified according to specified criteria by two nephrologists (P-O.A & M.A) Twelve patients diagnosed with lithium nephropathy in the previous study were alive at the new prevalence point and were also included. In total, 25 patients were found to have lithium as a sole or main etiological factor. Of these, 24 patients started their lithium treatment before 1980 and one patient after. Thus, 24 cases were observed before the breakpoint in a sample of 4,135 patients (0.58%). According to our hypothesis a decrease was expected to be found among patients who started their lithium treatment after 1980. A one-sided upper 95% confidence interval for the proportion of ESRD cases from the one observed case is 0.12%, indicating at least a 4-fold decrease in the proportion of patients with lithium-induced ESRD.

Conclusion

Our preliminary findings suggest that modern treatment principles of lithium have markedly reduced, but not eliminated the risk for lithium-induced ESRD.

Renal failure caused by prophylactic lithium treatment – still a threat to the patients?

Author: Jan Svedlund, Aiff H, Attman P-O, Aurell M, Bendz H, Schön S.

Harald Aiff,Per-Ola Attman, Mattias Aurell, Hans Bendz, Staffan Schön, Jan Svedlund

Departments of Psychiatry and Nephrology, Sahlgrenska University Hospital, Department of Clinical Sciences, Psychiatry, Lund University, Department of Internal Medicine, Ryhov County Hospital,Sweden, Sahlgrenska University Hospital, Blå Stråket 15,

SE 413 45 Gothenburg, Sweden, jan.svedlund@vgregion.se

Objective

The irreversible renal damage caused by lithium treatment remained unknown until 1977 when Hansen et al. reported permanent renal damage in lithium patients. Their observations together with confirmatory studies prompted considerable changes of the treatment routines to prevent the development of permanent kidney damage. The revised routines included lowest possible, individual lithium doses and regular monitoring of plasma lithium and renal function. They were widely adopted in Sweden already in 1980 and have been standard procedure since then. Studies by us and others 1978-2010 have shown that no renal damage is to be expected within the first few years of treatment. However, after ≥15 years of treatment chronic kidney disease and irreversible nephrogenic diabetes insipidus is found among a considerable proportion of patients. Recently we reported the new finding that prophylactic lithium treatment can cause end-stage renal failure (ESRD), and that the risk was increased sixfold among lithium patients compared to the normal population (Bendz et al. 2010).

The purpose of the present study was to replicate our previous study to investigate whether lithium ESRD remains a possible consequence of the treatment.

Method

study designs were identical. We identified in two major regions in Sweden all patients with past or present lithium treatment who were on renal replacement therapy (RRT = dialysis or kidney transplant). We reviewed their charts. Only patients with lithium treatment as the sole or contributing etiological factor for ESRD were included. We obtained the RRT population from the Swedish Renal Registry. We estimated the number of lithium patients from the number of prescriptions (in the previous study we counted the patients directly.)

Results

There were 25 patients with lithium-induced ESRD. Twelve of them were survivors from the first study.

The populations First study Replication

The general population 2,697,919 2,823,626

The RRT population 2,234 2,652

The lithium population 3,367 4,135

The prevalences First study Replication

RRT patients in the 0.8 ‰ 0.9 ‰ general population

Lithium patients in the 1.2 ‰ 1.5 ‰ general population

Lithium ESRD in the 5.3 ‰ 6.0 ‰ lithium population

Lithium ESRD in the 8.1 ‰ 9.4 ‰ RRT population

Conclusion

The prevalence of lithium-induced ESRD remained essentially unchanged for 6 years since 2005. ESRD remains a possible consequence of lithium treatment.

Additional Information

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Residual Symptoms in bipolar disorder: How to define and to manage them in clinical practice

Authors: Liova Yon, L. Samalin, B. Giordana, V. Milhet, L Marty, W. El Hage, P. Courtet,
F. Bellivier, PM. Llorca Pôle de Psychiatrie Hôpital Henri MONDOR, 15 ème étage, 94010 CRETEIL Cedex, France, liova.yon@hmn.aphp.fr

Objective

The aim of this study is to define RS and to describe their management using a qualitative analysis.

Method

A qualitative study was conducted. Data were collected from five focus groups including 46 psychiatrists all over France. An interview guide was used, including questions about definition of RS, their assessment and influence on the management of bipolar patients. Content analysis was used to identify themes emerging from the focus groups.

Results

No explicit definition of RS was associated with participants consensus. Definition appears to be multicriteria, interactive and scalable. It is based both on the psychiatrist's therapeutic objectives and patient's complaints. Eight major RS were identified: suicidal risk, emotional dysregulation, observance, cognitive impairment, sleep disorder, functional disability, patient's complaints, and comorbidities evolution.

Content analysis underline the fact that: Standardized tools are not used in clinical practice; RS are permanent preoccupation; they justify optimisation of medication and adjustment of visits frequency.

Conclusion

Qualitative study is helpful to define and describe RS. Identifying RS is an important way of achieving implementation strategies and improve management of bipolar patients.

DIAGNOSIS AND DEFINITIONS

Emigration and risk of depression by gender in Sardinian studies: Does Hypomanic temperament play a role?

Name: Mauro Giovanni Carta°, Cetkovich-Bakmans M, Krishna M, Bhat#, Moro MF°, Mura G° and Agermeyer, M*°
Viale Merello 22 Cagliari, Italy , °Department of Public Health, University of Cagliari, Cagliari, Italy
*Centre for Public Mental Health, Gösing am Wagram, Austria
#DEPARTMENT OF NEUROSCIENCE AND CELL BIOLOGY, University of Texas Medical Branch, Galveston, Texas,USA mgcarta@tiscali.it

Objective

The poster aims to determine if the difference in gender risk for mood disorder among Sardinian emigrants can be explained by the possibility that Sardinian emigration pre-selected men with hypomanic temperament.

Method

This is a narrative review that compares the results of studies on gender difference in motivation from the 60's, with the results on prevalence of depressive disorders in Sardinian emigrants from the studies in the last decades.

Results

In the 1960's, Rudas examined attitudes toward emigration in Sardinian couples waiting to emigrate and found that the decision for emigration was principally take by males; moreover, emigrant women showed a low self-esteem than emigrant men. A study carried out between 2001-02, in the peak of the economical crisis of the Argentinean default, on Sardinian immigrants to Argentina in the 60's, found high risk for depressive disorders only in women. These results were opposite to that of the findings ten years earlier in a survey on Sardinian immigrants to Paris in which the risk of Depressive Episode was higher only in young men.

Conclusion

In Sardinian emigrants the early motivations and self esteem seems to be related to the modalities of expression of mood disorders and the differences in the risk triggering situations in the host country. The data are suggestive of a bipolar disorder risk for young (probably hypomanic) men in competitive, challenging conditions and of unipolar disorder for women in trying economical conditions.

Additional Information

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Sensitivity and specificity of the Mood Disorder Questionnaire to detect comorbid bipolar disorder in complex depressed inpatients.

Authors: Fabienne Cyprien, Isabelle Jaussent, Guillaume Collin, Grégoire Mercier, Emilie Olié, Sébastien Guillaume, Philippe Courtet

Hôpital La Colombière, Inserm U1061, Pavillon 42 RDC Calixte Cavalier

39 avenue Charles Flahault, BP 34493, 34295 Montpellier CEDEX 5, France

fcyprien@orange.fr

Objective

Patients with bipolar disorder (BD) are often misdiagnosed as having major depressive disorders, and consequently receive ineffective treatment, leading to poorer prognosis. Here, we assessed the psychometric performances of the original Mood Disorder Questionnaire (MDQ) and its modified MDQ7 version, to screen for BD in depressive inpatients, in function of the depression severity and the number of co-occurring axis I psychiatric disorders.

Method

Depressed inpatients (n=195) were consecutively enrolled and asked to complete the French version of the MDQ. Psychiatric diagnoses were made using the standardized DSM-IV-TR structured interview MINI 5.0.0. The severity of depression was assessed with the Beck Depression Inventory and the Hamilton Depression Scale. Sensitivity (Se), specificity (Sp) and positive likelihood ratio (LR+) were used to compare the MDQ/MDQ7 performance according to the level of comorbidity and depression severity.

Results

MDQ and MDQ7 performed equally well independently of the comorbidity burden. In the absence of comorbidity, MDQ had a Se=66.67% [95%CI: 42.81-90.52] and Sp=90% [95%CI: 71.41-108.59], LR+=6.67 and in the presence of ≥2 comorbidities MDQ showed a Se=59.09% [95%CI: 38.55-79.64], Sp=83.72% [95%CI: 72.69-94.76], LR+=3.63. Severe depression did not impair the MDQ/MDQ7 performances.

Conclusion

In the clinical practice, MDQ and MDQ7 are reliable and useful instruments for systematic detection of BD in acute inpatients with complex depression.

Additional Information

Limitations: The transversal nature of the study.

