ECNP

european college of neuropsychopharmacology

ECNP Seminar Serbia

14-16 November 2014, Kastel Ecka

Introduction

ECNP is an independent, non-governmental, scientific association dedicated to the science and treatment of disorders of the brain. Founded in 1987, its goal is to bring together scientists and clinicians to facilitate information-sharing and spur new discoveries.

The objective of ECNP is to serve the public good by stimulating high-quality experimental and clinical research and education in applied and translational neuroscience. . It seeks to do this by:

- Co-ordinating and promoting scientific activities and consistently high-quality standards between countries in Europe.
- Bringing together all those involved in or interested in the scientific study of applied and translational neuroscience by arranging scientific meetings, seminars, and study groups.
- Providing guidance and information to the public on matters relevant to the field.
- Providing a format for the co-ordination and for development of common standards in Europe.

To fulfil this aim ECNP organises, amongst others, yearly the ECNP Congress that comprises of 6 plenary lectures, 28 symposia and 7 educational update sessions. The annual meeting attracts more than 6,000 participants and is considered to be the largest event in neuropsychopharmacology in Europe.

ECNP organises seminars, as the one you have been invited to participate, in areas of Europe where there are less opportunities for psychiatrists to participate in international meetings. Interaction is the keyword at these meetings and they have proved very successful both for the participants and for the experts. During the seminar we discuss clinical and research issues that the local organisers feel that are needed to be covered and using these topics as a model for teaching how to ask a research question and how to plan an effective study. Leading ECNP experts that are also talented speakers will facilitate mutual discussion in small groups allowing you to present your abstract and get feedback from your colleagues and local mentors.

So far, ECNP has organised this meeting in Poland, Estonia, Turkey, Bulgaria, Slovak Republic, Hungary, Czech Republic, Moldova, Romania, Greece, Russia,

Latvia and recently in Macedonia, Armenia, Georgia and Serbia. In some countries we have organised it more than once.

ECNP also supports on an annual basis participation of 100 junior scientists and researchers in an intensive three-day Workshop in Nice. Other educational activities of ECNP include the journal *European Neuropsychopharmacology* that promotes scientific knowledge along with publishing consensus statements. . In addition, since 2009 ECNP organises a summer school of neuropsychopharmacology in Oxford, since 2012 a school of child and adolescent neuropsychopharmacology in Venice and since 2013 a school of old age neuropsychopharmacology in Venice. We plan to start a workshop on methodology and clinical research in Barcelona in 2015..

This year we start with a pilot of a new initiative, The ECNP Research Internship. This is a new collaborative initiative of ECNP and the ECNP Junior Member Advisory Panel (JMAP) that aims to provide short-term research internship opportunities for junior researchers. Senior researchers from the list of ECNP Fellow members offer unpaid 2 week exploring research internship in their institutions.

Please see the ECNP website (www.ecnp.eu**)** where you can find information about all the above initiatives and additional information and look for the activity that fits you.

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

Gil Zalsman

Chair ECNP Educational Committee

PROGRAMME

ECNP Seminar in Neuropsychopharmacology

14-16 November 2014, Serbia

FRIDAY 14 NOVEMBER 2014

Arrival of participants and experts

19.00 Welcome and dinner

SATURDAY 15 NOVEMBER 2014

09.00 – 09.15 Introductions to the programme

Gil Zalsman, Israel

09.15 – 10.00 The suicidal patient-risk assessment and prevention
Gil Zalsman, Israel

10.00 – 10.45 Maintenance treatment of bipolar disorder- focus on the polarity index
Dina Popovic, Spain

10.45 – 11.30 Coffee break

11.30 – 12.15 The management of depressive illness in old age

Robin Jacoby, United Kingdom

12.15 – 12.30 How to give a talk

Gil Zalsman, Israel

12.30 – 13.30 Lunch

Presentations participants in 3 groups in 3 parallel workshops			
Round 1 13.30 – 15.00	*Gil Zalsman* *and* *Tamara Cavic* **Group 1**	*Dina Popovic* *and* *Janko Samardzic* **Group 2**	*Robin Jacoby* *and* *Dejan Stevanovic* **Group 3**

15.00 – 15.30 Break

15.30 – 16.30 How to prepare a scientific paper

Gil Zalsman, Israel

16.30 – 17.30 Discussion on career opportunities

All

19:00 Cultural event and dinner and group photo

SUNDAY 16 NOVEMBER 2014

Presentations participants in 3 groups in 3 parallel workshops			
Round 2 08.30 – 10.00	*Gil Zalsman* *and* *Tamara Cavic* **Group 2**	*Dina Popovic* *and* *Janko Samardzic* **Group 3**	*Robin Jacoby* *and* *Dejan Stevanovic* **Group 1**
10.00 – 10.30 Coffee break			
Round 3 10.30 – 12.00	*Gil Zalsman* *and* *Tamara Cavic* **Group 3**	*Dina Popovic* *and* *Janko Samardzic* **Group 1**	*Robin Jacoby* *and* *Dejan Stevanovic* **Group 2**
12.00 – 14.00 Lunch and preparation for plenary session			

Plenary 14.00 – 15.00	14.00 – 14.20	**Group 1** Presentation and discussion
	14.20 – 14.40	**Group 2** Presentation and discussion
	14.40 – 15.00	**Group 3** Presentation and discussion

15.00 – 15.15 Time to fill out evaluation forms and preparation of awards ceremony

15.15 – 15.30 Short break

15.30 – 15.45 Awards ceremony

15.45 – 16.00 Concluding remark and thanks,

Gil Zalsman, Israel

VENUE

The “Kastel Ecka” castle is situated about 60 kilometres north from Belgrade and only 7 kilometres away from Zrenjanin, in Ecka village. It was built in the English style. The constructing lasted from 1816 till 1820. The castle was built by the Lazar family and at the official opening ceremony, on August 28, 1820, Franz Liszt, a famous violinist, played.

Nowadays, this old edifice has been completely redecorated and adapted, so that today it is a object that can offer its guests unforgettable holiday in the authentic atmosphere, which is inspired by its aristocratic past.

Surrounded by the beautiful scenery and far away from the city rush, the castle Kastel Ecka is ideal for congresses, celebrations, promotions and other manifestations.

UTP Kastel ECKA AD

Novosadska 7

23203 Ecka, Serbia

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Prof. Gil Zalsman M.D., M.H.A., B.Sc.

Prof. Zalsman graduated from the Hebrew University and Hadassah Medical School in Jerusalem, Israel. He completed his psychiatry residency at the Geha Mental Health Center and Tel Aviv University and the Child Psychiatry residency at Geha and Yale Child Study Center in Yale University, Connecticut, USA with the late Prof. Donald J Cohen. He completed a two years Post-Doctoral Fellowship with Prof. J John Mann, in the Neuroscience Department, Columbia University, New York State Psychiatric Institute, where he holds an ongoing position as an Associate Research Scientist. He also holds a Master degree in health administration (MHA. summa cum laude) from Ben Gurion University, Israel. His academic research focuses on gene-environment interactions in childhood depression and suicidal behavior and other psychiatric disorders.

Prof. Zalsman has published more than a 200 papers, of them more than 90 original papers, dozens of reviews, book chapters, two edited books and actively participated in more than a 170 scientific meetings. Since 1 November 2013 he is the Director and Chief of Child Psychiatry Division at Geha Mental Health Center. He is an Associate Professor in Psychiatry at Sackler School of Medicine and former director of psychiatry continuing education program.

Prof. Zalsman is the past board member and president of the child psychiatry section at the Association of European Psychiatry (EPA). Currently he a counselor and chair pf education at the executive committee of the European College of Neuropsychopharmacology (ECNP) and the president of the Israeli Society of Biological Psychiatry (ISBP). He served as the deputy editor of the Israel Journal of Psychiatry and recently chaired the 14th European Symposium for Suicide and Suicidal Behavior (ESSSB), held in Tel Aviv.

Prof. Zalsman owns a private psychiatric outpatient clinic for children and adolescent in Tel Aviv, the Zalsman Institute.

He is married with two children and resides in Tel Aviv suburb, Israel.

Abstract: The suicidal patient-risk assessment and prevention

According to the WHO approximately 1.5 million people will die from suicide in 2020. The estimated global suicide rate is 14 suicides per 100,000 inhabitants. Last year, approximately 150,000 people completed suicide in Europe of them 63,000 in the European Union. The highest suicide rates are in Lithuania, Russian Federation, Belarus, Finland, Hungary and Latvia. There is approximately 4:1 male to female ratio in suicides. Suicide continues to be the first or second cause of premature death among 15-24 year olds and rates can be 6-8 times higher in the elderly

Extensive research during the past three decades has elucidated various biological, psychological and social risk factors to suicidal behavior, such as gender, age, previous suicide attempt, substance abuse, presence of psychiatric disorders and a family history of suicide. The most studied candidate polymorphism in suicide in the context of gene X environment interaction is the 5HTTLPR.

A clinical approach focusing in risk assessment in the single patient and some national prevention strategies will be discussed. Optional prevention and treatment options will be discussed.

