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Republic of Moldova 2011

The beautiful land of Moldova welcomes ECNP Seminar in October 2011

Local Organizer: Dr. Sinita Eugenia tomtit_bird@mail.ru

Republic of Moldova 2011

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 fulfil this aim ECNP organises, 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 every year 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. Young investigators from all over Europe are invited to spend some days in Nice discussing about the latest research in the area of neuropsychopharmacology.

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 organises a summer school of neuropsychopharmacology in Oxford. Next year ECNP will also organise a school of child and adolescent neuropsychopharmacology in Venice and in 2013 it is planned to organise a school of neuropsychopharmacology in geriatrics.

Finally, ECNP organises seminars, as the one you have been invited to participate, in areas where there are less opportunities for psychiatrists to participate in international meetings. So far, ECNP has organised this meeting in Poland, Estonia, Turkey, Bulgaria, Romania, Slovak Republic and Hungary. 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 Moldova!

Celso Arango, MD

Chair ECNP Educational Committee

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Psychiatry in Moldova – interesting facts:

Clinical Hospital of Psychiatry, funded 1893 – 1895, located in the capital of Moldova – Chisinau, is the second in Europe according to its territory and bed number, with its capacity to treat up to 2000 patients.

Today the Hospital encounters 1200 beds in several Units: Out –patient dispensary, Neurosis, Acute Psychosis Male and Female, Somatic Comorbidities, Epilepsy, Child Psychiatry, Compulsory Treatment, Chronic Estates, Consultation Unit (internal medicine, neurology, laboratory), Intensive Therapy Unit.

The unique situation in Moldova, being characterized by the process of decentralization, offers wide developing out-patient services in Mental Health Centers, general hospitals, primary care services, and in the same time – Clinical Hospital of Psychiatry remains the main center for scientific research, clinical trials, psychiatry residency studies, rehabilitation and recreational activities for patients and personnel. The reforms that are initiated in the last years focus on evidence – based approach in psychiatry, human rights respect aspect, continuous development of the services and well trained specialists. Collaboration with ECNP makes this development condense, including the most actual discoveries both on biological and clinical levels.

ECNP activities in Moldova:

The Seminar 2011 in Vadul lui Voda is the first event organized by ECNP in Moldova, that offers young specialists and local leaders possibility to get acquainted with up-to-date evidence – based data, as well as possibility to share opinions, discuss and make new conclusions that might change the practice for good. Together with the participation at ECNP Summershool and Regional Meetings in Eastern Europe and all over the world, open to Moldavian specialists – ECNP collaboration offers new possibilities of development for psychiatrists and thus, for Psychiatry as a Science and Medical Care.

We hope that the Seminar 2011 will open the door to an intensive and fruitful collaboration, because the Science does not have borders, except for those located in our own conscience!

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Republic of Moldova 2011

Programme

ECNP Seminar in Neuropsychopharmacology

17-19 October 2011, Vadul lui Voda, Moldova

MONDAY 17 OCTOBER 2011

Arrival of participants and experts

19.00 Welcome and dinner

TUESDAY 18 OCTOBER 2011

09.00 – 09.15 Introductions to the programme, Celso Arango, Spain

09.15 – 10.00 **Acute psychosis**, Celso Arango, Spain

10.00 – 10.45 **Dementia**, Michael Davidson, Israel

10.45 – 11.30 Coffee break

11.30 – 12.15 **Affective disorders**, Alessandro Serretti, Italy

12.15 – 12.30 **How to give a talk**, Celso Arango, Spain

12.30 – 13.30 Lunch

Presentations participants in 3 groups in 3 parallel workshops			
Round 1 13.30 – 15.00	*Celso Arango* *and* *Anatol Nacu* **Group 1**	*Michael Davidson and* *Grigorii Zapuhlih* **Group 2**	*Alessandro Serretti* *and* *Ludmila Bumacov* **Group 3**

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TUESDAY 18 OCTOBER 2011

15.00 – 15.15 Break

15.15 – 15.45 **How to prepare a scientific paper**, Celso Arango, Spain

16:00 – 21.00 Cultural event and dinner

WEDNESDAY 19 APRIL 2011

Presentations participants in 3 groups in 3 parallel workshops			
Round 2 08.30 – 10.00	*Celso Arango and Anatol Nacu* **Group 2**	*Michael Davidson and Grigorii Zapuhlih* **Group 3**	*Alessandro Serretti and Ludmila Bumacov* **Group 1**
10.00 – 10.30 Coffee break			
Round 3 10.30 – 12.00	*Celso Arango and Anatol Nacu* **Group 3**	*Michael Davidson and Grigorii Zapuhlih* **Group 1**	*Alessandro Serretti and Ludmila Bumacov* **Group 2**

12.00 – 14.00 Lunch and preparation for plenary session		
Plenary 14.00 – 15.00	14.00 – 14.20	**Group 1** Presentation
	14.20 – 14.40	**Group 2** Presentation
	14.40 – 15.00	**Group 3** Presentation

15.00 – 15.15 Time to fill out the 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**, Celso Arango, Spain.

Professor Celso Arango MD is Head of the Child and Adolescent Department of Psychiatry, Hospital Gregorio Marañón. He is also Associate Professor of Psychiatry at the Universidad Complutense de Madrid and Associate Professor of Psychiatry at the University of Maryland, School of Medicine in Baltimore.

Professor Arango is a M.D. and Ph.D. and has a specialist degree in Forensic Psychiatry from the Universidad Complutense de Madrid. He is an instructor for two undergraduate courses and 22 doctoral courses and thesis director for eight doctoral dissertations. He is the editor of five books and more than 30 book chapters and has authored more than 200 scientific articles published international journals. In addition he has presented more than 200 papers and presentations at international conferences from 1993 to 2011. His research involvement includes participation in 36 research projects, 21 as principal investigator, Coordinator of a Thematic Network of the Instituto de Salud Carlos III (ISCIII) and Scientific Director of the the Spanish Network in Mental Health (Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM).

Professor Arango's memberships include the editorial committees of 10 Spanish and international scientific journals and the Executive Committee of the ECNP. He has 19 awards conferred by Spanish and international scientific societies and the Cross of Civil Merit in Health. In addition, he is the Coordinator of the "European Child and Adolescent Neuropsychopharmacology Network." He is also Secretary of the Spanish Society of Biological Psychiatry and member of seven other Spanish and international scientific/professional societies and Consultant to the EMEA and AEM (Spanish Drug Agency).

Professor Arango´s main areas of research included neurobiological correlates of early-onset psychoses, developmental neuropsychopharmacology and psychopharmacology in schizophrenia.

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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. subespecialty 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 mensage, 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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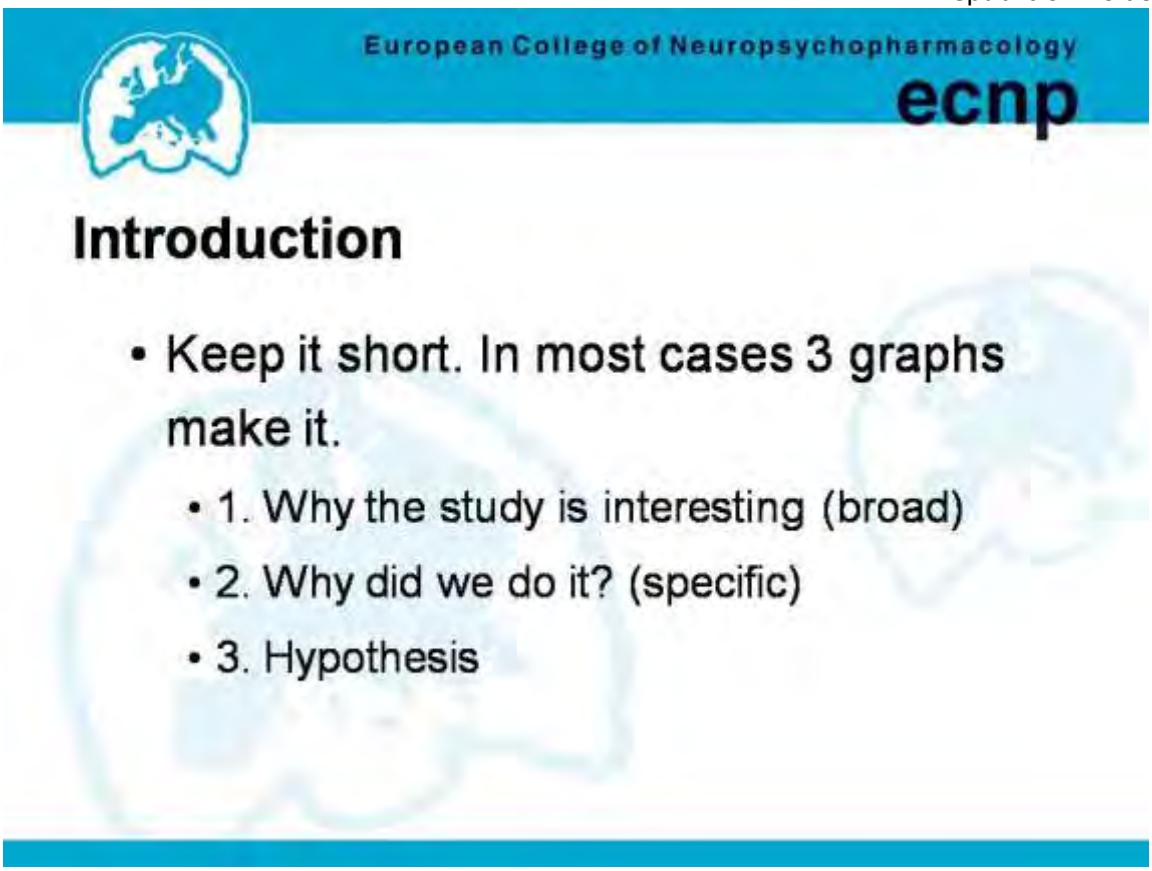
Discussion

- Refer Tables and Figures
- Do not repeat results
- Include limitations section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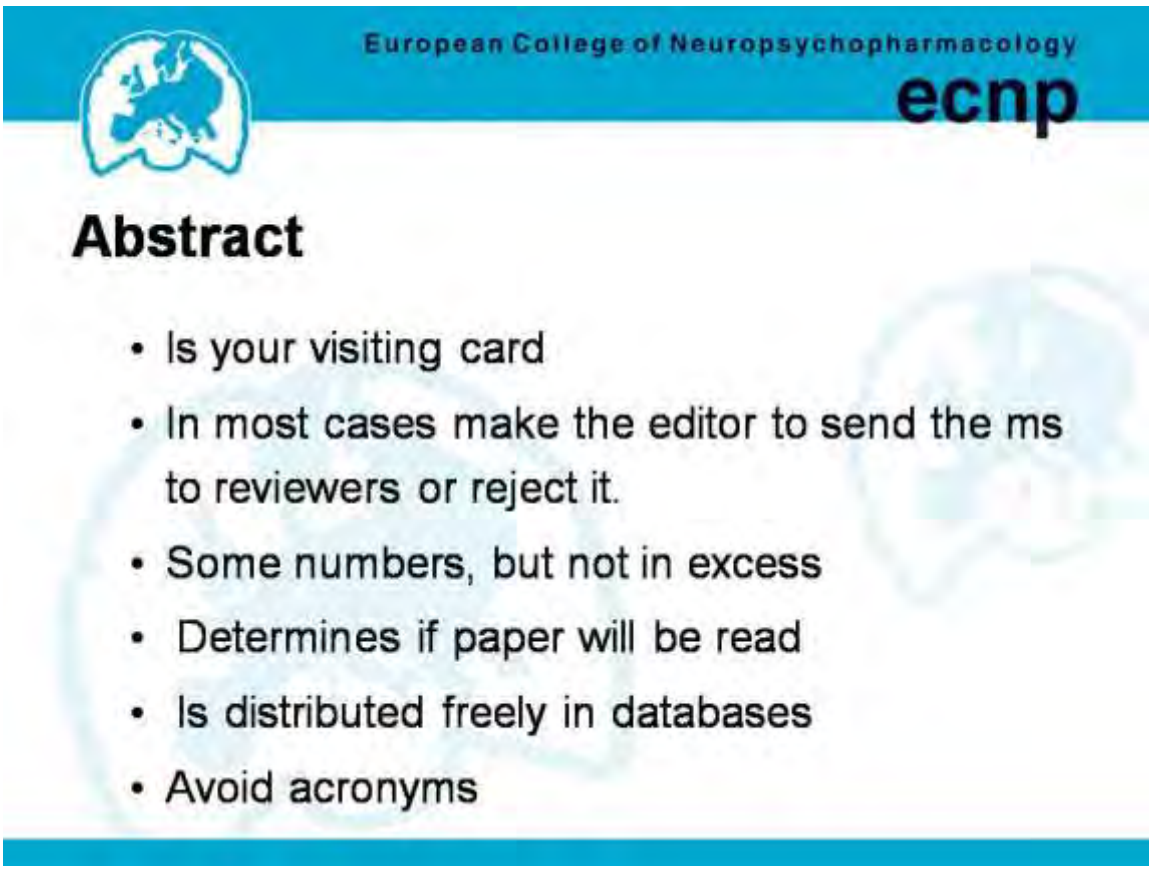
Introduction
• Keep it short. In most cases 3 graphs make it.
• 1. Why the study is interesting (broad)
• 2. Why did we do it? (specific)
• 3. Hypothesis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Abstract
• Is your visiting card
• In most cases make the editor to send the ms to reviewers or 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 senteces 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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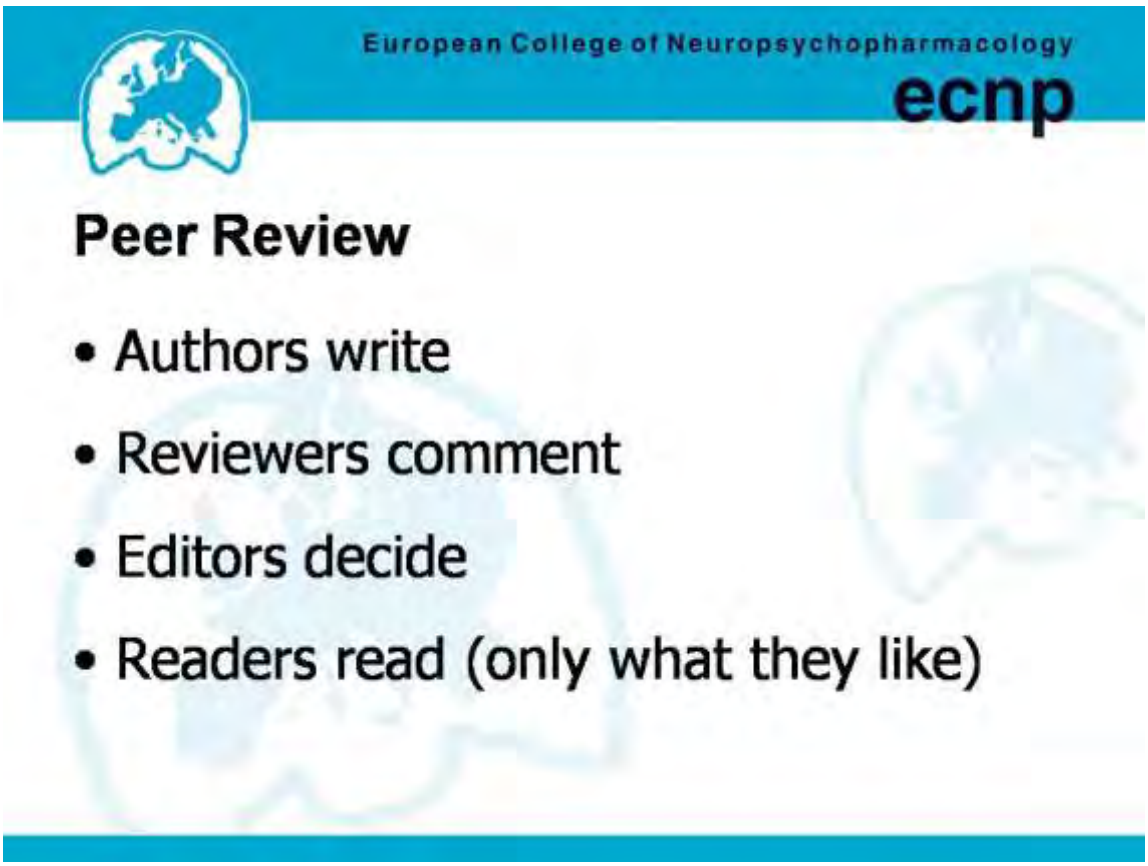
Authorship
• The manuscript is not under consideration elsewhere and will not be submitted elsewhere until a final decision has been made by the journal
• All funding sources must be acknowledged
• All conflicts of interest should be reported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Peer Review
• 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"

