



ECNP
Seminar in
Neuropsychopharmacology



2-4 November 2012

Bran

Romania

Introduction

The European College of Neuropsychopharmacology (ECNP) was established in 1987 on the initiative of scientists and clinicians working in Europe in the convergent disciplines in neuropsychopharmacology and related neurosciences.

ECNP aims to widen knowledge in regard to central nervous system disorders, and to increase awareness, recognition and improvement of the treatment of these disorders. To fulfill this aim ECNP organizes, amongst others, yearly the ECNP Congress that comprises at least 3 plenary lectures, 28 symposia and 6 educational update sessions. The latter sessions target issues such as updates on evidence-based treatment and new developments in the preclinical area that influence the clinical field. The annual meeting attracts more than 7,000 participants and is considered to be the largest event in neuropsychopharmacology in Europe.

ECNP also supports on an annual basis participation of 100 young psychiatrists and researchers in an intensive three-day Workshop in Nice. Other activities of ECNP include the journal *European Neuropsychopharmacology* that promotes scientific knowledge along with publishing consensus statements. These consensus statements are products of an annual meeting with delegates from the scientific community in neuropsychopharmacology (scientists and clinicians), European regulators and industry in which discussion about issues such as use of placebo, guidelines for long-term maintenance are discussed. In addition, since 2009 ECNP organizes a summer school of neuropsychopharmacology in Oxford and since 2012 a child and adolescent school of neuropsychopharmacology in Venice.

Finally, ECNP organizes seminars, as the one you have been invited to participate, in areas where there are less opportunities for psychiatrists to participate in international meetings. We have previously organized a Seminar in Romania. So far, besides our previous meeting in your country, ECNP has organized this meeting in Poland, Estonia, Turkey, Bulgaria, Slovak Republic, Hungary, Check Republic, Moldova. Interaction is the keyword at these meetings and they have proved very successful both for the participants and for the faculty.

Please see the ECNP website (www.ecnp.eu) where you can find information about the above initiatives and additional information.

I look forward to a fruitful and inspiring meeting in Romania!

Celso Arango, MD

Chair ECNP Educational Committee

Program ECNP Seminar in Neuropsychopharmacology 2-4 November 2012, Romania

FRIDAY 2 NOVEMBER 2012

Arrival of participants and experts

19.00 Welcome and dinner

SATURDAY 3 NOVEMBER 2012

08.15 – 08.30 Introductions to the programme
Celso Arango, Spain

08.30 – 09.15 Treatment of acute psychoses
Celso Arango, Spain

09.15 – 10.00 Benefit / risk assessment in medicine in general and psychiatry in particular
Michael Davidson, Israel

10.00 – 10.30 Coffee break

10.30 – 11.15 Unipolar and bipolar mood disorders – commonalities and differences in etiology and pathogenesis
Erkki T. Isometsä, Finland

11.15 – 11.30 How to give a talk
Celso Arango, Spain

Presentations participants in 3 groups in 3 parallel workshops			
Round 1 11.30 – 13.00	<i>Celso Arango and Alexandra Mihailescu</i> Group 1	<i>Michael Davidson and Valentin Matei</i> Group 2	<i>Erkki T. Isometsä and Radu Teodorescu</i> Group 3
13.00 – 14.00 Lunch			
Round 2 14.00 – 15.30	<i>Celso Arango and Alexandra Mihailescu</i> Group 2	<i>Michael Davidson and Valentin Matei</i> Group 3	<i>Erkki T. Isometsä and Radu Teodorescu</i> Group 1

15.30 – 16.00 How to prepare a scientific paper

16.00 – 21.00 Excursion Bran castle and dinner

SUNDAY 4 NOVEMBER 2012

Presentations participants in 3 groups in 3 parallel workshops			
Round 3 08.15 – 09.45	<i>Celso Arango and Alexandra Mihailescu</i> Group 3	<i>Michael Davidson and Valentin Matei</i> Group 1	<i>Erkki T. Isometsä and Radu Teodorescu</i> Group 2
09.45 – 10.00 Coffee break			
10.00 – 11.00 Preparation for plenary session			
Plenary 11.00 – 12.00	11.00 – 11.20	Group 1 Presentation	
	11.20 – 11.40	Group 2 Presentation	
	11.40 – 12.00	Group 3 Presentation	

12.00 – 12.15 Preparation of awards ceremony

12.15 – 12.30 Awards ceremony

12.30 – 12.45 Concluding remarks and thanks
Celso Arango, Spain

12.45 – 13.45 Lunch



Celso Arango

Celso Arango, MD, PhD

Associate Professor of Psychiatry, University of Maryland, Baltimore
Associate Professor of Psychiatry, Universidad Complutense, Madrid
Head of the Child and Adolescent Department of Psychiatry,
Hospital General Universitario Gregorio Marañón
Chair ECNP Educational Committee

Celso Arango, MD, PhD is a psychiatrist and Associate Professor of Psychiatry at the University of Maryland in Baltimore and the Universidad Complutense in Madrid. He is also Head of the Child and Adolescent Department of Psychiatry at Hospital General Universitario Gregorio Marañón. Dr. Arango is the Scientific Director of the Spanish Psychiatric Research Network with 25 centers and more than 400 researchers. He is also Coordinator of the Child and Adolescent First-Episode Psychosis Study (CAFEPS) funded by the Spanish Ministry of Health (with eight centers in Spain) and the Child and Adolescent Neuropsychiatry Network funded by the European College of Neuropsychopharmacology (ECNP). He has written more than 230 peer-reviewed articles, 6 books, and more than 35 book chapters. Many of his articles and book chapters have focused on the neurobiology of early-onset and first-episode psychoses as well as the safety of psychiatric medications in pediatric patients. In addition, his group has shown how patients with a first psychotic episode experience greater losses of gray matter than expected and a correlation of gray matter loss with antioxidant status. Dr. Arango has participated in more than 59 competitively funded research projects, as Principal Investigator in 43 of them, including projects with international funding (Stanley Foundation, NARSAD, European Commission, etc.) and several clinical drug trials. He is also coordinator of several multicenter projects that assess multiple prognostic factors and treatment in early-onset psychosis, and is currently participating in five EU projects funded by the VII Framework.



Michael Davidson

Professor Michael Davidson, MD

Sheba Medical Centre
Department of Psychiatry
Tel Hashomer, 52621, Israel
E-mail: mdavidson6@gmail.com

Michael Davidson, MD is psychiatrist, Professor of Psychiatry at the Sackler School of Medicine. Dr Davidson started his psychiatrist career at the Mount Sinai Medical School in New York where he stayed for about 15 years, the last 5 years as Professor of Psychiatry. His research career has begun studying dopamine activity in schizophrenic patients, which was cutting edge research in 1980 and his paper was published in Science. He has written more than 250 peer-reviewed articles. Many of his articles have focused on neurobiology of schizophrenia, risk factors of schizophrenia, bipolar disorder, Alzheimer's disease. In addition, his group is producing interesting results upon premorbid markers in schizophrenia. Dr. Davidson has awarded more than 50 research grants, including projects with international funding (Stanley Foundation, NIMH, European Commission, etc.). During the late eighties dr Davidson has initiated the set-up of the Schizophrenia Brain Bank at the Mount Sinai Medical School in New York. Dr Davidson initiated and conducted more than 40 clinical drug trials. He is presently Principal Investigator in a multicenter project that studies the link between diabetes and Alzheimer's Disease, and is currently participating in OPTiMiSE EU project funded by the VII Framework. Dr Davidson has been awarded with ECNP-Psychopharmacology Award 2004, CINP Neuroscience Award 2006 and he is was a ACNP Fellow. Dr. Davidson is Chief Editor for European Neuropsychopharmacology, he is reviewer or board member to the Archives of General Psychiatry; American Journal of Psychiatry; Biological Psychiatry; Schizophrenia Bulletin; Schizophrenia Research; Psychiatry, Dialogues in Neurosciences, Alzheimer's disease and Related Disorders Journal .



Erkki Isometsä

Erkki Isometsä, M.D., Ph.D.

Professor and Chair, Department of Psychiatry,
Institute of Clinical Medicine,
University of Helsinki &

Research Professor (part-time),
Dept. of Mental Health and Substance Use Services,
National Institute for Welfare and health,
Helsinki, Finland

Erkki Isometsä is professor and chair of psychiatry at the University of Helsinki, Finland. He is also part-time research professor at the National Institute of Health and Welfare in Helsinki, and Chief Physician at the Department of Psychiatry of the Helsinki University Central Hospital (HUCH). Dr. Isometsä started his scientific career in the late 1980's in the National Suicide Prevention Project in Finland, investigating completed suicides among subjects with mood disorders in his PhD thesis. Since then his main research foci have been clinical and epidemiological research on unipolar and bipolar mood disorders and suicidal behaviour. He has led clinical-epidemiological research on mood disorders as the PI of large cohort studies such as the Vantaa Depression Study (VDS), Jorvi Bipolar Study (JoBS), and Vantaa Primary Care Depression Study (PC-VDS). These studies have investigated the clinical outcome of mood disorders, and risk factors for suicidal behavior or long-term disability among these patients. Besides these longitudinal studies, he also leads research on molecular genetics and brain imaging in mood disorders. His more recent research interests include influence of mood disorders or antidepressants on processing of emotional information. Overall, he has published over 200 peer-reviewed scientific papers, which have been cited about 5000 times. He has supervised 14 psychiatric PhD dissertations, with nine dissertation projects ongoing. He has chaired the national Finnish Current Care Guidelines for Depression Task Force, is currently member of the Affective Disorders and Antidepressants Scientific Advisory Panel of the European College of Neuropsychopharmacology (ECNP), Secretary & Treasurer of the International Academy of Suicide Research (IASR), and member of the editorial boards of *Bipolar Disorders* and *Acta Psychiatrica Scandinavica*.



Radu Teodorescu

Radu Teodorescu, MD, PhD

Head of the Department for Community Psychiatry
and Psycho-social Rehabilitation

“Prof. dr. Al. Obregia” Clinical Hospital of Psychiatry

E-mail: tdrscrd@yahoo.com

Radu Teodorescu, MD, PhD is psychiatrist, Head of the Department for Community Psychiatry and Psycho-social Rehabilitation at “Prof. dr. Al. Obregia” Clinical Hospital of Psychiatry, Bucharest, Romania. Dr Teodorescu started his psychiatrist career in 1986 in Bucharest and worked in France between 1992-1994 as a psychiatrist and clinical researcher. In 1994 he has begun training and he specialized in Cognitive Behavioral Therapy. Dr Teodorescu is certified trainer of Cognitive Behavioral Therapy and has created the Romanian Association of Cognitive Behavioral Therapy, through which he has coordinated training of more than 300 CBT psychotherapists. Dr Teodorescu published more than 40 articles. Many of his articles have focused on Cognitive Behavioral Therapy in eating disorders, depression, anxiety disorders and schizophrenia. He has edited two books „Anxiety disorders” (1999) where he authored a chapter on cognition in anxiety disorders and one regarding social phobia; „Textbook of mental health” (2001) where he has authored two chapters one on personality disorders and one on Cognitive Behavioral Therapy. Dr Teodorescu conducted more than 10 clinical drug trials. Dr Teodorescu is reviewer or board member for the Dutch journal «Mental Health», the French journal «Art-Psy», the Romanian Journal of Psychiatry, and he is member of the following scientific societies Romanian Psychiatric Association, member of the Romanian Association for Rehabilitation, Association Française de Psychothérapie Comportementale et Cognitive, the Romanian Psychotherapeutic Association, International member of the American Psychiatric Association, the European Association of Psychiatry. He is national representative European Association of Behavioral Cognitive Therapies and president of the Romanian Association of Behavioral-Cognitive Therapies.



Valentin Matei

Valentin Matei, MD, PhD

Head of the Department XIII

“Prof. dr. Al. Obregia” Clinical Hospital of Psychiatry

E-mail: vm_matei@yahoo.com

Valentin Matei, MD, PhD is psychiatrist, Head of the Department XIII of Adult Psychiatry at “Prof. dr. Al. Obregia” Clinical Hospital of Psychiatry. Dr Matei started working as psychiatrist in 2002, and in 2004 he worked at the Queen Elisabeth Hosp. London, Old Age Psychiatry Ward (clinical attachment). His research career began in the early years of psychiatry specialty and in 2007 he worked as a Fellowship Researcher at the Institute Of Psychiatry London. He has written more than 20 articles, mostly in peer reviewed national journals, and he has presented the results of his work at international conferences. Many of his articles have focused on risk factors of depression and schizophrenia, correlations between cognitive functioning and early onset of schizophrenia or depression. Dr Matei was co-investigator in 4 clinical drug trials in the areas of schizophrenia and Alzheimer’s disease. He is presently Principal Investigator in several multicenter clinical trials that study treatment of schizophrenia, and is currently participating in OPTiMiSE EU project funded by the VII Framework. Dr Matei has been awarded for best presentations with ECNP -Seminar Award in 2005 and in 2008 with Romanian Congress of Psychiatry – best presentation award. Dr. Matei is reviewer for the European Journal of Neuropsychopharmacology.



Alexandra Mihăilescu

Alexandra Mihăilescu, MD

Specialist psychiatry Department XII
"Prof. dr. Al. Obregia" Clinical Hospital of Psychiatry
Assistant professor Medical Psychology
University of Medicine and Pharmacy Carol Davila, Bucharest
E-mail: andrast79@yahoo.com

Alexandra Mihailescu, MD, is psychiatrist, working at Department XII of Adult Psychiatry at "Prof. dr. Al. Obregia" Clinical Hospital of Psychiatry, and assistant professor and PhD student at the University of Medicine and Pharmacy Carol Davila, Bucharest. Dr Mihailescu has started her research career as undergraduate with small studies on stress biology and psychosomatics. Her research interests are stress, mood and anxiety disorders in young adults. Dr Mihailescu has published 9 articles, most of them in peer reviewed national journals and several book chapters. In addition, she edited Psychoneuroallergology – 2nd edition, ed. Ioan Bradu Iamandescu. Dr Mihailescu participated as co-investigator in 8 clinical drug trials and also worked as a clinical research associate in 2 drug trials (neurology and psychiatry areas). She is currently participating in OPTiMiSE EU project funded by the VII Framework. Dr Mihailescu has been awarded with Romanian Medical Academy prize for best poster in 2011. Dr. Mihailescu is reviewer for 2 online open access journals, Patient Preference and Adherence and Neuropsychiatric Disease and Treatment. Dr Mihailescu is member of the following scientific societies: Romanian Psychiatric Association, Romanian Society of Psychoneuroendocrinology and she is member in the operational committee and scientific secretary of Romanian Society of Applied Psychosomatics, where she participated in the organization of all national conferences. She is now local organizer of the ECNP Seminar in Neuropsychopharmacology, Romania, 2012.

ECNP Experts conferences

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How to prepare a scientific presentation

Celso Arango

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Before you start

- What does the audience already know about your topic?
- What are their interests?
- Why are you giving presentation?

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Before you start

- What is your desired outcome?
- How much time do you have?
- What are key points?