Impulsivity and Panic Disorder: the Role of Cyclothymia

Authors: Alessandra Del Carlo1, Marzia Benvenuti1, Valerio Manzo1, Salvatore Rizzato1, Francesca Casalini1, Liliana Dell'Osso1, Giulio Perugi1,2

Department of Psychiatry, Neurobiology, Pharmacology, Biotechnology, University of Pisa, Pisa, Italy - via Roma 67, Italy, 1 Department of Psychiatry University of Pisa, Pisa, Italy;

2 Institute of Behavioural Sciences G. De Lisio, Pisa, Italy, alessandra.delcarlo@gmail.com

Objective

Higher level of impulsivity, measured by different rating tools, has been reported in patients with anxiety disorders than in healthy controls. The presence of both trait and state impulsivity was associated with the presence of comorbid cyclothymic disorder. In this report, we evaluated impulsivity in Panic Disorder patients and healthy controls, hypothesizing that impulsivity may be related with Cyclothymic disorder comorbidity rather than the diagnosis of Panic Disorder.

Method

A sample including 66 subjects with panic disorder and 44 control subjects matched for demographic, educational and work characteristics underwent a diagnostic evaluation by the Mini Neuropsychiatric Interview (MINI); a symptomatological evaluation by the Bech-Rafaelsen Depression and Mania Scale (BRDMS), the State-Trait Anxiety Inventory (STAI), the Hypomania Check List (HCL-32) and the Clinical Global Impression (CGI); a temperamental and personological evaluation by the Questionnaire for the Affective and Anxious Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Modified (TEMPS-M), the Separation Anxiety Symptoms Inventory (SASI), the Interpersonal Sensitivity Symptoms Inventory (ISSI); and, finally, a psychometric and a neuro-cognitive evaluation of impulsivity by the Barratt Impulsiveness Scale (BIS) and the Immediate and Delayed Memory Task (IMT/DMT). The initial sample of patients with anxiety disorders was then subdivided into two subgroups depending on the presence of comorbid cyclothymia (Cyclo+ [n=22] and Cyclo- [n=44]). For the diagnosis of cyclothymic disorder, we used both the DSM-IV-TR criteria and also a modified threshold for hypomania with a duration of 2 days. Comparative analyses were made between the entire initial sample of patients and healty controls and among Cyclo+, Cyclo- and healty controls.

Results

Patients/controls comparisons showed higher levels of trait and state impulsivity in patients affected by Panic Disorder than in healty controls. The comparison between Cyclo+, Cyclo- and controls showed that Cyclo+ are the most impulsive subjects in all the investigated measures and are characterized by greatest symptomatological impairment, highest scores in temperamental scales, and highest levels of interpersonal sensitivity and separation anxiety.

Conclusion

In our patients with panic disorder, trait and state impulsivity resulted to be greater than in controls. In particular impulsivity was highest in patients with both panic disorders and cyclothymia. In anxious-cyclothymic patients also separation anxiety and interpersonal sensitivity were more severe than in anxious patients without cyclothymia and controls. Our findings confirm that impulsivity, rather than being directly related to the presence of panic disorder, could be associated with comorbidity with cyclothymia.

POSTERS

Clinical features of Borderline Personality Disorder: the role of Trauma and Affective Instability

Author: Alessandra Del Carlo1, Marzia Benvenuti1, Federica Dima1, Valerio Manzo1, Salvatore Rizzato1, Francesca Casalini1, Liliana Dell'Osso1, Giulio Perugi1,2

Department of Psychiatry, Neurobiology, Pharmacology, Biotechnology, University of Pisa, Pisa, Italy - via Roma 67, Italy, 1 Department of Psychiatry University of Pisa, Pisa, Italy;

2 Institute of Behavioural Sciences G. De Lisio, Pisa, Italy, alessandra.delcarlo@gmail.com

Objective

The relationship between inherited susceptibility and environmental factors in borderline personality is a controversial topic ever since Borderline Personality Disorder (BPD) was incorporated into DSM in 1980. In this report we evaluate the role of affective instability (a core biological characteristic of BPD) such as childhood trauma (an environmental factor frequently associated with BPD) on the clinical phenomenology of Borderline Personality Disorder.

Method

A sample including 50 subjects with "Borderline Personality Disorder" (DSM IV) underwent a diagnostic and clinical evaluation by the Diagnostic Interviw for Borderline Patients (DIB); the Mini Neuropsychiatry Interview (MINI), the Structured Interview for Mood Disorder-R (SIMDr); the Hypomania Check List (HCL-32), the Symptom Checklist-90-R (SCL-90-R), the Clinical Global Impression (CGI), the Global Assessment of Functioning (GAF), the Interpersonal Sensitivity Symptoms Inventory (ISSI), the Separation Anxiety Symptoms Inventory (SASI). Affective instability was evaluated by means of the Affective Lability Scale (ALS) while childhood traumatic experiences with the Child Trauma Questionnaire(CTQ).

For evaluating the role of childhood trauma, we subdivided the initial sample in two subgroups on the basis of CTQ ratings: CTQ+ subjects (n=24) that achieved scores higher than the median of the sample and CTQ- subjects (n=26) that achieved lower scores. Comparative analyses on demographic, clinical and illness course features were made between CTQ+ and CTQ- subjects.

Similarly, for evaluating the role of affective instability, we then subdivided the initial sample in two subgroups on the basis of ALS ratings: ALS+ patients (n=23) that achieved scores higher than ALS median score of the sample, and ALS- patients (n=27) that achieved lower scores. Comparative analyses on demographic, clinical and illness course features were made between ALS+ and ALS- subjects.

Results

Comparing CTQ+ and CTQ- subgroups, no significant differences were found regarding age at onset, diagnosis, number of previous mood episodes, history of suicide attempts, comorbidity with Panic Disorder or Substance Use Disorder, or other clinical features explored.

Comparing ALS+ and ALS- subgroups, no differences were found as regards demographic features or illness course. On the other hand, Chronic Feelings of Emptiness were overrepresented in subjects with higher affective instability (55% vs 45%, p=.01) and a higher percentage of these latter (63.8% vs 58%, p=.02) reported a history of childhood traumatic experiences. ALS+ subjects reported higher scores in the "Affect" (48.5% vs 42.%, p=.03) and "Interpersonal" section (46% vs 39.3, p.01) of DIB. Finally, higher ratings in the SCL90 subscales for "somatizations", "obsessive-compulsive", "depression", "anxiety", "anger-hostility", "paranoid ideation" (10.6 vs 7.3, p=.04) were reported in ALS+ than ALS- subjects.

Conclusion

In our sample childhood traumatic experiences reported by patients with BPD seemed to be unrelated to a specific clinical phenomenology while high levels of affective instability were associated with strong subjective feelings of emptiness, negative environmental factors such as childhood trauma, a greater severity of general and affective psychopathology and a greater impairment in social functioning.

Genetic basis of alcohol dependence: analysis of the 5HTTLPR polymorphism of the serotonin transporter gene in alcohol dependent subjects and comorbidity with psychiatric diseases.

Authors: Ferraguti G., Codazzo C., Lucarelli M., Pascale E., Squarcione C., Vitali M., Pacini M., Ceccanti M.

Sapienza University of Rome, V.le Regina Elena, 324 - 00161 Rome - Italy

ferraguti@bce.uniroma1.it

Objective

Genetic basis of alcohol dependence (AD) are well established. Different studies have underlined the involvement of genetic variants concerning not only ethanol metabolism, but also the neurobiology of addiction and the pathways of reward circuits. Serotonin transporter, molecular target of many antidepressant drugs, plays a key role in regulating serotonergic neurotransmission and has been associated with many different pathologies, including alcoholism, obsessive-compulsive disorders, major depression and other psychiatric diseases. Aim of this study is to verify the link between the 5HTTLPR polymorphism of the serotonin transporter gene (SLC6A4) and alcohol dependence, in a sample of 434 alcoholics outpatient at Alcohol Unit of Umberto I Hospital – "Sapienza" University of Rome.

Method

Genotyping was performed by PCR amplification of a DNA fragment that includes the polymorphic region; this produces in heterozygotes two amplicons of different size, and in homozygotes a single amplicon longer (L) or shorter (S) depending on the variable number of repeated elements that results, in most cases, in a 43 base pairs insertion/deletion. We genotyped 434 alcoholics and 268 healthy controls for the 5HTTLPR polymorphism. In our sample 326 patients were only alcohol dependent, while 108 subjects were diagnosed for mental disease

and alcohol dependence, according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV tr) criteria. In particular, 63 had Bipolar Disorders (BD), 21 had Major Depressive Disorders (MD) and 24 Anxiety Disorders (AD).

Results

Statistical analysis of our data, performed by using a two tailed chi square test, has not shown differences between the control and the whole population of alcohol dependent subjects. No statistically significant differences appeared comparing the control group with the different subsets of patients above described; either the allelic frequencies or genotypes distribution were analyzed. We noticed a slightly higher frequency of the (S) allele in the group of anxiety disorders patients (45,8% compared to 41,6% of healthy controls) and in the group of only alcohol dependent patients (44,5% compared to 41,6% of healthy controls).

Conclusion

According to our results, the 5HTTLPR polymorphism of the serotonin transporter gene (SLC6A4) seems to be not involved in alcohol dependence even if complicated by a concurrent psychiatric disease. Our results agree with other recently published data concerning the comorbidity between Bipolar Disorders and Alcohol Dependence and the association of serotonin gene polymorphisms. A significant number of patients with Anxiety Disorders have at least on short allele and, although it may not be statistically significant possibly due to the smallness of the sample, further studies should be extended to a larger population to investigate this result.