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"Surely you were aware when you accepted the position, Professor, that it was publish or perish."

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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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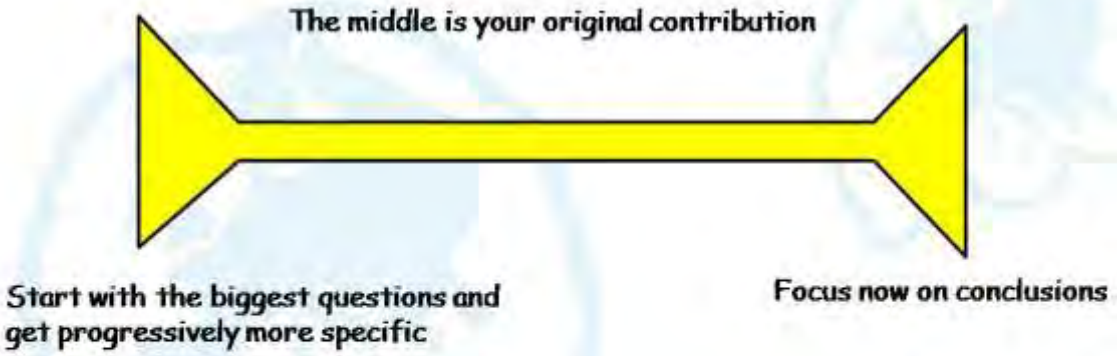
Start broad, get specific, and end broad



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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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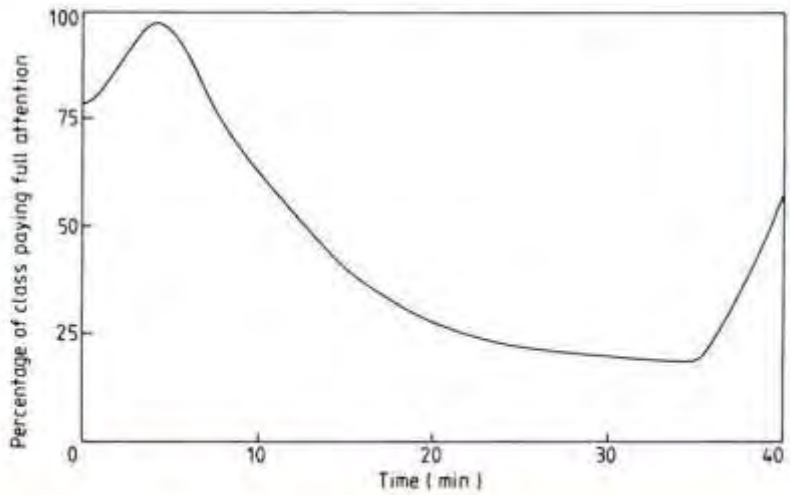
Audience attention curve



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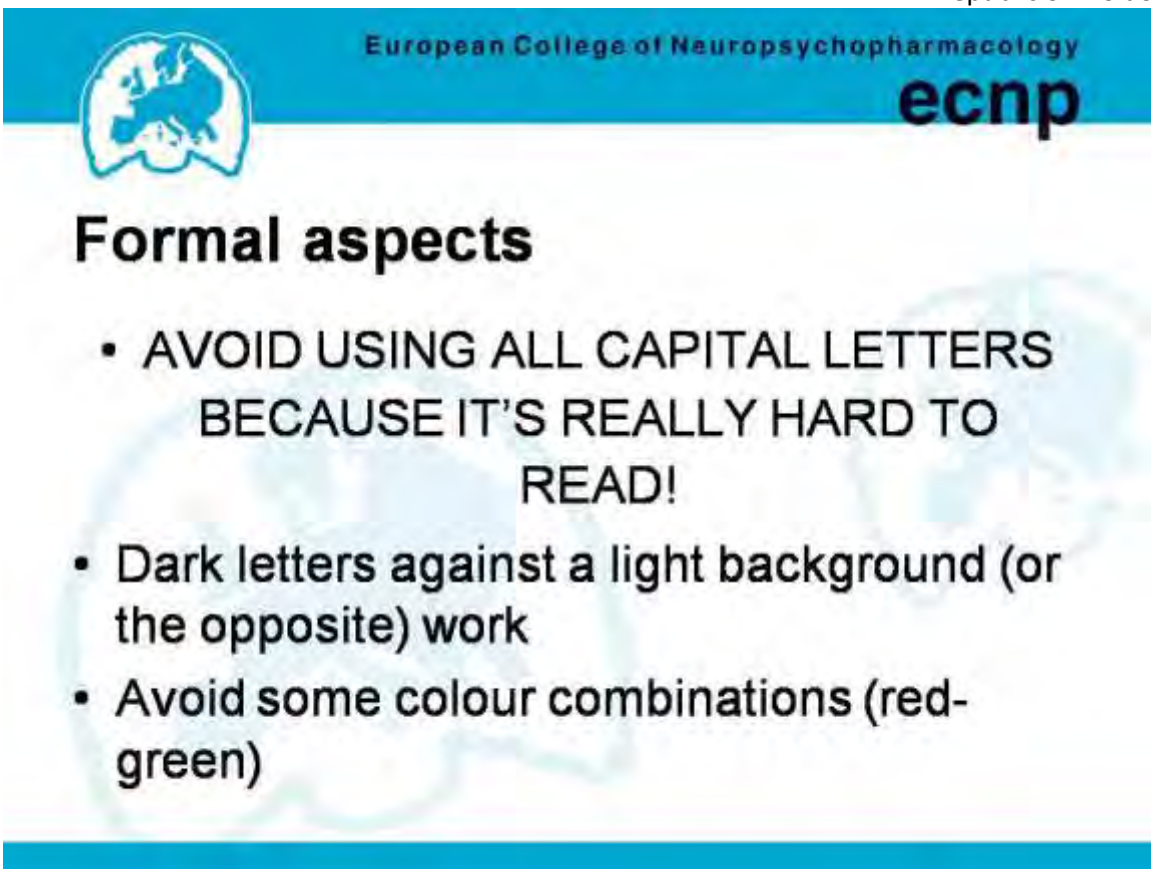
Conclusion and Recommendations

- 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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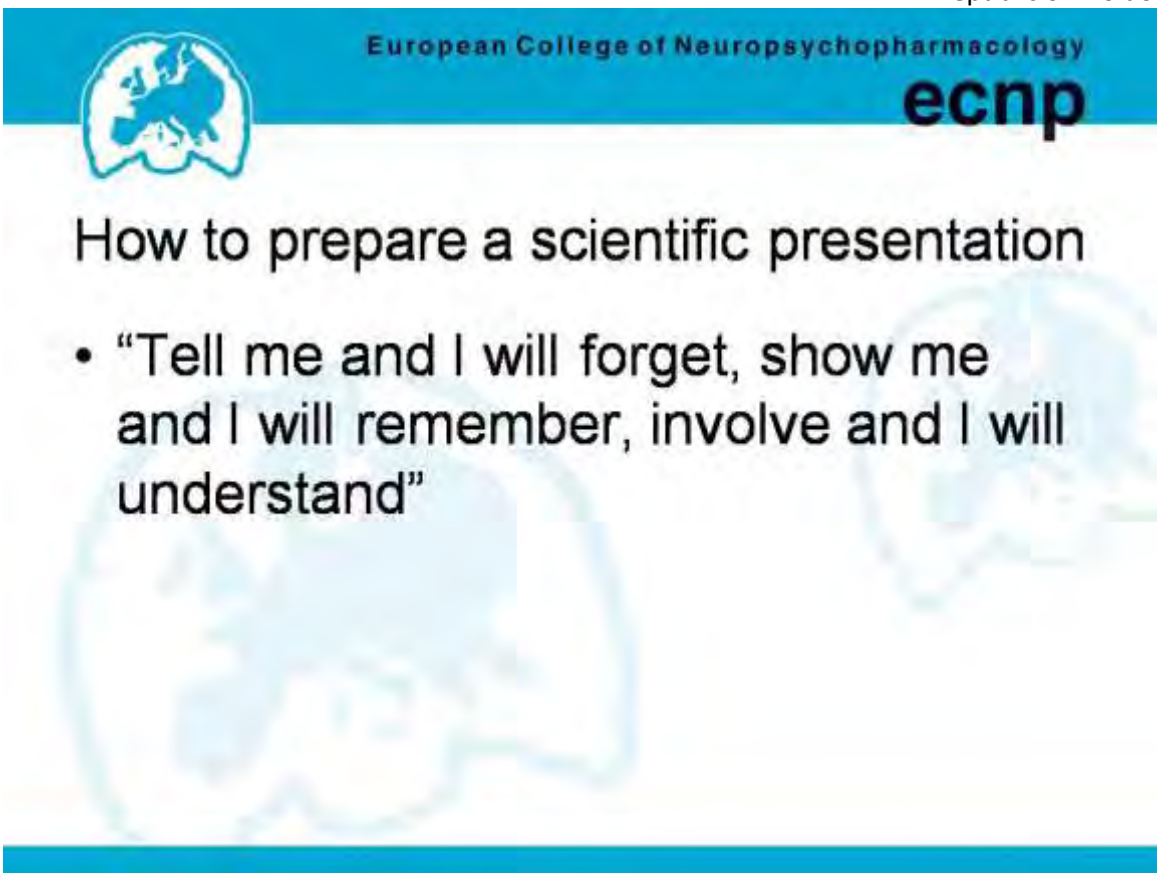
And do not forget to…….
Face the audience
Never underestimate your audience!
With time you will enjoy…..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How to prepare a scientific presentation
• "Tell me and I will forget, show me and I will remember, involve and I will understand"


Hospital General Universitario Gregorio Marañón
Treatment of Acute Psychoses
Celso Arango
Hospital General Universitario Gregorio Marañón,
Madrid, Spain
carango@hggm.es
Moldova, October 2011
ciber sam

Index

- Review of first episode studies
- Treatment in the acute setting
- Treatment 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

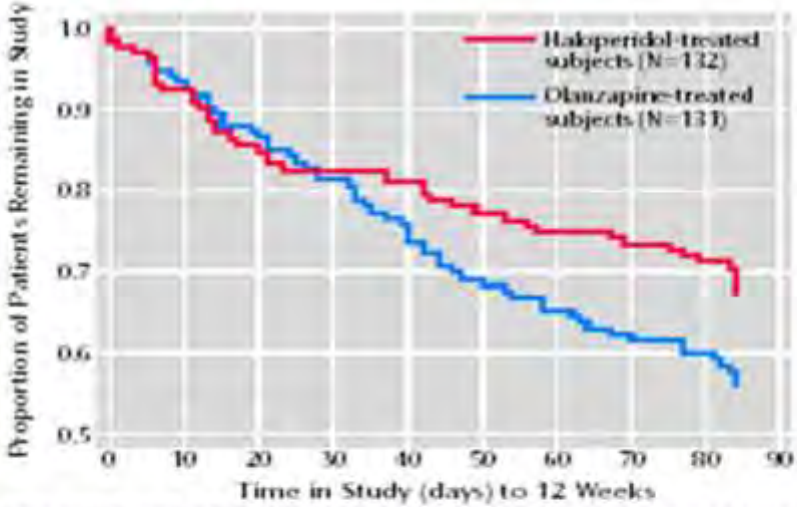
	Relapse Rate (%) Placebo	Relapse Rate (%) Antipsychotic	*P*-value
Kane et al, 1982	41 (7/17)	0 (0/11)	<0.01
Crow et al, 1986	62 (41/66)	46 (25/54)	0.002*
McCreadie, et al (Scottish Schizophrenia Research Group), 1989	57 (4/7)	0 (0/8)	NS
Hogarty and Ulrich, 1998	64	43	N/A