ECNP european college of neuropsychopharmacology

Diagnosis and Treatment of the Suicidal Patient

Prof. Gil Zalsman MD, MHA

Director, Child and Adolescent Division
Geha Mental Health Center
Psychiatry Department
Sackler Faculty of Medicine
Tel Aviv University, Israel
&
Associate Research Scientist
Molecular Imaging Division
Psychiatry Department
Columbia University
New York, NY

ECNP Seminar Serbia 2014

TEL AVIV UNIVERSITY
SACKLER FACULTY OF MEDICINE

REVIEW — CLINICIAN'S CORNER

Suicide Prevention Strategies
A Systematic Review

J. John Mann, MD
Alan Apter, MD
Jose Bertolote, MD
Annette Beautrais, PhD
Dianne Currier, PhD
Ann Haas, PhD
Ulrich Hegerl, MD
Jouko Lonnqvist, MD
Kevin Malone, MD
Andrej Marusic, MD, PhD
Lars Mehlum, MD
George Patton, MD
Michael Phillips, MD
Wolfgang Rutz, MD
Zoltan Rihmer, MD, PhD, DSc
Armin Schmidtke, MD, PhD
David Shaffer, MD
Morton Silverman, MD
Yoshitomo Takahashi, MD
Airi Varnik, MD
Danuta Wasserman, MD
Paul Yip, PhD
Herbert Hendin, MD

Mann et al., JAMA 2005, 294:2064-2074

Suicide in children & adolescents

- **Second leading cause of death until age 24y**
- **Suicide before puberty is rare** (Pfeffer 1996)
- **Adolescence- age of risk**

MOST COMMON DIAGNOSES IN TEEN SUICIDES

	MALE *(N=213)*	FEMALE *(N=46)*
Depression	**50%**	**69%**
Antisocial	**43%**	**24%**
Substance Abuse	**38%**	**17%**
*18- to 19-year olds**	*60–67%*	*13%*
Anxiety	**19%**	**48%**

66% of 17- to 19-Year-Old Male Suicides Have Substance/Alcohol Abuse

Brent et al. 1999, Shaffer et al. 1996; *N=120

D17

•Diagnosis

Definitions

- **CSSRS**
- **"An act of self harm with at least partial intent to die" (Posner et al., 2010)**
- **Spectrum Theory: ideation- justures-attempt (aborted/disrupted)-attempt-completed**

NSSI

- Non Suicidal self Injury
- New @ DSM 5
- No Intent to die
- Typically BLPD

DURATION OF DETAILED PLANNING

(N=106)

	N	%
Less than a day	77	73
More than a day	29	27
More than a week	17	16
More than a month	7	6

Fisher et al. 1995

C.M6

DEPRESSION AND SUICIDE

Not all depressed patients think about suicide.

Not all suicidal patients are depressed.

- **Risk Assessment**

Risk Assessment

- **Male!!!**
- **Psychopathology (MDD)**
- **Previous attempt**
- **Impulsive aggression**
- **Loss**
- **Leaving alone**
- **Support system**

Risk Assessment

- **Substance abuse**
- **Problem with the law**
- **Genetics**
- **Hopelessness- Despair**
- **Helplessness**
- **Poor decision making**

Evaluation after a suicide attempt

- Timing and consultation
- Letter (SMS/email)
- Medical lethality
- Access to means
- Support system
- Collaboration with therapist
- Personal connection

•Treatment

Tx of suicidal patients

- National prevention plan
- Safety plan
- Restriction of means
- No-suicide contract
- Aggressive treatment of psychopathology!!
- Postcard approach
- Human compassion and true care
- Effective treatment of depression
- Specific psychotherapies

Evidence- based psychotherapy for depression and suicidal behavior

- **CBT**
- **DBT**
- **IPT**
- **MBCT**

Third Generation of CBT

- **Dialectical Behavioral Treatment (DBT) . Linehan et al. 1991.**
- **Mindfulness-Based Stress Reduction (MBSR) Kabat-Zin 1994**
- **Acceptance and Commitment Therapy (ACT). Hayes et al. 1999**
- **Mindfulness-Based Cognitive Therapy (MBCT) Segal et al., 2002**
- ***Treat private events…to alter the function of internal phenomena… to diminish their behavioral impact***

Third Generation of CBT

- ***2500 years of Zen Buddhist ideology and practice***

- ***Mindfulness***
- ***Moment by moment***
- ***Acceptance***
- ***Dialectics***
- ***Don't change problematic thoughts but accept them for what they are-just private experience (Hayes 2004)***
- ***Dialectics: Balance acceptance and change Accept the thought and change relationships with the thoughts… gain flexibility (Linehan 1993).***

Third Generation of CBT

- **<u>MBSR (Kabat Zin 1979).</u>**
- **Mindfulness is a primary mode of Tx.**
- **Both clinical and school settings**
- **8 weeks program to reduce both medical and psychological symptoms**
- **Pediatric chronic pain**
- **Stress and Anxiety**
- **Age appropriate language. School age (Saltzman & Goldin, 2000)**
- **Mindful eating. Thoughts parade.**
- **Tai Chi and mindfulness in Boston schools (Wall 2005)**

Third Generation of CBT

- **<u>MBCT (Kabat Zin 1990).</u>**
- **Mindfulness is a primary mode of Tx.**
- **CBT+MBSR=MBCT**
- **Developed to <u>prevent relapse in MDD clinical patients.</u>**
- **The mindful way through depression (Mark Williams, John Teasdale, Zindel Segal and John Kabat Zin 2007)**

- **Acceptance and mindfulness treatment for children and adolescents (Laurie Greco, Missouri and Steven Hayes, Nevada, 2008)**

MBCT

(Ma & Teasdale, 2004; Teasdale et al., 2000).

Prevention clips

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www.zalsman.org

Dr Dina Popovic, M.D., PhD

Dr. Dina Popovic has received her degree in Medicine, *cum laude*, from the University of Bologna (Italy), has specialized in Psychiatry and was awarded a PhD with European label at the University of Pisa. Alongside with active clinical practice Dr. Dina Popovic performs clinical research at Bipolar Disorders Program of Hospital Clinic, University of Barcelona, Spain, headed by Prof. Eduard Vieta. Her scientific interests and publications primarily include Mood Disorders, Psychotic Disorders and Dual Pathology, with a special focus on clinical, pharmacological, genetic and neurophysiological aspects.

Abstract: Maintenance treatment of bipolar disorder- focus on the polarity index

Maintenance therapy is a critical part of treatment of Bipolar Disorder. Clinical practice requires deciding upon the most appropriate treatment for each patient, which is often challenging. Clinical markers for response to first-line therapy will be examined during this presentation. Another recurring issue in clinical practice is the difficulty in translating the results of research to therapeutic decision-making. For this reason, our group has developed Polarity Index, a metric retrieved by calculating Number Needed to Treat (NNT) for prevention of depression and NNT for prevention of mania ratio, as emerging from the results of randomized placebo-controlled trials, which indicates the relative prophylactic efficacy profile of existing treatments, and its external validity was examined in a naturalistic study. The Polarity Index provides a measure of how much antidepressant versus antimanic an intervention is in bipolar disorder prophylaxis. The available evidence on how to choose the most effective treatment for each patient with bipolar disorder, in the era of personalized medicine, will be critically examined.

Maintenance treatment of bipolar disorder - focus on the polarity index

Dina Popović, MD, PhD

Ecka, Serbia, 14-16 November 2014

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

popovic.dina@gmail.com

Goals of treatment in bipolar disorder

Goals of maintenance therapy

- Prevent relapse/recurrence of episodes
- Maintain optimal patient functioning
- Treat inter-episode subsyndromal symptoms

Expand response into remission and recovery

Malhi et al. *Acta Psychiatr Scand* 2009

Relapse prevention is a critical objective of treatment in bipolar disorder

•

- Why?
- What?
- To whom?

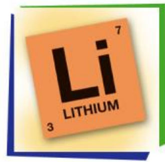
Clinical markers of response to Lithium

- Episodic clinical course with complete interepisodic remission. Mania-depression pattern
- Low comorbidity
- No rapid cycling
- Better efficacy in euphoric vs. dysphoric mania
- Bipolar family history with similar course of illness in the offsprings

Grof, 2010; Perugi et al., 2001; Vieta et al., 2005; Kleindienst, 2005; Rybakowski, 2013

Clinical markers of response to Lithium

- Later age at onset
- Low hospitalization rate
- Hyperthymic personality
- Preservation of cognitive functions and lack of cognitive disorganization



Rybakowski, 2012, 2013

Clinical factors of response to Carbamazepine

- CBZ> LI
  - psychiatric comorbidity
  -mood-incngruent delusions
  -EEG pathology, structural brain changes
- Bipolar I: Li >CBZ
- Bipolar II: Li = CBZ

Clinical factors of response to Valproate

- Atypical features ?
- More manic or mixed episodes VPA>LI

Kleindienst and Greil, 2000; Zarate et al., 1995: Rybakowsky et al., 2013

Clinical factors of response to Lamotrigine

- Chronicity of course, rapid cycling
- Comorbidity with anxiety disorders (panic disorder) and substance abuse
- Family history of schizoaffective disorder, recurrent depression, panic disorder

Clinical factors of response to Clozapine

- Severe manic episodes with psychomotor agitation and psychotic symptoms of great intensity

Passmore, 2003: Zarate et al., 1995

Clinical factors of response to Lamotrigine

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- Severe manic episodes with psychomotor agitation and psychotic symptoms of great intensity

Passmore, 2003: Zarate et al., 1995

Maintenance treatment choice: clinical considerations

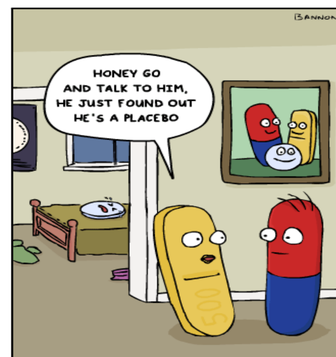
- Episode characteristics, including length and gravity
- Previous response
- Number of previous episodes
- Duration of interepisodic remission/ Time Interval since last episode
- Polarity of Initial or Index episode
- Predominant Polarity

Maintenance treatment choice: pharmacologic considerations

- Efficacy: NNT
- Safety : NNH
- Tolerability

EFFECTIVENESS

- Efficacy for each pole: Polarity Index
- Combination of drugs
  - Efficacy – sinergic actions
  - Safety/tolerability

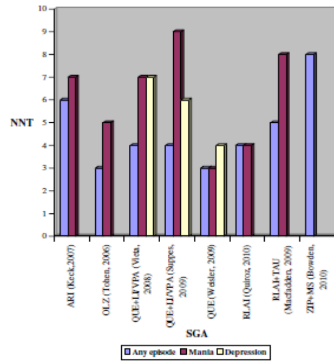


Psychopharmacology (2011) 213:657–667
DOI 10.1007/s00213-010-2056-8

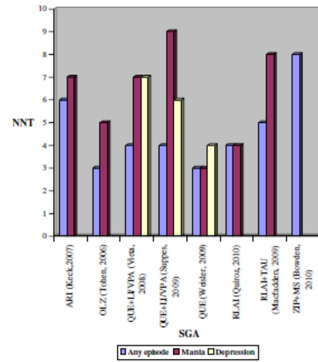
REVIEW

Number needed to treat analyses of drugs used for maintenance treatment of bipolar disorder