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Common Causes of Ineffective Presentations

- Failure to prepare the talk
- Confusing structure/not giving take home messages
- Gaps in logic
- Poorly designed slides
- Poor delivery

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Organizing a Presentation

- i. Outline
- ii. Problem and background
- iii. Design and methods
- iv. Major findings
- v. Conclusion and recommendations

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Making slides

- Main points only
- One idea per slide
- Short words, few words (5 per line)
- Strong statements: active voice

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The start

- Let audience know what they are going to hear
- Let them know how the presentation will be organized

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Start broad, get specific, and end broad

The middle is your original contribution



Start with the biggest questions and get progressively more specific

Focus now on conclusions

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Introduction

- Context
- Study question
- Relevant knowledge on issue

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Major findings

- Text and or table/graph
- One slide for each
- Message should be unambiguous

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Audience attention curve

Time (min)	Percentage of (lects paying full attention)
0	75
5	100
10	50
20	25
30	20
40	50

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Conclusion and Recommendations

- Key points
- Implications
- One slide for each message

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Formal aspects

- AVOID USING ALL CAPITAL LETTERS BECAUSE IT'S REALLY HARD TO READ!
- Dark letters against a light background (or the opposite) work
- Avoid some colour combinations (red-green)

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Formal aspects

- Choose style that supports the tone
- Apply the same style to each slide
- **Don't Say It, Show It**

Be consistent!

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Formal aspects

- Every slide should have a heading.
- Lists should contain no more than 3-4 items
- Limit text blocks to no more than two lines each.
- Be careful with the pointer!

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Formal aspects

Type size should be 20 points or larger:

- 18 point
- 20 point
- 24 point
- 28 point
- 36 point

* References can be in 14 point font

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And do not forget to.....

- Relax
- Listen to what you are saying
- Pace and time yourself

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And do not forget to.....

- Face the audience
- Never underestimate your audience!
- With time you will enjoy.....

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How to prepare a scientific presentation

- “Tell me and I will forget, show me and I will remember, involve and I will understand”

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How to prepare a manuscript

Celso Arango

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Categories

- Original research (focus of this talk)
- Reviews (invited vs. not invited)
- Case reports/series
- Letter to the editor

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The Journal

- Does the article fit the aims and scope of the Journal?
 - Choose before writing
 - General vs. subspecialty journal
- Read the table of contents of potential journals
- Examine several articles in potential journals
- Which journals will you cite in your article?

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Sequence

- The syndrome of the blank screen
- Figures, tracings, tables
- Methods and Results
- Discussion and Introduction
- Abstract and Title

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Tables and Figures

- Do before writing
- Exceed 1 sheet: redraw
- If small: move data to text
- Should be able to stand alone

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Methods

- Draft can be made while doing the study
- Enough information for an experienced investigator to repeat your work
- Avoid tiresome detail
- Tables preferred to long list of numbers or statistics

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Methods

- Refer to data (Fig. X, Table Y)
- Do not repeat numbers in Tables
- Include ethics information (with Ethics Committee approval and i.c.)
- Include complete statistics section

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Discussion

- First paragraph
 - State major findings
- Last paragraph
 - "In summary..." (2-3 sentences)
 - "In conclusion..." (biggest message, return to Intro, avoid speculation, avoid "need more work")

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Discussion

- Middle paragraphs
 - Base each on a major result
- Always focus on your results
- Explain what is new without exaggerating
- Never discuss prior work without reference to your work (but do not forget appropriate identification of prior research)

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Discussion

- Refer Tables and Figures
- Do not repeat results
- Include limitations section

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Introduction

- Keep it short. In most cases 3 graphs make it.
 - 1. Why the study is interesting (broad)
 - 2. Why did we do it? (specific)
 - 3. Hypothesis

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Abstract

- Is your visiting card
- In most cases make the editor to send the ms to reviewers or reject it.
- Some numbers, but not in excess
- Determines if paper will be read
- Is distributed freely in databases
- Avoid acronyms

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Title

- Max information in least words
- The title is an invitation to read the paper
- Use catchy titles
- State results

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Keywords

- Make them easy for indexing and searching! (if you want to be cited)

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References

- Cite the Journal you are submitting the paper to
- Reviewers may be selected from your references
- Use editing programs
- Relevant and recent

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The context

- Need stretch of several hours
- Avoid distractions: phone, e-mail
- Ideas come while writing

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First draft

- Write as quickly as possible
- As if thinking out loud
- Get everything down
- Ignore spelling, grammar, style
- Correct and rewrite only when the whole text is on paper
- Do not split the manuscript among the co-authors

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Introduction

- Context
- Study question
- Relevant knowledge on issue

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Major findings

- Text and or table/graph
- One slide for each
- Message should be unambiguous

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Formal aspects

- Avoid ambiguity
- Concise: Least words, short words, one word vs many
- Strengthen transition between sentences

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Formal aspects

- Check narrative flow: tell a story that the reader wants to read from start to end
- Smooth transitions
- Writing improves in proportion to deletion of unnecessary words
- Keep sentences short

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Formal aspects

- After the second draft send ms to your coauthors
- After the suggestions have been incorporated leave it for some time a re-read

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Formal aspects

- If you do not have time to check the spelling you may have not had time to check the quality of your experiments.....

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Formal aspects

- Prepare article, figures and table according to the journal's 'Guide for Authors'
- Adherence to the style of the journal is crucial
- Check references
- Check and double check your work

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Authorship

- Decided as early as possible
- The journal has instructions on who should/should not be an author
- Basically all authors should have done a major contribution to the study

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Authorship

- Approval of final version must be obtained from all coauthors before submission
- The first author is primarily responsible for collecting and analyzing data, and writing

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Authorship

- The manuscript is not under consideration elsewhere and will not be submitted elsewhere until a final decision has been made by the journal
- All funding sources must be acknowledged
- All conflicts of interest should be reported

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Peer Review

- Authors write
- Reviewers comment
- Editors decide
- Readers read (only what they like)

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Peer Review

- Peer review helps to determine the significance, contribution to what is already known and originality of research
- Most journals reject some paper prior to peer review (on basis of Editor's own evaluation)
- Usually 2-3 reviews sought (per manuscript)

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Possible Decisions

- Reject (up to 90-95% in good journals, do not give up!)
- Major revisions required (it will be reviewed again, may be rejected)
- Minor revisions needed (usually accepted)
- Accepted (congratulations! Enjoy and celebrate!)

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Response to the editor

- Reviewer's are (almost) always right. Editor is always right.
- Response to all the comments in a nice and polite way
- Thank the reviewers for their contribution

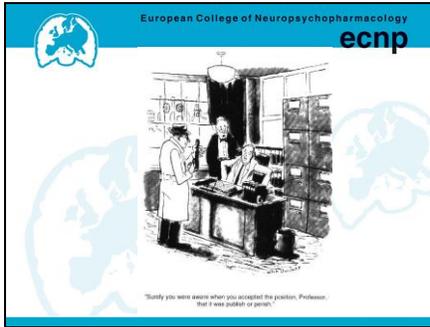
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When the study is negative

- If your result is not as expected, you should understand the reason. It may be something really new. (Must find out why it did "not work" in the expected way!)

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"Scientists are rated by what they finish, not by what they attempt"



Treatment of acute psychosis

Celso Arango

Hospital General Universitario Gregorio Marañón, CIBERSAM, School of Medicine, Universidad Complutense, Madrid, Spain.

The first episode of psychosis is a critical period in the course of each patient's illness and perhaps the most important opportunity for therapeutic intervention. The first experience of the patients with the psychiatric system should be less traumatic as possible. The treatment provided in the emergency setting should not jeopardize long-term objectives. This also includes that whenever is possible the patients is given the option to choose among different recommended treatments. Randomized controlled trials show no difference between different antipsychotics in terms of efficacy for the short-term acute treatment of psychosis. Main differences between antipsychotics are more markedly in side effects. This is even more important for pediatric patients that seem more vulnerable to some of these side effects. In the acute setting benzodiazepines are sometimes of great help. For the treatment of mania many different therapeutic options have shown to be effective. Second generation antipsychotics are used more frequently nowadays to treat acute mania. Patients usually need lower doses than used with more chronic patients. Recovery is a multidimensional process, improving psychotic symptoms is not the most difficult task for the clinician. Engaging the patient with a good therapeutic alliance, reducing the risk of lack of adherence and provide the proper psychoeducation are more difficult tasks that influence the long-term prognosis.



Treatment of Acute Psychoses

Celso Arango

*Hospital General Universitario
Gregorio Marañón,*

Madrid, Spain

carango@hggm.es

Romania, November 2012



Index

- **Review of first episode studies**
- **Treatment in the acute setting**
- **Treatment of acute mania**
- **Special Population: children and adolescents**
- **Discussion**

The first episode of psychosis is a **critical period** in the course of each patient's illness and perhaps the most important opportunity for therapeutic intervention

Placebo-Controlled First-Episode Maintenance Trials

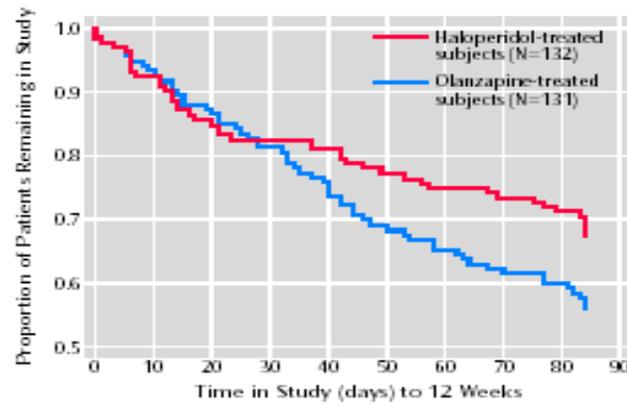
	Relapse Rate (%) Placebo	Relapse Rate (%) Antipsychotic	P-value
Kane et al, 1982	41 (7/17)	0 (0/11)	<0.01
Crow et al, 1986	62 (41/66)	46 (25/54)	0.002*
McCreadie, et al (Scottish Schizophrenia Research Group), 1989	57 (4/7)	0 (0/8)	NS
Hogarty and Ulrich, 1998	64	43	N/A

*When period between onset of index episode and hospital admission is taken into account

Kane JM et al. *Arch Gen Psychiatry*. 1982;39:70; Crow TJ et al. *Br J Psychiatry*. 1986;148:120;
McCreadie RG et al. *Acta Psychiatr Scand*. 1989;80:597; Hogarty GE, Ulrich RF. *J Psychiatr Res*. 1998;32:243

Olanzapine vs haloperidol

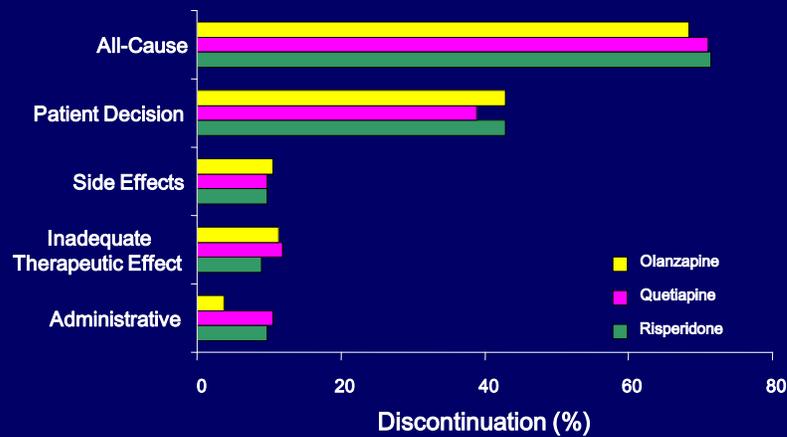
FIGURE 1. Time to Study Discontinuation for Any Reason of Subjects With First-Episode Psychosis in the 12-Week Acute Treatment Phase of a Long-Term Comparison of Olanzapine and Haloperidol^a



^a No significant difference between treatment groups in time to discontinuation ($p=0.06$, log rank test).

Lieberman et al, Am J Psychiatry 2003;160(8):1396-404

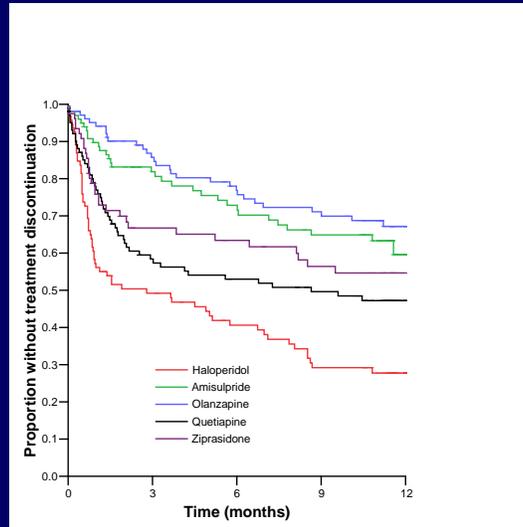
Primary Outcome: All-Cause Treatment Discontinuation



For each category above, the comparison of quetiapine vs olanzapine and quetiapine vs risperidone met the *a priori* test of noninferiority (20%) at $P<0.05$

McEvoy et al 2007

European first episode (EUFEST) Study



Time to treatment discontinuation for any cause

First-Episode Patients: Lower Medication Doses Than Multi-Episode Patients

Study	Mean Modal Daily Dose (mg)
Lieberman et al 2005	Haloperidol: 4.4
	Olanzapine: 9.1
Schooler et al 2005	Haloperidol: 2.9
	Risperidone: 3.3
Robinson et al 2006	Olanzapine: 11.8
	Risperidone: 3.9
McEvoy et al 2007, Am J Psychiatry. In press	Olanzapine: 11.7
	Quetiapine: 506
	Risperidone: 2.4

Lieberman J et al. *Eur Neuropsychopharmacol.* 2005;15(suppl 3):S526; Schooler N et al. *Am J Psychiatry.* 2005;162:947; Robinson DG et al. *Am J Psychiatry.* 2006;163:2096; McEvoy JP et al. 2007. *Am J Psychiatry.* 2007

Treatment goals in the emergency setting

Reducing acute symptoms

Minimising risk of harm

Calming agitation

Improving role functioning

Achieving these goals must not be at the expense of long-term treatment objectives

Arango & Bobes 2004

Patient requirements and preferences in the acute setting

Receive a rapid and accurate diagnosis

Be offered a choice of treatment

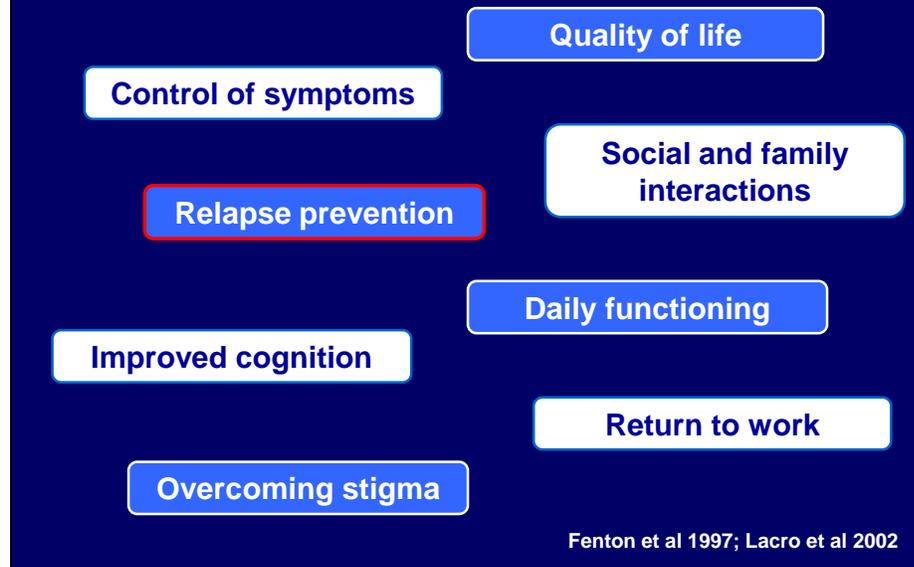
Benefit from a good therapeutic alliance