*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

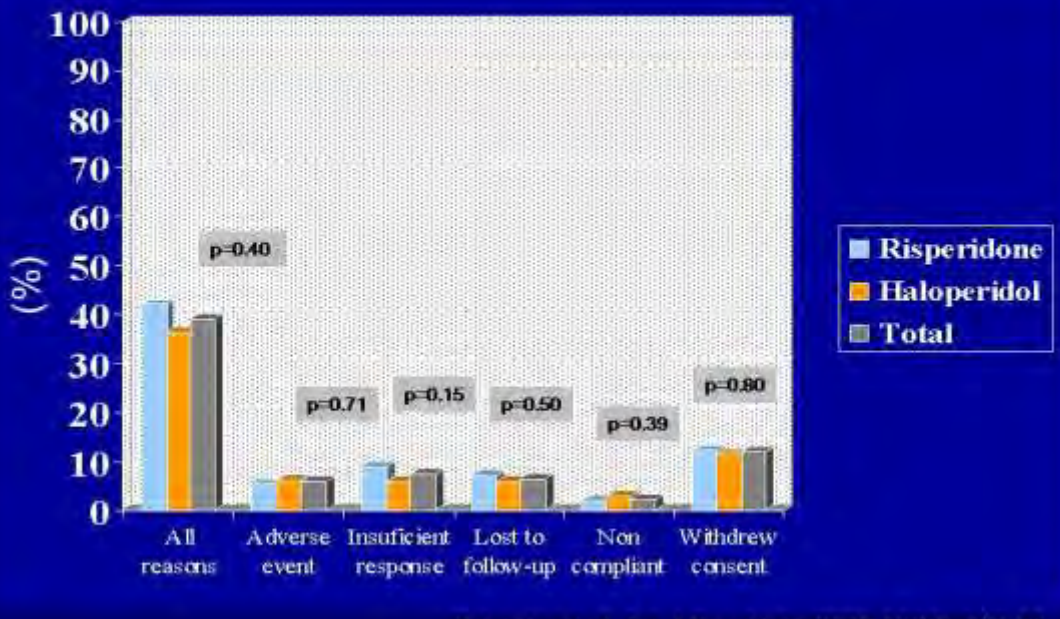
FIGURE 1. Time to Study Discontinuation for Any Reason of Subjects With First-Episode Psychosis in the 12-Week Acute Treatment Phase of a Long-Term Comparison of Olanzapine and Haloperidol[a]



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

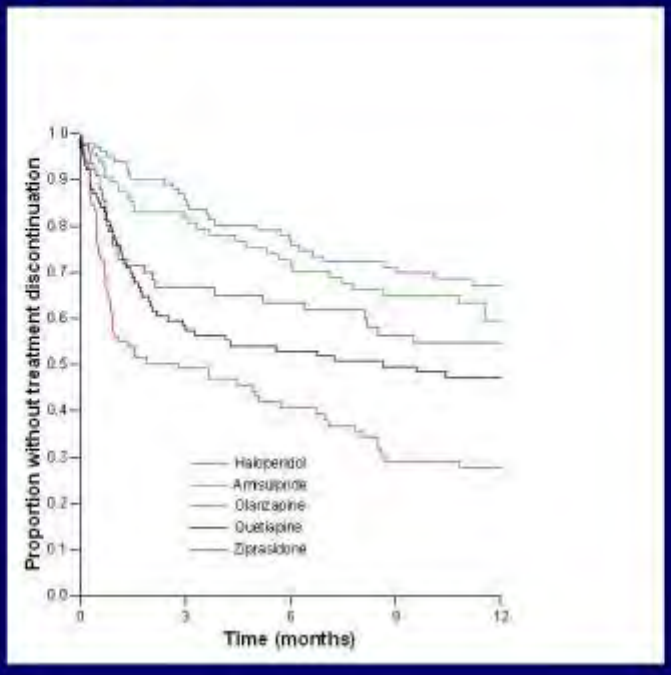
Lieberman et al, Am J Psychiatry 2003;160(8):1396-404

Discontinuation rates and reasons among patients



Schooler et al. Am J Psychiatry 2005;162(5):947-53

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 perception: the person behind the illness

'They were attentive to my needs, bringing food and drink, blankets and pillows. I was not made to disrobe and don a gown, but allowed to remain in street clothes.'

'I was immediately strapped down, given two injections and my clothes were taken.'

'A charge nurse took time out of her busy schedule to answer some questions I had and alleviated some of my fears.'

'I felt that my treatment was bad because I felt no one was listening to me.'

'I had tried to kill myself. The staff were very helpful at the time, they gave me hope to keep on living.'

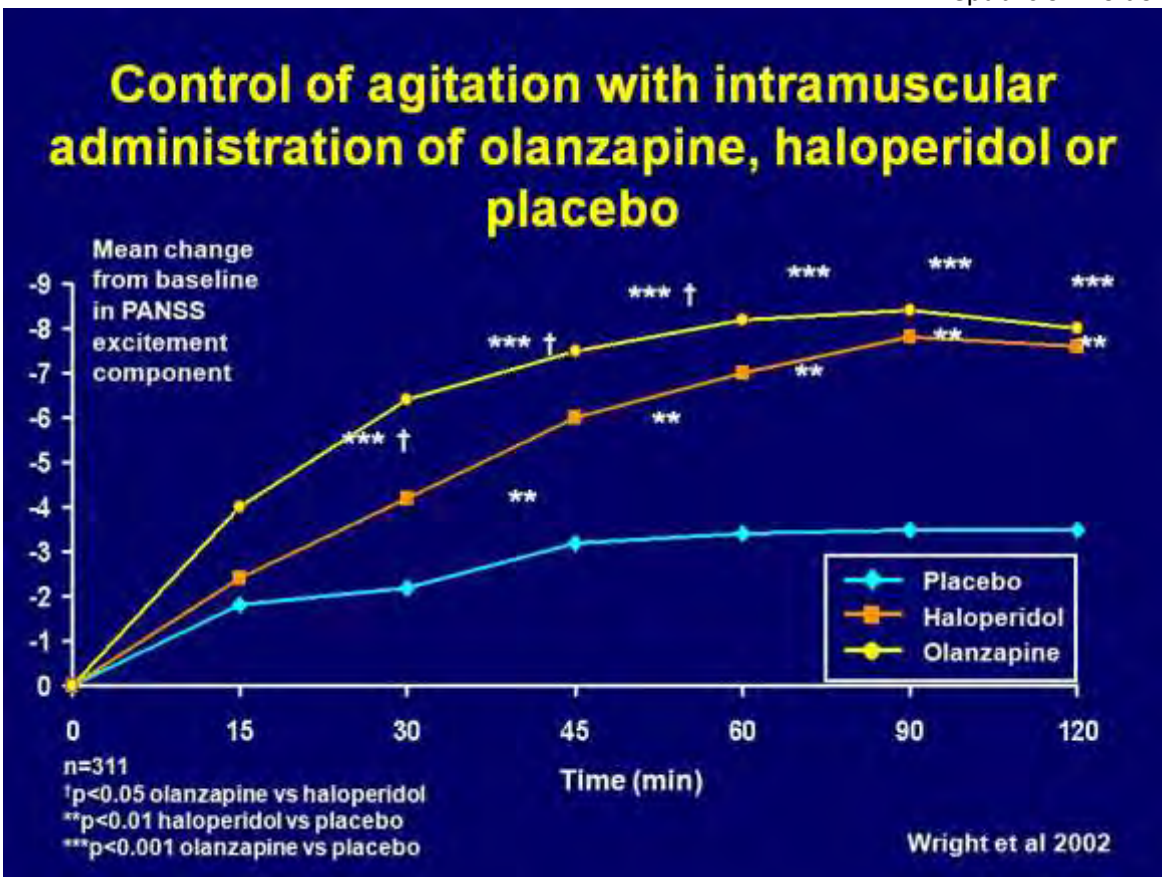
'They just seemed to ignore me. I was locked in a room and could see staff through the window.'

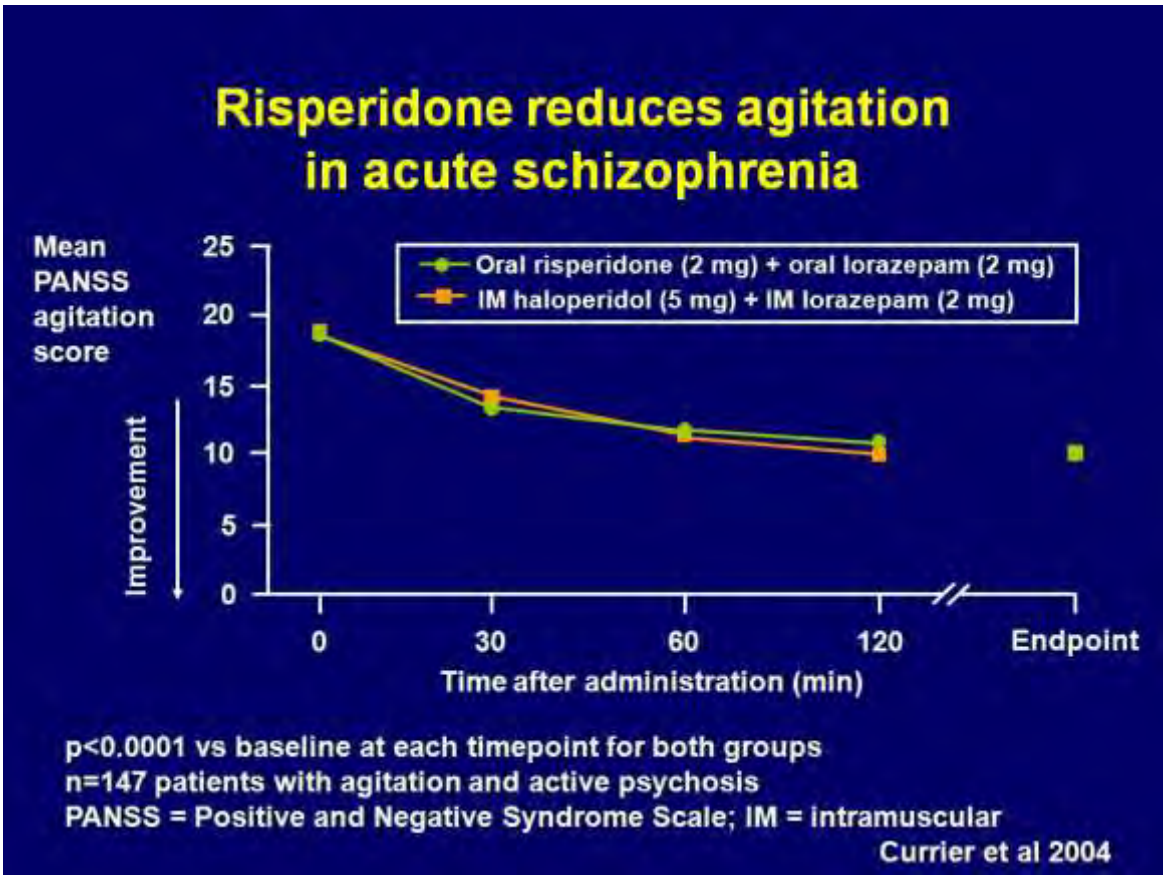
Allen et al 2003

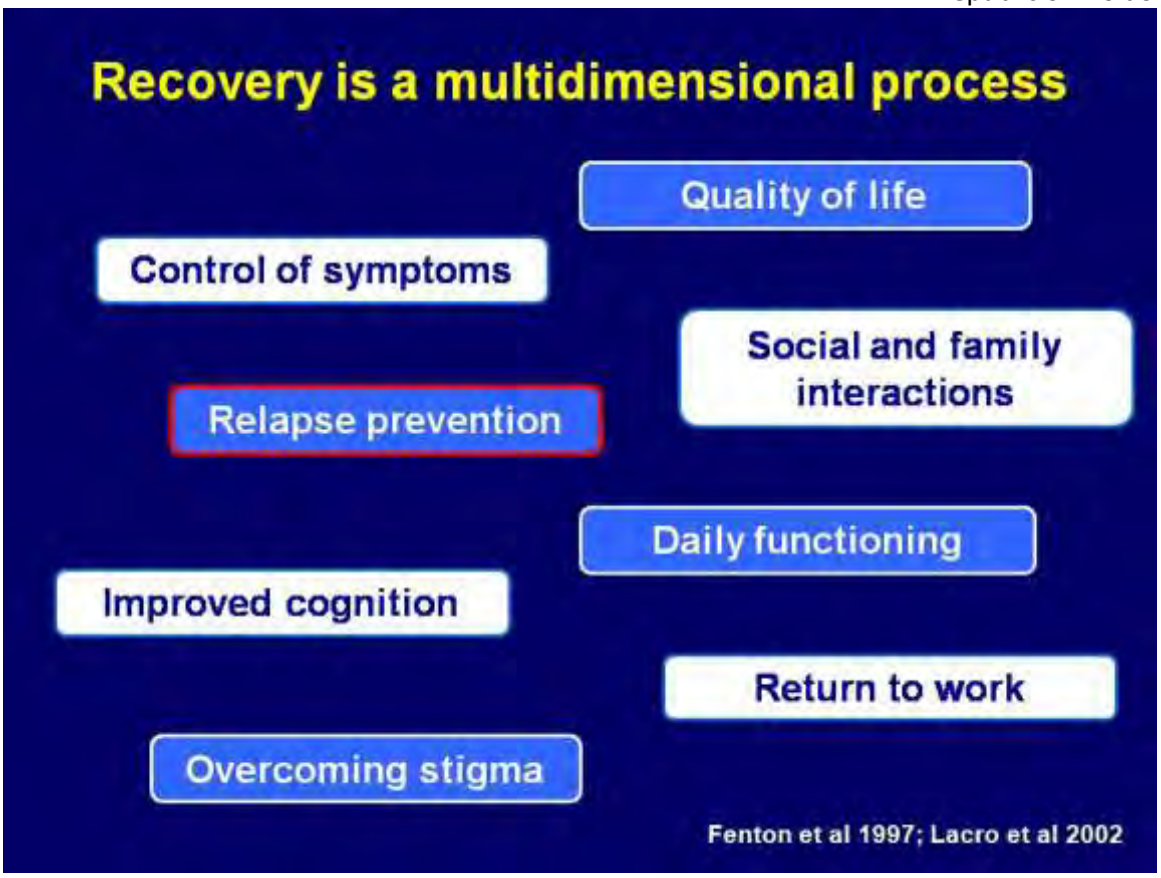
Patient requirements and preferences in the acute setting