Dina Popovic · Maria Reinares · Benedikt Amann · Manel Salamero · Eduard Vieta



SGA= second generation antipsychotic, MS= mood stabilizer, PLA=placebo, ARI= aripiprazole, OLZ= olanzapine, LI=lithium, VPA= valproate, QUE=quetiapine, RLAI= risperidone long acting injection, TAU= treatment as usual, ZIP=ziprasidone



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European Neuropsychopharmacology (2012) 22, 339–346

www.elsevier.com/locate/euroneuro

Polarity index of pharmacological agents used for maintenance treatment of bipolar disorder

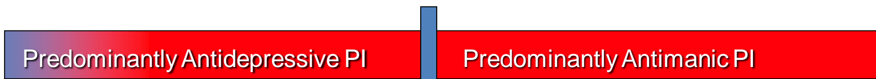
Dina Popovic [a, b], Maria Reinares [a], Jose Manuel Goikolea [a], Caterina Mar Bonnin [a], Ana Gonzalez-Pinto [c], Eduard Vieta [a,*]

[a] Bipolar Disorders Program, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERSAM, Barcelona, Spain
[b] Department of Psychiatry, Neurobiology, Pharmacology and Biotechnology, University of Pisa, Italy
[c] Santiago Apóstol Hospital, University of the Basque Country, CIBERSAM, Vitoria, Spain

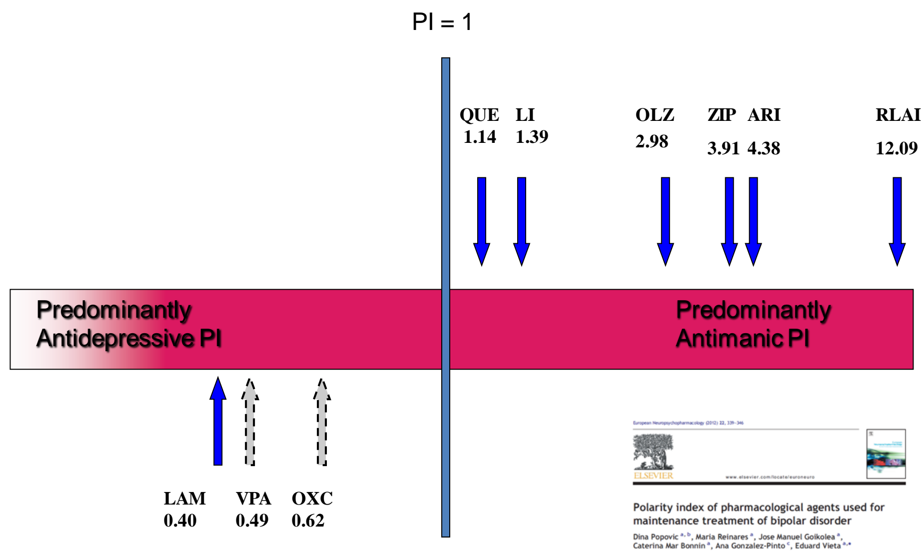
A measure of the relative prophylactic efficacy of drugs used in bipolar disorder maintenance treatment

$$\text{Polarity Index} = \frac{\text{NNT depression}}{\text{NNT mania}}$$

PI = 1



Polarity Index of medicaments used in maintenance treatment of BD



Adjunctive ADs in maintenance treatment of BD

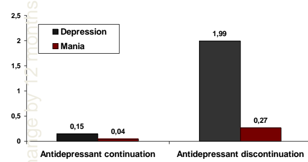
1) 2 RCTs examined the continuing AD treatment after good short-term response in BD I depression.

a) Responders to VFX/BUP/ SER + MS continued treatment for 1 year ➡ 15-25% had no further episodes [1] [2]

b) STEP-BD: 70 responders to MS + AD (SSRI/VFX/BUP) [3] , remitted for ≥8 weeks

[1] Post, 2006; [2] Leverich, 2006; [3]Ghaemi, 2010

b) STEP-BD: Antidepressant continuation *vs.* discontinuation (Clinical Monitoring Form)

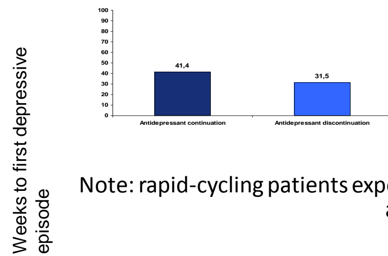


Change by 12 months

Trend to develop less severe depressive symptomatology

Significance of 12-month interaction effects: *Depression*, P=.06; *Mania*, P=.64

Weeks to first depressive episode



Significant delay in recurrence of new depressive episodes

Note: rapid-cycling patients experienced more depressive recurrences with an antidepressant

Ghaemi et al., J Clin Psychiatry, 2010

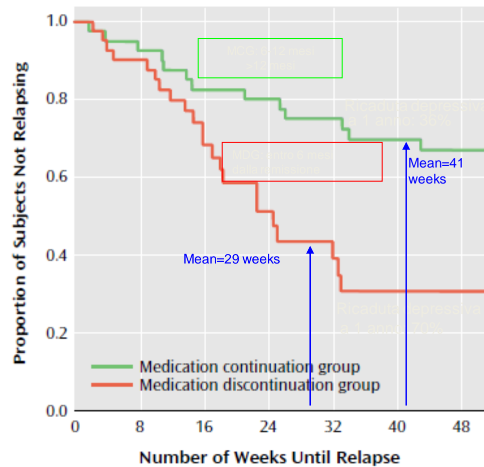
2) Impact of AD discontinuation on depressive recurrences over 1 year of follow-up

Patients with BD I or II who remitted for ≥ 6 weeks after addition of AD to MS. After 1 year AD cotinued or discontinued

Discontinuation group:

- Shorter latency to depressive relapse (χ^2=8.92, df =1, p=0.003)

- Higher risk of relapse (70% vs 36%)

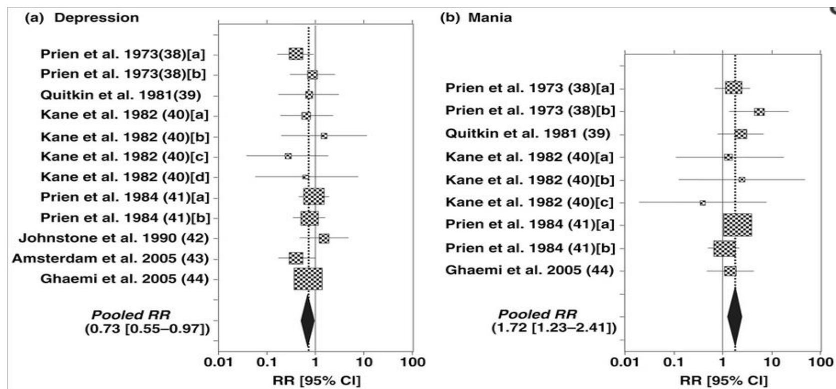


Altshuler et al., *Am J Psychiatry*, 2003

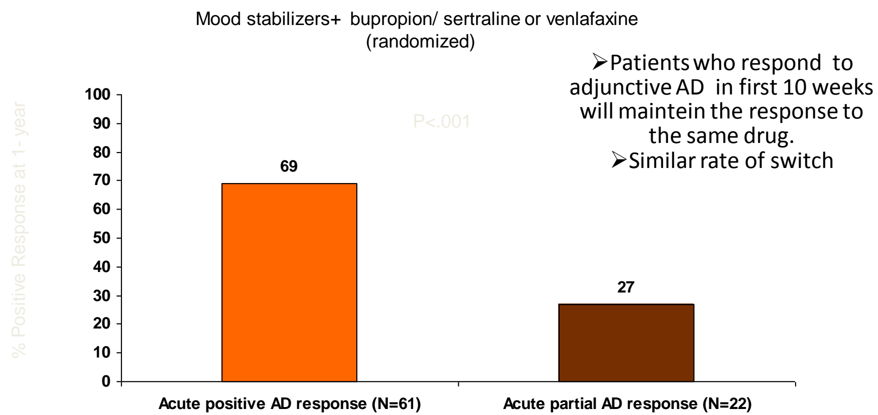
Meta-analysis of 7 maintenance trials (350 patients)

- 27% lower risk of new depression vs. MS-only or no treatment (RR = 0.73, 95% CI 0.55-0.97, NNT = 11)
- 72% greater risk for new mania (RR = 1.72; 95% CI 1.23-2.41; NNH = 7)
- Long-term adjunctive AD treatment was not superior to MS-alone in BPD

Ghaemi et al., 2008



4) Predictors of long-term responsiveness to adjunctive ADs



- Patients who respond to adjunctive AD in first 10 weeks will maintein the response to the same drug.
- Similar rate of switch

Altshuler et al., J Clin Psychiatry, 2009

✓Long-term trials involving adjunctive AD therapy are scant and have yielded ambiguous, inconclusive findings, despite a moderately favorable quality score (C) for the evidence

✓For predictors of response, the lack of adequate controls and reliance on enriched patient samples led to a D rating of available evidence(low)

Maintenance treatment

3. Maintenance treatment with adjunctive antidepressants may be considered if a patient relapses into a depressive episode after stopping antidepressant therapy.

CONCLUSIONS

- Maintenance treatment is crucial for prevention of recurrences and their neurobiological consequences
- Polarity Index measures the relative prophylactic efficacy of maintenance treatments for BD
- Polarity Index may be helpful for selecting the most appropriate intervention for each patient and for assessing the quality of maintenance prescription for Bipolar patients

CONCLUSIONS

- Evidence concerning the efficacy and safety of antidepressant treatment in BD is limited, and much of it is methodologically weak.
- Further research is necessary to clarify the many remaining questions concerning maintenance treatment in BD in general, in particular regarding effective and safe treatment of depressive episodes in BD

Prof Robin Jacoby DM. FRCP. FRCPsych.