An early diagnosis of bipolar spectrum disorders needs of valuing the somatisation symptoms of patients

Authors: Tavormina Giuseppe, M.D.

President of “Psychiatric Studies Centre” (Cen.Stu.Psi.), Piazza Portici, 11 - 25050 Provaglio d’Iseo (BS)
www.censtupsi.org
dr.tavormina.g@libero.it

Objective

An observational study of the diagnosis of 423 consecutive new patients in a period of six years (2003-2008) led to focus a high percentage of soft bipolar spectrum diagnosis (4), followed to a new classification of “the bipolar spectrum” (ten sub-types of bipolar spectrum mood, included the sub-threshold forms), in which there is a fluctuation concept between the manic/ipomanic phase of the bipolar spectrum and the depressive phase, and inside them all the mixed states with very high and rapid fluctuation of the mood.

I also put in evidence in this study the presence of their temperaments emerging from their personal anamnesis and analyzed at their ”first visit”, as sub-clinical evidence of the bipolar spectrum (hyperthymic temperament: 35%; cyclothymic-irritable temperament: 49%; depressive temperament: 16%), (6). The cyclothymic-irritable temperament also includes the “Softly-instable temperament” (a soft cyclothymic temperament).

Method

All the clinical cases-history of 400 patients of this group of 423 (161 men and 239 women; 23 patients with organic diagnosis have been excluded) have been revalued to put in evidence the presence of their eventual somatizations at their ”first visit” in my office, to value if this evidence might begin useful to do an early diagnosis of bipolar spectrum mood disorders.

Results

The main somatizations found at their ”first visit” in my office have been: colitis (45% of the patients), gastritis (25%), migraine (8%) others (above all with dermatological symptoms: 2%). All the patients presented muscolar tension at their ”first visit”.

Only the 20% of the patients did not present any somatization at their ”first visit” (almost all of this ”no-somatization” group were men, only 16% were women).

Conclusion

The subthreshold presence of the temperaments in the history of the patients with bipolar spectrum disorders allow us to consider this crucial way for early diagnosis of bipolar spectrum mood disorders. But, the chronic presence in the life of the patients of some somatizations (above all colitis, gastritis and migraine) needs to catch the attention of the psychiatrist and/or the GP as key-symptoms for an early diagnosis of bipolar spectrum mood disorder.

All the described somatization symptoms disappeared during the months of the pharmacological treatment of their bipolar mood disorders, except then some residual and soft symptom that periodically increases togheter with other mood disorders symptoms (during phases of disease exacerbation).

The pharmacological treatment of the bipolar mood disorders consists in a combination therapy between mood-regulators (mainly: lithium, carbamazepine, valproate, gabapentin, oxcarbazepine, lamotrigine, topiramate, olanzapine, pipamperone) and antidepressants (mainly: SSRI, SNRI); never using the antidepressants alone and/or in combination with benzodiazepine (and never using long time the benzodiazepine) in order to avoid an increase in instability and the development in patients of diphoric-mixed states.

When the patients with bipolar mood disorders present somatisations, very often these symptoms are mis-diagnosed or mistaken with somatic symptoms followed to organic diseases: with the consequence of the use of a long series of blood and instrumental tests, often useless for the illness of the patient.

There is a public health issue regarding the correct diagnosis of bipolar mood disorders : these diseases are often underreferred, underdiagnosed and undertreated/mistreated. To fail to treat bipolar mood disorders may sometimes result in serious complications (loss of work, relationship crisis, substance-abuse, suicide, rapes, etc).

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A Tale of Two Diatheses: Temperament and BIS/BAS as Risk Factors for Mood Disorder

Author: Anna Van Meter, John Irvin, Jessie Manthey, Eric Youngstrom

University of North Carolina, CB 3270, Chapel Hill, NC 27514, United States

avanmeter@unc.edu

Objective

Two major models of risk for mood disorder focus on affective temperament styles (cyclothymic, hyperthymic, depressive, anxious, irritable) and sensitivity in the behavioral inhibition (BIS) and behavioral activation (BAS) systems (Alloy et al., 2008; Evans et al., 2005; Kochman et al., 2005; Meyer, Johnson, & Carver, 1999; Vázquez et al., 2008). Temperament and BIS-BAS are important to biological models of risk.

Given the potential overlap in traits measured by the TEMPS-A and by Carver and White's BIS/BAS Scales, we investigated relations between the BIS/BAS Scales and TEMPS-A, and determined each scale's unique contribution to depressed and elevated mood symptoms.

Method

Young adults (N=499; average age 19; 63% female) were recruited from the University of North Carolina at Chapel Hill. Each participant completed a series of self-report questionnaires, including the TEMPS-A (Akiskal, 2005), the BIS/BAS Scales (Carver & White, 1994), Beck Depression Inventory (BDI, Beck, 1961), and Hypomanic Checklist (HCL, Angst, 2005). Linear regression quantified relations between mood symptoms and temperament and BIS/BAS scales.

Results

BIS/BAS Scales correlated with one another, consistent with previous research (p<.05). The temperament scales also correlated with one another (p><.01).

Temperament and BIS-BAS were distinct but associated constructs: cyclothymic temperament correlated with BAS Fun (r=.09, p<.05) and BIS (r=.24, p><.001). Hyperthymic temperament correlated with BAS positively (r= 23-.40, p><.001) and with BIS negatively (r= -.23, p><.001). Depressive temperament correlated with BIS (r=.32, p><.001). Anxious temperament correlated with BAS Reward (r=.16, p><.001) and BIS (r=.32, p><.001). Irritable temperament correlated with each of the BAS scales (r=.17-.26, p><.001).

Regressing BDI scores on temperament, cyclothymic (B=.69, p

<.001), depressive (B=1.66, p><.001), and anxious (B=.66, p><.001) predicted significantly. BIS/BAS scales explained 2% of the variance in BDI scores above and beyond temperament, which accounted for 45% of the variance. Only BIS was a significant predictor (B=.19, p><.01). >

Regressing the HCL scores on the temperament scale scores; cyclothymic (B=.42, p

<.001), hyperthymic (B= .46, p><.001), and irritable (B=.31, p=.05) predicted significantly. BIS/BAS scales explained 6% of the variance above and beyond temperament, which accounted for 14% of variance. BAS Reward was a significant predictor (B=.42, p><.01), as was BAS Fun (B = .27, p><.05). >

Conclusion

We investigated whether affective temperament and BIS/BAS represent overlapping constructs of mood disorder diathesis. Small to moderate correlations indicated that these are complementary but distinct constructs.

The affective temperaments showed stronger relations with depressive symptoms, with larger coefficients and R2 values in the regression model. This suggests that the TEMPS may more accurately describe the multifaceted nature of depression than BIS, which is more narrowly focused on inhibition. The role of affective temperament and BIS/BAS in the development of hypomanic symptoms is less clear. Limitations include that the population was not clinical and, therefore, the symptoms are likely not as severe as found in previous investigations, which may affect the predictive validity of the scales used.

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EPIDEMIOLOGY

French validation of the Circadian Type Inventory in a sample of remitted bipolar patients

Name: Carole Boudebesse, Lajnef, Milhiet, Henry, Bellivier, Leboyer, Etain Hôpitale Albert Chenevier, Pôle de Psychiatrie, centre expert troubles bipolaires, pavillon Hartmann, 40 rue de Mesly, 94000 Créteil, France, carole.boudebesse@gmail.com

Objective

Circadian rhythms disturbances were associated to bipolar disorder during both mood episodes and periods of remission. The circadian model of instability postulates to higher vulnerability to circadian rhythm disturbances in patients with bipolar disorder. Better characterization of circadian rhythms in bipolar disorder can help to better understand the pathophysiology of the disorder and to develop novel therapeutic strategy. Circadian rhythms are defined by three characteristics: phase, amplitude, stability. The circadian type inventory (CTI) is 11 items self-questionnaire first develop to measure circadian rhythms amplitude and stability. Especially, the CTI describes circadian rhythms as flexible/rigid (reflecting rhythms stability) and as languid/ vigorous (reflecting rhythms amplitude). Rigid types are described less able to sleep at unusual hours, languid types are described lethargic following reduced sleep. The CTI use in common practice with bipolar patients can help to define profile of vulnerability to irregular sleep/wake pattern. The CTI was validated in several languages but not yet in French. The first aim of the study is to validate the French version of the CTI. The second aim of the study is to compare bipolar patients and healthy controls for circadian parameters assessed by the CTI and for eveningness/morningness.

Method

The CTI was completed by remitted patients with bipolar disorder (n=140) evaluated by the French Bipolar Expert Centers Network. Remission was defined by a score < 8 to the Young Mania Questionnaire and a score

<8 to the Hamilton Depression Rating scale. They also completed the Composite Scale of Morningness (CSM) and the Epworth questionnaire to assess concurrent validity of the CTI. For the test-retest analysis, a sub-group of bipolar patients completed the CTI a second time six months later. The CTI and the CSM were also completed by healthy controls. >

Results

The internal reliability, the inter-items correlations, the concurrent validity and the test-retest reliability of the French version of the CTI will be presented. Comparisons of the CTI and the CSM scores between the group of remitted patients with bipolar disorder and the group of healthy controls will also be discussed.