- 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


Control of agitation with intramuscular administration of olanzapine, haloperidol or placebo
Mean change from baseline in PANSS excitement component
-9
-8
-7
-6
-5
-4
-3
-2
-1
0
0
15
30
45
60
90
120
Time (min)
Placebo
Haloperidol
Olanzapine
n=311
†p<0.05 olanzapine vs haloperidol
**p<0.01 haloperidol vs placebo
***p<0.001 olanzapine vs placebo
Wright et al 2002

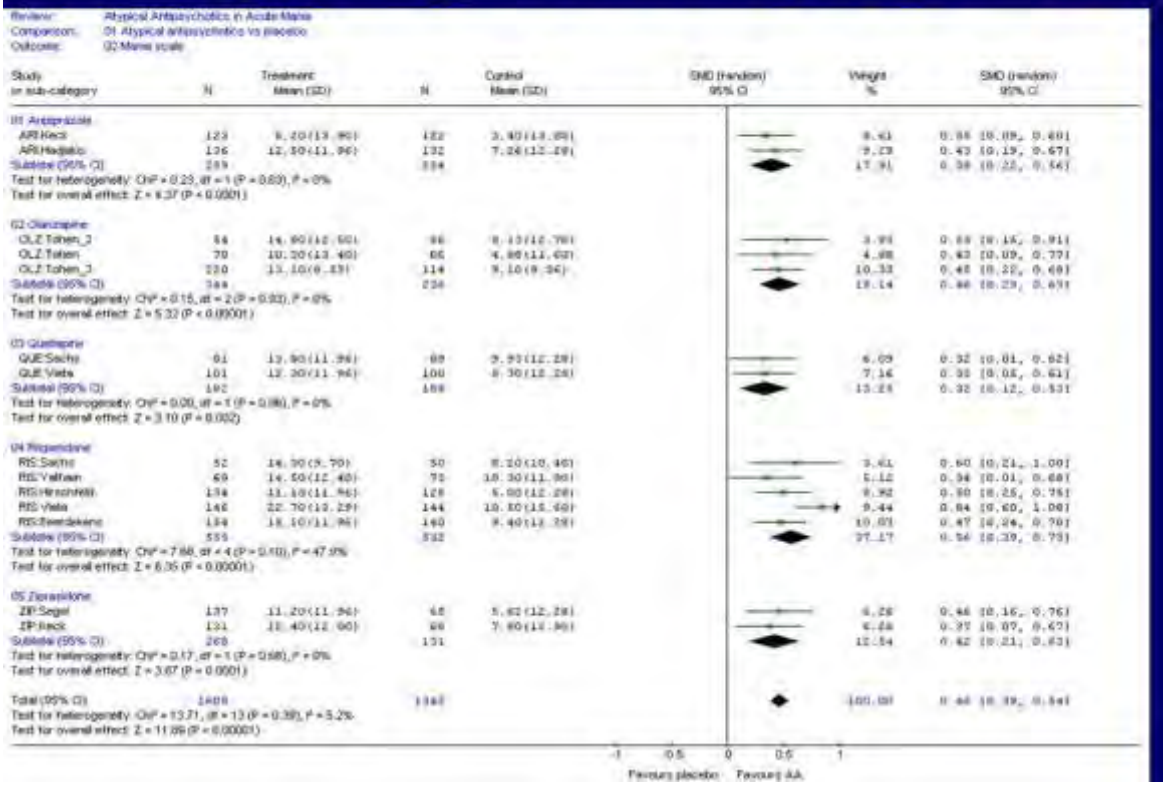

Risperidone reduces agitation in acute schizophrenia
Mean PANSS agitation score
25
20
15
10
5
0
Improvement
Oral risperidone (2 mg) + oral lorazepam (2 mg)
IM haloperidol (5 mg) + IM lorazepam (2 mg)
0
30
60
120
Endpoint
Time after administration (min)
p<0.0001 vs baseline at each timepoint for both groups
n=147 patients with agitation and active psychosis
PANSS = Positive and Negative Syndrome Scale; IM = intramuscular
Currier et al 2004



Treatment Options for Acute Mania

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

Metanalysis of Atypicals in Mania (Capapey & Vieta, 2005)



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

At risk for adverse health outcome
- BMI≥95 or
- BMI>85 +
  - hypertension >90 or
  - fasting cholesterol≥ 200mg/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

Treating first-episode patients

- More responsive than chronic patients
  - therapeutic and adverse effects
- Require lower doses of medication
- Effective early treatment can improve long-term outcome

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
- Patient adherence to their prescribed medication
- 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
- Ensuring a positive experience in the acute setting and establishing an interactive therapeutic alliance

European College of Neuropsychopharmacology
ecnp

Republic of Moldova 2011

Alessandro Serretti MD, PhD (1991- mark 110/110 with honours, Catholic University, Rome, Italy), Specialization in Psychiatry (1996 - mark 70/70 with honours, Milan University).

Since 1999 to 2006 Director of the Unit of Genetics in Mood Disorders, Dept. of Psychiatry, IRCCS Ospedale S.Raffaele, Milan.

2001-2008 Professor of Statistical Genetics at University Vita-Salute, IRCCS Ospedale S.Raffaele, Milan.

2006-present Associate Professor of Psychiatry (Ricercatore) at Bologna University, Bologna, Italy (main position), Director of the Mood Disorders Unit.

Author of more than 280 scientific papers in peer reviewed journals. Reviewer and member of the editorial board for 100 journals and 25 funding agencies. Principal Investigator in national and international scientific collaborative projects. Coordinator of a research unit active in genetic and clinical studies of major psychoses. H-Index=42.

Local Organizer: Dr. Sinita Eugenia tomtit_bird@mail.ru

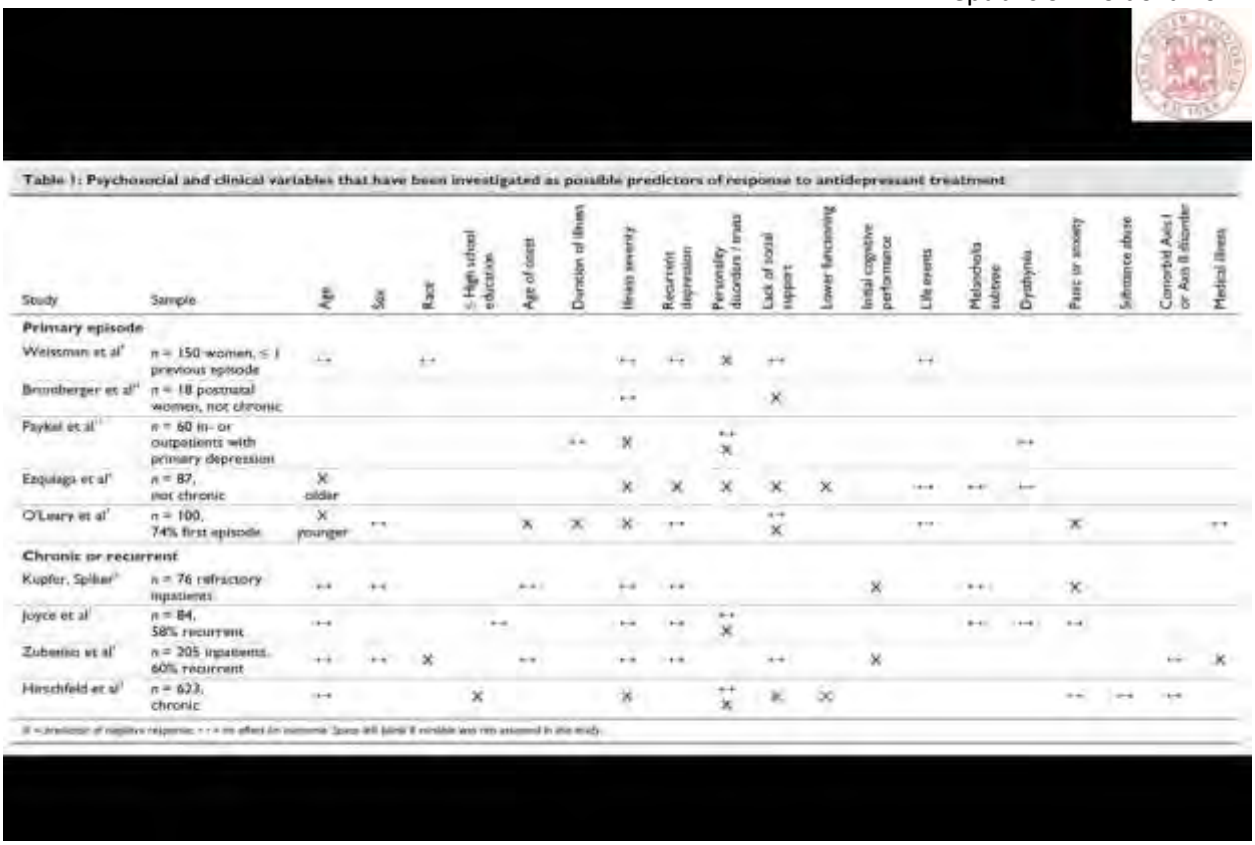


Table 1: Psychosocial and clinical variables that have been investigated as possible predictors of response to antidepressant treatment

Study	Sample	Age	Sex	Race	≤ High school education	Age of onset	Duration of illness	Illness severity	Recurrent depression	Personality disorders / traits	Lack of social support	Lower functioning	Initial cognitive performance	Life events	Melancholia subtype	Dysthymia	Panic or anxiety	Substance abuse	Comorbid Axis I or Axis II disorder	Medical illness
Primary episode																				
Weissman et al[7]	n = 150 women, ≤ 1 previous episode	↔		↔				↔	↔	×	↔			↔						
Bromberger et al[11]	n = 18 postnatal women, not chronic							↔			×									
Paykel et al[12]	n = 60 in- or outpatients with primary depression						↔	×		↔ ×						↔				
Ezquiaga et al[13]	n = 87, not chronic	× older						×	×	×	×	×		↔	↔	↔				
O'Leary et al[14]	n = 100, 74% first episode	× younger	↔			×	×	×	↔		↔ ×			↔			×			↔
Chronic or recurrent																				
Kupfer, Spiker[15]	n = 76 refractory inpatients	↔	↔			↔		↔	↔				×		↔		×			
Joyce et al[16]	n = 84, 58% recurrent	↔			↔			↔	↔	↔ ×					↔	↔	↔			
Zubenko et al[17]	n = 205 inpatients, 60% recurrent	↔	↔	×		↔		↔	↔		↔		×							↔ ×
Hirschfeld et al[18]	n = 623, chronic	↔			×			×		↔ ×	×	×					↔	↔	↔	

× = predictor of positive response; ↔ = no effect on outcome. Space left blank if variable was not assessed in the study.

Sociodemographic Features Predict Antidepressant Trajectories of Response in Diverse Antidepressant Pharmacotreatment Environments

*A Comparison Between the STAR*D Study and an Independent Trial*

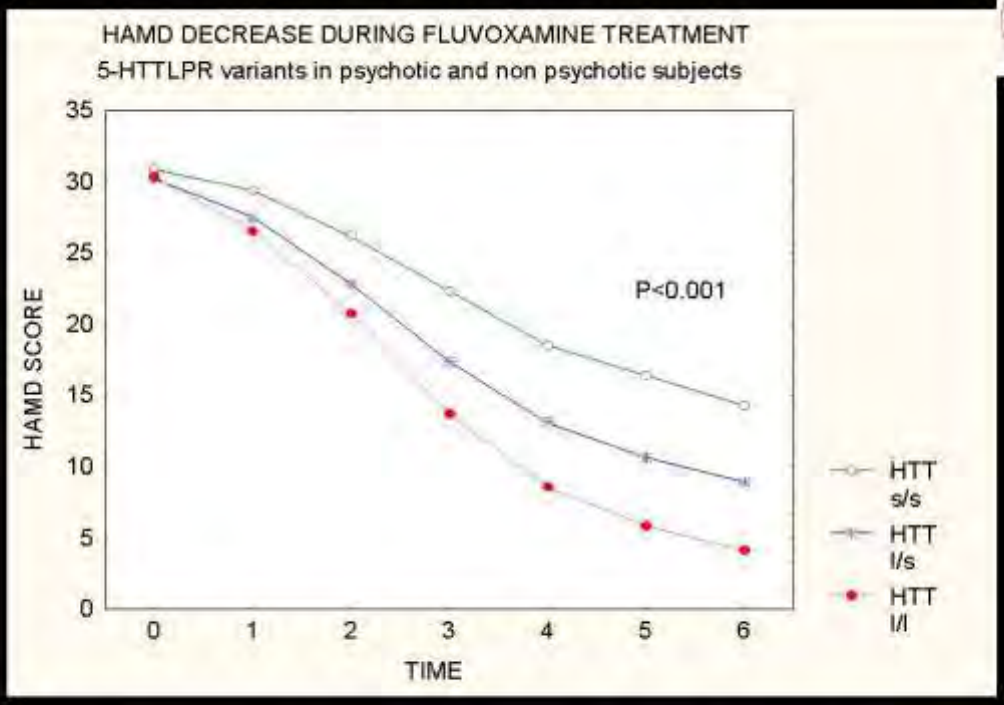
Antonio Drago, MD and Alessandro Serretti, MD, PhD

ORs for response were 2.6 and 2.2

higher education
higher money income
not living alone
good employment status.