Robin Jacoby studied Russian & French at Oxford University, followed by medicine at Oxford and Guy's Hospital, London. He undertook postgraduate training in internal medicine at Southampton University Hospitals and psychiatric training at the Bethlem Royal and Maudsley Hospitals, where he was also a consultant for ten years before moving to Oxford in 1994. Currently he is Professor Emeritus of Old Age Psychiatry at the University of Oxford. With Dr Catherine Oppenheimer he edited three editions of Psychiatry in the Elderly which became *The Oxford Textbook of Old Age Psychiatry* its 4th edition. He was Chairman of *The Global Initiative on Psychiatry* (www.gip-global.org) an international charity dedicated to reform of psychiatry, especially in countries of the former Soviet bloc. He has a particular interest in testamentary capacity, and has considerable experience in contentious probate cases. He shares virtual chambers with Prof Robert Howard at www.banks-v-goodfellow.com

Abstract: The Management of Depression in Old Age

The first step is to make the correct diagnosis. This means being aware of the differences and emphases that are found in older compared with younger patients. The next step is to make a risk assessment in order to decide where to treat the patient, i.e. as an outpatient or in hospital. SSRI antidepressants are now the standard treatment, but what is the evidence that they are effective? Which antidepressant should be used? What is the place of electroconvulsive therapy (ECT) in the treatment of depression in old age? These are the questions which show how finely balanced medical treatment is between art and science: questions I shall seek to answer in my lecture.

Managing Depression in Older People

Србија Новембар 2014

I am not going to talk about the following 9 slides. They are from the NICE Guidelines. I shall explain what those are, but the purpose of these first slides is for you to have some of the relevant guidelines in print. We shall start at slide 13

NICE Guidelines

Effective delivery of interventions for depression
All interventions for depression should be delivered by competent practitioners. Psychological and psychosocial interventions should be based on the relevant treatment manual(s), which should guide the structure and duration of the intervention. Practitioners should consider using competence frameworks developed from the relevant treatment manual(s) and for all interventions should:
receive regular high-quality supervision
use routine outcome measures and ensure that the person with depression is involved in reviewing the efficacy of the treatment
engage in monitoring and evaluation of treatment adherence and practitioner competence – for example, by using video and audio tapes, and external audit and scrutiny where appropriate.

NICE Guidelines

Case identification and recognition
Be alert to possible depression (particularly in people with a past history of depression or a chronic physical health problem with associated functional impairment) and consider asking people who may have depression two questions, specifically:
During the last month, have you often been bothered by feeling down, depressed or hopeless?
During the last month, have you often been bothered by having little interest or pleasure in doing things?

NICE Guidelines

Low-intensity psychosocial interventions

For people with persistent sub-threshold depressive symptoms or mild to moderate depression, consider offering one or more of the following interventions, guided by the person's preference:
individual guided self-help based on the principles of cognitive behavioural therapy (CBT)
computerised cognitive behavioural therapy (CCBT)[6]
a structured group physical activity programme.

NICE Guidelines
Drug treatment
Do not use antidepressants routinely to treat persistent subthreshold depressive symptoms or mild depression because the risk–benefit ratio is poor, but consider them for people with:
a past history of moderate or severe depression **or**
initial presentation of subthreshold depressive symptoms that have been present for a long period (typically at least 2 years) **or**
subthreshold depressive symptoms or mild depression that persist(s) after other interventions.

Treatment for moderate or severe depression
For people with moderate or severe depression, provide a combination of antidepressant medication and a high-intensity psychological intervention (CBT or IPT).

NICE Guidelines

Continuation and relapse prevention

Support and encourage a person who has benefited from taking an antidepressant to continue medication for at least 6 months after remission of an episode of depression.
Discuss with the person that:
this greatly reduces the risk of relapse
antidepressants are not associated with addiction.

NICE Guidelines

Psychological interventions for relapse prevention

People with depression who are considered to be at significant risk of relapse (including those who have relapsed despite antidepressant treatment or who are unable or choose not to continue antidepressant treatment) or who have residual symptoms, should be offered one of the following psychological interventions:
individual CBT for people who have relapsed despite antidepressant medication and for people with a significant history of depression and residual symptoms despite treatment
mindfulness-based cognitive therapy for people who are currently well but have experienced three or more previous episodes of depression.

NICE Guidelines

1.5.2.2 When an antidepressant is to be prescribed, it should normally be an SSRI in a generic form because SSRIs are equally effective as other antidepressants and have a favourable risk–benefit ratio. Also take the following into account:
SSRIs are associated with an increased risk of bleeding, especially in older people or in people taking other drugs that have the potential to damage the gastrointestinal mucosa or interfere with clotting. In particular, consider prescribing a gastroprotective drug in older people who are taking non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin.
Fluoxetine, fluvoxamine and paroxetine are associated with a higher propensity for drug interactions than other SSRIs[10].
Paroxetine is associated with a higher incidence of discontinuation symptoms than other SSRIs.

NICE Guidelines

Choice of antidepressant [11]

1.5.2.1 Discuss antidepressant treatment options with the person with depression, covering:
the choice of antidepressant, including any anticipated adverse events, for example side effects and discontinuation symptoms (see 1.9.2.1), and potential interactions with concomitant medication or physical health problems[12]
their perception of the efficacy and tolerability of any antidepressants they have previously taken.

NICE Guidelines

1.5.2.3 Take into account toxicity in overdose when choosing an antidepressant for people at significant risk of suicide. Be aware that:
compared with other equally effective antidepressants recommended for routine use in primary care, venlafaxine is associated with a greater risk of death from overdose
tricyclic antidepressants (TCAs), except for lofepramine, are associated with the greatest risk in overdose.

NICE Guidelines

When prescribing drugs other than SSRIs, take the following into account:
The increased likelihood of the person stopping treatment because of side effects (and the consequent need to increase the dose gradually) with venlafaxine, duloxetine and TCAs.
The specific cautions, contraindications and monitoring requirements for some drugs. For example:
the potential for higher doses of venlafaxine to exacerbate cardiac arrhythmias and the need to monitor the person's blood pressure
the possible exacerbation of hypertension with venlafaxine and duloxetine
the potential for postural hypotension and arrhythmias with TCAs
the need for haematological monitoring with mianserin in elderly people.[13]
Non-reversible monoamine oxidase inhibitors (MAOIs), such as phenelzine, should normally be prescribed only by specialist mental health professionals.
Dosulepin should not be prescribed.

Modern Medicine

- National Institute of Health and Care Excellence (NICE)
- Национални институт за одличну бригу

  - Government Control of Doctors
  - Владине контроле лекара

Teaching the private soldier what to do without having to think

Наставу Радовој шта да ради без потребе да мисле

Principles for assessment

When assessing a person who may have depression, conduct a *comprehensive assessment that does not rely simply on a symptom count*. Take into account both the degree of functional impairment and/or disability associated with the possible depression and the duration of the episode.

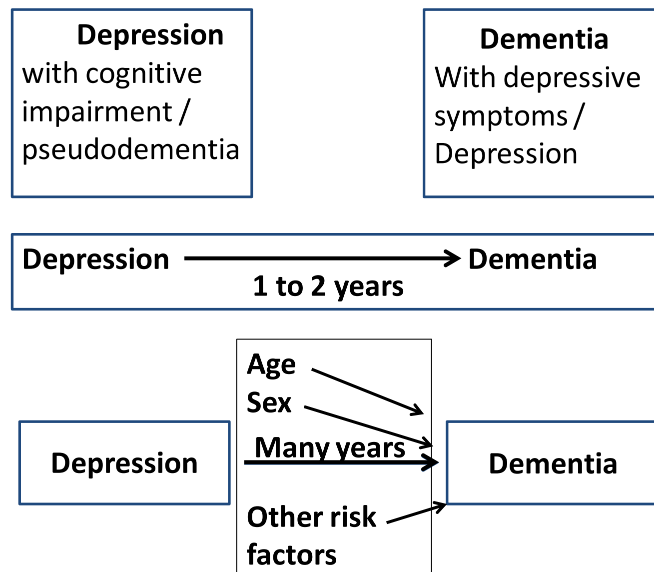
http://www.nice.org.uk/guidance/CG90/chapter/Key-priorities-for-implementation

Making the Diagnosis

Manifestations that everyone knows

Manifestations that not everyone knows

- Absence of obvious depression
- Pain or illness behaviour
- Behaviour change
- Anxiety
- Weight loss that seems like cancer
- Cognitive impairment
- Physical co-morbidity



Management 1st Decision

Careful risk assessment
- Suicidal ideas
- Delusions: for example, believes
  - has serious illness
  - is in financial ruin
  - has committed a crime
  - marriage on the rocks

What support is there at home?

Risk assessment determines where to treat.
Where to treat is first decision

The stepped-care model 1

STEP 1: All known and suspected presentations of depression	Assessment, support, psychoeducation, active monitoring and referral for further assessment and interventions
STEP 2: Persistent subthreshold depressive symptoms; mild to moderate depression	Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions

The stepped-care model 2

STEP 3: Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions; moderate and severe depression	Medication, high-intensity psychological interventions, combined treatments, collaborative care and referral for further assessment and interventions
STEP 4: Severe and complex depression; risk to life; severe self-neglect	Medication, high-intensity psychological interventions, electroconvulsive therapy, crisis service, combined treatments, multiprofessional and inpatient care

Prescribing for Older People

Bioavailability alters with age.

Hepatic metabolism reduced
⟶ First pass effect and biotransformation reduced
⟶ more drug available.

Reduction in GFR ⟶ more drug available

In principle, therefore, older people require lower doses. But this is not always the case.

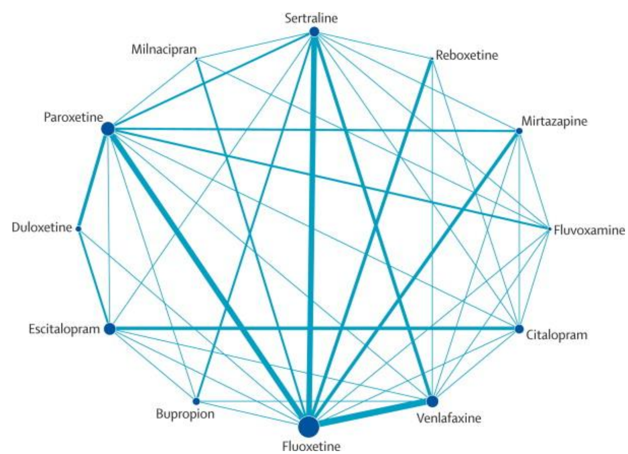
Polypharmacy Problem in Prescribing

Many older people taking many drugs:-
Statins, Anticoagulants, Beta Blockers
Aspirin, Cholinesterase inhibitors
NSAIDs ………….to mention only a few

- Be aware of interactions
- ?need proton pump inhibitors

Polypharmacy probably cannot be avoided. So psychiatrists are physicians and NOT doctors escaping from medicine.