Conclusion

The French version of the CTI would appear as a valid and robust non invasive tool to assess the vulnerability to disturbed sleep/wake pattern in patients with bipolar disorder. Detection of this vulnerability would help to define preventive therapeutic strategy.

The risk of bipolar disorders and major depressive disorders in Wilson's disease: results of a case-control study

Name: Mauro Giovanni Carta*, GC Farina*, O Sorbello*, MF Moro*, E Demelia*, F Cadoni*, A Serra*, G Mura*, M Piga*, L Demelia*

* Università di Cagliari, Italy , Viale Merello 22 Cagliari, Italy, mgcarta@tiscali.it

Objective

The aim of this study was to determine the risk for mood disorders in Wilson's disease (WD) using standardized mental health diagnostic tools

Method

This was a case control study. The cases were 23 consecutive patients with WD treated at the University Hospital in Cagliari, Italy, and the controls were 92 sex- and age-matched subjects with no diagnosis of WD who were randomly selected from a database used previously for an epidemiological study. Psychiatric diagnoses according to DSM-IV criteria were determined by physicians using structured interview tools (ANTAS-SCID).

Results

Compared to controls, WD patients had lower scores on the SF-12, which measures quality of life, and a higher lifetime prevalence of DSM-IV major depressive disorders (OR = 5.7, 95% CI 2.4-17.3) and bipolar disorders (OR = 12.9, 95% CI 3.6-46.3). The SF12 scores were much worse in patients with SPECT positivity for pathological perfusion, and such patients had a high risk of

Conclusion

This study was the first to use standardized diagnostic tools to study the association between mood disorders and WD. WD patients showed a higher risk for bipolar and major depressive disorders compared to controls. Reports in the literature about increased schizophrenia-like psychosis in WD and a lack of association with bipolar disorders may thus have been based on a more inclusive diagnosis of schizophrenia in the past. Our findings may explain the frequent reports of loss of emotional control, hyperactivity, loss of sexual inhibition, and irritability in WD patients.Limits: this study was limited by a small sample size.

Burden of metabolic diseases in patients with Bipolar Disorder

Name: Francesca Casalini, S.Belletti, N.Mosti, V.Mastria, S.Rizzato, G.Ceraudo, L.Dell'Osso, G.Perugi, Department of Psychiatry of the University of Pisa, via dell'omodarme, 38, Italy

casalinifrancesca@gmail.com

Objective

High rates of comorbidity between bipolar disorder and metabolic diseases (such diabetes, obesity, metabolic sindrome) have been reported in clinical and epidemiological studies. Few research explored the possible

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relationships between clinical and course characteristics of the mood disorder and these physical illnesses.

Method

We reported data derived from a sample of 244 bipolar patients consecutively referred to outpatients and inpatients units of the Department of Psychiatry of the University of Pise, Italy. All patients have been selected on the basis of DSM IV criteria for Bipolar I, II and NOS and have been evaluated by means of structured and semi-structured interviews, exploring diagnostic criteria (Structured Clinical Interview for diagnosis-SCID) and familial, clinical, course, comorbidity and treatment characteristics of the mood disorder (Structured Interview for Mood Disorders-SIMD). CGI for severity of the illness, GAF score for functional adjustement and TEMPS-35 for affective temperaments have been also administred. Finally, all patients have been carefully screened for physical illnesses by anamnestic interview and physical examination.

Results

In our sample high rates of metabolic diseases have been founded. More than 40% of our patients reported at least one metabolic disease. Such a comorbidity was not influenced by the subtype of Bipolar Disorder, but was related to the age of patients. Bipolar patients with meabolic diseases reported higher rates of anxiety disorders (GAD and social phobia). Life-style and drug tratment may play a role in this type of comorbidity, although our results don't suggest a strong relationship with previous therapy with neuroleptics.

Conclusion

Our results suggest the existence of many factors for the comorbidity between Bipolar Disorder and metabolic diseases, in addition to pharmacologic therapy. Further research is necessary in order to better define this association and improve clinical practice.

The Reliability and Validity of the Korean version the Body Shape Questionnaire

Author: Ik-Seung Chee, Tae-Seong Kim, Seoung-Min Cha, Jeong-Lan Kim, Seong Keun Wang

33. Munhwa-ro, Jung-gu, Daejeon, 301-721, Korea, Department of Psychiatry, Chungnam National University Hospital, Korea, Republic of, ischee@cnu.ac.kr

Objective

The aim of this study is to assess the reliability and validity of the Korean version of the Body Shape Questionnaire(BSQ).

Method

1.Subjects and procedure: Participants were 467 adults(M:96,F:371)in Daejeon(age M=27.4±8.8). IRB approval for this study was obtain from Chungnam National University Hospital. Body Shape Questionnaire(BSQ) was translated into korean and the cross-translated back again by bilingulaist.

2. Measures: All participants completed the BSQ, Body dysmorphic disorder-self Report Korean version(BDDE-SR), Eating Disorder inventory Korean version(EDI-2), and their body mass indices(BMI) were calculated.

Results

1.The mean BSQ score was 84.6±33.2, and the mean BMI score was 21.1±2.8.

2.The BSQ showed high test-retest reliability(r=0.926), very high internal consistency(Cronbach's alpha=0.966), and Spearman-Brown split-half reliability (0.940).

3.The correlation of the BSQ with BDDE-SR was 0.685(P<0.001), and body dissatisfaction subscale of of EDI-2 was 0.655(P><0.001).

4. Factor analysis of the BSQ found four factors explaining 62.1% of the total variance . Four factors were named as "dissatisfaction about feeling fat", "shame and inferiority about body shape", "attitude concerning body image perception", and "purging behavior".

Conclusion

This present results suggest that the Korean version of BSQ is a reliable and valid tool for assessing body image concern.

Validation of the French version of the Functioning Assessment Short Test (FAST) in patients with Bipolar Disorder. A study from the French Bipolar Expert Centers Network

Author: Daban Claire, Raust A, Fouques D, Barbato**A, Etain B, Henry* C. and the French Bipolar Expert Centers network. Hopital A.Chenevier

Pole de Psychiatrie, Centre Expert Bipolaire, 40 rue de Mesly, 94000 Créteil, France

* Fondation Fondamental, Créteil, France

**Epidemiology and Social Psychiatry Unit, Mario Negri Institute for Pharmacological Research, Milan Italy, claire.daban-huard@ach.aphp.fr

Objective

Measuring functional outcome in Bipolar Disorder is essential. Bipolar patients often experience functional impairment such as work absenteeism, but also important domains of functioning such as autonomy, interpersonal relationships and cognition inducing a higher burden of the disease. The concept of functioning is complex and involves many different domains including the capacity to work, capacity to live independently, capacity for recreation, capacity for romantic life, and capacity to study. Because the use of the Global Assessment of Functioning (GAF) Scale, or other generic scales, is not specific enough to assess specific areas of functional impairment, a specific scale has been developed by the Bipolar Disorder Program in Barcelona: the Functioning Assessment Short Test (FAST) (Rosa et al.; 2007). The FAST was developed to be sensitive to change and capture the main areas of disability for patients with BD and to require a short time for its administration. It is a simple interview, with 24 items, divided into 6 domains of functioning: Autonomy, Occupational functioning, Cognitive functioning, Financial issues, Interpersonal relationships, and Leisure time.

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Method

First designed in Spanish, then translated in English, validated in Italian and Brazilian bipolar patients, we propose a validation of the French version of the FAST. The translation was made by a psychologist and the back translation was confirmed by the authors. One hundred and 78 euthymic bipolar patients were evaluated from the French Bipolar Expert Centers Network. They were also evaluated with the GAF and the Clinical Global Impression (CGI) to assess the concurrent validity of the scale. For the test-retest analysis, after a week from the first FAST administration, 10 patients will be reassessed by the same rater.

Results

The results of the reliability, validity and clinical significance of the French version of the FAST will be presented.

Conclusion

The first result of this study will be presented in order to show that the FAST, a brief interview designed to evaluate the impact of mental illness on functioning, is a reliable and a valid measure in a sample of patients with BD in a French specialized treatment facility, with the capacity to successfully discriminate euthymic patients and controls and, moreover, to evaluate the impact of residual symptoms on levels of functioning.

Overweight and obesity in patients with bipolar disorder or schizophrenia compared with a non-psychiatric sample

Authors: Luis Gutiérrez-Rojas, Manuel Gurpegui, José María Martínez-Ortega, Lola Jurado.

Avenida Federico García Lorca nº 31, escalera 1, 2º C, Spain, gutierrezrojasl@hotmail.com

Objective

Multiple studies suggest an association of overweight and obesity with bipolar disorder (BD) and schizophrenia. The goal of this presentation was to determine the magnitude of this association and its relationship with previous course-of-illness and other variables of clinical interest.