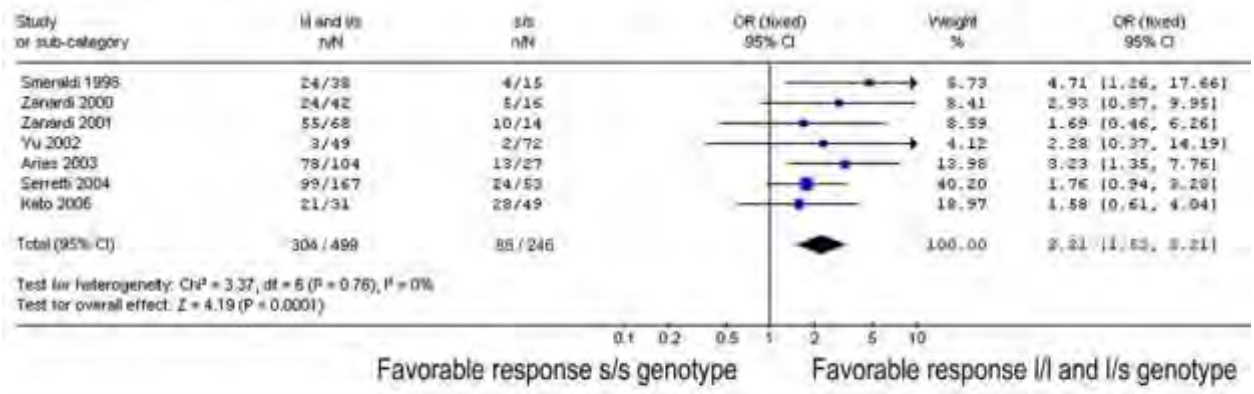
Examples of PGx: FDA

Drug	Indication	Effect measure	Gene-allele	FDA guidelines
Cetuximab	Colorectal cancer	Disease-free survival	*EGFR+*	Required
Trastuzumab	Breast Cancer	Disease-free survival	Her2 *overexpression*	Required
Lapatinib	Breast cancer	Disease-free survival	*Her2+*	Required
Azathioprine 6MP	childhoold leukemia	myelotoxicity	*TPMT Variants*	For information only
Busulfan	Myelogenous leukemia	Disease-free	*Philadelphia chromosome +*	For information only
Carvedilol	Heart failure	Ejection fraction; survival	*β1-AR* (arg389)	none
Pravastatin	Dyslipidemia	HDL and total cholesterol levels, atherosoclerosis progression	*CETP-B1* *HMGCR* (HAP7)	none
Donepezil	Alzheimer's Disease	Improvement in ADAS-Cog	*ApoE4+*	none
Rosiglitazone	Alzheimer's Disease	Improvement in ADAS-Cog	*ApoE4-*	none



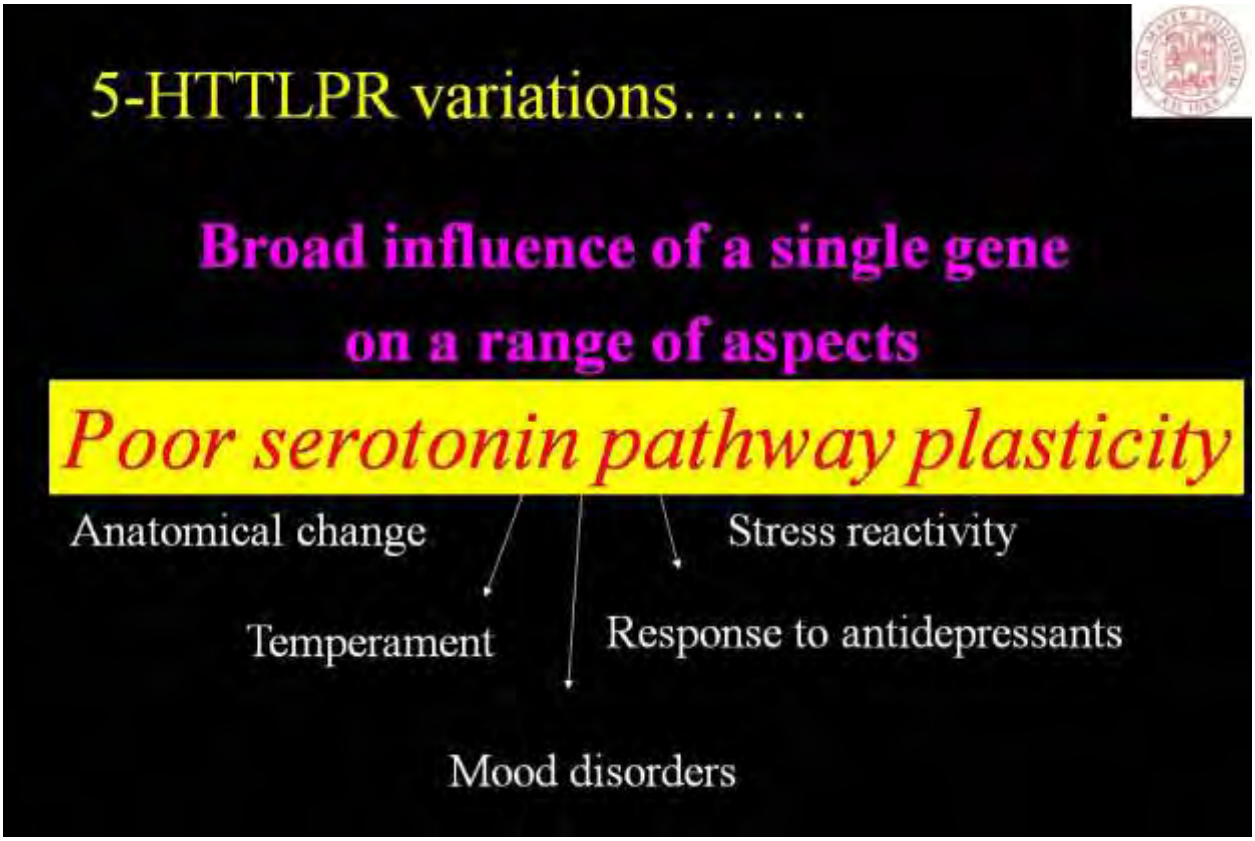
5-HTTLPR variants explained 7% of the variance of antidepressant efficacy

Remission



FEATURES MODULATED BY SERTPR	POSITIVE AND NEGATIVE STUDIES
NEUROANATOMIC SITES	
Hippocampal volume	– –
Amygdala response	+ –
ANXIOUS PERSONALITY TRAITS	
Infants	+ – +
Infants (l/l)	+ + +
Adults	+ + + + + + + + + + ** – – – – – – – – –
Cluster C diagnosis	–
ANXIETY DISORDERS	
Obsessive Compulsive Disorder	– – – +
Panic Disorder	– – – –
Generalized Anxiety Disorder	–
Post Traumatic Stress Disorder	–
Compulsive Buying	–
PSYCHOSOMATIC DISORDERS	
Chronic Tension-type Headache	–
Diarrhoea Irritable Bowel Syndrome phenotype	+
Fibromyalgia	– + –

FEATURES MODULATED BY SERTPR	POSITIVE AND NEGATIVE STUDIES
MOOD DISORDERS	
Major Depressive Disorder	+ * *
Bipolar Disorder	+ * * *
Total depressive symptomatology	-
Psychic anxiety symptomatology	+
Depression, Mania, Delusion and Disorganization symptomatologic factors	-
Early age at onset	+ + - +
Lower illness recurrence	+
Rapid cycling (l or s allele)	+ +
Antidepressant induced mania	+ - + +
Better response to serotoninergic treatments (l allele)	* + + +
Better response to total sleep deprivation (l/l)	+
Side effects (nausea)	-
Stressful life events	+ + - + +
SUICIDE	* * - - - +



Main replicated genes

- *HTT* ++
  ++++++++++++++++++++++++++----------
- *5-HT1A* ++++++++++++-----
- *5-HT2A* ++++++++++++++++++++++++----------
- *BDNF* ++++++++++++++++++++-----
- *COMT* ++++++++++++++++++--
- *MAO-A* +++++++------
- *NET* ++++++--
- *Gbeta3* ++++++----
- *FKBP5* ++++++----
- *PGP* +++++++-----

Less replicated genes

- *TPH1* +++++----------
- *TPH2* ++++--
- *ACE* ++++---
- *CRHR* ++++-
- *CLOCK* +++
- *APOE* +++-
- *NR3C1* +++
- *PDE* +++
- *GSK-3β* ++++
- *GRIK4* +++-

Preliminary findings

5-HT1B	+--	GRM3	-	CACNA1C	+
5-HT3A	++++-	GRIK2	++	FGF	+
5-HT3B	++--	GRIA1	+	RGS4	-
5-HT5A	-	GRIA3	++	p75NTR	+
5-HT2C	---	GRIN3A	+	MCR1	+
5-HT6	+----	CREB	+-	MCR2	+
DAT	++	HRH1	+	PPGAL	+
DRD2	-	IL-1β	++	GNB3	-
DRD3	+	nNOS	--	CHRBP	+
DRD4	+	DTNBP1	++-	OPRM1	+-
ADRB1	+-	VAMP2	-	SIGMAR1	-
ADRA2A	++	TREK1	++		
GRM2	-	NTRK2	+-		

Pharmacogenetics: problematic issues…*and possible solutions*

- Low variance explained by polymorphisms (HTTLPR=2.8%, TPH=2.7%, Gß3=1.2%) → Other variables influence drug response: Life events, social support, temperament, hormons…*and should be included in the model! Neural Network?*
- Epigenetic factors, CNV, Splicing, Regional expression, gene interactions…*should be controlled with multivariate or neural network models.*
- Drug response may differ across episodes…*longer follow up*

Interaction between SERTPR and stressful life events on response to antidepressant treatment

Laura Mandelli [a,*], Elena Marino [b], Adele Pirovano [b], Raffaella Calati [a], Raffaella Zanardi [b], Cristina Colombo [b], Alessandro Serretti [a]

[a] Institute of Psychiatry, University of Bologna, Bologna, Italy
[b] Department of Psychiatry, San Raffaele Scientific Institute, Milan, Italy

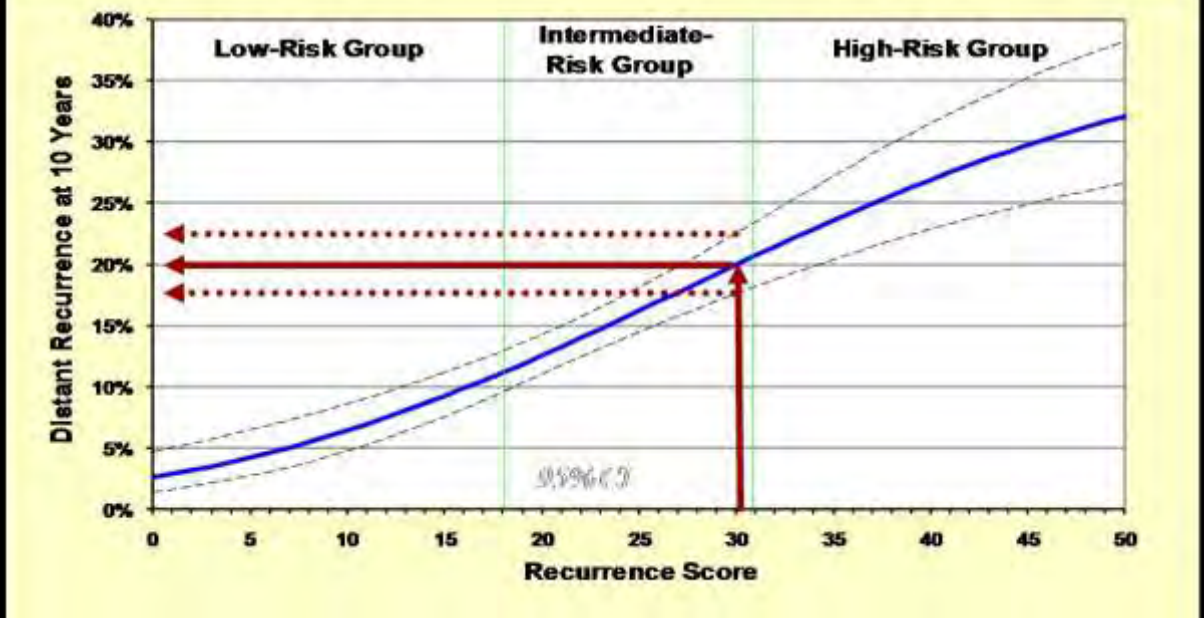
Eur Neuropsychopharm (2009) 19, 64–67

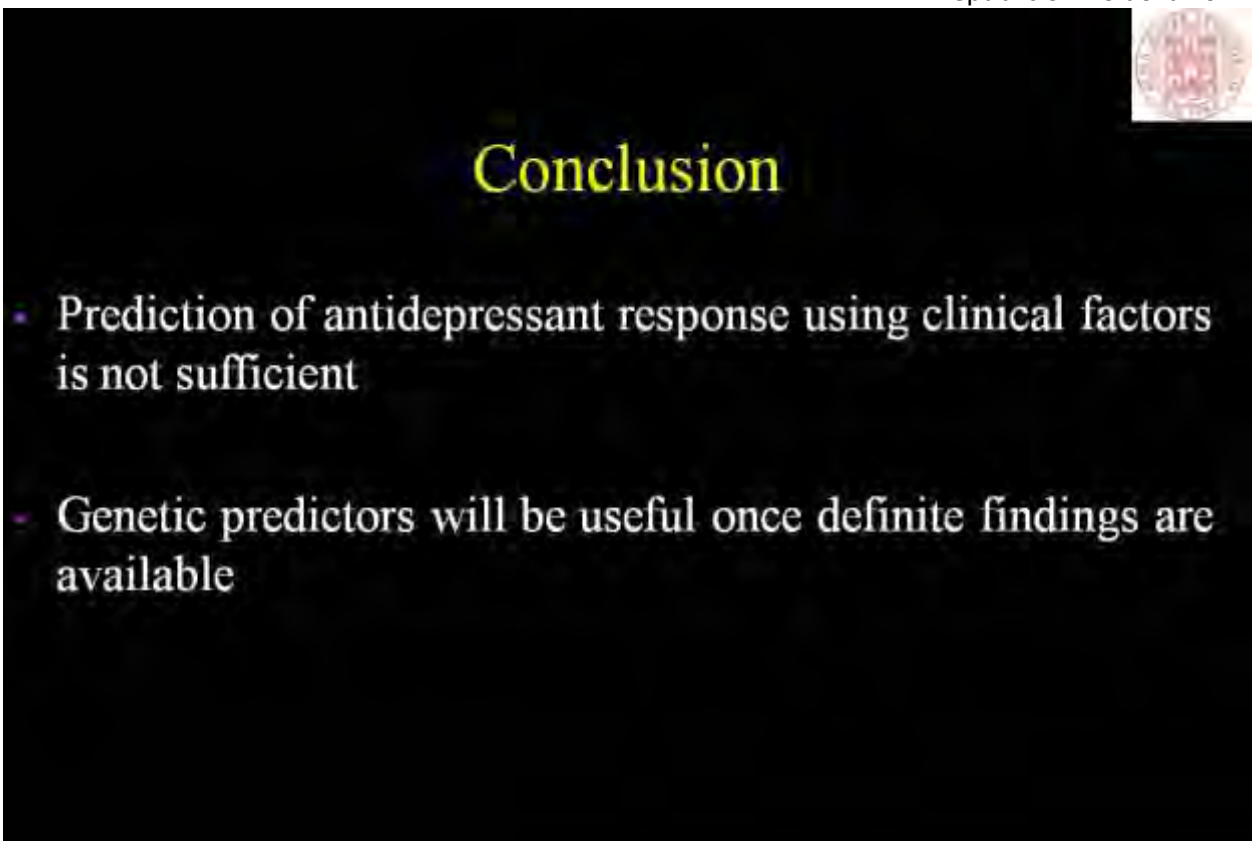
Table 1 Response to treatment, according SERTPR genotype and exposure to adverse life events at the onset of Mood disorder