Older Tricyclics	**e.g. amitriptyline**
Newer Tricyclics	e.g. lofepramine
Atypical antidepressants	Trazodone, nefazodone, mianserin
Monoamine oxidase inhibitors (non-reversible)	Phenelzine, tranylcipramine
Reversible inhibitors of monoamine oxidase (RIMAs)	Moclobemide
SSRI's	Citalopram, escitalopram, sertraline, paroxetine etc.
Noradrenaline and specific serotonin enhancers	Mirtazepine
Noradrenaline reuptake inhibitors	Reboxetine
Serotonin/noradrenaline reuptake inhibitors	Venlafaxine, duloxetine

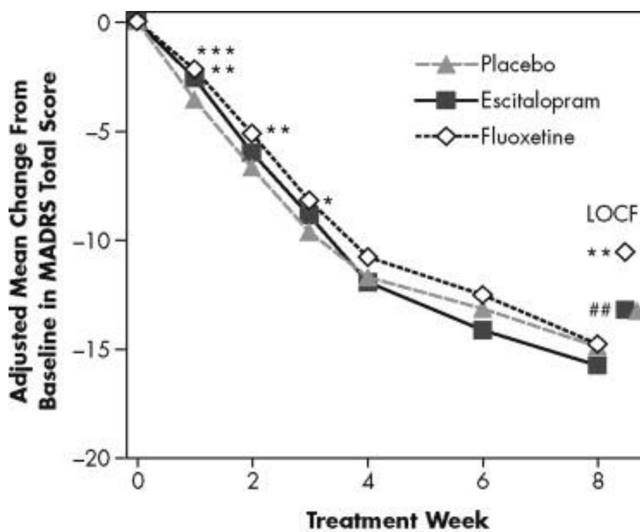


Network of eligible comparisons for the multiple-treatment meta-analysis for efficacy. The width of the lines is proportional to the number of trials comparing each pair of treatments, and the size of each node is proportional to the number of randomised participants (sample size). The network of eligible comparisons for acceptability (dropout rate) analysis is similar.

- Many trials of antidepressants in younger people.
- Most show overall benefit, but not all.
- Results cannot necessarily be extrapolated into old age populations.
- Nelson trial heterogeneous population.
- Large number of sites with much variation in outcomes

Antidepressants versus placebo for the depressed elderly (Review)
Wilson K, Mottram PG, Sivananthan A, Nightingale A

THE COCHRANE COLLABORATION®

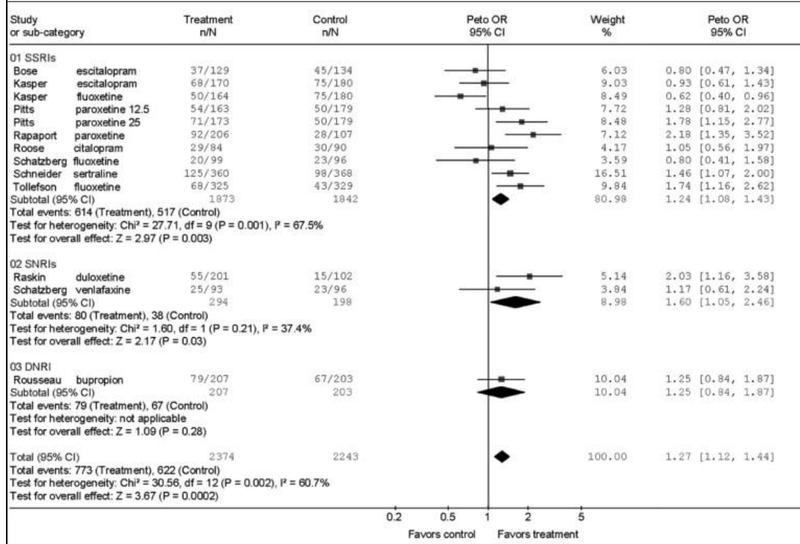


Note: MADRS: Montgomery-Åsberg Depression Rating Scale; LOCF: last observation carried forward.
*p <0.05; **p <0.01; ***p <0.001 for active treatment (escitalopram or fluoxetine) versus placebo; ##p <0.01 escitalopram versus fluoxetine.

Kasper et al 2005 American J of Geriatric Psychiatry 13, 884

73 Sites

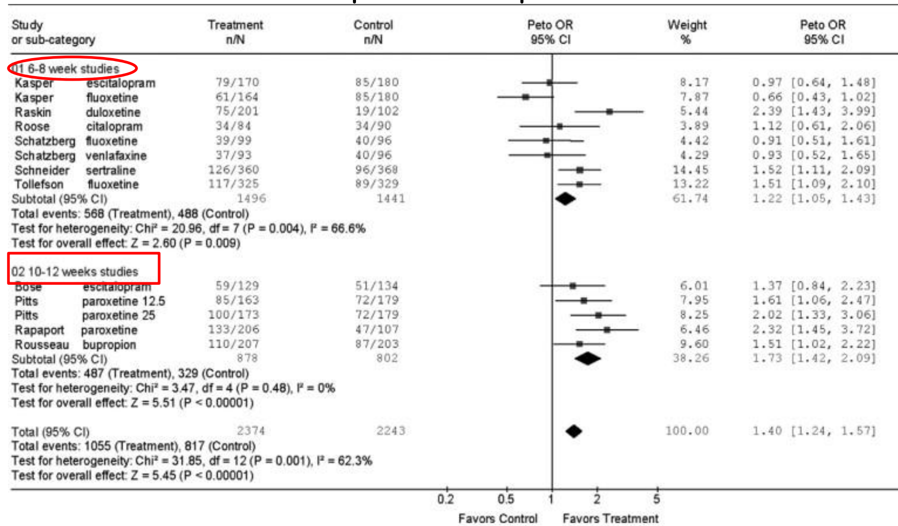
Response rates by individual trial, drug class, and overall compared with placebo



Nelson et al. 2008 American Journal Geriatric Psychiatry 16, 558

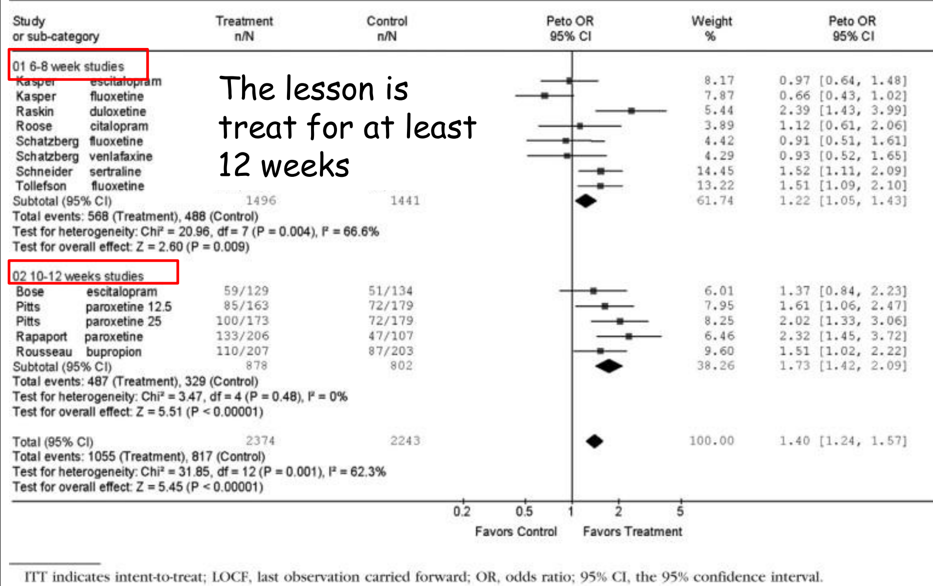
ITT indicates intent-to-treat; LOCF, last observation carried forward; OR, odds ratio; 95% CI, the 95% confidence interval; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor; DNRI, dopamine norepinephrine reuptake inhibitor.

Remission rates by individual trial, drug class, and overall compared with placebo



ITT indicates intent-to-treat; LOCF, last observation carried forward; OR, odds ratio; 95% CI, the 95% confidence interval.

Response Rates by Individual Trial, by Study Duration, and Overall Compared With Placebo



ITT indicates intent-to-treat; LOCF, last observation carried forward; OR, odds ratio; 95% CI, the 95% confidence interval.

Reasons for poor response to antidepressants

Technical trial reasons:

- Low sample size / underpowered
- Between site variation
- Demographically heterogeneous sample
- Protocol violations
- et cetera, et cetera

Patient reasons

- Wrong diagnosis?
- COGNITIVE IMPAIRMENT

Stroop Test

Green Red Blue
Purple Blue Purple

Синий Фиолетовый Красный
Зеленый Фиолетовый Зеленый

STROOP TEST

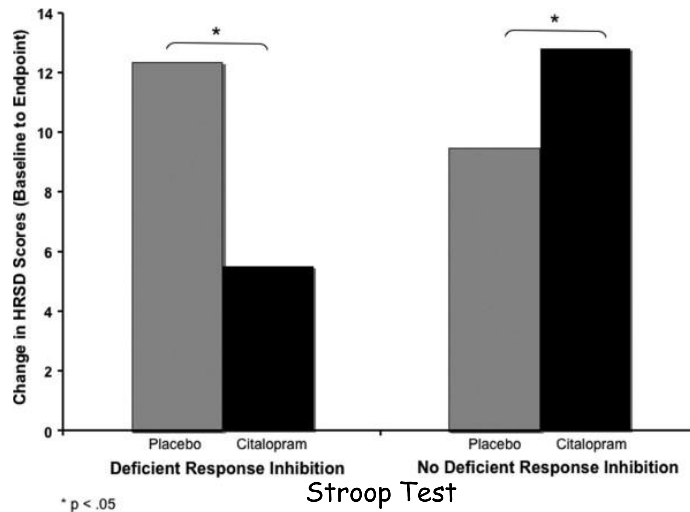
red blue orange purple
orange blue green red
blue purple green red
orange blue red green
purple orange red blue
green red blue purple
orange blue red green
purple orange red blue

СТРУП ТЕСТ

ЦРВЕНА ПЛАВА ОРАНГЕ
ПУРПЛЕ ЗЕЛЕНА ЗЕЛЕНА
ЦРВЕНА

ОРАНГЕ ПЛАВА ЦРВЕНА
ЗЕЛЕНА

Executive Dysfunction and Response to Citalopram



Stroop Test

Sneed et al 2010 American Journal of Geriatric Psychiatry 18, 128

Electroconvulsive therapy – ECT

- Treatment of choice for psychotic and/or suicidal patients
- Age is no bar.
- No age-associated increase in adverse effects
- The most life-saving treatment in psychiatry

Acute Efficacy of ECT in the Treatment of Major Depression in the Old-Old

Tew, et al *Am J Psychiatry 1999;156:1865-1870*

% Responding (HRS≤10)	63.2	79.3	75.7
Bilateral % Responding (HRS≤10)	50	100	100

Despite a higher level of physical illness and cognitive impairment, even the oldest patients with severe major depression tolerate ECT in a manner similar to that for younger patients and demonstrate similar or better acute response.