Method

The prevalence of overweight and obesity was compared among patients with BD (n=108), patients with schizophrenia (n=250) and a non-psychiatric control group (n=290). Moreover, within each group we analyzed the variables associated with overweight [including obesity, i.e., body mass index (BMI) ≥25] and obesity (BMI≥30) adjusting for a possible confounding effect of sex, age and educational level by logistic regression.

Results

In comparison with the non-psychiatric sample, a strong association of both BMI≥25 and obesity was observed with BD and schizophrenia (adjusted odds ratios between 3.4 and 4.6; P-values

<0.001). Overweight was significantly associated with male sex and increasing age in both control and BD groups; and with female sex among schizophrenia patients. Moreover, for BD patients, earlier onset of first BD symptoms, presence of a non-psychiatric illness, current use of mood-stabilizing medication, and being a non-smoker were significantly associated with overweight; and male sex and the presence of a non-psychiatric illness, with obesity. Within the schizophrenia patients, obesity was significantly associated with female sex, intermediate age range and lower PANSS score. >

Conclusion

Among patients with BD or schizophrenia, the chronic course of their illness and their current treatment with psychotropic medication might be more relevant for becoming overweight or obese than the specific psychiatric illness.

Validation of a Global Assessment Measure for Fatigue

Authors: Howard Hassman(1), Steven D. Targum(2), Maurizio Fava(3), Maria Pinho(1)

1 CRI Worldwide, Willingboro, NJ

2 Clintara LLC, Boston, MA

3 Massachusettes General Hospital, Boston, MA, 16000 Horizon Way, Suite 100

Mount Laurel, NJ 08054, United States, jsacco@criww.com

Objective

To facilitate assessment of fatigue-related symptoms, we developed a customized global assessment scale based upon the original CGI(2). The CGI is subject to scoring variability that can obscure the assessment of the intended symptoms(3). 3 In this study, CGI-severity and Patient Global Impression of severity (PGI-S) for Fatigue instruments were developed to focus on “targeted” symptoms of fatigue. We have demonstrated that the CGI-S and PGI-S for fatigue are both reliable and valid as used in a psychiatric population.

Method

56 subjects consented to participate in this study. There were two clinic visits during which the CGI-S and PGI-S for fatigue rating instruments were administered. The MGH cognitive and physical functioning questionnaire (MGH-CPFQ), a validated self-rated 7-item scale was also used as a validation instrument4. The patient-rated MGH-CPFQ and PGI-Severity for fatigue preceded the clinician-rated CGI-S at screen and the CGI-S and CGI-Improvement (CGI-I) at the second visit.

Results

Most subjects revealed mild to moderate levels of fatigue associated with a range of Axis I psychiatric disorders. Clinical and Patient Impressions of fatigue were well correlated. Both CGI-S and PGI-S for fatigue were well correlated with the CPFQ. At the second visit the CGI-S for fatigue revealed temporal stability (r=0.81) in the test-retest assessment. The correlation between CGI-S and PGI-S remained high (r= 0.61) as did convergent validity for the CPFQ (r=0.74 for CGI-S and 0.61 for PGI-S).

Conclusion

In this study, we have demonstrated that the customized CGI-S and PGI-S for fatigue are reliable measures of fatigue in a population of psychiatric patients.

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The St. Göran Bipolar Project: A Prospective Longitudinal Study on Bipolar Disorder

Author: Olofsson Haydeh, 2 Wennberg M.,2 Carlswärd-Kjellin A.,2 Gezelius B.,3 Blom A.,3 and Landén M.,1, 2, 3.

1Karolinska Institutet, Department of Clinical Neuroscience, Sweden; 2Centre of Psychiatric Research, Affective Centre at Northern Stockholm Psychiatry, Sweden; 3Affective Unit in Mölndal, Sahlgrenska University Hospital, Sweden.Centre of Psychiatric Research,

Affective Centre at Northern Stockholm Psychiatry, Vårdvägen 3, 112 81 Stockhlom, Sweden haydeh.olofsson@sll.se

Objective

Considering the broad variety of patterns and symptoms in bipolar disorder (BP), there is a need to conduct research based on clinical populations that take this heterogeneity into account. The St. Göran Bipolar Project (SBP) is a prospective longitudinal study based on a clinical population in two defined catchment areas in Stockholm and Gothenburg, Sweden. It is designed as a clinical work-up program with yearly follow-ups, and collects phenotypic data in terms of diagnosis and neuropsychological testing, along with biological samplings of blood and cerebrospinal fluid (CSF), and magnetic resonance imaging (MRI) scans of the brain. The goals of SBP are to study pathological mechanisms and prognostic factors by virtually following patients for life, but also to provide a structured clinical work-up of highest quality to secure the best available care for bipolar patients. Population-based, age- and sex-matched controls are recruited through Statistics Sweden.

Method

Patients are recruited from two centers in Sweden: the Affective Centre at Northern Stockholm Psychiatry and the Affective Unit in Mölndal. The Affective Disorder Evaluation (ADE, originally developed for the STEP-BD program) and the M.I.N.I.-international neuropsychiatric interview are performed to establish a bipolar disorder diagnosis. This is followed by blood work, including but not restricted to analyses of high sensitive C-reactive protein, hormones and sex hormones. Lumbar puncture is performed under standard conditions and the CSF is immediately analysed with respect to monoamines and albumin quotient. Thereafter a MRI scan of the brain is done. An extensive neuropsychological evaluation is conducted. The interplay of the collected information allows performance of many types of studies including genetic, brain morphological, neuropharmacological, and psychological.

Results

Clinically, this program has resulted in considerably higher quality in the health care provided. Structured diagnostic instruments are used to a higher degree and somatic disorders are excluded by means of standardised blood work. A more secure health care is an immediate result of implementing this structured work-up program. Research-wise, this large sample (approximately 500 patients) allows for cross-sectional analyses and a variety of research findings have been published with respect to neurochemical, biochemical, and genetic data. Examples are correlations of grey-matter volume reduction to manic episodes, detection of increased levels of kynurenic acid and cytokines in CSF of patients as compared to controls and also an association between manic/hypomanic irritability in male patients, and distinctive gene variants involved in progesterone metabolism. Differences in CSF monoamine concentrations in bipolar patients with and without ADHD have also been documented. Finally, one investigation with electron microscopy showed a presence of yet unidentified globular-/threadlike structures in CSF of patients.

Conclusion

The cross-sectional composition of SBP has been a mutual benefit for clinical work and research. It has shown to be effective in offering the best available work up, providing solid grounds for clinical decision making. Several potential biomarkers have been studied. The future perspectives include repeating all investigations, including lumbar puncture and MRI scans of the brain, and neuropsychological testing, after 6 years. This would allow the study of prognostic factors and the study of how brain morphology, cognitive function, and neurochemical markers develop over time.

Rates and predictors of rehospitalization after the first lifetime hospitalizations for manic or mixed episode . A naturalistic study in Spanish sample of Bipolar I inpatients

Author: Villar Laura, Carreras J, Rius M, Malo M, Perez A, Bonet P and Nieto E

ALTHAIA XARXA ASSISTENCIAL., Department of Psychiatry, C/ Dr. Joan Soler sn.

08243 Manresa, Spain, maktub16@hotmail.com

Objective

The first objective was to estimate the rate of rehospitalization in bipolar manic or mixed inpatients admitted consecutively and for the first time in his life in our Psychiatric Hospitalization Unit of General Hospital of Althaia Xarxa Assistencial , Manresa, Spain)

The second objective was determine the type of phase (manic, mixed or depressed) causing the first rehospitalization and the clinical predictors of each type of relapse.

Method

This is a retrospective study, based on the review of the

clinical charts of all patients between 18 and 65 years old , admitted to our Psychiatryc Unit between 1996 and 2010 for the first time in his life and diagnosed according to DSM IV criteria of Bipolar I manic or mixed episode. Multiple clinical, sociodemographics and biological variables are collected in the charts of all inpatients admitted in our psychiatric unit. All these patients were followed in our Hospital as outpatients from discharge until today for an average of 6, 4 years (range 1 to 15 years). We recorded all readmissions of patients including the time in days to first rehospitalization and subtype (manic, mixed or depressive) of the same. Patients were classified according to their first rehospitalization:

Those who had no rehospitalizacion.

Those who were readmitted for the first time in a manic phase, Those who were readmitted for the first time in a mixed phase Those who were readmitted for the first time in a depressive phase We compared basal clinical , biological and sociodemographic variables between the 4 subgroups ob Bipolar patients. We used the Chi-square test for qualitative variables, the Student t test for the numeric with normal distribution and the U of Mann-Whitney test for the numeric without normal distribution.

Results

Patients: Of the 125 first-episode type I BPD patients, 90 presented in mania and 35 in DSM-IV mixed episodes (28%). Both groups were very similar in sex-distribution: 52 % men with initial mania vs. 43% with mixed-states. Manic first-episodes requiring hospitalization occurred at similar ages than did mixed-states (33.5±11.9 vs. 32.06±10,9 years; F=0,49, p<0.5).