The first G x E Pgx study

		Responders		Non-responders	
		N	(%)	*N*	(%)
L/L Non-exposed	(*n*=26)	22	(85%)	4	(15%)
L/L Exposed	(*n*=30)	24	(80%)	6	(20%)
S-carriers Non-exposed	(*n*=31)	22	(71%)	9	(29%)
S-carriers Exposed	(*n*=72)	49	(68%)	23	(32%)

IVDMIA example: Oncotype DX®




Conclusion
Prediction of antidepressant response using clinical factors is not sufficient
Genetic predictors will be useful once definite findings are available

Prof. Michael Davidson is currently the Head of the Department of Psychiatry at the Sheba Medical Center and Professor of Psychiatry at the Sackler School of Medicine. Prof. Davidson has trained in psychiatry at the Mount Sinai School of Medicine in New York City between 1981 and 1985 where remained on staff until 1995 and became Professor of Psychiatry. Prof. Davidson has accumulated experience both as an administrator and as a researcher. He has been hospital deputy director both in New York State and in Israel and has contributed to the movement of deinstitutionalization.

As a researcher Prof. Davidson has published over 200 articles mostly in peer reviewed prestigious journals in the area of Schizophrenia and of Alzheimer's disease. In the area of Schizophrenia he has investigated and published data focused on the biology of the disease (neurochemistry and molecular biology) as well as experimental treatments. Recently he as embarked in the study of the premorbid and prodromal manifestations leading to Schizophrenia. In the areas of Alzheimer's Diseases most of his research work has been devoted to developing novel treatments for this condition. Lately his research has been focused on determining the contribution of cardiovascular risk factors and pathology to the manifestation of Alzheimer's disease. Prof. Davidson is a board member of several professional organizations as well as a reviewer for professional journals.

Clinical and Research Dilemmas In Dementia

Michael Davidson MD

What is dementia?

- How did the definition evolved?
- What aspects of cognition are relevant?
  - Be aware, cognition alone is not sufficient to diagnose dementia
- The Differential Diagnosis
  - Reversible vs. irreversible vs. pseudo-demenita
  - Education, culture, motivation, anxiety/depression,
  - Delirium vs. dementia
  - Dementia as a presenting symptom of a medical illness

Dubois 2011 diagnostic criteria

Probable Alzheimer's disease: A plus one or more supportive features B, C, D, or E

Core diagnostic criteria

A Presence of an early and significant episodic memory impairment that includes the following features:

1 Gradual and progressive change in memory function reported by patients or informants over more than 6 months

2 Objective evidence of significantly impaired episodic memory on testing: this generally consists of recall deficit that does not improve significantly or does not normalise with cueing or recognition testing and after effective encoding of information has been previously controlled

3 The episodic memory impairment can be isolated or associated with other cognitive changes at the onset of Alzheimer's disease or as Alzheimer's disease advances

Supportive features

B Presence of medial temporal lobe atrophy: volume loss in the hippocampus, entorhinal cortex, or amygdala on MRI with qualitative ratings by visual scoring (referenced to well characterised population with age norms) or quantitative volumetry of regions of interest (referenced to well characterised population with age norms)

C Abnormal cerebrospinal fluid biomarker: low amyloid β_{1-42} concentrations, increased total tau concentrations, or increased phosphotau concentrations, or combinations of the three; or abnormalities in other well-validated markers that will be discovered in the future

D Specific pattern of reduced glucose metabolism in bilateral temporal parietal regions on functional neuroimaging with PET or with other well validated ligands, such as Pittsburgh compound B or FDDNP (2-(1-(6-[(2-[^{18}F]fluoroethyl)(methyl)amino]-2-naphthyl) ethylidene)malononitrile)

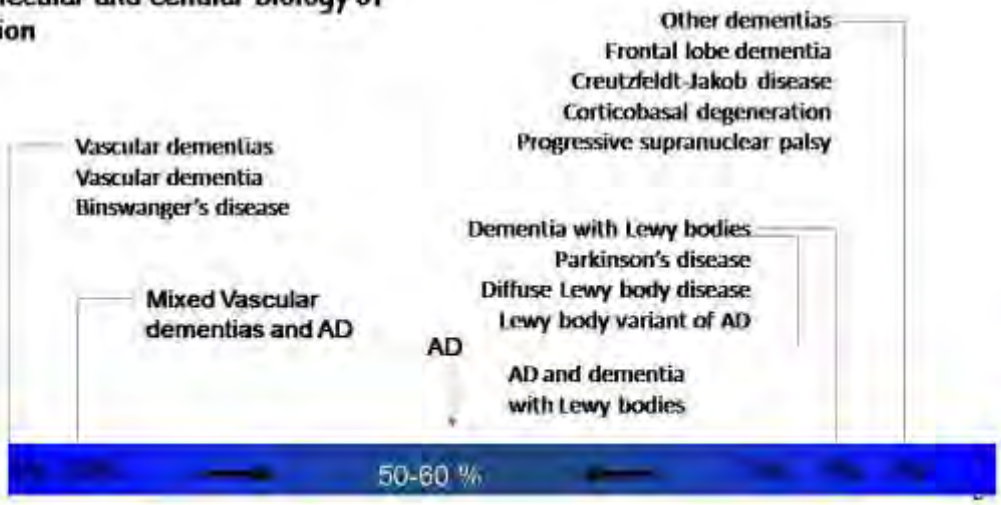
E Proven Alzheimer's disease autosomal dominant mutation within the immediate family

Is the dementia classification possible and does the phenomenology correlates with histology or etiology?

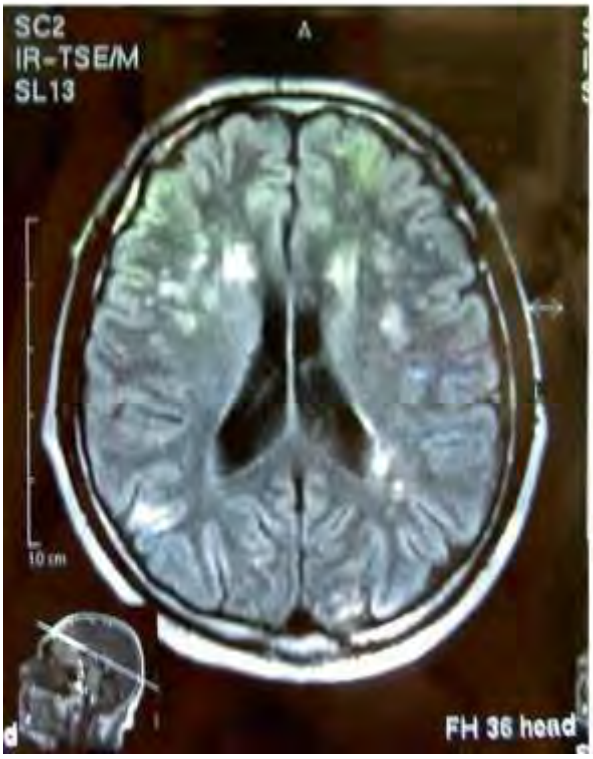
Symptom	Alzheimer's disease	Vascular dementia	Diffuse Lewy body	Fronto-temporal
Psychomotor agitation	+++	+++	+++	+
Aggresive behaviour	++	++	++	+
Delusions	++	++	+++	+
Hallucinations	+	+	+++	-
Depression	++	+++	++	+
Anxiety	++	+++	+	+
Apathy/ retardation	++	+++	++	++++
Sleep changes	++	++	++	+++
Appetite Changes	+	+	+	+++
Sexual disinhibition	+	+	+	+++

How many types of dementias exist?
Is there a correlation between phenomenology and neuropathology ?

- Phenomenology and course
- Histology
- Anatomical distribution of lesion
- Combination of lesion
- Molecular and cellular biology of
- lesion

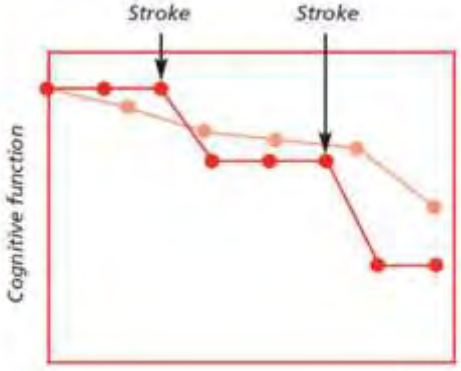


Stroke and dementia

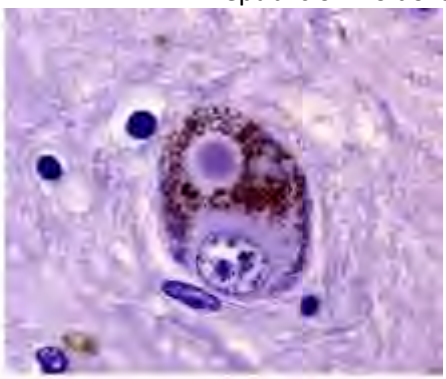


Stroke related dementia
The symptoms of stroke related dementia may appear suddenly. Over a period of time, the person may have further strokes which result in cognitive and, frequently, physical disabilities

Small vessel disease related dementia
Small vessel disease related dementia tends to be more like Alzheimer's disease, developing slowly over time



What is Lewy body dementia ?



A form of dementia with some overlap with Alzheimer's disease

Characterised by some features of Parkinsonism

Often, have gait instability and falls

Formed visual hallucinations (usually non-frightening)

Marked fluctuation within and between days

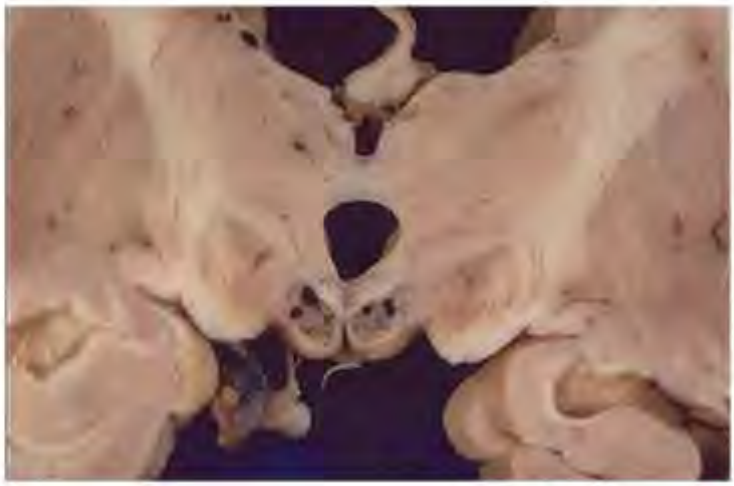
Daytime sleepiness with sleep reversal and bad dreams

Extreme sensitivity to neuroleptics

Wernicke-Korsakoff syndrome

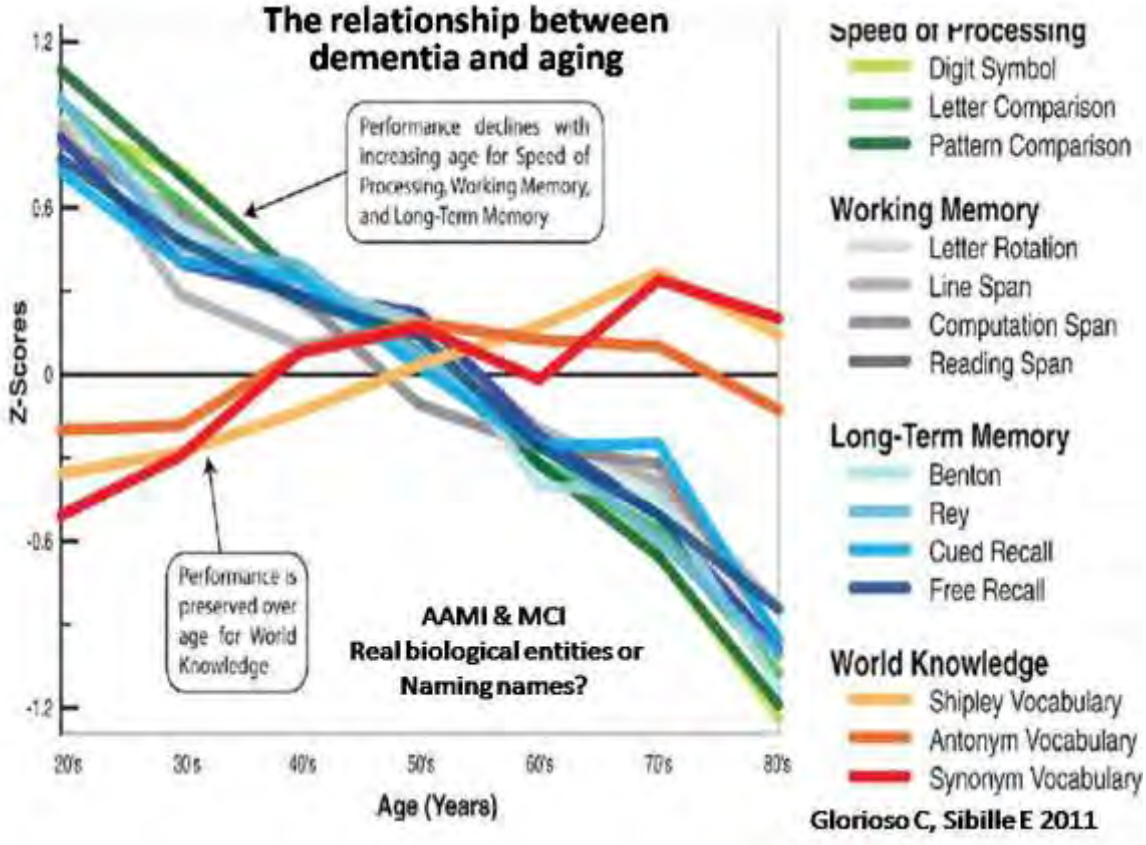
Wernicke's encephalopathy - delirium with ophthalmoplegia
Korsakoff's psychosis - amnesic/confabulatory disorder

Thiamine deficiency: alcoholics, malnourished people



Dementia associated with gait disorder

- Lewy Body disease
- Vascular dementia
- Normal pressure hydrocephalus
- Mass lesion (tumour/haematoma)
- Co-incidence of dementia plus another cause of gait disturbance
- "Parkinsons-plus" disorders



Which cognitive functions decline with age?