How long should treatment continue?

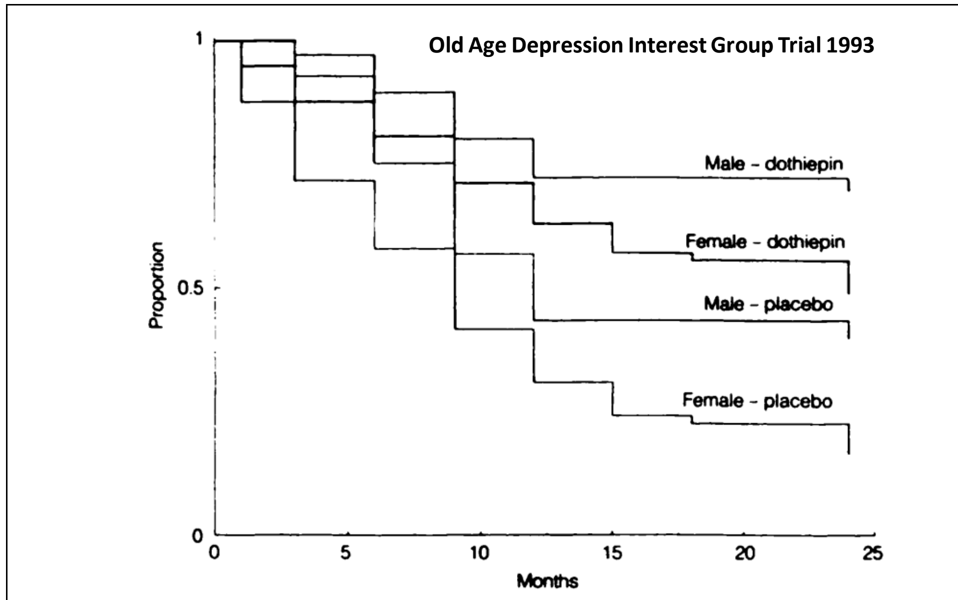
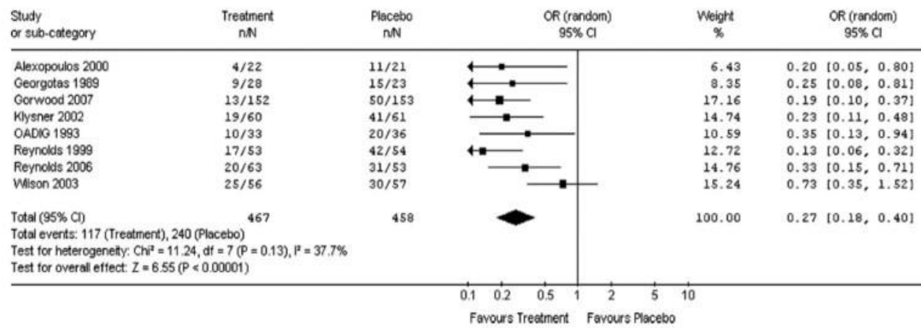


Fig. 1 Survival curves, from Cox regression, with Efron correction for ties and stratification for sex.

Continuation Treatment for Old Age Depression



Review: Double-blind RCTs antidepressants
Comparison: 71 Maintenance studies
Outcome: 06 Number of relapses or recurrences

Study or sub-category	Treatment n/N	Placebo n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Alexopoulos 2000	4/22	11/21		6.43	0.20 [0.05, 0.80]
Georgotas 1989	9/28	15/23		8.35	0.25 [0.08, 0.81]
Gorwood 2007	13/152	50/153		17.16	0.19 [0.10, 0.37]
Klysner 2002	19/60	41/61		14.74	0.23 [0.11, 0.48]
OADIG 1993	10/33	20/36		10.59	0.35 [0.13, 0.94]
Reynolds 1999	17/53	42/54		12.72	0.13 [0.06, 0.32]
Reynolds 2006	20/63	31/53		14.76	0.33 [0.15, 0.71]
Wilson 2003	25/56	30/57		15.24	0.73 [0.35, 1.52]
Total (95% CI)	467	458		100.00	0.27 [0.18, 0.40]

Total events: 117 (Treatment), 240 (Placebo)
Test for heterogeneity: $Chi^2 = 11.24$, df = 7 (P = 0.13), $I^2 = 37.7\%$
Test for overall effect: Z = 6.55 (P < 0.00001)

The data of nortriptyline and phenelzine from the Georgotas et al. study are combined in Figure 1.

Kok et al American J Geriatric Psychiatry 2011, 19, 249

Dr Tamara Cavic, M.D., PhD

Dr Cavic graduated in University in Belgrade School of Medicine, attained a title Specialist in Psychiatry, Master degree, and PhD. From 1993 up to date she is working at the Clinic for Mental Disorders „Dr Laza Lazarević“. She was Coordinator of the WHO Regional Model for Mental health. Dr Cavic is a Trainer in the BPC (Belgrade Psychodrama Center) and the ECP (European Certificate for Psychotherapy) holder. She was assigned with the tasks in several national interdisciplinary projects. As a member of EEPSI (Eastern European Psychiatric Scientific Initiative) she participated in several multicentric international studies and she was awarded by WPA (World Psychiatric Association) with Okasha Award for extraordinary contribution to psychiatry in developing countries.

Her fields of interest are psychotic disorders and psychological trauma.

Dr Cavic published more than 50 scientific papers.

She is the co-author of the books: „Psychology of refugees“ (2000) and „Teaching ethics in Psychiatry - Case Vignettes“ (2005). She is the author of two monographs: „On exile- psychosocial aspects“ (2001) and „Trauma and psychotherapy“ (2013).

Dr Cavic is a Scientific Associate at the Belgrade School of Medicine.

Dr Janko Samardzic M.D., PhD

Dr Janko Samardzic is a medical doctor-specialist in Clinical Pharmacology at the Institute of Pharmacology, Clinical Pharmacology and Toxicology in Belgrade. He is teaching at the Medical Faculty, University of Belgrade, Serbia. Dr Samardžić has a master degree in Experimental Pharmacology and PhD in the field of Medical Pharmacology. He completed postgraduate courses in the pharmaco-epidemiology and clinical trials at Erasmus University Medical Center Rotterdam, The Netherlands. Currently, he also holds the position of Chief for Pharmacoeconomics in Republic Health Insurance Fund.

As a researcher, Dr Samardzic is a member of the Science Project by the Ministry of Education, Science and Technological Development, Republic of Serbia. He is a member of Serbian Pharmacological Society, Austrian Pharmacological Society and European Colleague of Neuropsychopharmacology (ECNP). Also, he is an expert for preclinical and clinical drug evaluations at the regional Agencies for Medicines and Medical Devices.

Dr Samardzic has extensive experience and expertise in Neuropsychopharmacology, he is the author of a large number of peer reviewed papers, and also a regular speaker at international medical and pharmaceutical workshops and conferences.

Dr Dejan Stevanovic, M.D., PhD

Dr Stevanovicis a child psychiatrist working at Clinic for Neurology and Psychiatry for Children and Youth Belgrade, Serbia. His main research interests are child neuropsychiatry, cognition and neuropsychology, and pharmacoeconomics. His research career has begun studying quality of life and functioning in pediatric epilepsy, but his main research articles are dealing now with cross-cultural aspects in child psychopathology, pediatric psychopharmacology, and with pediatric depression and anxiety disorders in particular.

He has published 30 articles in international, peer-reviewed journal.

The current projects are „Cognition in anxiety and depressive symptoms in children“, „Psychopathology in pediatric epilepsy“, and „Trauma in adolescents - International Child Mental Health Study Group (ICMH-Study Group)“.

Dr Stevanovic is a member of ECNP Child and Adolescent Neuropsychopharmacology Network.

ECNP Seminar Serbia was organised by:

Dr Gorica Djokic, ECNP Ambasador for Serbia
Assistant Director, Psychiatric Clinic Laza Lazarevic,Visegradska 26,Belgrade,Serbia
Email:neurogoga@vektor.net

Abstracts

Aleksandar Misojcic, Institute of Mental Health

Denying a mental disorder and fear of stigma – case report

Denying a mental disorder and stigma result in reduced motivation for treatment. Presented is a case report of a female patient with manifesting alterations of premorbid behavioural patterns in early adolescence. She is refusing to be treated, with her parents supporting her, believing that problems are transient and not wanting their child 'to be poisoned with medications'. In the further course, apparent is progression of illness, exhibiting mental impoverishment, isolation, dysfunction. Treatment is commenced two decades after initial occurrence of problems, immediately after her father's death. This paper covers influence of denial and stigmatization on the quality of life of patients.

Amir Peljto, Institute of Mental Health

The symptoms of depression in schizophrenia based on the phase of illness

This prospective clinical study enrolled 100 patients with schizophrenia in acute impairment phase and remission phase. Psychometric assessments were made by using Positive and Negative Syndrome Scale for Rating the Symptoms of Schizophrenia, Scale to Assess the Unawareness of Mental Disorder, the Calgary Depression Scale for Schizophrenia and Global Assessment of Functioning Scale. Depressive symptomatology prevalence in patients with schizophrenia in the acute phase of the illness was 23% in the study group, while in the remission phase was low - 13% of the sample. Based on logistic regression, clinical factors in our findings were better predictors of depression in the acute phase than sociodemographic factors, while in remission phase it was the other way round. Depressive symptomatology often occurs in patients with schizophrenia. Better insight was significantly correlated with lower mood, as well as marital status and parenthood.