Fifty-three patients (42,4%) required at least one readmission in the follow-up period , 29 (23,2%) for manic phase, 13 (10,4%) for mixed phase and 11 (8,8 %) for depressive phase 2.Variables significantly associated in univariante analysis with the subgroup or manic readmission were : first hospitalization for mania (93% vs 66% P

<0.003), lower age (29 vs 35 P><0.05) lower cholesterol (3,84 vs 4,41 mmol/l) P><0.02) and higher creatinine levels (0,94 vs 0,84 mg/100ml) P><0.01) in the first hospitalization. The mean time to readmission for a manic phase was 842 days. The average number of readmissions when the first rehospitalization was for mania was 1,83>3. Variables significantly associated in univariante analysis with the subgroup or mixed readmission were: first hospitalization for mixed phase (69,2% vs 23,2 % P

<0.001) , suicide attempt in the first hospitalization (30,8% vs 1,8%, P><0.001). The mean time to readmission for a manic phase was 891 days. The average number of readmissions when the first rehospitalization was for mixed phase was 2,38.>4. Variables significantly associated in univariante analysis with the subgroup or depressive readmission were . psychiatryc comorbidity (82%vs 49,6%, P

<0.05) , onset of bipolar disorder in a depressive episode (82% vs 46,5% P><0.03). The mean time to readmission for a depressive phase was. significantly shorter than in the case of readmission for manic or mixed phase (368 vs 868, P><0.05) The average number of readmissions when the first rehospitalization was for depressive phase was 2,55 >

Conclusion

1. At a mean follow-up period of 6 years after the first admission for manic or mixed phase 42% of bipolar patients were readmitted at least once.

2. The readmission for manic phase (23%) is significantly related to the first hospital admission for mania and also biological variables (younger age, lower cholesterol levels , and higher creatinine levels)

3. The readmission for mixed phase (11%) is significantly related to the first admission for mixed phase and the presence of suicidal behavior

4. The readmission for depressive phase (10%) is significantly related to initial depressive polarity ,greater comorbidity and shorter time to first readmission

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Rates and predictors of rehospitalization after the first lifetime hospitalizations for manic or mixed episode . A naturalistic study in Spanish sample of Bipolar I inpatients

Authors: Villar Laura, Carreras J, Rius M, Malo M, Perez A, Bonet P and Nieto E

Departament of Psychiatry. Althaia Xarxa Assistencial of Manresa.

C/ Dr. Joan Soler sn., Manresa. CP:08243, Spain., maktub16@hotmail.com

Objective

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- Those who had no rehospitalizacion.
- Those who were readmitted for the first time in a manic phase,
- Those who were readmitted for the first time in a mixed phase
- Those who were readmitted for the first time in a depressive phase

We compared basal clinical , biological and sociodemographic variables between the 4 subgroups ob Bipolar patients. We used the Chi-square test for qualitative variables, the Student t test for the numeric with normal distribution and the U of Mann-Whitney test for the numeric without normal distribution. F

Results

Patients: Of the 125 first-episode type I BPD patients, 90 presented in mania and 35 in DSM-IV mixed episodes (28%). Both groups were very similar in sex-distribution: 52 % men with initial mania vs. 43% with mixed-states. Manic first-episodes requiring hospitalization occurred at similar ages than did mixed-states (33.5±11.9 vs. 32.06±10,9 years; F=0,49, p<0.5).

Fifty-three patients (42,4%) required at least one readmission in the follow-up period , 29 (23,2%) for manic phase, 13 (10,4%) for mixed phase and 11 (8,8 %) for depressive phase

2.Variables significantly associated in univariante analysis with the subgroup or manic readmission were : first hospitalization for mania (93% vs 66% P

<0.003), lower age (29 vs 35 P><0.05) lower cholesterol (3,84 vs 4,41 mmol/l) P><0.02) and higher creatinine levels (0,94 vs 0,84 mg/100ml) P><0.01) in the first hospitalization. The mean time to readmission for a manic phase was 842 days. The average number of readmissions when the first rehospitalization was for mania was 1,83>3. Variables significantly associated in univariante analysis with the subgroup or mixed readmission were: first hospitalization for mixed phase (69,2% vs 23,2 % P

<0.001), suicide attempt in the first hospitalization (30,8% vs 1,8%, P><0.001). The mean time to readmission for a manic phase was 891 days. The average number of readmissions when the first rehospitalization was for mixed phase was 2,38.>4. Variables significantly associated in univariante analysis with the subgroup or depressive readmission were psychiatric comorbidity (82%vs 49,6%, P

<0.05) , onset of bipolar disorder in a depressive episode (82% vs 46,5% P><0.03). The mean time to readmission for a depressive phase was. significantly shorter than in the case of readmission for manic or mixed phase (368 vs 868 , P><0.05) The average number of readmissions when the first rehospitalization was for depressive phase was 2,55 >

Conclusion

1. At a mean follow-up period of 6 years after the first admission for manic or mixed phase 42% of bipolar patients were readmitted at least once.

2. The readmission for manic phase (23%) is significantly related to the first hospital admission for mania and also biological variables (younger age, lower cholesterol levels , and higher creatinine levels)

3. The readmission for mixed phase (11%) is significantly related to the first admission for mixed phase and the presence of suicidal behavior

4. The readmission for depressive phase (10%) is significantly related to initial depressive polarity ,greater comorbidity and shorter time to first readmission.

Additional Information

References

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Screening for bipolar disorder in a group of children hospitalized in psychiatry

Authors: Sami Othman, Soumya Halayem, Asma Bouden, Mohamed Bechir Halayem

Professional adress : service de pédopsychiatrie, RAZI Hospital, PB 2010, La Manouba, Tunisia

sami.oithman1@yahoo.fr

Objective

Determine the frequency of bipolar disorder in a group of children and adolescents hospitalized in psychiatry using arab version of the Child Bipolar Questionnaire

Method

during one year all patients aged 6 to 17 years hospitalized in the department of children and adolescent psychiatry at Razi hospital in Tunis, Tunisia were assessed using K-SADS-PL and arabic version of the CBQ. patient with Pervasive developmental disorders, Mental retardation, or Organic diseases were excluded

Results

N = 70

- patients were aged 7 to 17 years
- average age: 13.2 years
- Sex ratio = 1
- 15 children had positive score of bipolar disorder with two cases of comorbid ADHD-BP. Only 9/15 had a mood disorder confirmed by clinical examination and the K-SADS-PL:
- 3 cases of early onset bipolar disorder.

- 1 case ADHD-hypomania
- 5 cases of depression

the remaining 6 cases, considered initially bipolar, were diagnosed with ADHD and conduct disorder.

Conclusion

the CBQ is a sensitive questionnaire but not specific. It induces overdiagnosis. Actually, there are controversial discussions about bipolar disorder criteria in children and adolescent and one of the biggest challenges for child psychiatrist has been to differentiate early onset bipolar disorder from attention deficit hyperactivity disorder (ADHD).

Validation of the Mood Disorders Questionnaire for bipolar disorder in the postpartum period

Author: Verinder Sharma, Bin Xie

Regional Mental Health Care – London, Mood Disorders, 850 Highbury Ave.

London ON N6A 4H1, Canada vsharma@uwo.ca

Objective

We aimed to validate the Mood Disorders Questionnaire for the screening of bipolar postpartum depression.

Method

Women with histories of major depressive disorder or bipolar disorder (type I or II) attending an outpatient perinatal clinic were administered the Mood Disorder Questionnaire during the first month after delivery. An experienced research coordinator, blind to the Mood Disorder Questionnaire results, conducted a face to face diagnostic interview using the Structured Clinical Interview for DSM-IV.

Results

A total of 57 women with bipolar disorder (30 with bipolar II disorder and 27 with bipolar I disorder) and 68 women with major depressive disorder completed the Mood Disorder Questionnaire between two to four weeks after delivery. The traditional scoring criteria yielded a sensitivity of 75.44% [95%CI: 62.24%-85.87%] and a specificity of 86.76% [95%CI: 76.36%-93.77%]. The optimal cut-off score was eight or more endorsed symptoms without the supplementary questions (a sensitivity of 87.72% [95% CI: 76.32%-94.92%] and a specificity of 85.29 % [95%CI: 74.61%-92.72%]).

Conclusion

The Mood Disorder Questionnaire with alternate scoring is a useful screening instrument for bipolar disorder in the postpartum period.

Prevalence of unrecognized lifetime bipolar disorders in patients currently diagnosed with major depression: an explorative study

Authors: Kaloyan Stoychev (1), Krasimir Ivanov (1), Mariya Aleksandrova (1), Angelika Velkova (2)

(1) Medical University Pleven, Department of Psychiatry and Medical Psychology

(2) Medical University Pleven, Department of Public Health

24-A-10 Hadji Angel str., 5800 Pleven, Bulgaria, kaloyan_stoichev@abv.bg

Objective

Recent reanalyses of data from large longitudinal epidemiological studies show that about 40% of patients diagnosed with major depressive disorder (MDD) actually have unrecognized bipolar illness. Misdiagnosed bipolarity might be a major reason for treatment resistant depression. To check the validity of such possibility, we made a small explorative study for presence of underdetected bipolarity in patients presenting with MDD.