Receive verbal rather than physical interventions

Receive oral medication

Allen et al 2003; Arango & Bobes 2004; Allen et al 2005

Recovery is a multidimensional process

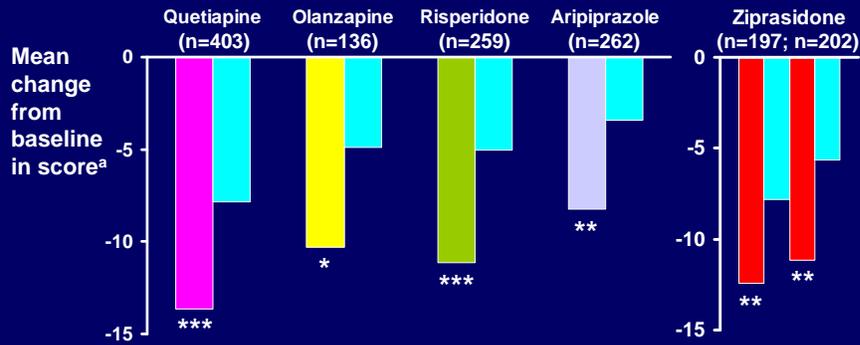


Treatment Options for Acute Mania

- Classical antipsychotics
- Atypical antipsychotics
- Lithium
- Valproate
- Carbamazepine
- Combinations
- Benzodiazepines
- ECT

Efficacy of atypical antipsychotics: improvement in manic symptoms

Data from 6 selected monotherapy studies

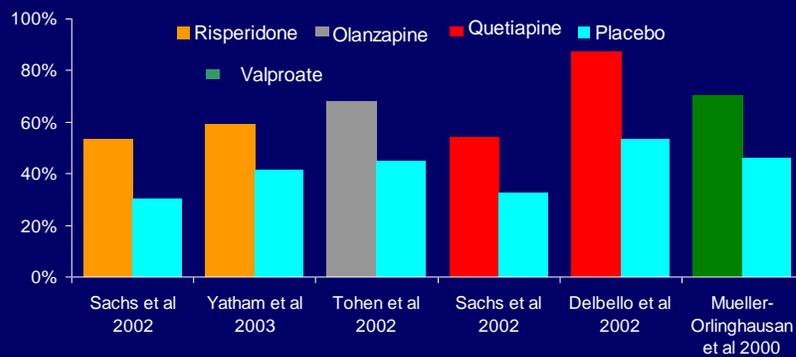


^aZiprasidone: SADS-C MRS; others: YMRS; columns are active drug vs placebo
*p<0.05; **p<0.01; ***p<0.001 vs placebo

Vieta et al, 2005; Tohen et al 1999;
Hirschfeld et al 2002; Keck et al 2003; Keck et al 2003; Segal et al 2003

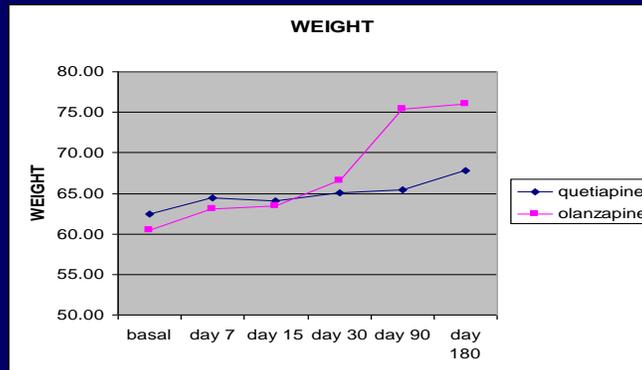
Atypical Antipsychotics As Adjunct to Mood Stabilizers Vs. Mood Stabilizer Monotherapy

Response Rate (≥50% Reduction YMRS)



Sachs et al. 2002 (3 wks, n=156, YMRS=28), Yatham et al. 2003 (3 wks, n=151, YMRS=29),
Tohen et al. 2002 (6 wks, n=344, YMRS=22), Sachs et al. 2002 (3 wks, n=190), Delbello et al. 2002 (6 wks, n=30, YMRS=33).

Change in weight over time by treatment group olanzapine/quetiapine



Arango et al, 2009

Metabolic side effects in young people treated with second-generation antipsychotics

At risk for adverse health outcome

- BMI ≥ 95 or
- BMI > 85 +
 - hypertension > 90th or
 - fasting cholesterol ≥ 200 mg/dl or
 - LDL cholesterol > 130 or
 - HDL cholesterol < 40 or
 - TGC ≥ 150 or
 - Hyperglycaemia ≥ 110 mg/dl)

At risk adverse	Baseline	6 month
RIS	22.7%	36.4%
OLZ	15.0%	60.0%*
QTP	12.5%	20.8%

* p < 0.05

Significant weight gain

Defined as > 0.5 increase in body mass index (BMI) z-score (adjusted for age and gender) at 6 months

RIS: 50%
OLZ: 75%*
QTP: 29%

* p < 0.01

• **Total cholesterol** increased in patients receiving olanzapine (p=0.047) and quetiapine (p=0.016).

• Treatment with quetiapine was associated with a decrease in **free thyroxin** (p=0.011).

Fraguas et al, J Clin Psychiatry 2008

SATIETY study design

Treatment with all antipsychotics was associated with changes in metabolic parameters at 12 weeks

All values refer to mean change from baseline (p value)

	Aripiprazole (n=41)	Olanzapine (n=45)	Quetiapine (n=36)	Risperidone (n=135)	Untreated (n=15)
Weight (kg)	4.44 <0.001	8.54 <0.001	6.06 <0.001	5.34 <0.001	0.19 0.77
Fat mass (kg)	2.43 <0.001	4.12 <0.001	2.82 <0.001	2.45 <0.001	0.35 0.39
Waist (cm)	5.40 0.001	8.55 <0.001	5.27 <0.001	5.10 <0.001	0.70 0.40
Glucose (mg/dl)	0.54 0.76	3.14 0.02	2.64 0.12	1.14 0.26	0.69 0.81

Correll CU, *et al.* *JAMA* 2009;302:1765–1773.

Treating first-episode patients

The most difficult task is not getting them to respond to treatment, but getting them to **continue** to take medication

The course of an acute episode of psychoses can be directed towards successful treatment outcomes by...

- Prompt intervention with agents that are well tolerated
- Initiating a programme of long-term therapy (including social services, psychoeducation, accessibility to health facilities and intervention with family is possible) to maintain and build upon the initial success of treatment
- Consider polypharmacy in the acute treatment of bipolar disorders
- Ensuring a positive experience in the acute setting and establishing an interactive therapeutic alliance

Unipolar and bipolar mood disorders – commonalities and differences in etiology and pathogenesis

Erkki Isometsä

The etiology of mood disorders is multifactorial. The central domains of etiological risk factors comprise genetic vulnerability, predisposing personality features, childhood adversity, and precipitating psychosocial stress. The predisposing and precipitating roles of early adversity and current psychosocial stressors have been well documented for unipolar depression, but are more equivocal for bipolar disorders, and qualitative differences are likely to exist. Family, twin and adoption studies provide compelling evidence for moderate to high heritability of depressive (35-40%) and bipolar disorders (60-80%). A large genome-wide association study of bipolar disorder found significant associations for four allelic variants from two genes, ODZ4 and CACNA1C. Some personality features, in particular the personality dimension of neuroticism, are likely to mediate at least part of inherited predisposition to mood disorders; bipolarity may be specifically related to abnormalities in regulation of behavioural activation. Patients with mood disorders have structural brain abnormalities, and alterations both in neurons and glia in the prefrontal cortex, likely progressing as a function of illness duration. In functional brain imaging studies, limbic (e.g. amygdala) overactivity poorly controlled by prefrontal cortical structures is commonly found. The structural and functional abnormalities observed in brain imaging studies may imply either genetic vulnerability, disturbances of early development, or progression of illness. However, differences between unipolar and bipolar patients are found both in structure and function. For research on mood disorders, elucidating the complex interplay of genetic vulnerability, brain structure and function, predisposing temperamental features and factors mediating psychosocial stress in the brain during early development as well as in adulthood (e.g. HPA axis, inflammation) is of fundamental importance. While great advances have been made in understanding etiology and pathogenesis of mood disorders, nevertheless the major obstacle for advance in developing more effective treatments for them is still limited understanding of their illness mechanisms.



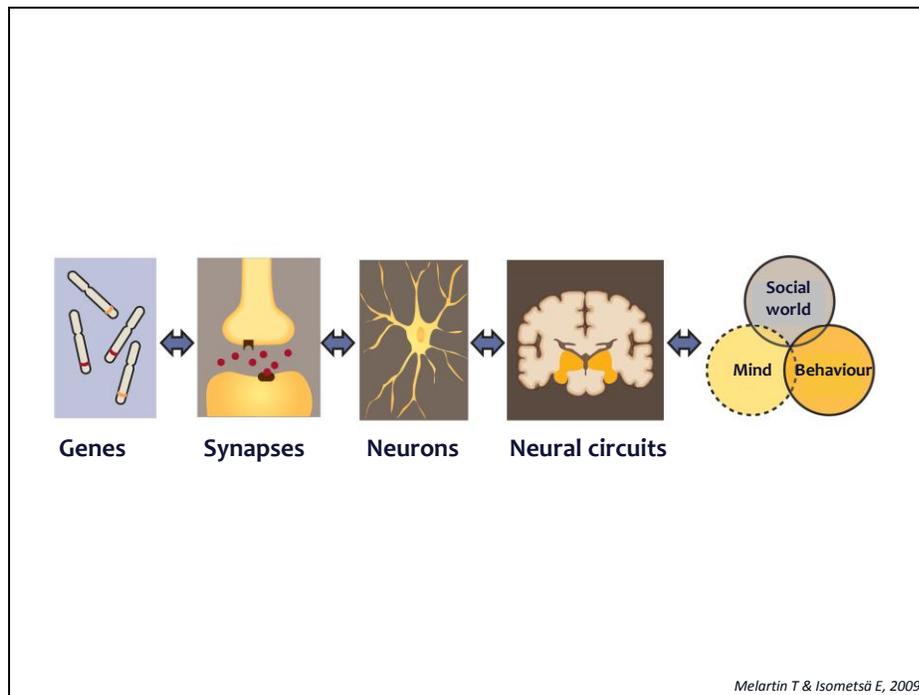
ECNP Seminar in Neuropsychopharmacology, Romania 3.11.2012

Unipolar and bipolar mood disorders – commonalities and differences in etiology and pathogenesis

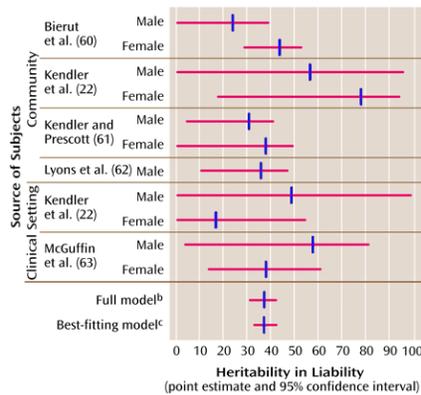
Erkki Isometsä, M.D., Ph.D.
 Professor of Psychiatry,
 Department of Psychiatry, University of Helsinki &
 Research Professor, National Institute for Health and Welfare
 Helsinki, Finland

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Are mood disorders heritable?



From Sullivan et al. Genetic epidemiology of major depression: review and meta-analysis. *Am J Psychiatry* 2000;157:1555-1562

Major depression

- Often familial (for several possible reasons).
- In twin studies concordance of monozygotic twins about 50%, dizygotic about 20%, i.e. markedly lower.
- Few adoption studies, overall pattern similar
- **Heritability about 35-40%**

Bipolar disorder

- Very often familial
- **Heritability about 60-80%**

Genome-wide association studies (GWAS) of mood disorders conducted and ongoing.

Problems:

- Heterogeneity of phenotype
- Polygenic inheritance, small genetic effects
- Genetic heterogeneity



ORIGINAL ARTICLE

A mega-analysis of genome-wide association studies for major depressive disorder

Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium¹

Prior genome-wide association studies (GWAS) of major depressive disorder (MDD) have met with limited success. We sought to increase statistical power to detect disease loci by conducting a GWAS mega-analysis for MDD. In the MDD discovery phase, we analyzed more than 1.2 million autosomal and X chromosome single-nucleotide polymorphisms (SNPs) in 18759 independent and unrelated subjects of recent European ancestry (9240 MDD cases and 9519 controls). In the MDD replication phase, we evaluated 554 SNPs in independent samples (6783 MDD cases and 50695 controls). We also conducted a cross-disorder meta-analysis using 819 autosomal SNPs with $P < 0.0001$ for either MDD or the Psychiatric GWAS Consortium bipolar disorder (BIP) mega-analysis (9238 MDD cases/8039 controls and 6998 BIP cases/7775 controls). No SNPs achieved genome-wide significance in the MDD discovery phase, the MDD replication phase or in pre-planned secondary analyses (by sex, recurrent MDD, recurrent early-onset MDD, age of onset, pre-pubertal onset MDD or typical-like MDD from a latent class analyses of the MDD criteria). In the MDD-bipolar cross-disorder analysis, 15 SNPs exceeded genome-wide significance ($P < 5 \times 10^{-8}$), and all were in a 248 kb interval of high LD on 3p21.1 (chr3:52 425 083–53 822 102, minimum $P = 5.9 \times 10^{-9}$ at rs2535629). Although this is the largest genome-wide analysis of MDD yet conducted, its high prevalence means that the sample is still underpowered to detect genetic effects typical for complex traits. Therefore, we were unable to identify robust and replicable findings. We discuss what this means for genetic research for MDD. The 3p21.1 MDD-BIP finding should be interpreted with caution as the most significant SNP did not replicate in MDD samples, and genotyping in independent samples will be needed to resolve its status.

Molecular Psychiatry advance online publication, 3 April 2012; doi:10.1038/mp.2012.21

ORIGINAL ARTICLE

The Heritability of Bipolar Affective Disorder and the Genetic Relationship to Unipolar Depression

Peter McGuffin, MB, PhD, FRCP, FRCPsych; Fruhling Rijsdijk, PhD; Martin Andrew, MB, MRCPsych; Pak Sham, BM, PhD, MRCPsych; Randy Katz, PhD; Alastair Cardno, MB, PhD, MRCPsych

Background: Twin studies of bipolar affective disorder (BPD) have either been small or have not used explicit diagnostic criteria. There has been little use of genetic model fitting and no analyses to explore the etiological overlap with unipolar depression (UPD).