Misplacing the keys or failing to put a name no a familiar face not cognitive decline!

- Forgetfulness in young and middle age versus cognitive decline in elderly
- Speed of performance versus judgment and experience
- Learning new information versus remembering old information
- Anxiety, depression, drugs, alcohol abuse versus cognitive decline
- AAMI and MCI what overlaps with what?

Is all this necessary for diagnosis ?

- **Lab** CBC with diff, serum electrolytes, Ca++, glucose, BUN/CR, LFTs, TFTs, B12 & folate, U/A, RPR, head imag Sed. rate, HIV, CXR, heavy metals, LP, EEG, functional imaging, Lyme titers, endocrine studies, rheumatologic studies, **Neuropsychological Te**sting
- **LP**: Suspicion of metastatic CA, CNS infections, neuropsyphilis, hydrocephalus, vasculitis. Also for dementia <55 and rapidly progressive dementias
- **Neuroimaging** - consider in all new cases. However without focal symptoms or signs, seizures or gait disturbances in an individual over age 70 - *consider this optional*
- **Functional Imaging** (SPECT, PET, MRS, fMRI): to clarify type of dementia when necessary (and in the future to track course of illness and response to tx)
- **EEG** - can help distinguish delirium from dementia, can help with seizure disorder and JCD

Risk Factor *(why me?)*

a life-long endeavor starting with the choice of genes

Factor (Reference)	Studies, n	Participants, n	Follow-up, y	Association With Cognitive Decline
Nutritional				
Saturated fat (8)	1	2960	5.6	Inadequate evidence*
Trace metals (9–11)	2	6335†	4–9	Copper (no association except in subgroup)
Mediterranean diet (12, 13)	2	3285	4.5–7.0	Decreased risk
Fruits and vegetables (14, 15)	2	17 056	2.0–5.5	Decreased risk (vegetables) or no association (fruits)
Medical				
Diabetes (16–27)	12	47 629	2–25	Possibly increased risk
The metabolic syndrome (19, 28–30)	4	5713	1–14	Increased risk, except for age >85 y
Hypertension (19, 21, 31–46)	19	>43 000	1–14	No consistent association
Hyperlipidemia (37, 47, 48)	5	20 184	3–6	No consistent association
Homocysteine (49–53)	5	3409	2–10	No consistent association
Obesity (18, 19, 54)	3	8479	4–8	No consistent association
Depression (18, 38, 55–65)	13	32 969	1.5–6.0	Probably increased risk
Anxiety (18, 66–68)	4	6297	6	No consistent association
Traumatic brain injury	0	–	–	–
Resiliency	0	–	–	–
Sleep apnea	0	–	–	–
Social, economic, or behavioral				
Childhood exposure (69–71)	3	6861	2.0–5.6	No association
Education (19, 34, 72–83)	14	43 201	1–11	No consistent association
Occupation (73, 84–86)	4	7277	4–14	Individual studies showed possible decreased risk, but exposures were too heterogeneous to synthesize
Social engagement (19, 37, 71, 80, 87–97)	†54	42 9505	2–21	No consistent association for marital status, social network, or social support
Other leisure activities (89, 98, 99)	3	9999	1.5–6.0	Probably decreased risk
Alcohol (18, 19, 100–105)	7	15 581	2.2–8.0	No association
Tobacco (18, 19, 33, 38, 100, 105)	14	33 685	2–7	Increased risk
Toxic environmental exposure				
Pesticides	0	–	–	–
Genetic				
Apolipoprotein E ε4 allele (19, 21, 33,	15	8509	1–14	Increased risk

Ann Intern Med. 2010;153:182-19

Using CSF Biomarkers to Predict Progression from MCI to AD*

Measure	Cutoff Value	Sensitivity/ Specificity	Hazard Ratio†
T-Tau $A\beta_{1-42}$	>350 ng/L <530 ng/L	95% / 83%	17.7 (p<0.0001)
$P\text{-}Tau_{181}$ $A\beta_{1-42}$	>60 ng/L <530 ng/L	95% / 81%	16.8 (p<0.0001)
T-Tau $A\beta_{1-42}$/ $P\text{-}Tau_{181}$	>350 ng/L <6.5	95% / 87%	19.8 (p<0.0001)

*4-6 year follow up

Hansson O et al., *Lancet Neurol* 2006;5:228–34

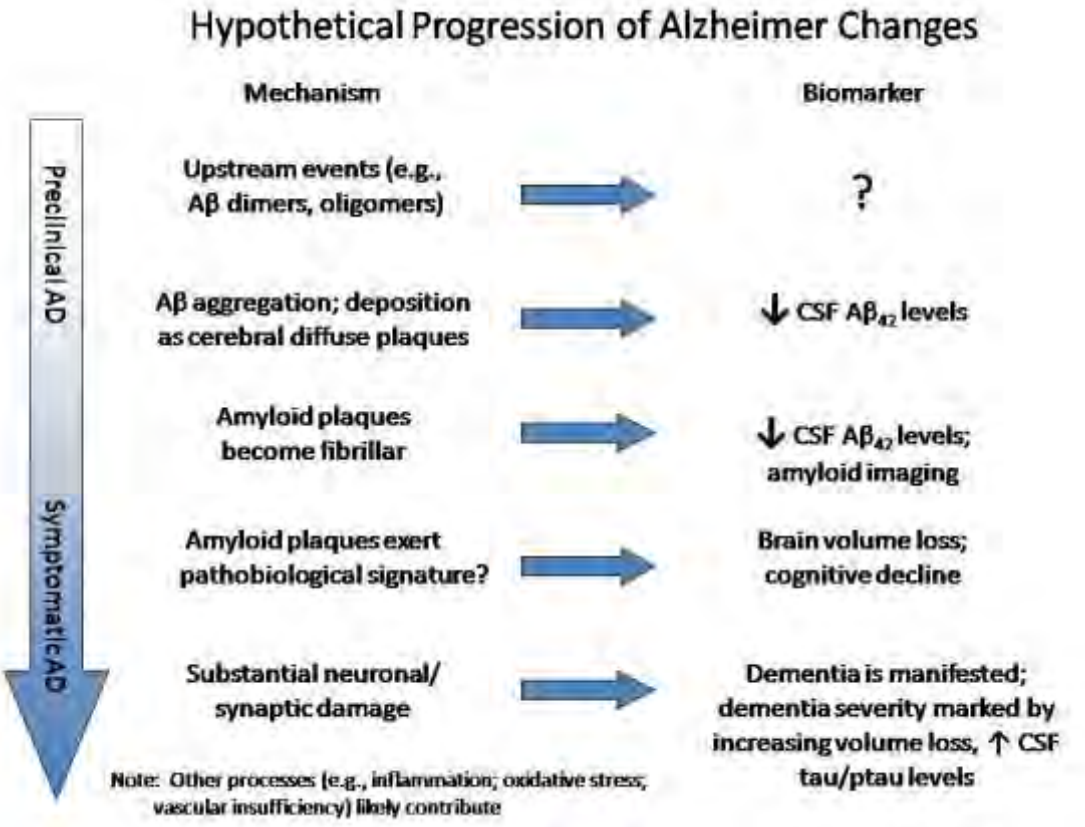
†Adjusted for age, sex, ApoE4, and educational level

How clinically relevant is it?

Volumetric MRI

- Serial volumetric MR images
  - Regional (hippocampal and entorhinal cortex) and whole brain volume change are validated markers of disease progression
    - **Regional** best for *early* progression
      - AD: 3.0 – 6.0 versus Control: 0.3 – 2.2
    - **Whole brain** better for progression *after onset* of clinical AD
      - AD: 1.4 – 2.2 versus Control: up to 0.7
- **Best validated marker for disease progression**

Frisoni GB et al., *Nat. Rev. Neurol.* 6, 67–77 (2010)



Current therapeutics

- 1906 Alzheimer's description
- 1970's Cholinergic hypothesis
- 1985 first THA trial
- 1993 Tacrine approved
- 1997 Vitamin E
- 1997 Donepezil
- 2000 Rivastigmine
- 2001 Galantamine
- 2003 Memantine

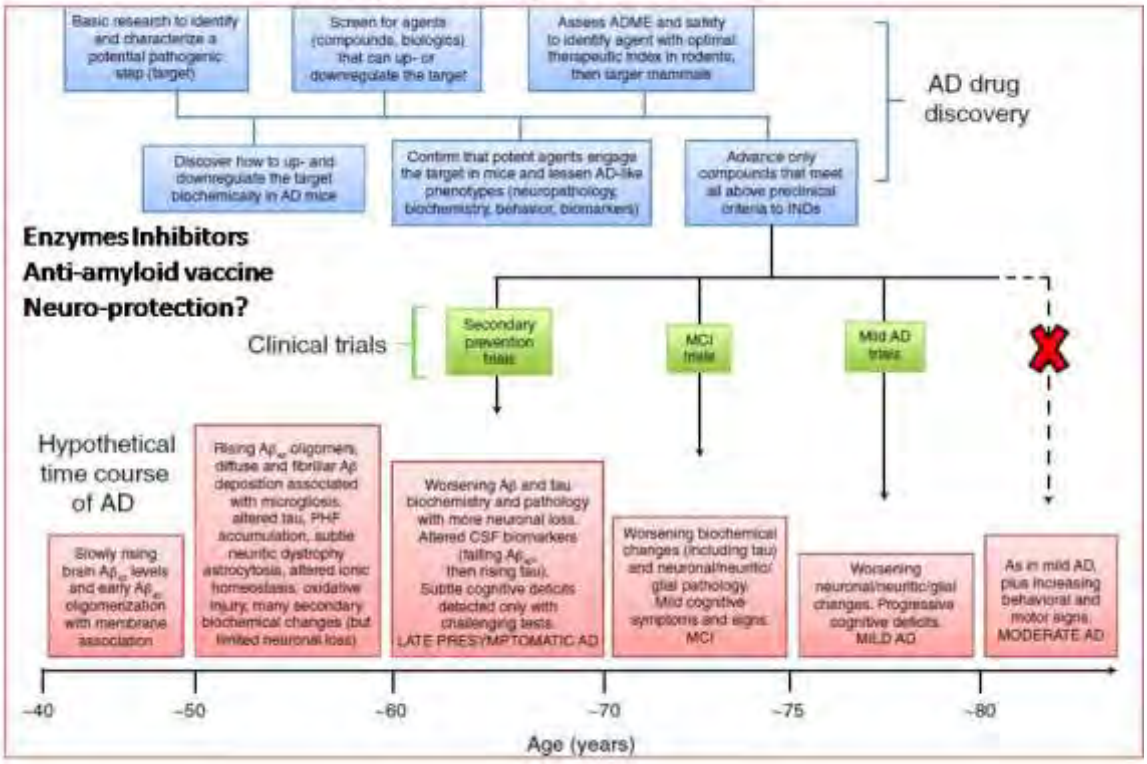
Improve scores on psychometric scales (equivalent of the natural deterioration over 3 months *(Lancet June 23, 2004)*

Occasionally benefit behavior and activity of daily living

- Have dose dependent reversible Gastro-intestinal adverse effects
- The mechanism of action might be
  - Delay of intra-synaptic Ach degradation
  - Neuro-protection
  - Decreased amyloid deposits

The occasional irrationality of the current Rx

Drug Development for AD



Age-dependent success

3 years:	not wetting your pants
10	having friends
18	having a driver's license
20	having sex
35	having money
50	having money
60	having sex
70	having a driver's license
75	having friends
80	not wetting your pants

"Age is not a particularly interesting subject; anyone can get old. All you have to do is live long enough." - *Groucho Marx*

Getting old is not so bad, considering the alternative." *Maurice Chevalier*

European College of Neuropsychopharmacology
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Republic of Moldova 2011

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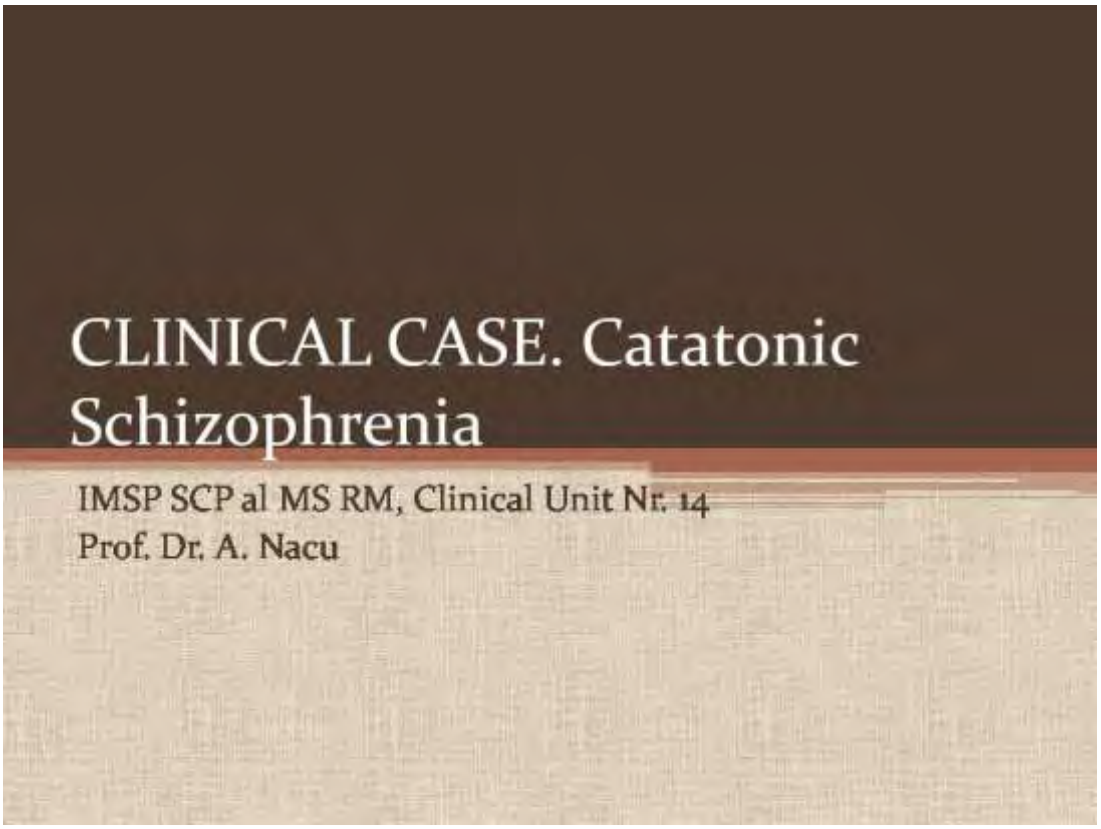

Local Organizer: Dr. Sinita Eugenia tomtit_bird@mail.ru

General data

- The female patient P. Iulia, 1977, mun. Chisinau,
- Inpatient, Acute Pschosis Unit nr. 14
- Psychiatric dispensary registration from 2003, after the first hospitalization. 5 hospitalizations.