Method

Using a cross-sectional design and predefined inclusion/exclusion criteria, we recruited 26 patients with DSM-IV major depressive episode (MDD) referred to treatment at the psychiatry department of Pleven University Hospital from February to March 2011. No patients with previously known bipolar disorder (BD) were sampled. Participants were assessed with a semi-structured interview covering all relevant sociademographic, clinical, medical and treatment history data. For identification of lifetime mania/hypomania we developed a structured inventory detecting changes in level of activity, mood variability and presence of short (under 4 days) episodes of mood elevation on a lifetime basis. Collateral confirmation of data was obtained by means of interview with patients' significant others. Thus, a diagnosis of BD was justified by several different diagnostic algorithms. Analysis of data was directed at:

(1). Measuring the lifetime prevalence of unrecognized bipolar I (BP-I) or bipolar II (BP-II) disorder in the sample.

(2). Comparing BP-I and BP-II patients with pure MDD patients in terms of course and severity of illness, clinical characteristics of depression and presence and duration of intra-episodic manic symptoms.

(3) Analyzing rates of treatment resistance and intolerance to SSRIs in patients with bipolar and unipolar depression.

Statistical analyses were carried out in SPSS 13.00 for Windows.

Results

16 (62%) out of 26 patients met DSM-IV-TR criteria for bipolar disorder on a lifetime basis. Three of them were diagnosed with BP-I and thirteen had BP-II. Ten patients (7 women and 8 men) were identified as having pure MDD. BP-I disorder was more common in women (8 out of 13 cases) while all BP-I cases were found in men.

Bipolar patients had younger mean age, earlier onset of depressive symptoms and earlier age of clinical diagnosis (BP-I patients only), more mood episodes and hospitalizations. In pure MDD cases substantially longer duration of current symptoms was observed. Only bipolar patients showed positive family history for bipolarity, had history for suicide attempts and co-occuring anxiety disorders.

Presence and duration of intraepisodic manic symptoms (distractibility, irritability, and mood lability) was notably higher in bipolar patients. They also more often showed atypical depressive symptoms like mood reactivity, increased appetite and hypersomnia.

Regarding SSRSs treatment history, both groups did not differ in terms of treatment resistance, but bipolar patients had higher rates of drug induced irritability and anxiety.

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Conclusion

A diagnosis of MDD based on current classification systems is problematic because it includes significant number bipolar cases. Bipolar depression is associated with earlier onset, more mood episodes and greater variability of symptoms including more atypical ones. Although rate of treatment resistance in bipolar patients did not exceed those in MDD ones, there are some indications of poorer tolerance to SSRIs in the former.

The STANLEY project – a large scale Swedish bipolar DNA collection

Authors: Emma Flordal Thelander, Marie Lundin, Birgitta Ohlander, Radja Dawoud, Leila Nyrén, Sebastian Paulsson-Magné, Mikael Landén

Dept of Medical Epidemiology & Biostatistics, Karolinska Institutet, Box 281, SE-171 77 Stockholm, Sweden, emma.flordal.thelander@ki.se

Objective

The aim of this study is to collect blood samples from 5000 individuals in Sweden diagnosed with bipolar disorder in order to perform Genome Wide Association Studies (GWAS). Linkage of data with Swedish national health registers will enable analyzes of gene-environment interactions. Samples from 6500 individuals without a psychiatric diagnosis have already been collected and genotyped and will be used as control material. Our sample collection is part of the International Cohort Collection for Bipolar Disorder (ICCBD) with the overall goal to collect 19000 bipolar samples.

Method

This study was initiated in 2009 after a pilot study performed in 2007. Subjects are identified from two sources; the Swedish National Quality Assurance Registry for Bipolar Disorder (QR) and the Swedish Hospital Discharge Registry (HDR). In the QR, patients are registered at their local psychiatric clinic by their treating doctor or nurse, and phenotype data such as psychiatric history is also available. In the HDR, all over-night hospitalizations in Sweden are registered and subjects hospitalized at least twice with a diagnosis of bipolar disorder were selected.

Initially, the subjects receive an invitation letter describing the study process and a request for participation. The letter is followed up by a call from a research nurse when questions can be answered. If the subject wants to participate, a phone interview with questions regarding background, health status and psychiatric symptoms is conducted. A blood sample kit is sent by mail and the patient goes to a health care unit to take the blood sample. The sample and a signed informed consent is sent to our Biobank for DNA extraction and thereafter shipped to Broad Institute (Boston, USA) for GWAS and sequencing analysis.

All subjects are also asked for permission to access data from other registries, such as the Medical Birth Registry and the Prescribed Drug Registry, as well as consent to access medical records to be able to confirm that diagnostic criteria are fulfilled in a proportion of the cases.

Results

So far, about 7600 subjects have been contacted. Almost 4000 individuals have so far consented to participate in this study, hence donated a blood sample and responded to a questionnaire. All in all, 13% of the subjects have been excluded since they do not fulfill the inclusion criteria, due to recent demise or acute illness, 12% we could not get in contact with, 18% rejected participation and 55% accepted to participate in this study. So far, the vast majority of subjects have been identified through the QR, but a tendency can yet be seen that these persons are more willing to take part in the study than patients identified through the HR.

The data collection will be finished by the end of 2012.

Conclusion

We have developed a logistic process for high throughput, large-scale sample collection of blood from individuals with bipolar disorder identified through Swedish national registers. This will be one of the largest sample collections of this kind and together with additional Swedish register data, this will hopefully serve as a valuable source in bipolar disorder research for many decades ahead.

PSYCHOLOGICAL ASPECTS

The effectiveness of brief cognitive psychotherapy in the reduction of patients' depressive symptoms in relation to the number of episodes

Authors: Luciana de Avila Quevedo, Adriana Carvalho, Karen Jansen, Luciano Dias de Mattos Souza Ricardo Tavares Pinheiro, Ricardo Azevedo da Silva

Praça 20 de Setembro 904 b/203, Brazil

lu.quevedo@bol.com.br

Objective

To determine whether cognitive therapy is more effective in reducing depressive symptoms in first-episode patients or in patients with previous episodes.

Method

Randomized clinical trial with youth aged 18 to 29 years who met diagnostic criteria for depression assessed by the Structured Clinical Interview for DSM (SCID). Participants who were in psychological or psychiatric treatment and / or who showed suicide risk, or who used some psychoactive substance (except tobacco and alcohol) were excluded. Depressive symptoms were assessed using the Hamilton Depression Scale (HAM-D), in addition, young people were asked about the number of episodes. The models of psychotherapy were used: Cognitive Therapy Narrative (TCN) and Cognitive Behavioral Therapy (CBT), both with 7 sessions. At the end of treatment, the final evaluation was performed with the HAM-D and HAM-A. The statistical analysis was realized in the SPSS 13.0 for Windows. All subjects gave written informed consent for the analysis and anonymous publication of research findings.

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Results

We randomized 91 patients diagnosed with depression. Of these, 46 received CBT and 45 received TCN. 46 participants completed the treatment, 18 in CBT and 28 TCN. Thirty-six (78.3%) of the sample had experienced previous episodes. The mean difference between patients treated in CBT was 8.22 (95% CI: 6.03, 10.42) points in the average Hamilton`s Scale (depressive symptoms, while the difference between the averages of those treated in NCT was 5.57 (95% CI: 3.10, 8.04). Participants who were in first depressive episode declined 4.20 (± 11.02) points in the average Hamilton´s Scale (depressive symptoms), while those who had previous episodes, showed a reduction of 12.16 (± 6.82) points in mean score of depressive symptoms (p = 0.07).

Conclusion

There was remission of depressive symptoms in two models of intervention and on the number of episodes; the reduction of depressive symptoms was higher in those who were not in the first episode.

RAINBOW, Psychosocial Therapy for Pediatric Bipolar Disorder (PBD):Adaptation to Portuguese Families

Authors: Sónia Fernandes, Isabel Sá, Mani Pavuluri
Rua do viveiro nº402 6ºesq., 2765-428 Estoril, Portugal
sonia.fernandes@cadin.net

Objective

Despite the prevalence of pediatric bipolar disorder (PBD) in Portugal, there are no formal or organized therapies designed to treat these children. The current study aims to address the gap in Portugal by examining the feasibility of RAINBOW therapy to Portuguese families.

Method

It was necessary to adapt the RAINBOW programme to meet the unique needs of the PBD population in Portugal. Our aim was to enhance the core RAINBOW curriculum via supplemental modules to address the following areas of need: (1) limited awareness and acceptance of the PBD diagnosis; (2) limited advocacy for the rights and needs of children with psychiatric disorders within the school setting; and (3) cultural differences in parenting styles that impact the treatment content. The development and implementation of the adapted RAINBOW model will be presented, along with results from an open trial examining the feasibility, acceptability, and efficacy for PBD in Portuguese families. Youth ages 6-15 with bipolar disorder and their families were recruited from the Child Development Disorders Support Center in Cascais, Portugal. Parents and children were assessed pre- and post-treatment.

Results

Results suggest that the RAINBOW programme was feasible and acceptable to Portuguese families. Parents reported significant improvement in their child's behavior, reductions in parent-child conflict, and reductions in parental conflict.

Conclusion

Evidence suggests that RAINBOW is feasible and acceptable to Portuguese families and warrants further development to meet the need in the Portuguese community.