Methods: Sixty-seven twin pairs, 30 monozygotic and 37 dizygotic, in which the proband had BPD were ascertained, and lifetime diagnoses were made using DSM-IV criteria. Univariate models were applied to estimate the contribution of additive genetic and environmental effects. Bipolar data were then combined with those from 68 monozygotic and 109 dizygotic pairs in which the proband had UPD. Two models were explored: a classic 2-threshold approach, in which BPD and UPD occupy the same continuum of liability but differ in severity, and a correlated liability model of mania and depression.

Results: Heritability of BPD was estimated at 85% (95%

confidence interval [CI], 0.73-0.93) using narrow concordance and 89% (95% CI, 0.61-1.0) using broad concordance, with no shared environmental effects detected. A 2-threshold model was an unsatisfactory fit. Fitting a correlated liability model revealed a genetic correlation of 0.65 (95% CI, 0.58-0.75) between mania and depression and a correlation of 0.59 (95% CI, 0.15-0.84) for nonfamilial environment. Approximately 71% of the genetic variance for mania was not shared with depression.

Conclusions: As defined by the DSM-IV, BPD is highly heritable. There are substantial genetic and nonshared environmental correlations between mania and depression, but most of the genetic variance in liability to mania is specific to the manic syndrome.

Arch Gen Psychiatry. 2003;60:497-502

LETTERS

nature
genetics

Large-scale genome-wide association analysis of bipolar disorder identifies a new susceptibility locus near *ODZ4*

Psychiatric GWAS Consortium Bipolar Disorder Working Group¹

We conducted a combined genome-wide association study (GWAS) of 7,481 individuals with bipolar disorder (cases) and 9,250 controls as part of the Psychiatric GWAS Consortium. Our replication study tested 34 SNPs in 4,496 independent cases with bipolar disorder and 42,422 independent controls and found that 18 of 34 SNPs had $P < 0.05$, with 31 of 34 SNPs having signals with the same direction of effect ($P = 3.8 \times 10^{-7}$). An analysis of all 11,974 bipolar disorder cases and 51,792 controls confirmed genome-wide significant evidence of association for *CACNA1C* and identified a new intronic variant in *ODZ4*. We identified a pathway comprised of subunits of calcium channels enriched in bipolar disorder association intervals. Finally, a combined GWAS analysis of schizophrenia and bipolar disorder yielded strong association evidence for SNPs in *CACNA1C* and in the region of *NEK4-ITIH1-ITIH3-ITIH4*. Our replication results imply that increasing sample sizes in bipolar disorder will confirm many additional loci.

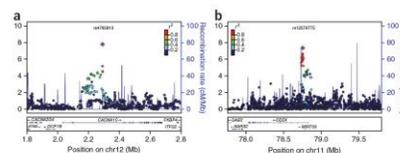


Figure 1 Results are shown as $-\log_{10} P$ for genotyped and imputed SNPs. The most associated SNP in the primary analysis is shown as a small purple triangle. The most associated SNP in the combined analysis is shown as a large purple triangle. The colors of the remaining markers reflects r^2 values with the most associated SNP. The recombination rate from CEU HapMap data (second y axis) is shown in light blue.

Nature Genetics 2011;43:977-983.

What is the CACNA1C doing? Influences frontolimbic emotional processing

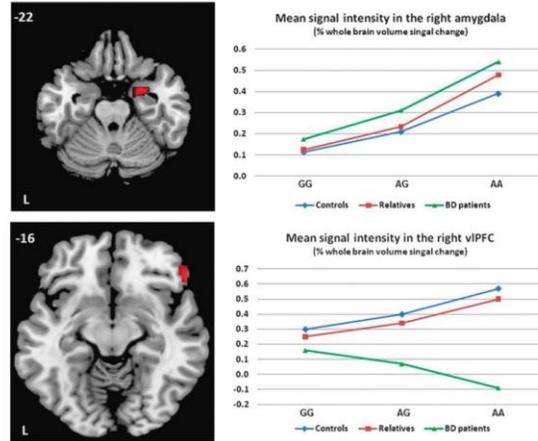


Figure 1 Statistical parametric map (SPM) showing the effect of *CACNA1C* rs1006737 polymorphism on amygdala function during fear-face processing in bipolar disorder (BD) patients, their unaffected relatives and controls (top), and genotype \times diagnosis interaction in the ventrolateral prefrontal cortex (vLPFC) (bottom); SPM thresholded at $P < 0.05$, family-wise error corrected.

Jogia J et al, *Molecular Psychiatry* 2011;16:1070-71.

Resilience – why do not all individuals at risk become ill?

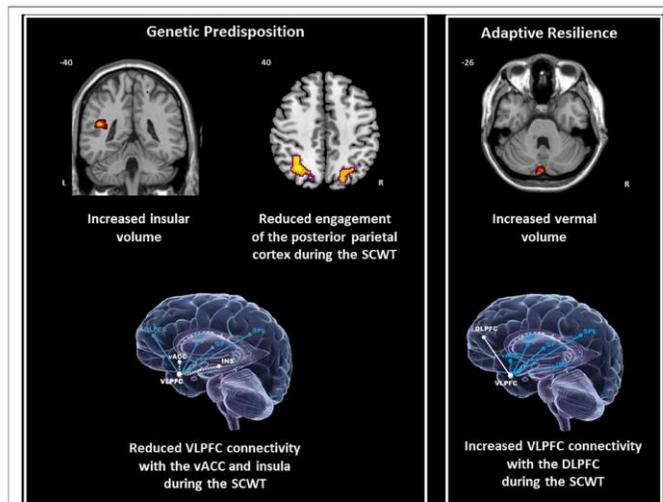


FIGURE 1 | Neural correlates of genetic predisposition and resilience in relatives of bipolar patients. DLPFC = dorsolateral prefrontal cortex; CN = caudate nucleus; GP = globus pallidus; Ins = insula; SPL = superior parietal cortex; vACC, ventral anterior cingulate cortex; VLPFC = ventrolateral prefrontal cortex; coordinates are presented in Talairach and Tournoux space x = sagittal; y = coronal; z = axial.

Frangou S. Brain structural and functional correlates of resilience to bipolar disorder. *Frontiers in Human Neuroscience* 2012;5:1-10

Childhood maltreatment and risk of mental disorders in young adulthood:

- A prospective national cohort study from New Zealand, N= 2144, age of interviewees 16-27 years

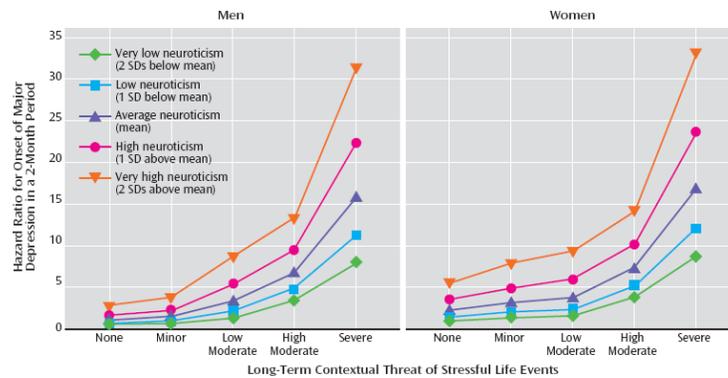
Table 5. DSM-IV Lifetime Disorders Among Young Adults With Child Protection Agency History Compared With Those Without^a

DSM-IV Lifetime Mental Disorder	Child Protection Agency Group		Comparison Group Including Retrospectively Reported Childhood Maltreatment ^b		Comparison Group			
	No. (%)	SE	No. (%)	SE	Including Retrospectively Reported Childhood Maltreatment ^b		Excluding Retrospectively Reported Childhood Maltreatment ^b	
					Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^c	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^c
Major depressive disorder	50 (23.91)	3.63	252 (14.40)	1.11	1.87 (1.21-2.89) ^d	1.76 (1.13-2.73) ^d	2.30 (1.47-3.61) ^d	2.10 (1.32-3.35) ^d
Dysthymia	12 (5.57)	1.98	27 (1.83)	0.44	3.16 (1.32-7.59) ^d	3.64 (1.46-9.07) ^d	4.35 (1.71-11.09) ^d	4.82 (1.74-13.38) ^d
Bipolar disorder	23 (7.72)	1.97	144 (5.74)	0.65	1.38 (0.76-2.49)	1.23 (0.67-2.24)	1.86 (1.00-3.47)	1.68 (0.88-3.20)
Panic disorder	12 (4.27)	1.83	65 (2.97)	0.45	1.46 (0.57-3.71)	1.23 (0.45-3.36)	1.69 (0.66-4.38)	1.44 (0.50-4.11)
Specific phobia	48 (20.61)	3.35	236 (11.68)	0.90	1.96 (1.26-3.04) ^d	1.81 (1.15-2.85) ^d	2.37 (1.50-3.72) ^d	2.20 (1.37-3.53) ^d
Social phobia	46 (18.67)	3.25	212 (10.05)	0.82	2.05 (1.29-3.26) ^d	2.06 (1.26-3.39) ^d	2.49 (1.54-4.03) ^d	2.70 (1.58-4.61) ^d
GAD	19 (6.38)	1.74	73 (4.03)	0.61	1.62 (0.85-3.11)	1.66 (0.83-3.33)	2.00 (1.01-3.99) ^d	2.16 (1.03-4.51) ^d
PTSD	33 (14.16)	3.03	100 (4.40)	0.62	3.59 (2.05-6.28) ^d	2.46 (1.25-4.85) ^d	7.04 (3.80-13.06) ^d	4.86 (2.26-10.45) ^d
OCD	12 (5.43)	2.03	39 (2.41)	0.55	2.33 (0.94-5.77)	2.28 (0.94-5.54)	3.03 (1.11-8.31) ^d	4.00 (1.63-9.82) ^d
Alcohol abuse/dependence	81 (32.76)	4.01	353 (16.36)	1.09	2.49 (1.69-3.67) ^d	1.89 (1.24-2.88) ^d	3.16 (2.12-4.71) ^d	2.50 (1.59-3.91) ^d
Drug abuse/dependence	59 (25.85)	3.77	218 (10.05)	0.90	3.12 (2.04-4.77) ^d	2.27 (1.39-3.71) ^d	3.95 (2.54-6.16) ^d	3.03 (1.78-5.15) ^d

Scott KM et al. Arch Gen Psychiatry 2010;67:712-719.

Neuroticism modifies risk of depression in the context of adverse life events

FIGURE 1. Hazard Ratios Indicating Risk of Onset of Major Depression for a Population-Based Sample (N=7,517) Classified by Sex, Neuroticism, and Stressful Life Events^a



^a A hazard rate of unity was defined as the risk level for a man with a mean score on the 12-item neuroticism scale from the shortened Eysenck Personality Questionnaire (21) and no exposure to stressful life events. Descriptions of the types of stressful life events and the scoring of long-term contextual threat are given in text.

Kendler KS, Am J Psychiatry 2004;161:631-636

Differences between unipolar and bipolar mood disorders in structural brain imaging studies: a meta-analysis

Table 5. Statistical Comparison of the Present MDD Meta-analysis With a Previous Meta-analysis of BD^a

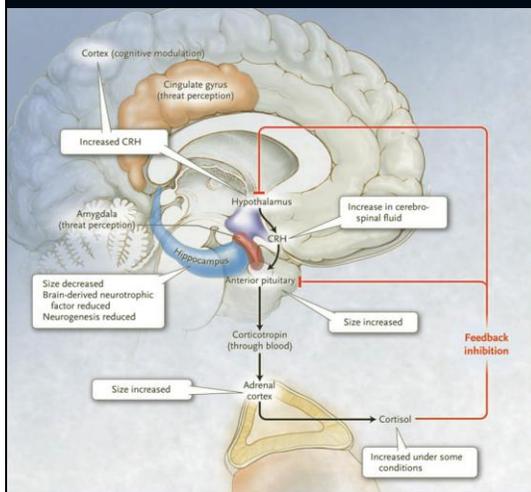
Region	MDD vs Control Meta-analysis			BD vs Control Meta-Analysis			MDD vs BD ^a	
	No. of Studies	Effect Size	P Value	No. of Studies	Effect Size	P Value	Effect Size	P Value
Lateral ventricles, total	15	0.44	<.001	17	0.39	<.001	0.04	.73
Caudate, total	13	-0.22	.006	17	0.03	.69	-0.25	.03
Putamen, total	8	-0.25	.009	10	0.05	.56	-0.30	.02
Globus pallidus, total	3	-0.31	.04	6	0.39	.10	-0.70	.01
Thalamus, total	7	-0.34	.01	13	-0.05	.73	-0.29	.13
Hippocampus, total	37	-0.47	<.001	18	-0.06	.48	-0.41	<.001
Corpus callosum, cross-sectional area	6	0.06	.75	4	-0.43	.006	0.49	.04
DWMH	14	OR, 1.09	.51	13	OR, 2.49	<.001	OR, 0.44	.001
ScGMH	8	OR, 1.90	.03	6	OR, 2.84	.01	OR, 0.67	.42

Abbreviations: BD, bipolar disorder; DWMH, deep white matter hyperintensities; MDD, major depressive disorder; OR, odds ratio; ScGMH, subcortical gray matter hyperintensities.

^aFor the MDD vs BD comparison, negative effect sizes indicate that the region is smaller in MDD patients; positive effect sizes indicate that the region is smaller in BD patients. An OR less than 1 indicates that hyperintensities are less common in MDD patients compared with BD patients. Effect sizes for BD have been recalculated by combining left and right measures (see the "Methods" section) and, as such, may vary from those reported in the previous BD meta-analysis.³ Boldface indicates significant differences between BD and MDD patients.

Kempton MJ et al. Arch Gen Psychiatry 2011;68:675-90.

Hyperactivity of HPA axis in depression and bipolar disorder



- Perceived stress results in hypersecretion of CRH.
- Long-term hypercortisolism reduces activity of neuronal growth factors (e.g. BDNF).
- Disturbed neuronal energy metabolism, vulnerability to apoptosis.
- Reduced neurogenesis and plasticity.
- Reduced hippocampal volume (< 10%) in chronic or recurrent depression; less often observed in bipolar disorder.
- Programming in early life?
- Reversible or not?

Belmaker RH & Agam G. Major depressive disorder. N Engl J Med 2008;358:55-68.