Ana Kuzmanovic, Psychiatric Clinic Laza Lazarevic

Pharmacological treatment and suicidal risk in schizophrenia- a case report

It was estimated that the suicidal risk in schizophrenic patients is 10 times higher than in general population which represents great challenge for adequate assessment and pharmacological treatment. We are presenting a case of a schizophrenic patient treated with clozapine who attempts suicide during hospitalization. After that patient was treated in Intensive care Unit with olanzapine, which stabilized patient's condition into satisfactory remission. Although, according to literature, clozapine shows superiority against all other antipsychotics while treating suicidal patients, this specific vulnerable group requires constant and meticulous personalized approach and treatment.

Ana Munjiza, Institute of Mental Health

Role of Th1, Th2 and Th17 cytokines in major depressive disorder

Cytokines are implicated in the pathophysiology of major depressive disorder. The aim of our study is to investigate correlation between serum levels of representative Th1, Th2 and Th17 cytokines and clinical features such as suicidal ideation, duration of depression and symptomatology severity in patients with major depresive disorder. Serum concentrations IL-4, IL-6, IL-17A, INFγ and TGFβ will be determined by using ELISA technique in 80 patients fulfilling the DSM-IV-TR criteria for a current major depressive episode. Assessment of intensity of psychopathology will be measured by Hamilton Depression Rating Scale. We are hoping this study will help in confirming some aspects of the inflammatory hypothesis in depression.

Anamarija Petek Erić, Psychiatric Clinic- Clinical Centre Osijek

Correlation of personality traits and suicidality in patients suffering from mood disorders

This research focuses on finding crucial personality features based on genetic-neurobiological model among population of patients with mood disorders (predominantly depression, bipolar affective disorder- depressive or mixed episode) who, at the beginning or during the treatment, express suicidal thoughts, ideas or attempt. We are also investigating the role specific psychopharmacological therapy in these patients in order to find correlations between medication effectiveness, expression of suicidal thoughts/attempts and specific personality structure.

Bojana Dunjić- Kostić, Clinic for psychiatry- Clinical Center of Serbia

Psychoimmunological aspects of schizophrenia

According to the current literature, individuals with mental illnesses (especially schizophrenia and affective disorders) have altered immunological status. We investigate differences in immunological status between acutely exacerbated schizophrenic patients and healthy individuals, as well as correlation between proinflamatory cytokines (Interleukine-6 and Tumor necrosis factor-alpha) and some clinical variables. Acutely exacerbated individuals with schizophrenia had different immunological status than healthy controls. Cytokines levels correlated with some clinical variables.

Bojana Ristovski, Specialized Psychiatric Hospital Kovin

Link Between Levels of C-reactive Protein and Duration of Schozophrenia

Increased levels of inflammatory markers have been reported in schizophrenia, but few studies have examined levels of high sensitivity C-reactive protein (CRP), a non-specific inflammatory marker and its connection with the duration of disease.
All patients will be tested by sociodemographic inventory and PANSS in the second week after the hospitalization, Levels of high sensitivity CRP will be measured in individuals with first episode schizophrenia, between 5 and 10 ill duration group , more than 10 ill duration group, and non-psychiatric controls. The study is expected to additionally clear the etiopathological mechanisms in schizophrenia, in the light of inflammatory processes.

Bojana Vidovic, University of Belgrade- Faculty of Pharmacy Email:

Associations of oxidative stress status parameters and metabolic syndrome in schizophrenia

Metabolic syndrome (MetS) is highly prevalent in people with schizophrenia and conveys a significantly increases risk of type 2 diabetes and cardiovascular disease. In recent years there has been an increasing interest in the oxidative stress in the schizophrenia. However, up to now, there have been no studies investigating the association between oxidative stress status and MetS in schizophrenia. Analysis of oxidative stress parameters showed that schizophrenia patients with MetS have significantly higher lipid peroxidation and impaired antioxidant defense than patients without MetS. Patients with more MetS components have a higher level of oxidative stress. Assessment of oxidative stress might be useful for determining cardiovascular risk in patients with schizophrenia.

Danilo Pešić, Institute of Mental Health

The owerlap between borderline personality disorder and cerebellar cognitive affective syndrome

We describe a young woman who was treated since sixteen of polysubsance abuse, affective instability, and self-harming and was diagnosed as borderline personality disorder. Since the neurological and neuropsychological reports pointed to signs of cerebellar dysfunction and dysexecutive syndrome, we performed magnetic resonance imaging of brain which demonstrated partially developed vermis and rhombencephalosynapsis. These findings shed a new light on the severity and nonresponsiveness to medication and show the overlap between the clinical manifestations of cerebellar cognitive affective syndrome and severe borderline personality disorder.

Dina Dabbas, Psychiatric Clinic Laza Lazarevic

Quetiapine super-responder schizophrenic patient

Super-responders are schizophrenic patients on stabile treatment with overall improvement greater than 50-60% and ability to live alone, work, and have long-term relationship. Based on clinical studies regarding the efficacy of antipsychotics in treatment of schizophrenia, quetiapine has equal efficacy in reducing both Positive and Negative symptoms as other first-line atypical antipsychotics such as risperidone and olanzapine,. CATIE study proves early cognitive improvement for patients treated with quetiapine. CASE REPORT:35 -year old highly educated schizophrenic patient with delusions, aggressive behaviour and significant cognitive impairment with previous partial response to all other antipsychotics who is super-responder to quetiapine monotherapy.

Djordje Curcic, Psychiatric Clinic Laza Lazarevic

The effects of prescribed physical activity on people with schizophrenia

People with schizophrenia are overall less physical active than general population. Aerobic capacity, that is an indicator of the overall health and oxygenation, is lower in patients with schizophrenia, than the expected average value in healthy people the same age. Unfortunately, no general concept for a therapeutic application of physical exercise has been developed so far. Prescribed physical exercise could improves aerobic capacity and oxygen supply to the central nervous system. It's a good inducer of neurogenesis. Prescribed physical activity could be an effective adjunct treatment for patients with schizophrenia (for decreasing psychiatric symptoms and increasing quality of life).

Dragana Pavicevic, Psychiatric Clinic Laza Lazarevic

Correlation of neurological soft signs and negative symptoms in psychotic patients

Neurological soft signs (NSS) are described as subtle, nonlocalizing neurological abnormalities. According to literature neuroleptic-naive schizophrenia patients had significantly more NSS than controls; patients who were more neurologically impaired had more negative symptoms. Atypical antipsychotics are more preferred for the treatment of negative symptoms. In this ongoing study, we are performing *Heidelberg* neurological soft sign scale and PANSS to neuroleptic-naive psychotic patients. The hypothesis is that patients with higher scores on Negative and Heidelberg scale would have a better response to atypical antipsychotics. Such patients can be potentially identified by neurological soft signs examination; it is very important prognostic and includes improved methods of treatment of patients.

Dusko Stupar, Clinic For Child Neurology and Psychiatry

Klein-Levin syndrome

Kleine-Levin syndrome is a rare disorder of sleep diagnosed mainly on clinical grounds. It presents a unique diagnostic dilemma for neurologists and psychiatrists; especially due to a high risk of being diagnosed as a psychiatric condition like a mood disorder. Patients with Kleine-Levin syndrome experience reoccurring feelings of excessive tiredness and prolonged sleep, excessive appetite and increased sexual urges. Several other symptoms usually accompany the syndrome, including changes in mood and cognitive ability and even psychotic symptoms. Case presentation: The patient is a 9 year old boy who initially presented with symptoms such as hypersomnia, hyperphagia, withdrawal into himself and anxiety at the age of seven. His personal and family history is unremarkable. These episodes of behavioral and mood changes usually lasted up to ten days followed by several months of remission. Routine blood, urine and hormone analysis were within normal ranges. There were also normal findings in neurological, EEG, neuro-ophthalmology and MRI examinations. Result of psychological examination – IQ=98.

Igor Radosavljevic, Psychiatric Clinic Laza Lazarevic

Using of REBT in psychosis treatment

The aim of this research is considering the possibility apply REBT (Rational Emotional Behaviour Therapy) in psychosis treatment. One of crucial criteria in establishing a psychosis diagnosis had been the presence of thought process interruption in form and content. REBT, on the other hand, aims to strengthen a logical approach in thought process which is difficult to accomplish in treating psychoses. Pharmacotherapy remains the dominant approach in treatment. In the experience of this research, further adaptation to reality and progress in resocialization can be accomplished through REBT. The therapy can be applied equivalently in individual and group modalities.

Jelena Jovic, University of Prishtina- Kosovska Mitrovica

The Level of Serum Lipids and Depression in the Elderly

It is considered that the changes that emerge in the concentration of cholesterol in the cell membranes as a response to the serum level of cholesterol, have an influence on the number of serotonin receptors in patients suffering from depression. There have not been any clear conclusions yet. The study which included 246 examinees older than 65 proved the existence of the interrelation between the level of serum cholesterol and the level of depression. GDS was used for the evaluation of depression. I propose that a similar study should be carried out on a larger sample with the parallel use of another scale for evaluation of depression and determination of cholesterol fractions as well.

Katarina Zoric, Psychiatric Clinic Laza Lazarevic

Schizophrenia and smoking

Co-morbidity of schizophrenia and smoking is a well-known phenomenon. Smoking rates (78-88%) in schizophrenic patients are much higher than in general population. Cigarette smoking may reduce plasma levels of antipsychotics up to 50%. The goal of this study was to investigate effects of smoking on antipsychotics treatment of schizophrenia.The results of our study suggest that cigarette smoking have significant effect on antipsychotic therapy of schizophrenia, and that smoking more than 20 cigarettes per day significantly reduces effects of antipsychotics measured on PANSS.