Recovery is Such a Huge Word: Understandings of 'Recovery' in People with Bipolar Disorder and Implications for Psychiatric Care

Authors: Hou, Sharon; Michalak, Erin; Hole, Rachelle; Holmes, Cindy; Velyvis, Vytas; Austin, Jehannine; Pesut, Barbara; CREST.BD.

Objective/Background

Bipolar disorder is a challenging psychiatric condition characterized by complex and varying symptoms, course and outcomes. This complexity is compounded by differing understandings of recovery from no hope of recovery, to clinical recovery characterized by a linear diminishing of symptoms, to personal recovery characterized by meaningful quality of life. These understandings have profound implications for individuals living with bipolar disorder, and yet, we know little about the meaning of recovery from their perspective. The purpose of this study was to explore what the term recovery means in a sample of Canadian individuals living with bipolar disorder via qualitative research methods.

Methods

Three focus groups, including 13 individuals who self-reported as being diagnosed with bipolar disorder type I or II, were conducted to better understand the meaning of recovery. Focus groups were digitally recorded and transcribed. Transcripts were coded manually and analyzed thematically.

Results

"The Meaning of Recovery" was a rich category with numerous supporting themes and nuanced dimensions. Four themes dominant themes were identified through coding and thematic analysis: "Re-thinking the Language of Recovery", "Shifting the Framework", "The Art of Managing BD", and "Understanding the Journey."

Conclusion

Four important practice implications arise from this study. Firstly, it is important to find a language of recovery that reflects the complexities of living with a chronic mental health condition. Secondly, quality of life should be given priority in the treatment process. Short well validated scales are available to facilitate this exploration. Thirdly, emphasis should be placed upon the capacity of people living with bipolar disorder to self-manage their condition. A variety of techniques and tools are available to assist clinicians. Lastly, a collaborative therapeutic relationship is foundational to enabling individuals to rebuild a sense of self and lower the stigma associated with living with bipolar disorder.

Insights such as these into the meanings of recovery for individuals living with bipolar disorder are essential to high quality care. Individuals in this study provided complex and nuanced understandings of recovery that were meaningful in relation to their lives. However, it is important to note that this was a small sample, all self-referred and not ethnically

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diverse. Research is required to further our understandings of recovery in more diverse populations.

Additional Info (bio):

Sharon Hou received her BA (Honours) in Psychology and French from the University of California, Los Angeles. She is currently the Research Coordinator for the Collaborative RESearch Team to study Bipolar Disorder (www.crestbd.ca). Through her work, Sharon is acquiring experiences in conducting psychological research, such as mixed-methods (qualitative and quantitative) research, translational research, and community-based participatory research. She is interested in studying the psychosocial facets of bipolar disorder, such as interpersonal traits, life events, and quality of life. Sharon is currently in pursuit of her doctoral degree in Clinical Psychology.

Bipolar disorder and psychotherapy: patients characteristics in Lombardy Region (Italy)

Authors: Buthaina Ibrahim, Antonella Zambon, Antonio Lora, Emiliano Monzani, Giovanni Corrao Università di Milano-Bicocca, Facoltà di Scienze Statistiche: Ed. U7, Via Bicocca degli Arcimboldi, 8 - 20126 Milano, Italy b.ibrahim.84@gmail.com

Objective

The study aims to describe clinical and socio-demographic charateristics of bipolar disorder (BD) patients treated with pharmacological therapy alone and BD patients also treated in combination with psychotherapy in the current Italian clinical practice.

Method

The target population consisted of all patients aged 18 years or older, with an ICD-10 diagnosis of bipolar disorder between January 2006 and December 2009, residents in Lombardy – an Italian region with about 9 million residents (16% of the national population). All patients were followed for 1-year of follow-up. Data on these individuals was extracted from PSICHE, a large electronic database designed to monitor the mental health and the use of mental health services of Lombardy residents. Pharmacotherapy included antidepressants, mood stabilizers and antipsychotics agents. Psychotherapeutic interventions included cognitive behavioural therapy, psycho-education, family therapy and group therapy. Chi-square tests were applied to test for differences in the measured variables – including age, educational level, occupational status and comorbidity profile - between patients treated with pharmacotherapy alone or in combination with psychotherapy.

Results

Out of 4635 individuals aged 18 years or older diagnosed as having bipolar disorder, 1750 (37.8%) were treated with psycho- and pharmaco-therapy and 2885 (62.2%) with pharmacotherapy only. Compared with patients treated with pharmacotherapy alone during the first year of follow-up, those treated with psychotherapy in addition to pharmacotherapy were significantly younger (mean age 48.4 versus 49.7, p=0.005), and more often unemployed (17.2% versus 15.5%, p <0.0001). The two groups did not show a statistically significant difference in gender (female were 57.5% versus 56.4%, respectively), Charlson comorbidity score (absence of any comorbidities was 85.3% versus 85.1%, respectively), years of education (1-5, 6-7, 8-13 and ≥14 years of education were 22.1%, 39.9%, 29.2% and 8.8% versus 20.8%, 38.6%, 29.9% and 10.7%, respectively) and marital status (married patients were 47.3% versus 48.6%, respectively). >

Conclusion

Although several reviews on the efficacy of psychotherapeutic interventions for bipolar disorder are already available in the literature, not all patients receive psychotherapy treatment. Most importantly, our findings show that there was no difference in the Charlson comorbidity score in patients treated with psychopharmacologic therapy and those treated with only pharmacotherapy, while it is well known in literature that patients with a low comorbidity score are more likely to be non-adherent to pharmacotherapy. So, for these BD patients combining drug therapy with non pharmacologic interventions might improve adherence and achieve better treatment outcomes because a better monitoring of drug treatment intake is possible due to the more frequent contacts with health-care professionals facilitates. The additional support of psychotherapy to pharmacotherapy therefore deserves more research

Advancing bipolar disorders research via collaborative knowledge translation

Authors: McBride, Sally; Michalak, Erin; Youngstrom, Eric; CREST.BD

Background

The Collaborative RESearch team to study psychosocial factors in BD (CREST.BD) is a multidisciplinary, Canadian network dedicated to both fundamental research and knowledge exchange on bipolar disorder (BD).

The team's core mandate is to focus on research, clinical practice, and social change informed by a focus on psychosocial factors in BD.

CREST.BD bridges traditional and newer research approach, with a special emphasis on community-based participatory research methods, whereby people with BD and their family members, and other key stakeholders (e.g., mental health providers), are active participants in research and knowledge exchange.

Method

Membership of CREST is broad, including academic researchers, people with BD and their family members, and a variety of health care providers.

Although there are other excellent teams internationally specialising in BD research, CREST.BD is unique in its multidisciplinary configuration; it now includes team members from a diverse range of disciplines (including psychology, psychiatry, criminology, nursing, social work, gerontology, occupational therapy and genetic counselling), expertise in a breadth of traditional research

methods and wide ranging fields of BD specialisation (including stigma, psychosocial treatments, advocacy, advanced statistics and psychometrics, assessment, cognition, spirituality, coping, novel technologies, indigenous, youth and aging populations). Further, it is the only cross-sectoral BD network (integrating 'lived experience' or community expertise, the public health sector, community agencies and academia) to specialise in research committed to integrated KT.

Integrated KT' represents a collaborative and participatory approach where researchers, healthcare providers and patients work together as partners to design, conduct and evaluate research.

Results

Key research projects within CREST.BD portfolio have generated knowledge on: effective self-management strategies for BD, methods for the utility of quality of life assessment in clinical care and methods and the rational for mental illness stigma. The team's 'Knowledge to Action' (KTA) translational research study, for example, has used novel knowledge translation (KT) strategies to swiftly and effectively disseminate research findings in these areas.

Conclusions

Model epitomised by CREST.BD has the potential to pay real dividends in terms of improving the quality and effectiveness of BD research. Collaborative research methods can:

- Allow for the development of research hypotheses that are of high relevance to those affected by BD
- improve research recruitment and retention, and the quality of research data because research participants have a vested interest in the process
- increase the relevance and pragmatism of new treatment interventions
- empower patients and reduce BD-related stigma

Acknowledgment: CREST.BD's work is made possible by a 3-year Canadian Institutes for Health Research (Network Catalyst – Knowledge Translation) grant.

Additional Info (bio):

Sally McBride is a public health professional, with a BA in Medical Anthropology from the University of Victoria (British Columbia, Canada) and a Masters in Public Health from Simon Fraser University (Burnaby, Canada). She has seven years' experience working in communications, community engagement and population health research in Canada. Currently, she is the Knowledge Translation Manager for The Collaborative RESearch Team to study Bipolar Disorder (www.crestbd.ca), a national network committed to taking an interdisciplinary approach to participatory research and knowledge exchange. In this position she facilitates the development of innovative ways to share mental health research, engages diverse stakeholders in knowledge exchange initiatives and supports people with mental health diagnoses and healthcare providers to work in academic research. Over the past 10 years, Sally's career scope has included the faciliation of community engagement initiatives for a population health research network, and engaging in the health systems research with the Pan American Health Organization.

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Creativity and schizotypy in Bipolar Illness Painting "Mania"

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