NeuroImage 61 (2012) 677–685



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A meta-analysis of neurofunctional imaging studies of emotion and cognition in major depression

Carsten Diener ^{a,*}, Christine Kuehner ^b, Wencke Brusniak ^a, Bettina Ubl ^a, Michèle Wessa ^c, Herta Flor ^a

^a Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Germany
^b Research Group Longitudinal and Intervention Research, Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Square J5, 68159 Mannheim, Germany
^c Section for Experimental Psychopathology and Neuroimaging, Department of General Psychiatry, Center of Psychosocial Medicine, Heidelberg University, Germany

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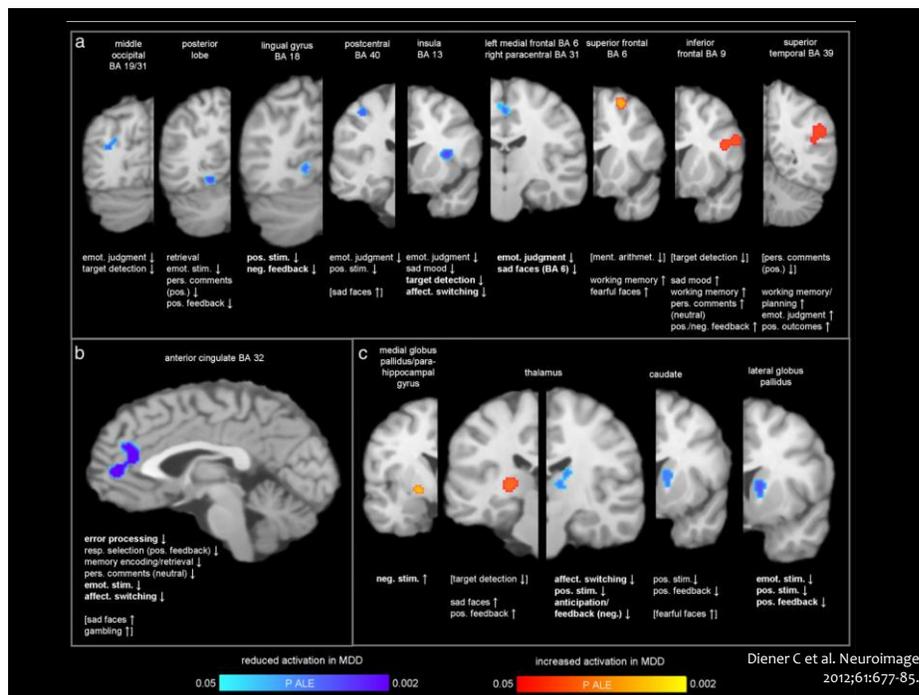
ABSTRACT

Major depressive disorder (MDD) is characterized by altered emotional and cognitive functioning. We performed a voxel-based whole-brain meta-analysis of functional neuroimaging data on altered emotion and cognition in MDD.

Forty peer-reviewed studies in English-language published between 1998 and 2010 were included, which used functional neuroimaging during cognitive–emotional challenge in adult individuals with MDD and healthy controls. All studies reported between-groups differences for whole-brain analyses in standardized neuroanatomical space and were subjected to Activation Likelihood Estimation (ALE) of brain cluster showing altered responsivity in MDD. ALE resulted in thresholded and false discovery rate corrected hypo- and hyperactive brain regions.

Against the background of a complex neural activation pattern, studies converged in predominantly hypoactive cluster in the anterior insular and rostral anterior cingulate cortex linked to affectively biased information processing and poor cognitive control. Frontal areas showed not only similar under- but also overactivation during cognitive–emotional challenge. On the subcortical level, we identified activation alterations in the thalamus and striatum which were involved in biased valence processing of emotional stimuli in MDD. These results for active conditions extend findings from ALE meta-analyses of resting state and antidepressant treatment studies and emphasize the key role of the anterior insular and rostral anterior cingulate cortex for altered emotion and cognition in MDD.

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Neural correlates of emotional processing in MDD vs. BD:
- a voxel-based meta-analysis of fMRI studies

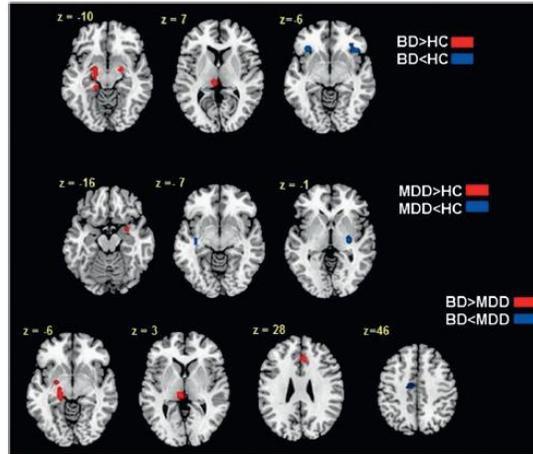
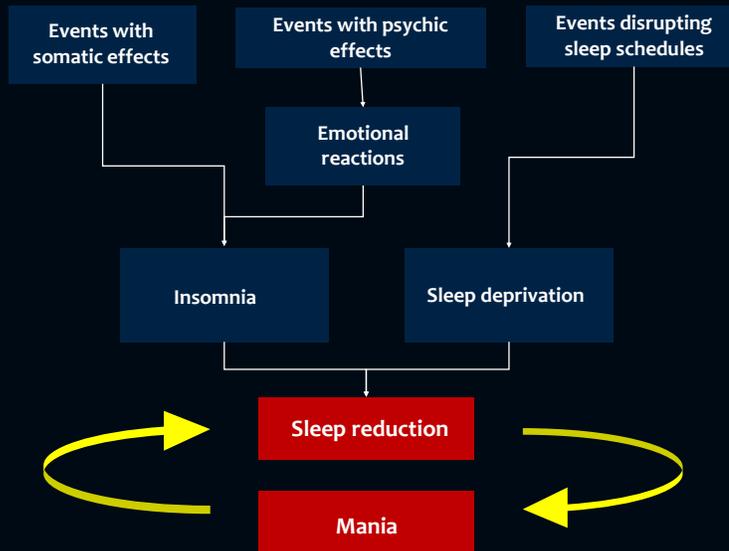


Figure 1 Activation Likelihood Estimation (ALE) maps representing regional activity consistently associated with Bipolar Disorder (BD) or Major Depressive Disorder (MDD). Clusters of relative overactivation or underactivation are shown in red and blue respectively; numbers represent axial (z) coordinates of each slice in Talairach space; $p < 0.05$ False Discovery Rate corrected for multiple comparisons. Top row: statistical map of significant ALE clusters for the comparison of BD patients to healthy controls (HC). Middle row: statistical map of significant ALE clusters for the comparison of MDD patients to healthy controls (HC). Bottom row: statistical maps of significant ALE clusters associated with the contrast of BD and MDD.

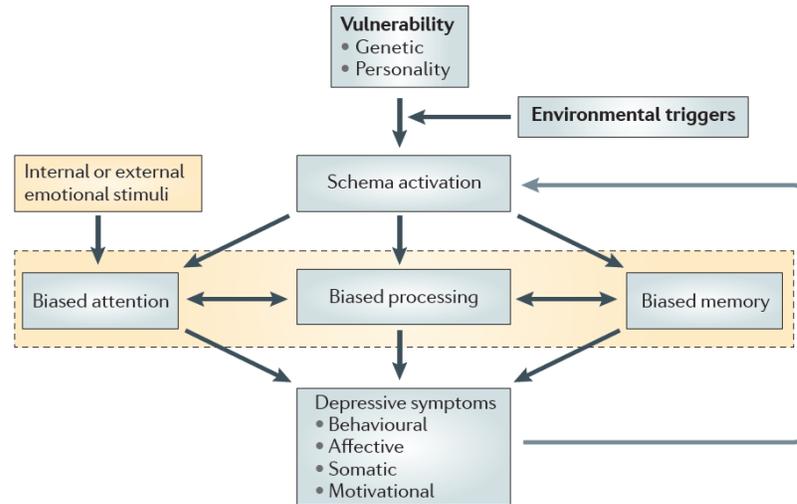
Delvecchio G et al. *European Neuropsychopharmacology* 2012;22:100-13.

Sleep reduction as the final common pathway to mania



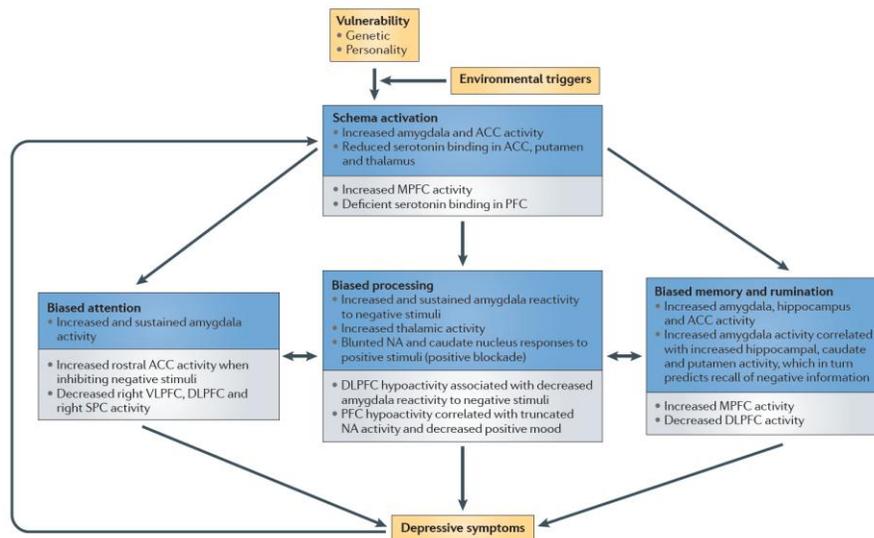
Wehr TA et al. *Am J Psychiatry* 1987;144:201-4.

Information processing in the cognitive model of depression



Disner SG et al. Nat Rev Neurosci 2011;12:467-77.

An integrated cognitive neurobiological model of depression



Disner SG et al. Nat Rev Neurosci 2011;12:467-77.

Benefit/risk assessment in medicine in general and psychiatry in particular

Michael Davidson

Medicine is a science of uncertainty and an art of probability said the famous internist William Osler. Decision making in an environment of uncertainty is the rule for many human activities (ex. financial investing, pharmaceutical R&D) and, for most specialties in the clinical practice of medicine. The benefits of treating sustained ventricular tachycardia, the harm of not treating it and the risk of treating but causing more harm than benefit, can be quantified with the help of hard outcome measures and are not clouded by personal value systems. This is also true for less dramatic conditions and for treatments with smaller effects sizes such as pain, nausea or pruritus. Most people want to stay alive and be free of nausea.

Because psychiatric do not have neither dramatic effects nor hard outcomes to prove efficacy benefit/harm/risk assessment at the societal level and at the individual level are more difficult to assess yet accurate assessment is not less essential. Regulatory agencies, health care providers and individual physicians are all struggling to address these issues.

How much weight to give evidence when it contrasts with personal experience? How vulnerable is the observant psychiatrist to generate for herself faulty feedback? How to handle good quality but opposing or uncertain evidence and how much uncertainty to share with the patient? Are NNT and NNH helpful in assessing risk and communicating it to the patient despite the fact that they measure different phenomena? Are we blinded by the glitter of numbers?

We need to address these dilemmas since they exist in every moment of our clinical practice. For example are the GI disturbances caused by cholinomimetics in AD patients justified despite the fact that benefits cannot be observed clinically or measured psychometrically in individual patients? Is addition of antipsychotics in AD to treat psychosis justified despite the fact that the benefit is questionable but there is a very small increase in risk of death? How much psychotropic is justified in affective disorders despite the fact that it is almost impossible to gather good effectiveness evidence? Is there a point where treatment refractory psychosis or depression should not be treated with medication? We all make every day 10 to 20 such decisions but we very rarely turn back to try to understand how we reached the decisions. Is it "scientific intuition" and is so can it be improved?

Risk assessment in psychiatry

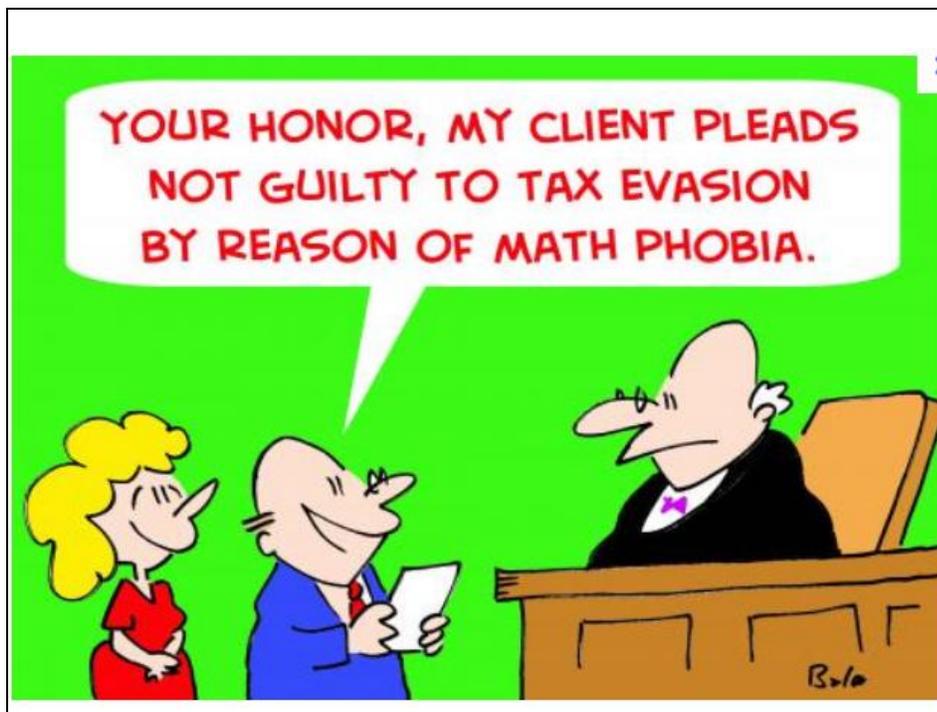
risk-uncertainty-decisions

How well can physicians do risk/benefit assessment and how well can they communicate it to patients?

Statistical literacy and illiteracy



Michael Davidson MD



Can we live in a risk free world?

too much risk prevention is bad for your health

- Paradoxically it might cause stagnation in drug development
- Chases events rather than real risks
(irreversible and irrelevant legislation as a reaction to an unexpected but very rare event)
- Shifts responsibilities from the individual to society

Why are most risk/benefit assessments in medicine made under condition of uncertainty?

- For many questions no RCT exist or we infer from RCT cohorts to individuals but individuals present
 - Genetic polymorphism leading to pharmacodynamic and pharmacokinetic variations
 - variable response to Rx in terms of benefits and AE
 - Cohorts in RCT are not the same as the cohorts in daily practice
- The information (on illness presentation, course and response to treatment) we gather is neither objective nor reliable
- Biological markers don't necessarily reduce biological heterogeneity (ex. Amyloid plaque in AD)

Benjamin Franklin "In this world, there is nothing certain but death and taxes".

Differences between risk in medicine vs. risk in insurance, finances or gambling

- Asymmetric information
 - present in both cases but with different consequences
- Agent vs. principal
 - convergence of interest vs. potential conflict
- Moral hazard
- Time-dependent risk
 - Postpone versus binary
- Cohort vs. individual
 - Problematic in medicine but useful in gambling*

* The winnings are unpredictable for the gambler but predictable for the owners of the slot machines. The physician who has to make decisions based on cohorts is like owner of the slot machine

Can risk (as damage) be quantified?

- Option X has a probability of 0.01 for complication A, with a loss of 1000 $\text{risk of a loss} = 10 \text{ or } 0.01 \times 1000.$
- Option Y has a probability of 0.01 for a complication A, with a loss of 1000, and a probability of 0.000001 of complication B, with a loss of 2,000,000, then total risk is a loss of 12 $(0.01 \times 1000) + (0.000001 \times 2,000,000)$

But what is the meaning of 1000 or how do we calculate the value of the loss ?

Can risk/benefit ratio be quantified?

- Personal preferences
- Cultural biases
- Can short term immediate benefits be weighted against long term future benefits?
- Benefits – AE (NNT - NNH) or QALY- ?
- Benefits and AE are not measured on the same units
 - How many patients with pain relief or MI(s)(the benefit) are needed to balance GI bleeding (the risk) when prescribing aspirin?
 - How much short-term risk is acceptable for long-term benefit (e.g., statins and blood pressure medications that yield long-term benefit)?
 - How much individual risk is acceptable for societal benefit (e.g., vaccines)?
 - How much societal risk is acceptable for individual benefit (stringent commitment policies)?