Marija Mitkovic Voncina, Institute of Mental Health

Linking child abuse history and child abuse potential: The moderating role of temperament

Aim of our study was to investigate the differential role of temperament in the relationship between abuse experiences in childhood and child abuse potential. The sample of 372 parents from non-clinical population responded to the general questionnaire, Childhood Trauma Questionnaire, Child Abuse Potential Inventory, Temperament and Character Inventory – Revised, Symptom Checklist 90 – Revised, and Experiences in Close Relationships - Revised. The results showed significant relationship between childhood abuse history and child abuse potential, with Reward Dependence as a moderator of this association, controlling for socio-demographics, personality dimensions, attachment, psychiatric symptom distress and somatic illness. Findings may have practical implications in preventive strategies.

Milana Poznic- Jesic, Psychiatric Clinic- Clinical Centre Vojvodina, Novi Sad

Brain parenchime ultrasound in opiate addicts

Our goal was to evaluate the frequency and significance of the size of the hyperechogenicity of the substantia nigra measured by transcranial parenchymal ultrasound in a population of untreated opiate addicts and opiate addicts on methadone therapy. This was a comparative, single-blinded, controlled study.We found significantly higher prevalence of hyperechogenicity of substantia nigra in untreated opiate addicts. Further evaluation on bigger samples are required to confirm the validity of these results.

Milica Borovcanin, Psychiatric Clinic- Clinical Centre Kragujevac

Role of cytokines in the onset and development of schizophrenia

In broad spectrum of possible causes or contributing factors, immune system and cytokines were investigated in the onset and development of schizophrenia. The aim of our study was to analyze the serum concentrations of type-1, type-2, type-17 and regulatory cytokines in drug-naive patients with first episode psychosis and schizophrenia in relapse in patients. Analysis showed that TGF-β can be a valuable marker for psychosis. The presence of enhanced anti-inflammatory/immunosuppressive activity in schizophrenia may be an attempt to counteract or limit ongoing pro-inflammatory processes and down regulating chronic inflammation. The increased type-2 cytokine serum levels appear to be down regulated by antipsychotic treatment.

Milutin Kostic, Institute of Mental Health

BDNF, COMT and SERT genetic polymorphism combinations and their effect on susceptibility for depression and brain cortical thickness

Depression is a mental disorder that affects around 350 million people worldwide. Studies have shown that genetic polymorphisms in the SERT 5-HTTLPR, BDNF val66met and COMT val158met are linked to depression. In our study 77 patients who fulfilled the DSM-IV-TR criteria for current major depressive episode and 66 healthy controls underwent an MRI scan and genetic screening for those three polymorphisms. The aim of our study is to analyze combinations of those three polymorphisms in patients and controls, and possibility of specific combinations that might lead to a higher susceptibilty to depression and the way the combinations affect cortical thickness in the brain.

Nikola Jovanovic, Institute of Mental Health

D personality prevalence in the population of psychiatry residents

D (Distressed) personality type has a tendency towards increased negative affectivity and inhibition of negative emotions in social situations. Type D personality has been associated with an increased risk of adverse cardiac events in patients with a cardiovascular condition and higher prevalence of metabolic syndrome. It is also a vulnerability factor for other medical conditions. D personality was associated with poor physical and mental health status and poor self-management of the disease. The aim of the study is to distinguish prevalence of D personality type in the population of psychiatry residents.

Romana Petrovic, Psychiatric Clinic Laza Lazarevic

Hypothetical mechanism of the antidepressive effect of ketamine

If the depression could be defined as a state of constriction of mindfulness, than psychodelic drugs such as ketamine may improve depression through the neuropharmacological expansion of mindfulness or by the chemical removal of mental barriers to the natural expansion of mindfulness.
I would propose a prospective study to investigate the associations between changes of severity of depression and changes of mindfulness, before and after ketamine antidepressant treatment. The sample would consist of 30 depressive patients assessed by the Montgomery–Åsberg Depression Rating Scale and Kentaky inventory of mindfulness skills, before and after ketamine treatment.

Slavica Minic, Psychiatric Clinic- Clinical Centre Kragujevac

Evaluate symptoms of depression in patients with type 2 diabetes mellitus

Correlation between depression and diabetes has been known for several centuries. Comorbidity in patients with diabetes or depression as a primary disorder has been the focus of numerous studies dealing with the prevalence of depression in patients with diabetes, the relationship between depression and insulin resistance, hyperglycemia and complications of diabetes, risk factors for developing diabetes in patients with depression, as well as the influence of depression on mortality in patients with diabetes. Project of the Ministry of Health this year in Serbia introduced screening for depression in primary care and the aim of this study is to assess depressive symptoms in patients by screening for depression and to pay special attention to patients suffering from type 2 diabetes treated with oral antidiabetic and to observe if there is a connection, it would be of great importance.

Tamara Timic Stamenic, University of Belgrade- Faculty of Pharmacy

Role of α_5GABA_A receptors in cognitive functions relevant to schizophrenia

It is postulated that cognitive impairments associated with schizophrenia are caused by hypofunction of NMDA receptors. NMDA receptor antagonist, MK-801, induces dose-dependent impairment of learning and memory. The dose of 0.1 mg/kg MK-801 consistently induced prominent cognitive impairment in rats in different behavioural tests (Morris water maze, novel object recognition test, social novelty discrimination procedure). The aim of my research is to investigate the role of α_5GABA_A receptors in cognitive functions relevant to schizophrenia by using an agonists (SH-I-75, SH-053-2'F-R-CH_3) or inverse agonist (PWZ-029) with functional selectivity for these receptors after treatment with MK-801.

Tijana Antin Pavlovic, “Dr Selakovic” Child and adolescent Clinic

Cognitive side effects of antiepileptic drugs in children- case report

We report a 12 year old girl who has been introduced treatment with topriamat instead of carbamazepin due to poor seizure control. Psychological evaluation prior to the change of medication showed that her intelligence level was in the range of average (IQ t =96, Iqv=98, Iqn=92). After 14 months of therapy there was a visible decline in cognitive abilities, as well as cessation of seizures and stabilization of EEG changes. Psychological reevaluation showed borderline intelligence (IQ t= 78, IQ v=77, IQ n=80). Cognitive side effects should be taken into consideration when using antiepileptic therapy in children.

Tijana Mirjanic, Specialized Psychiatric Hospital Kovin

Schizotypy and vulnerability for psychosis- sibling study

We used Structured Interview for Schizotypy-Revised to compare nonpsychotic siblings of patients with schizophrenia to age and gender matched controls from Serbia in the levels of positive and negative shizotypy. We divided group of sibling to siblings with higher risk for schizophrenia and to lower risk group based on patients scores of Wechsler Digit Symbol Coding Task, the central feature of the cognitive impairment in schizophrenia.

We hypothesized that siblings might have higher levels of schizotypy in comparison to controls, and more probable -siblings with higher risk for psychosis will have higher shizotipy levels in compare to control group.

CK elevation due to malignant neuroleptic syndrome or hypokalemia?

At presentation patient with frank psychosis was admitted for the second time in 8 months. He denied alcohol consumption but stopped using 10 mg Haloperidol for a while. After application of second im haloperidol injection (due to noncompliance to oral AP), he developed symptoms that fulfilled criteria for malignant neurolepic syndrome (MNS). In spite application of adequate therapy, CK was rapidly raising up to 27 067Ul/l. Additional tests revealed hypokaliemia. Afterwards, patient admitted that he used alcohol and was sleeping immobilised for a while.

Not only application of incisive AP after drug free period can be risk for MNS with CK elevation, but also alcohol abuse could cause hypokaliemia that further influence elevation of CK, especially after immobilisation.

Vanja Mandic Maravic, Institute of Mental Health

Sex differences and autism spectrum disorders: clinical and functional aspects

Introduction: Findings on sex differences among persons with autism spectrum disorders are inconsistent. Method: The study included 134 participants diagnosed with autism spectrum disorders, assessed for autistic symptoms and adaptive functioning. Results: Males were more often diagnosed with typical autism, while there were no sex differences in the adaptive functioning or the autistic symptoms. We found different, sex-specific correlations of autistic symptoms with age and adaptive functioning. Conclusion: The possibility that sex moderates the change of autistic symptoms with age, and that it affects the expression of core autistic symptoms in adaptive functioning is discussed.

Visnja Banjac, Psychiatric Clinic- Clinical Centre Banjaluka

Diagnostic dilemma: organic or psychological

Method: a retrospective analysis of case. Case report: 38 year old woman, was first examined by internist because of the intense headaches followed by sleep difficulties, loss of appetite, anxiety, agitation and fear of death. The beginning of symptoms she linked to loss of her brother. After that she was admitted to the psychiatric hospital under the diagnosis of suspected depression. During the psychiatric examination she showed symptoms of reactive depression. Because of persisting symptoms of headache and frequent hypertensive crisis a detailed diagnostic evaluation was performed. It was found that the levels of cortisol were increased. Furthermore, CT of the adrenal glands showed the presence of tumor. At the end surgical treatment was recommended. After completing the surgery, symptoms of depression disappeared.

Vladimir Djuric, Psychiatric Clinic Laza Lazarevic

Clinical aspects of dysmorphic disorder

The research is about etiology, neurobiology, symptomatology, diagnosis, diferential diagnosis and treatment of a special type od body dysmorphic disorder called muscle dysmorphia. There are lot of photos and video materials about this clinical entity. Also, there is a short vignette about a patient with a muscle dysmorphia, that was hospitalised in Clinic for psychiatric disorder “Dr Laza Lazarevic”, with diferential diagnostics procedure and treatment guidelines.

Vladimir Knezevic, Department for psychiatry and medical psychology- Medical Faculty University of Novi Sad

Degree of hostility as a poor indicator of severity of illness in persons with schizophrenia

Objective: We observed the intensity of hostility as a function of illness severity in hospitalized patients diagnosed with schizophrenia. Materials and Methods: This study involved 110 hospitalized schizophrenic patients with scores ≥ 3 on item P7 (hostility) of Positive and Negative Syndrome Scale (PANSS). The PANSS scale was administered on the first day of patient's hospitalization. Results: Intensity of the hostility was not associated with the severity of illness, measured by the total PANSS scale score and by the Positive scale score. Conclusion: Although hostility is very common and important symptom of schizophrenia it's etiology is not fully clarified. Further clarification of the etiology of hostility could contribute to its better prevention and more effective treatment.

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