* QALY(quality of life years) Perfect health for a year = 1 death = 0. For each extra year lived if a person is not in full health (wheelchair, dyspnea, depressed) they are given a value between 0 and 1 for each of the remaining years of their life.

Papers of participants

Cornelia Aipu

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia” , Clinical Department IV, Bucharest

‘Medicinal plant’ induced psychosis

Abuse of psychogenic substances sold as ‘natural ways to cure’ has escalated in recent years in Romania.

Currently there are only limited studies describing the real clinical effect associated with reported ‘natural plant miracles’. Many of them induced psychosis and other psychiatric symptoms. Knowing which natural substances may be responsible for that helps us to manage better the differential diagnostic and treatment.

Cecilia Andronic

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia” , Clinical Department XII, Bucharest

Over the past decade advances in the management of psychotic episode in the community have involved increasing emphasis on the psychosocial dynamics of care, coordinated through a care programme approach, and the introduction of new medication.

The purpose of this case study was to use an evidence based medicine approach and cognitive behavioral therapy to work through an unusual way of treating a common problem. We looked at an example of an in-patient with severe psychotic episode.

During hospitalization, the patient received treatment with antipsychotic, that helped the patient to have less psychotic symptoms , and CBT improved social adjustment and quality of life, and diminished psychotic symptoms and the related distress.

Her symptoms improved to the point where she was successfully discharged home on a combination of antipsychotic treatment and programed therapy sessions. The improvement was sustained until present day.

In particular, the use of cognitive behavioral therapy (CBT) proved to be a promising additive treatment and has been shown to be an effective means of tackling symptoms associated with psychotic episode.

Maria Magdalena Blaj

Department of Psychiatry, Faculty of Medicine and Pharmacy, Western University “Vasile Goldis”, Arad”

DEPRESSION IN LATER LIFE

Maria Magdalena Blaj^a, Delia Marina Podea^a

Depression and old age are often regarded as inextricably linked, but it seems likely that old age depressive disorders are not particularly well encompassed by the DSM and ICD. The studies shows that between 10 and 15% of elderly people in the community have depressive symptomatology at a given point in time and only about 3% of the same community have depressive episodes meeting ICD-10 and DSM-IV criteria.

The studies revealed a symptom-cluster profile unique to people older than 60 years, characterized by depressed mood, psychomotor retardation, poor concentration, constipation, and poor self-perception of health.

Just because a patient does not meet the diagnostic threshold it does not mean that their symptoms are unimportant. Having a few symptoms persistently, especially if accompanied by impaired function or quality of life, is a key risk factor for major depression.

Nicoleta Bobutanu

Clinical Hospital Of Psychiatry “ Socola” Iasi

Perspectives the administration of antioxidants in patients with schizophrenia

Pharmaceutical treatment for tens of millions of people worldwide suffering from schizophrenia is limited to only several antipsychotics. Despite the proven efficacy of these drugs somehow, overall result remains suboptimal. Thus, alternative treatment options are needed. In this way a possible therapeutic approach could be represented by antioxidant therapy.

Oxidative stress is increasingly attracting more attention, more research in medical and biological fields were oriented towards deciphering the mechanisms underlying this process, given the increasing importance of oxidative stress in many degenerative diseases and mental illnesses including schizophrenia.

Studies are necessary to better systematize how antioxidant therapy could be applied in clinical practice. These studies should answer questions such as: what kind of antioxidants can be used in the effective dose and the period of time, would be administered alone or in combination therapy, when treatment could be initiated and if that antioxidants should be combined with supplements of omega 3 fatty acids.

Georgeta Boscu

Centre Hospitalier Andree Rosemon, Cayenne, French Guiana

Treatment efficacy evaluation and alternatives in patients with obsessive compulsive disorder symptoms and certain psychotic symptoms.

Case study of a 28 years old male patient admitted in the service with important anxiety, persecution feelings, castration thoughts, food deprivation. He arrived with a part of his crane and one eyebrow shaven. Couple of days later he told us that “the logical explanation” of those persecutory forces is that his brain produces them.

The obsessive and compulsive symptoms started when he was 14, and he had the first psychiatric hospitalization when he was 20 for atypical depression with psychotic elements.

Several treatments were tried between 2004 and 2012: Olanzapine, Paroxetine, Fluoxetine, Risperidone, Aripiprazole, Haloperidol, Valproic Acid, Amisulpride. Longest stable period was with 400 mg/d of Amisulpride and 500 mg/d of Valproic Acid per day (2006 to 2009). He stopped treatment in 2011 and December 2011 symptoms aggravation during several months and hospitalization in mai 2012. Quetiapine treatment started in april. During this current

hospitalization, we maintained Quetiapine 600 mg/d and added Sertraline 200 mg/day. Clinical partial improvement.

Alin Ciobica

Alexandru Ioan Cuza University, Molecular Biology, Iasi

Oxidative stress could play an important role in the major depression disorder (MDD). However, there are very few studies regarding this aspect.

We evaluated the enzymatic antioxidants (superoxide dismutase–SOD/glutathione peroxidase–GPX) and the levels of a lipid peroxidation maker: malondialdehyde–MDA.

We showed an increased oxidative stress status in the serum of patients with MDD, expressed by decrease of both SOD/GPX and an increase of lipid peroxidation marker MDA.

Additionally, we demonstrated here for the first time in our knowledge a difference in terms of antioxidant enzymes and lipid peroxidation between the first episode and recurrent depression patients.

Marius Cocu

Clinical Hospital of Psychiatry Socola Iasi

Growing evidence suggests that oxidative stress, inflammation, changes in glutamatergic pathways and neurotrophins play important roles in many psychiatric illnesses including mood disorders, schizophrenia and addiction. Minocycline is an antibiotic that can modulate glutamate-induced excitotoxicity, and has antioxidant, anti-inflammatory and neuroprotective effects. Given that these mechanisms overlap with the newly understood pathophysiological pathways, minocycline has potential as an adjunctive treatment in psychiatry. Case reports of individuals with schizophrenia, psychotic symptoms and bipolar depression have shown serendipitous benefits of minocycline treatment on psychiatric symptoms.. However, taken together, the current evidence suggests minocycline may be a promising novel therapy in psychiatry.

Raluca Costinescu

Quintiles Romania, Clinical Operations, Bucharest

Facial Emotion Processing Ability of Children with ASD after Intranasal Oxytocin and Interventions for Emotion Recognition Training

Children with autism exhibit a range of social dysfunction. Recognizing faces is critical to social functioning, and can be improved by using **intervention software- FEFA emotion recognition training**. The effects of this type of social intervention may be amplified with the concurrent use of **Oxytocin (Syntocinon)** (24 UI) per day.

The objective of this study is to determine efficacy of intranasal **Oxytocin** in children with autism spectrum disorders when paired with a intervention that is designed to enhance face perception skills.

Two pediatric patient groups will participate in this study: male, 8-18 years; **mental age \geq 10**; parent consent; **ability to complete tasks** (adequate vision, motor control of a keyboard/mouse); **participant must be on a currently stable treatment regimen**; are not **sensitive to Syntocinon**; diagnosed according with DSM-IV and ADI-R, ADOS.

Facial recognition will be assessed by a slide set developed Matsumoto and Ekman's Japanese and Caucasian Facial Expressions of Emotion.

Oana Cristina Cretu

Clinical Hospital Of Psychiatry “ Socola” Iasi

Effect Of Memantine Treatment At Patients With Moderate – Severe Alzheimer’s Disease Treated With Donepezil

Objective of the study was to investigate the behavioral and cognitive effect of memantine in moderate to severe patients with Alzheimer’s disease receiving donepezil. 43 patients were enrolled in this prospective, randomized, parallel group study. There were no significant imbalances between the treatment groups in demographic and baseline clinical characteristics. Cognitive and global measures were collected at baseline and at the end of weeks 4, 8, 12 and 24. Behavioral measures were collected at baseline, at the end of week 12 and at week 24. Results: Memantine – treated patients showed significantly less deterioration in their functionality. Of patients who exhibited agitation / aggression at baseline, those treated with memantine and donepezil showed significant reduction of symptoms compared with donepezil – treated patients. Conclusions: Treatment with memantine was well tolerated and reduced agitation / aggression, irritability, and appetite eating disturbances in patients who were agitated at baseline and delayed its emergence in those who were free of agitation at baseline.

Ioana Dan-Silion

Clinical Psychiatry Hospital “Prof. Dr. Alexandru Obregia”, Clinical Department I, Bucharest

Features of treatment in patients with medico-legal onset of schizophrenia

The medico-legal onset of schizophrenia is a controversial topic in the history of relations between forensic psychiatry and justice, as basically, the fact that for the first time a person has committed an offense under the criminal law, comes as proof of recognition of schizophrenia diagnosis. Typically, in these situations, the act is violent, unexpected and without any apparent logical motive, but with fewer elements of cruelty (which would allow compliance with the most serious category of homicide).

During this period, the debut, with subject managing to hide the delirium, he can not be diagnosed and there can not be applied any medical safety measure.

Violent behavior in patients with schizophrenia appears just before the first hospitalization.

Treatment of such patients with psychotic disorders who committed an offense under the Criminal Code, must consider primarily the interests of society, compared to the mentally ill subject.

Principles of mental health treatment recommend primary and secondary prevention (ante-factum treatment, avoiding the re/occurrence of an offense under the Criminal Code) and tertiary prevention (post-facto treatment that is designed to prevent relapse).

Razvan Dan-Silion

ICON Clinical Research, Clinical Operations, Bucharest

Psychopharmacology – changing human perception on psychiatric diseases – a short history

Drugs obtained from certain plants have been used for millennia by humans to ease suffering or change awareness, but until the modern scientific era nobody knew how these substances worked.

Psychiatry was conceived largely as a phenomenological medical domain, as patient behaviors or themes which were observed in patients could often be correlated to a limited variety of factors such as childhood experience, inherited tendencies, or injury to specific brain areas. Models of mental function and dysfunction were based on such observations.

But until World War II, no clear clinical benefit could be observed. No breakthrough.

Neuropsychopharmacology may be regarded to have begun in the earlier 1950s with the discovery of drugs such as MAO inhibitors, tricyclic antidepressants, phenothiazines and benzodiazepines which showed some clinical specificity for mental illnesses such as anxiety, depression and schizophrenia.

The field now known as neuropsychopharmacology has resulted from the growth and extension of many previously isolated fields which have met at the core of psychiatric medicine, and engages a broad range of professionals from psychiatrists to researchers in genetics and chemistry.

Adriana Mihaela David

Sp.Universitar de Urgenta Bucuresti, Psihiatria de legatura

This paper presents the quality of life in patients with cancer and depression-anxiety comorbidity from bio-psycho-socio-spiritual point of view. The impact of the psychological component on the assessment of the quality of life is outlined, using unsystematic personal observations. The double determinism of somatic and mental pathology, with emphasis on the interference of depression and anxiety with the quality of life is reviewed and strategies about how to improve the quality of life in patients with cancer and comorbid anxiety disorders or depression are described.

Keywords: quality of life, depression, anxiety disorders, oncology

Liliana Veronica Diaconescu

University of Medicine and Pharmacy “C. Davila” Bucharest, Medical Psychology

Variables involved in therapeutic adherence of somatic patients with psychiatric comorbidity treated by general practitioner

Study group: patients with chronic somatic diseases (cardiovascular, respiratory, gastrointestinal diseases) which are receiving general medical practice and are presenting psychiatric comorbidity (anxiety, depression) **Method:** Administration of psychological tests regarding anxiety (Hamilton Anxiety Scale), depression (Center for Epidemiologic Studies Depression Scale, CES-D Ratlof, 1970), adherence (Medication Adherence Report Scale -MARS, Horne, 2004) and social support (Duke-UNC Functional Social Support Questionnaire, 1988). Variables that may influence adherence and to be considered in the study : age, sex, disease, disease severity, the level of anxiety, respective depression, social support.

Rodica Dogaru

Diagnostic Centre Clinic, Bucharest

The literature of neuroimaging of pain and learning processes shows that chronic pain is characterized by learning related and memory related plastic changes of the central nervous system with concomitant maladaptive changes in body perception. These alterations share many similarities with brain changes in emotional disorders. Learning influences subjective, behavioural, neurophysiological and biochemical aspects of pain that outlast the phase of acute pain and may contribute to experience of chronic pain.

My presentation is based on a case of patient with chronic anxiety disorder. In the last 6 months he has experienced a chronic sciatic nerve pain with significant functional impairment with no improvement after a many clinical and paraclinical specific investigations and also after specific treatment for pain; anxiolytic treatment and cognitive behavioural therapy has led to significant decrease in pain intensity.

Iolanda Maria Dumitrescu

“Eftimie Diamandescu” Hospital, Cernica, Ilfov

Sleep deprivation and post partum depression (ppd) – is there a link? A research project

BACKGROUND: Research concerning sleep deprivation in early post partum period show divergent results. While some studies elicited a negative effect of poor sleep quality and fewer hours slept on the new mothers' mood others suggest that sleep deprivation may be a cure for PPD.

METHOD: Pregnant women will be enrolled at their last visit with the GP before delivery, usually within the last month of pregnancy. They will be administered a questionnaire regarding the presence of predictors for PPD and asked to take home a daily sleep chart to fill in in the first month after giving birth. 1-2 months postpartum they will be screened for PPD according to the DSM IV-TR criteria.

RESULTS: This study aims to find whether there is a correlation between the average number of hours slept per day in the first month after delivery and the presence of PPD.

LIMITATIONS AND DISCUSSION: A large sample may be necessary to control for all the risk factors. If a correlation exists, further research is needed to tell whether there is a causal relation between the two.

Radu Mihai Dumitrescu

“Regina Maria” Obstetrics-Gynecology Hospital, Bucharest

Correlations between treatment with oxytocin peripartum and prevalence of postpartum depression

Oxytocin is a hypothalamic neuropeptide which seems to facilitate at central level adaptive social attachment processes and to modulate anxious response to stress (Cyranowski J.M., 2008).

major depression is associated with dysfunction of hypothalamic-pituitary-adrenal axis, which may involve also dysfunctions at the level of oxytocin (Ozsoy S., 2009). post-partum depression is present in aprox 19% of the total women after birth (Skrundz M., 2011). Oxytocin obstetrical administration is related to labor, to stimulation of uterine contractions, to prevention of postpartum bleeding and to help milk let-down postpartum.

This study's objective is to identify if there are significant differences in prevalence of postpartum depression and other symptoms in the anxiety spectrum, between the parturient which received oxytocin and those who do not. We will use a depression scale (e.g. Edinburgh Postnatal depression Scale-EPDS) at the prenatal assessment in the third trimester and in postpartum period at 2 and 6 weeks.

The results would bring data upon the use of oxytocin as treatment for prevention of postpartum depression.

Maria Magdalena Dumitru

Clinical Hospital Of Psychiatry “Socola” Iasi

SOMATIC COMORBIDITIES IN PATIENTS WITH BIPOLAR DISORDER

Bipolar patients have a high risk for somatic comorbidities that need to be treated by non-psychiatrist medics. Factors related to unhealthy lifestyle, disease and treatment may confer some additional risk of morbidity in people with bipolar disorder.

The primary endpoint of the study was to detect risk factors for the development of somatic comorbidities in patients with bipolar disorder wich will allow appropriate treatment to improve their quality of life.

The study was conducted by interviewing and physical examination of a group of 21 consecutive patients who were hospitalized between 1 to 28 February 2011 in the Clinical Hospital of Psychiatry “Socola” Iasi and were diagnosed with bipolar disorder according to DSM-IV-TR criteria.

Patients age range was 24 to 58 years. Of the subjects 57% were female and 43% men. The study shows that 67% of patients with bipolar disorder smoked regularly, and 52% consumed alcohol abusively. The most common somatic diseases associated were dyslipidemia, arthrosis, obesity, hypertension, liver diseases, type 2 diabetes mellitus. Metabolic syndrome criteria were met by one third of patients.

The patients with bipolar disorders showed a high proportion of alcohol abuse and smoking. Most somatic diseases recorded were related to metabolic syndrome and other disturbances typically caused by unhealthy diet and lifestyle.

Olguta Maria Dumitru

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Clinical Department XII Bucharest

Metabolic changes among psychiatric inpatients receiving antipsychotics - cross-sectional study on patients admitted in a psychiatric unit in Bucharest in a 12 month period

Background: Antipsychotic drugs can be of great benefit in a range of psychiatric disorders, including schizophrenia and bipolar disorder, but all are associated with a wide range of potential

adverse effects. These can impair quality of life, cause stigma, lead to poor adherence with medication, cause physical morbidity and, in extreme cases, be fatal.

Persons taking antipsychotics are at a greater risk of developing obesity, diabetes type 2, hypertension and dyslipidemias than those in the general population. The metabolic side effects are due to a number of factors: the type of antipsychotic (classical or atypical), the dose of the drug and the individual response to treatment.

Materials and methods: medical records of 84 inpatients randomly selected from all admissions to a public psychiatric hospital between June 2011-June 2012 and diagnosed, according to DSM-IV criteria, with different types of schizophrenia, schizoaffective disorder or bipolar disorders.

Results: 18/84 (21.43%) patients were treated with Haloperidol, 24/84 (28.58%) with Olanzapine, 21/84 (25%) with Risperidone, 16/84 (19,04%) with Quetiapine, 3/84 (3.57%) with Aripiprazole and 2/84 (2.39%) with Amisulpride. 10/84 patients (2 treated with Haloperidol and 8 with atypical antipsychotics) had high levels of cholesterol. 33/84 patients (2 treated with Haloperidol and 31 with SGAs-second generation antipsychotics) had higher mean triglyceridaemia (>150 mg/day). Values of total lipids over 800 mg/day were observed in 4 patients (all 4 treated with SGAs). 17/84 patients had higher mean glycaemia (>110 mg/day), 9/84 patients have been diagnosed with type 2 diabetes mellitus, 7/84 patients with obesity, and 4/84 patients with metabolic syndrome (all treated with SGAs).

Conclusions: The rate metabolic disorders observed in this study were higher in patients treated with second generation antipsychotics.

Catalina Giurgi-Onucu

SCJUT, “Eduard Pamfil” Psychiatry Clinic, Timisoara

The depressive-delusional spectrum is currently under-researched. It is of importance to psychiatric nosology to identify the differences between the two pathologies of this spectrum. Social functioning and social cognition are some of the points of interest for long-term evolution, when psychotic elements are present. In literature, there are very scarce information regarding the comparative assessment of social functioning or social cognition between people suffering with a depressive-delusional pathology and those with a delusional-depressive disorder. We hypothesize that social functioning and social cognition are reduced in subjects suffering with psychotic depression. The participants were diagnosed by using the SCAN interview (ICD-10).

Adrian Horvath

Targu Mures County Hospital, Psychiatry II

The effectiveness of Aripiprazole as SDA-DPA-SPA in treatment of brief and chronic psychotic disorder

Keywords: Aripiprazole, antipsychotics, Serotonin-dopamine antagonism, dopamine partial agonism, serotonin partial agonism.

Objective: To evaluate if Aripiprazole as the only SDA-DPA-SPA is more or less effective in treatment of psychosis, comparative with other SGA

Method: In a retrospective analysis developed in Psychiatry Clinic II, Targu Mures, we studied the effectiveness of Aripiprazole as SDA-DPA-SPA at the patients with brief or chronic psychotic disorder, with or without previous antipsychotic treatment.

Results: At the time in development

Conclusion: At the time in development

Denisa Elena Ivanovici

Spitalul Judetean de Urgenta Targoviste

THE ASSOCIATION BETWEEN SPIRITUALITY AND DEPRESSION IN THE ELDERLY

The religion and the spirituality had become variables of interest in medical research, being recognized their potential to prevent, to heal or to cope with the illness. This paper studies the correlation between these variables and the depression in the elderly.

We have investigated the spiritual or religious beliefs, the nature of any religious belief and their practice and importance in daily life. It was included questions about the communication with a spiritual force and the purport and the impact on the illness, using "The Royal Free Questionnaire for Spiritual and Religious Beliefs", created by Professor Michael B King.

Forasmuch the depression in the elderly has its peculiarities, we used The Geriatric Depression Scale for the screening of the depression in the elderly populations.

In our study, applied to an urban population with ages over 65 years, as well as in the studies from the specialty literature, the high scores obtained through the investigation of religious and spiritual beliefs has been correlated with the decreasing of the depressive symptoms. The faith in a superior force, the relation with this and the belief in the power of the prayer had differed substantially between the depressed and no depressed persons.

In conclusion, the finding of the ways to encourage the intrinsic beliefs of the elderly patients may have a benefic impact in the treatment of the depression. The relation between spirituality, medicine and mental health remains an area of enthralling research with the purpose to describe the therapeutically modalities most effective.

Ovidiu Marginean

Mărginean Ovidiu Cabinet Individual de Psihologie, Campung Moldovenesc

Research proposal. Psychoeducation in Severe Mental Illness: Survey of all Psychiatric Institutions in Romania

Psychoeducation for severe psychiatric illnesses, mainly for schizophrenia, is generally is not systematically provided in Romanian mental health settings. In order to promote psychoeducation implementation into clinical practice on a large scale it is necessary first to map to what extent and for what diagnoses psychoeducation is provided (to investigate the percentage of persons that took part at psychoeducation programs - patients and family members - in the past 5 years) as well as to explore possible critical areas that hinder from psychoeducation implementation and dissemination (such as financing, leadership, training and attitudes). The study population is represented by all psychiatric facilities in Romania, the managers and the moderators of psychoeducation programs conducted in those facilities. Data will be collected through postal survey, telephone interviews and focus groups. Proposed strategies for overcoming barriers in the implementation of psychoeducation programs will be described.

Roxana Mihaela Marginean

Clinical psychologist at Campulung Moldovenesc Hospital of Psychiatry, Mental Health Center

The psychosocial rehabilitation of people with severe mental health problems: a quasiexperimental study of the impact of an assertive community treatment program

The psychosocial rehabilitation of people with severe and persistent mental health problems is a relatively new field in the Romanian psychiatric care. Despite the existent legislation and international recommendations, the practice of assertive community treatment is still scarce and hasn't been, until now, investigated with scientific methods. Accordingly, in the present study we aim to analyze the impact of an assertive community treatment program, implemented in rural and micro-urban regions within the psychiatric sector of Câmpulung Moldovenesc. Using a pretest- posttest quasi-experimental design of non-equivalent groups, we have evaluated the program's impact in comparison with standard treatment, on reducing symptoms and improving social and independent living skills in a sample of 143 participants diagnosed with depression and schizophrenia. The findings indicate that after 6 month of assertive community treatment the intervention group obtained significant lower mean scores on clinical scales and significant higher mean scores on the social functioning scale compared to the initial evaluation and the control group. The reform of the system of mental health services can become a concrete reality through joined and active involvement of researchers and clinical practitioners in implementing and studying psychosocial rehabilitation programs.

Alina Elena Miu

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Clinical Department IX, Bucharest

Recurrent Depression with somatic phenomena at old versus adult patients

Depression is frequently associated with somatic pathology, especially if it is recurrent. I would like to study if there are more frequent somatic phenomena for patients older than 65 years old diagnosed with recurrent depression in Psychiatric Hospital than for the patients under 65 years old with the same Psychiatric pathology.

Simona Ana Mudava

SC Acord Med SRL, Bucharest

Finding a possible common core of major depression, dementia and schizophrenia

This article aims to present the common features of three major psychiatric disorders, dementia, major depression disorder and schizophrenia, covering the symptomatic, imagistic, neuroanatomical and receptorial areas, as well to raise the question (without pretending to find a such pretentious answer) whether a common organic dysfunction exists.

Leonard Nastase

Institute of Mother and Child Care “Professor Dr. Alfred Rusescu”, Bucharest

The correlation between the prediction of the theoretical efficiency through molecular modeling and clinical effectiveness in ssri antidepressants

Năstase Leonard¹, Năstase Sorina², Avram Speranța³

Aim: Our study has sought to correlate the QSAR analysis (quantitative structure-activity relationship) of SSRIs (Selective serotonin reuptake inhibitors) and their receptorial affinity with a serie of clinical cases of depression treated with SSRIs.

Materials and method: Through molecular modeling and analysis of quantitative structure-activity relationship (QSAR), we analyzed and compared the activity of serotonergic antidepressants - escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine and we have performed their hierarchy based on their theoretical antidepressant effectiveness. Were constituted five lots of 50 patients with depression in order to determine the clinical efficacy of these antidepressants. Each of these groups received treatment with one of the five antidepressants. The initial distribution of patients was made based the severity of untreated depression, in each group being included in equal proportions of patients with severe, medium and middle depression. The Hamilton Depression Scale and Beck Depression Inventory were applied to the patients before the start of antidepressant treatment, at 2 weeks and 2 months after treatment.

Results: The theoretical ranking aquired from molecular modeling and QSAR analysis was, in the order of increasing effectiveness of antidepressants, paroxetine, fluvoxamine, fluoxetine, sertraline, escitalopram, while the practice ranking has been: fluvoxamine, fluoxetine, sertraline, paroxetine and escitalopram.

Conclusion: Our clinical study has not fully confirmed the theoretical prediction, so that we consider the improvement of theoretical models of molecular simulation, including exploring the interaction of antidepressants with ions (sodium, potassium, magnesium, calcium).

Sorina Nastase

MedLife Hyperclinic, PhD student

Study of interactions between antipsychotics and their membrane receptors by qsar methods – towards new antipsychotics drug design

Năstase Sorina, David Adriana Mihaela

* Adriana Mihaela David and Sorina Năstase have equal contributions to this article.

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1. Dr. Năstase Sorina, psychiatrist, in Faculty of Biology, Bucharest University and Medical and Farmaceutical University “Carol Davila” Bucharest
2. Dr. David Adriana Mihaela, psychiatrist, Departamentul de Psihiatrie de Legătură SUUB, PhD student in Medical and Farmaceutical University “Carol Davila” Bucharest

Abstract: Affinity of typical and atypical antipsychotic drugs at membrane dopaminergic D2 and serotonergic 5HT1A receptors have been studied using quantitative structure activity relationship (QSAR) analysis. Using computational chemistry the antipsychotics affinities expressed as (-log Ki) at dopaminergic D2 and serotonergic 5-HT1A were correlated with pharmacokinetic descriptors namely: the Solvent Accessible Surface Area (SASA), molecular

volume (V), globularity (G), Octanol/water partition coefficient ($\log P$), solubility (S), dipole moment, polarizability, and most important, the Blood/Brain barrier permeability. The statistical results indicated that the simultaneous contribution of $\log P$, molecular volume and solvent accessible surface, polarizability and dipole moment are important for antipsychotics activity. The best correlation between predicted and experimental biological activities of antipsychotics was recorded when interaction between antipsychotics and membrane receptor D2 was analyzed.

Raluca Nicoara

Timisoara County Hospital, Psychiatric Clinic “Eduard Pamfl”, Timisoara

The Placebo Effect In Clinical Trials: Reality Or Fiction?

The placebo effect has always been a source of fascination, irritation and confusion in the medical field. Very many clinical trials performed in the past years in the psychiatric field have demonstrated a concerning rise in the placebo response. There are recent scientific discoveries that show some of the possible neurobiological mechanisms of the placebo effect that appear to be capable of releasing endogenous neurotransmitters that mimic the expected pharmacological effect.

The placebo response obtained in clinical trials appears to be more than a simple error. There is additional research needed in order to exploit this therapeutic potential, if it really exists.

Manuela Padurariu

Socola Hospital Iasi, III B

Mild cognitive impairment(MCI) is a transitional stage between normal cognitive aging and Alzheimer's disease(AD). The aim of this study was to determine the oxidative stress in MCI and AD patients.

We assessed some enzymatic antioxidants like superoxid dismutase(SOD)/glutathione peroxidase(GPX) and a lipid oxidation maker-malondialdehyde(MDA).

Alterations in the activity of both antioxidant enzymes were found in MCI and AD peripheral blood. Also, MDA levels were increased in the AD/MCI patients.

Conclusion:peripheral markers of oxidative stress appear in MCI with a similar pattern to that observed in AD, which suggest that oxidative stress might represent a signal of the AD pathology.

Corina Panzaru

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Bucharest

Global disability in depressed people treated with SSRI or TCA

Key words: disability, depression, antidepressive treatment

Introduction: Depressive disorder have a large impact on psychosocial functioning. Since lower functioning predicts recurrence of a depressive episode, insight into the course of social and

physical functioning of persons with depressive disorders, and into the determinants of an impaired recovery of functioning may facilitate recurrence prevention and limit the burden of disease. Psychosocial disability is important in the course of the disease in order to estimate the efficacy of the treatment, the progress under treatment and the quality of life in depressive patients.

Methods: Forty-nine patients with MDD treated with SSRI and twenty-five depressed patients with TCA were compared on global disability using SDS self- scale both in acute phase, and in remission phase, during 2 years of treatment.

Results: The patients from both groups showed a decrease of disability level during the remission phase compared with acute phase. The patients treated with SSRI demonstrated a statistically improvement in global psychosocial functioning (Shehan Disability Scale) than the TCA-treated patients after 1 year of treatment ($p=0.015$) and at the end of study meaning 2 years of treatment ($p=0.001$).

Conclusions: Global psychosocial functioning, improves over time in patients successfully treated for MDD. Patients treated with SSRI have significantly better performance in psychosocial functioning than patients treated with TCA

Lucian Paziuc

Spitalul de Psihiatrie Campulung Moldovenesc

Psychosocial rehabilitation of chronically mentally ill - Community support integrated services in a psychiatric sector

This paper aims to reflect the day to day work of multidisciplinary team in a well defined geographical area with many cultural, social, economic and spiritual peculiarities. Mental health care in Romania focusing currently in psychiatric hospitals.

There is only formal communication between bed units and the ambulatory service, the continuity of care is often limited to a certain continuity of psychotropic drug administration. We can not talk about a particular specialization, no concept of therapeutic team and the less that community care.

The general objective is to increase quality, accessibility and targeting of mental health services in the psychiatric sector Câmpulung Moldovenesc.

Specific objectives

1. Development of alternative and integrated community care into the Mental Health Center Câmpulung Moldovenesc with the involvement of local community and users of psychiatric services for medical and psycho - social rehabilitation.
2. The increase of Quality of life of people with mental health problems.
3. Forming a multidisciplinary team of medical and social intervention in the psychiatric sector Campulung Moldovenesc.
4. Combating discrimination and social exclusion through measures to support and complement existing national strategies and policies.

The community services are aimed at setting up favorable frameworks recovery, even in the wild life of the beneficiary. They require to accompany the person on the tortuous road to recovery.

Alina Petricean

Clinic of Psychiatry No 2, Targu Mures

Oral atypical antipsychotics are most commonly prescribed class of medicine for the treatment of severe mental illness

An electronic excel based audit tool has been designed and used to allow individual mental health organisation to review the use of oral atypical antipsychotic medicines in patients with severe mental illness and depression admitted on three Inpatient units

The audit reports were generated automatically and included: a summary of oral atypical antipsychotic prescribing, the use by diagnosis, dosing and titration regimes, the length of stay in psychiatric unit, the date when medically fit for discharge compared to actual date of discharge Results showed that 89 patients were admitted to Psychiatric Units between 1/2/11 – 31/3/11 and 37 inpatients were placed on atypical antipsychotic. Diagnosis used were: Schizophrenia, Bipolar Mania, Bipolar Depression, Major Depressive Disorder (with psychotic symptoms), Borderline Personality Disorder, Schizoaffective Disorder, Substance induced psychosis, Psychotic episode.

Quetiapine XL and Olanzapine were used the most and Quetiapine XL, the Olanzapine and Aripiprazole were usually titrated. Average time in days to target dose for Olanzapine is higher compared to Quetiapine XL. The highest mean stay (in days) is for Risperidone (51 days), followed by Quetiapine XL (25 days) and Olanzapine (20 days). Non-medical delay in days for discharge: the higher for Risperidone and Aripiprazole. The reason for discontinuation of initial atypical were lack of response and adverse events. The average final dosage of atypical AP: Aripiprazole 15 mg, Olanzapine 14 mg, Quetiapine XL 433 mg, Quetiapine IR 300 mg, Risperidone 5 mg.

Florina Rad

University Of Medicine & Pharmacy “Carol Davila”;

“Al. Obregia” Clinical Psychiatry Hospital, Child And Adolescent Psychiatry Department, Bucharest

Possible predictive factors for the evolution of children with Autistic Spectrum Disorder comorbid with Attention Deficit Hyperactivity Disorder

Hypothesis

ASD and ADHD are comorbid in 50-80% of cases

About 80% of children with ASD comorbid with ADHD can progress to ADHD after behavior therapy

Parents of children with ASD have a high systemizing quotient and a low empathy quotient

Parent phenotype (systemizing quotient and empathy quotient) can influence the evolution of child

Primary objective

To identify the predictive value of parents' phenotype for children evolution

Secondary objectives

To identify the prevalence rate of ADHD in children with ASD

To identify parental phenotype (systemizing and empathy quotient)

Method

50 children (2-6 years old) will be evaluated at baseline and after 1 year of applied behavior therapy with: KID SCID, ADOS and ADHD RS

Their parents will be evaluated at baseline with SQ (Systemizing Quotient) and EQ (Empathy Quotient)

SPSS 19 will be used to determine the predictive value of variables

Florina Ratoi

County Emergency Clinical Hospital of Arad

Adherence / non-adherence issue in psychotic disorders

Florina Rățoi¹, Delia Marina Podea¹

¹“Vasile Goldiș” Western University of Arad

Most recent trials showed that 74% patients with psychotic illness discontinued antipsychotic treatment before 18 months, underlining the point that adherence to treatment is challenging for patients with long-term mental illness. A similar high discontinuation rate was reported in a comparative study of antipsychotic therapy tolerability and efficacy on first psychotic episode. This suggests that medication non-adherence is a major consideration, even at the beginning of treatment. Moreover, medication non-adherence rates for psychiatric conditions are generally worse than for other medical conditions

Great attention was rightly paid to improving adherence to treatment with innovations in medicine industry.

Rational use of atypical antipsychotics may confer benefit with regard to medication adherence. Furthermore, use of long-acting injectable antipsychotic formulations may improve medication adherence.

Keywords: adherence, non-adherence, psychotic disorders, antipsychotic, long-acting

Cristina Luana Roata

Psychiatry Hospital Campulung Moldovenesc

Female depression and sexual disfunction

Dr. Cristina–Luana Roată – psychiatrist doctor, Psychiatry Hospital Câmpulung Moldovenesc

Ovidiu Mărginean – clinician psychologist, Individual Psychology Practice, Câmpulung Moldovenesc

The purposes of this research were: the study of a often health situation, depression, alltogether with one of the comorbidities, sexual disfunction. This study was realized developing a quality analyze by applying a female sexual disfunction specific questionnaire and establishing a correlation between sexual disfunctional beliefs and demografic parameters, in specialy with age.

This research studied a representative group of 30 women with the diagnosis of different forms of depression. The 30 women were hospitalized in Clinical County Emergency Hospital Cluj – Clinic Psychiatry II and in Psychiatry Hospital Campulung Moldovenesc, in the period 16.11.2010 – 15.04.2011.

Daniela Claudia Sabau

Spitalul Clinic Judetean Tg.Mures, Clinica Psihiatrie I Ac.

This paper is focused on the role of cognitions in depressive disorders, from a diagnostic and a therapeutic point of view. After a brief review of the diagnostic criteria stated in ICD - 10 and

DSM-V, we call into question the cognitive model of depression proposed by A.Beck, based primarily on negative cognitive productions and negative cognitive schemata, and the model proposed by M.Seligman, concerning the learned helplessness theory of depression. Finally, we expose the issues of the cognitive therapy in depression. **KEY-WORDS:** cognitions in depression learned helplessness, cognitive therapy

Irina Sacuiu

Clinical Hospital of Psychiatry Socola Iasi

Objectives: The study aimed was to defining the cognitive deficit in schizophrenia and the influence of the atypical antipsychotics on it. Another objective was to compare the neurocognitive effects of olanzapine, quetiapine, risperidone, ziprasidone, clozapine and sertindole and to establish the relationship between cognition and social functioning in schizophrenia.

Methods: The study was of the observational prospective type, lasting for 40 weeks was made on 7 groups of 20 patients each, according to the type of the antipsychotic used in therapy: olanzapine, quetiapine, risperidone, aripiprazole, ziprasidone, clozapine and sertindole. The test batteries used in the CATIE (*Clinical Antipsychotic Trials of Intervention Effectiveness*) and BACS (*Brief Assessment of Cognition in Schizophrenia*) studies have been applied.

Results: After 40 weeks, corresponding V10, every antipsychotic drug improved the compound score of the CATIE and BACS neurocognitive battery comparing to the moment of the inclusion in the study (Vi). There was a positive correlation: the patients who displayed a cognitive improvement at the V10 moment, also displayed benefits in the social and occupational fields, which suggests a functional relevance for the improvement of cognition, cognition amelioration has been positively correlated with the improvement of social performance and professional qualification.

In conclusion, there is an important cognitive deficit in the majority of the schizophrenic patients. Olanzapine, quetiapine, risperidone, aripiprazole, ziprasidone, clozapine and sertindole have displayed similar results in terms of their effects on various neurocognitive deficits. There is a strong relationship between the level of the cognitive deficits in schizophrenia and the social performance as well as compliance with treatment and the quality of life.

Diana Catalina Sfat

Emergency County Hospital Timisoara, Psychiatric Clinic

Pseudocyesis is a very rare syndrome (prevalence 1-6 cases per 22,000 births). Three etiological theories are widely accepted: conflict theory, wish-fulfillment theory and depression theory. This syndrome is often associated with borderline and histrionic personality disorders. This paper presents a case report of pseudocyesis. A 26-year-old woman, married, childless, was admitted to psychiatric department for amenorrhea, unilateral galactorrhea, tender and sore breasts, abdominal distension and a strong belief that she was nine month pregnant. Based on anamnesis, clinical, laboratory and psychometric tests, the established diagnosis was pseudocyesis (F45.1 undifferentiated somatoform disorder, according to ICD-10) and mixed personality disorder.

Elena Daniela Stefan

“Eduard Pamfil” Timisoara County Hospital

Background: In literature the duration of untreated psychosis (DUP) was correlated with treatment outcome.

Objective: The study aims to evaluate if there are significant correlations between the DUP and the number of days spent during hospitalization in schizophrenic patients admitted to Psychiatric Clinic Timisoara 2nd department.

Method: 47 schizophrenic patients admitted from 2005 till 2012 were included in the study. The diagnosis was established according to ICD-10 criteria.

Results: in schizophrenic patients the DUP median was 5 months, with an average duration of hospitalization of 37 days.

Conclusion: No significant correlations were found between DUP and the duration of hospitalization.

Andreea Stefanache

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Clinical Department XVI, Bucharest

Therapeutic Management of the Psychotic Symptoms in Patients of Methadone Maintenance Treatment

A. Stefanache ¹, V. Rusanu ², M. Siderencu ³

Methadone maintenance treatment (MMT) is an effective treatment for opiate addiction. Many patients in treatment do not have complete control over their addictions at all times and many times they continue using heroin or other drugs such alcohol or legal highs after admission to treatment. Legal highs or “bath salts” and/or “herbal incense” have serious adverse psychiatric effects including acute psychosis, delirium, violent behavior. Treatment of acute psychosis in MMT patients can be a challenge. We would like to study on 20 MMT male patients with acute psychosis, the efficiency of the neuroleptic treatment and the adverse events patient report.

Carmen Ioana Trutescu

University Of Medicine & Pharmacy “Carol Davila”; “Al. Obregia” Clinical Psychiatry Hospital, Child And Adolescent Psychiatry Department, Bucharest

Usefulness of neuroleptic medication in the early treatment of comorbidities TSA - ADHD

Hypotesis

High frequency of cases in which TSA is comorbid with various forms of disorder and ADHD hiperchinetica as well as ESSENCE definition (Gillberg), have generated an intense preoccupation with the course of treatment in these cases. Usefulness of of drug therapy is currently controversial although the use of medication efficacy and improve cognitive and social functioning.

Objectives

Identify the benefits obtained by children with ASD with comorbid ADHD who received associated neuroleptic medication to psychotherapy.

Method

60 children with ASD/ ADHD (3-6 years old), in two sample, evaluated at baseline and after 6 month of applied behavior therapy associated or not with neuroleptic medication

Children will be evaluated using KID SCID, ADOS and ADHD RS

SPSS 19 will be use to determine the predictive value of variables

Otilia Carmen Turiac

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Clinical Department XII, Bucharest

Bipolar Disorder-OCD Comorbidity: A Case Report and Treatment Dilemma

Background

A growing number of epidemiological and clinical studies have found that bipolar disorder significantly co-occurs with anxiety disorders at rates that are higher than those in the general population.

Anxiety symptoms tend to be more prevalent in Bipolar II than Bipolar I disorder also anxiety symptoms often resolves when the mood disorder is treated.

Case presentation

We present a 54 years old man with obsessive-compulsive disorder who also suffers from bipolar disorder, currently experiencing a severe depressive episode.

In the past he had many admissions to hospital, mainly for antidepressant- induced mania. The last admission was in 2002 and since then he only experienced depressive symptoms, but also the OCD symptoms were more prominent.

Conclusion

The biggest challenge is the treatment of the OCD-bipolar disorder comorbidity, given the fact that antidepressants, while proven effective in anxiety disorders, may worsen the course of bipolar disorder, especially if initiated before treatment with a mood stabilizer.

Claudia-Cristina Vasilian

Emergency County Hospital Timisoara, Liaison Psychiatry

Prevention of post surgery delirium in elderly

Delirium, defined as an acute decline in attention and cognition, is a major complication following hip fracture surgery in the elderly. The etiology is multifactorial, and the underlying mechanisms are not clearly understood. Postoperative delirium is associated with longer hospitalization, higher mortality, greater costs and long term cognitive dysfunction.

The objective of this study is to determine if preoperative administration of Piracetam, Folic acid and group B vitamins reduces the incidence and duration of this common hip fracture surgery complication in the elderly.

Roxana Elena Vornicu

“Al. Obregia” Psychiatric Hospital, IV Clinic, Bucharest

Recent theories propose that the impairment of the memory-prediction function represents the core feature of schizophrenia and accounts for the cognitive and perceptual deficits associated with the disease.

Two findings that support this theory state that schizophrenic patients have difficulties in processing and recognizing incomplete visual stimuli and have a tendency of extracting spurious messages from meaningless noise.

I would like to investigate how atypical antipsychotics affect the memory-prediction function in regard to the above-mentioned reality distortion parameters.

Madalina Ionelia Vrabie

Clinical Hospital of Psychiatry “ Prof. Dr. Al. Obregia”, Clinical Department VII Bucharest

Identifying the cognitive deficits in bipolar affective disorder during manic episodes
M Vrabie^a, I Miclutia^{bc}, V Marinescu^{ad}, C Popescu^c

^a7Ward, Clinical Hospital of Psychiatry “Al. Obregia” Bucharest, Romania, ^bDepartment of Psychiatry, University of Medicine & Pharmacy “Iuliu Hatieganu” Cluj-Napoca, Romania, ^cSecond Psychiatric Clinic, Emergency County Hospital Cluj-Napoca, Romania, ^dDepartment of Psychiatry, University of Medicine & Pharmacy “Carol Davila”, Bucharest, Romania

Objective: Identifying specific domains of cognitive dysfunction for manic episodes in bipolar affective disorder.

Methods: 60 bipolar (HAMD score ≥ 17 , manic/hippomanic: YMRS score ≥ 12 , euthymic: 6 month of remission, HAMD score ≤ 8 , YMRS score ≤ 6) patients (DSM IV TR). The cognitive battery included standardized test of IQ, attention, working memory, visual memory, verbal memory and executive functioning. Demographic data, data about family history, psychiatric history, past/current treatment, history of psychosis, duration of illness, age of onset were collected. We analyzed statistically these data and identified specific domains of cognitive dysfunction for manic episode.

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.

Conclusions: 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.

Andrea Zamfirescu

Sf. Luca Hospital, Geriatrics, Bucharest

We investigated two groups of 10 patients, diagnosed with mild to moderate dementia, on specific dementia medication. The intervention consisted in 40 minutes of aerobic exercise training, 5 days per week, 3 months.

We used neuropsychological tests: MMSE, Clock Drawing Test, GDS, R-ACER (Romanian version of Adenbrooke's Cognitive Evaluation Revised), Geriatric Depression Scale, ADL/IADL and "physical" measurement tests.

The results show that multimodal intervention in dementia, considering both pharmacological treatments and non-pharmacological treatment's development seem to be the hope for a better management of patients diagnosed with dementia.

Mathilda Zavoianu

SCUMC "Carol Davila" Bucharest

Mild cognitive impairment refers to the clinical state of individuals who are memory impaired but do not meet clinical criteria for dementia and are functioning well.

ApoE4 is a known genetic risk factor for Alzheimer disease.

A number of studies showed no significant grey matter loss in non- apoE4 carriers with MCI , but a MRI pattern of atrophy associated with progression to AD in MCI.

As the objective of the study: to assess the efficacy of donepezilum in preventing progression of MCI to AD by comparing neuropsychological performances and hippocampal volume decline.