DIAGNOSIS: CATATONIC SCHIZOPHRENIA. Catatonic agitation syndrome.

Anamnesis

Epidemiological and allergy data favorable. Mother was weird in behavior, relatives tell about lack of emotional attachment of the mother towards her child. Mother was not treated by psychiatrist. In 2009 dies, colonorectal cancer. The patient is the only child. Early development without any particular features. Was communicable, calm, active, friendly, attentive. Studies: 10 years school, Pedagogic University. Works as Laboratory Assistant. Not married, no children.

Catamnesis

After the last hospitalization in 2000 (2 months long, including Intensive Therapy Unit, the cause not being clear – neuroleptic malignant syndrome?) was living with father and paternal grandmother. Daily **clozapin 25 mg/day**, was feeling well. From 2005 – till 2010 did not come to psychiatrist for usual control visits. In august 2010 the patients estate has changed: became agitated, did not manage to find a place, was constantly moving, repeated the words of other persons addressed to her, did not sleep. Is hospitalized.

Father.

From the communications of the medical personnel – fathers behavior during the visits is suggestive for the presence of intimate relationship with the patient. Father replies that this is not true.

The evolution: 1st day of hospitalization

Is orientated in time, space and her person. Does not stay at one place, exterior – not arranged properly. Answers are not related to questions, repeats doctors words and gestures. Tells psychiatrist that he know him, reveals details of "the first meeting". Is agitated, jumps, cries, tells poems. Emotional estate is mostly depressive. Attention perturbed. Critical attitude absent. Appetite present, sleeping troubled.

2nd week: Oneiroid Estate

- After one week in Unit, the patient reveals that she does not sleep, but is in "Paradise", and "sees, that everyone is there, including doctors from the Unit". This lasts 3 – 4 days, disappears on higher clozapine doses.
- The patient tells that everyone "is yellow and is dead", including herself. Medical assistant reports that the patient frequently tells that she dies and then gets back to life.

Actual estate

Is orientated in time and space. Knows that she is hospitalized, can tell some dates with approximation. Is accessible to verbal contact, answers questions. Repeats doctors words in stereotype manner. Tells that she is afraid of death and of not seeing her father again. Spontaneously says that psychiatrist is her father , or, seeing another patient says "look, father has come". Tells poems made of words, with correct rhythm and without any logical links. Clear periods of motor agitation and motor inhibition. Repeats another persons gestures. Medical personnel reports that the patient sleeps all night, although the patient tells that she just "stays in bed" and does not sleep.

Treatment evolution.

- 1) **Typical antipsychotics** (chlorpromazine, haloperidol, levomepromazine) – neuroleptic syndrome that is hard to differentiate with stuporous estate.
- 2) **RISPERIDONE** – at doses of **4 mg/day** sdr. Neuroleptic: muscular hypertonus, deglutition troubles, walking troubles. FEVER 37,5 - 12 hours.
- 3) **CLOZAPINE** – dose of **350 mg/day 4 weeks the same psychic estate**. Critical sense appears for a short period of time: the patients does suicide attempt, recognizes that she is hospitalized, and that "she will die here".
- 4) **OLANZAPINE** – 20 mg/day. The same estate. Clear periods of stuporous and agitation estates

DISCUSSIONS

- Diagnosis
- Catatonia as a syndrome
- Treatment: discussion of the current treatment, propose a treatment plan.

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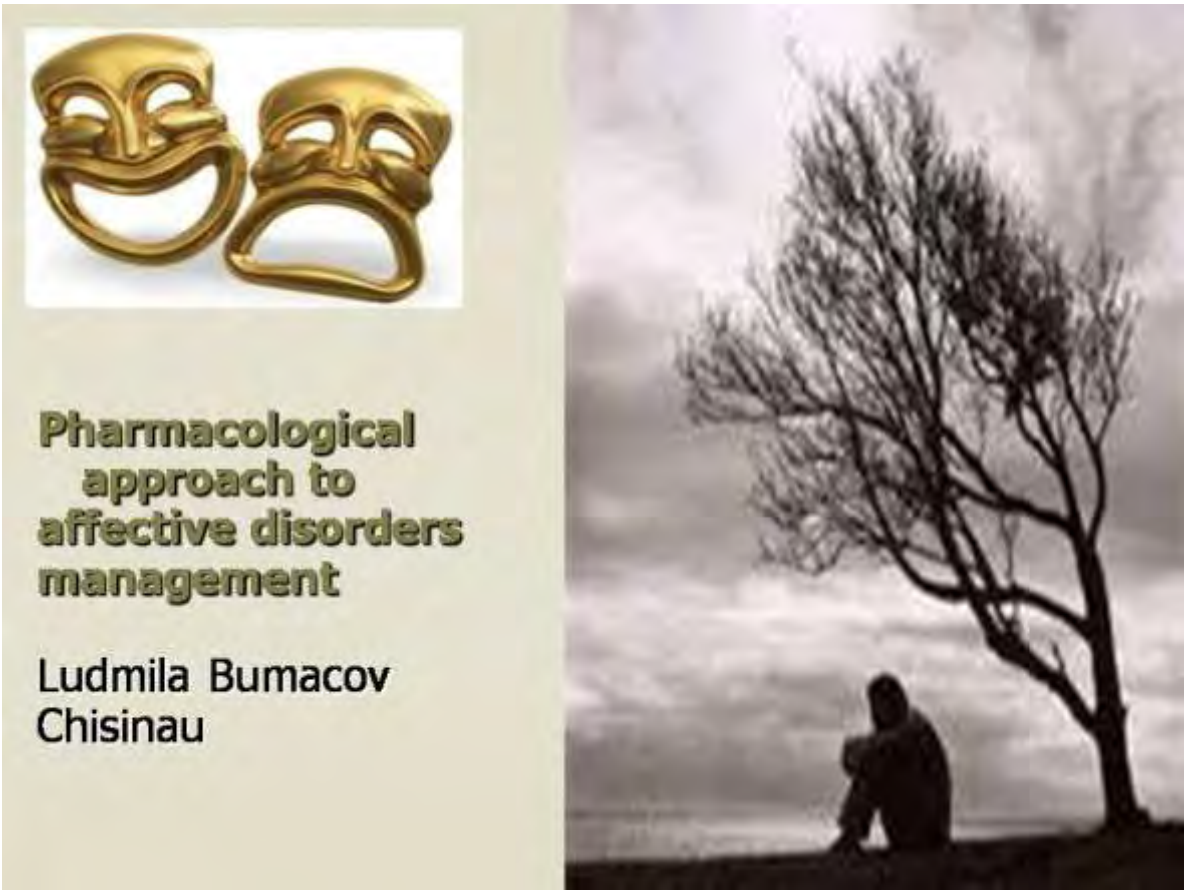
Conf. Dr. Ludmila Bumacov, Associate professor; clinical pharmacologist ; neurologist

Member of Bioethical Comity

Member of Expert Comity of Academy of Science (projects evaluation)

Member of Comity for Comity Accreditation and Evaluating of Medical Institution

Member of Expert Group for drug registration.



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What do they have in common?






Affective disorders

Presently, the goals of treatment are:
-Reduction in symptoms;
-Decreasing the frequency or preventing future episodes;
-Optimizing overall functioning,
especially during episode intervals.
- Treatment thus may be thought
of as having three stages:
acute, continuation and
maintenance.

Haw to treat ?

Which are the general principle
of correct drug choice

Pharmacological approach

Appropriate Pharmacological treatment

- ***Depend on:***
- **1. Disease properties**
- **2. Patient's properties**
- **3 Pharmacodynamic and pharmacokinetic properties of the drugs**

1. Disease properties

- Getting an accurate diagnosis: (correct assessment of mood disorders - differential diagnosis should be made)
- The onset of mood episodes (acute or insidious)
- Aetiologi- genetic or organic factors
- The type, phase and severity of the illness – acute, chronic ; BP I, BPII, Cyclothimia, unipolar depression.

- Stage of the affective disorder the patient is experiencing:

- manic episodes – (with or without psychotic symptoms);
- Depression – (mild, moderate, severe, typical, atypical)
- cycling between manic and depressive states.
- MDD symptoms (panic syndromes, anxiety, sleeping problems, eating disorders, suicide intentions etc.)
- Severity of the illness (milder, moderate or severe cases)

2. Particular patient characteristics

- Genes - Pharmacogenetics

  Genes can impact on medication effects in a variety of ways, including changes in drug metabolism, biodistribution, in varying disease neurobiology and in susceptibility to side effects.

  Drug metabolism categorization is based on hepatic CYP2C19 and CYP2D6 drug-metabolizing enzyme genotypes. According to this:

- *88% of H.sapiens* metabolize most drugs at the same rate and are labelled *extensive metabolizers*. Most of these people receive their medication based on their weight in kilogram to achieve a therapeutic range.

Genes - Pharmacogenetics

- *10% of H.sapiens* are known as *poor metabolizers (PMs).* most of these 10% metabolize drugs so slowly that *significant side effects occur* and they are taken off their medications or they stop them on their own.

  PMs may actually reach toxic levels of medications, often at relatively low clinical doses.

- *2%* have a different genetic architecture; they complain of absolutely no improvement after taking medications because they rapidly metabolize the medication *as ultra-rapid metabolizers (UMs).* Clinicians may mistakenly try a new medication with the UMs in the belief that they were treatment refractory to that particular medicine.

Patparticular patient characteristics

- There are also intermediate metabolizers who are heterozygous in their relevant genotypes and whose activity varies greatly.

  The four categories affect psychotropic dosing regimens.
- Impact on brain neurochemistry (alcohol and drug abuse; CNS diseases; trauma; medications).
- Co-morbidities (major depression and generalized anxiety, somatic and neuro vegetative symptoms)
- Pharmacological agents used for the treatment of somatic disorders (diuretics, antidiabetics, anticoagulants, NAID, glucocorticosteroids etc.)

Patparticular patient characteristics

- Previous treatment (efficiency, inefficiency; previous episode of an unacceptable side effect or therapeutic failure);
- Age - Age specific indications for adolescents, adult or senile people);
- Sex (male, female)-*drugs avoid in young women; in males*
- Body weight (*some drugs produce wight gain*)
- Patient Satisfaction and Compliance-*Major barriers to treatment adherence are thought to include the complexity of modern medication regimens ; poor "health literacy" and lack of comprehension of treatment benefits, the occurrence of undiscussed side effects, the cost of prescription medicine, and poor communication or lack of trust between the patient and his or her health-care provider . (Improvement of patient compliance through the use of packaging solutions through dialogue not monologue; Developing strong patient relationships etc.)*

3. Drug properties

- ***Pharmacological groups Choice according to disease peculiarities and drugs characteristics (efficiency, inoffensivety , adaptability of dosage regimen and cost)***
- Mood stabilizers : Lithium or Valproate or Lamotrigine or Carbamazepine or combination;
- Antidepressants :

-Tricyclics-TCAS -(Imipramine, amitriptyline) or -Second generation - Amoxapine, maprotiline (resemble the structure of the TCAS); or

Trazodone and bupropion (distinctive) or

-Third generation -Venlafaxine, mirtazapine, nefazodone, and duloxetine: or

- Selective serotonin reuptake inhibitors

SSRI- Fluoxetine, fluvoxamine, sertraline, paroxetine; or

-Monoamine oxidase inhibitors (MAOIs)

-*irreversible* – Phenelzine, tranylcypromine, *or*

-*reversible* – Moclobemide; or

-The novel antidepressant Agomelatine,

-a melatonergic MT(1)/MT(2) receptor agonist with serotonin 5-HT(2C) receptor antagonist activity.

- Antipsychotics :
- Typical: *phenothiazines* :Aliphatic derivatives (eg, chlorpromazine)- intense sedative eff, moderate antipsychotic, minor extrapiramidal eff.
- *piperidine derivatives* (eg, thioridazine) – *moderat sedative; intense antipsychotic and extrapiramidal eff.*
- *or piperazine derivatives* (flufenazine, perfenazine) all effects are moderate.
- Butyrophenones - Haloperidol,droperidol – very potent *antipsychotic and intense extrapiramidal eff, moderate sedative or*
- *Thioxantenes* – Chlorprotixene, thiothxitene - there are pharmacodinamic differences between drugs.
- Atypical) - Risperidone, quetiapine, olanzapine - potent *antipsychotic (against negative symptoms) without extrapiramidal eff, moderate sedative;*
- OR Combinations of drugs: Lithium + Valproate; Lithium + Antipsychotics; Lithium + antidepressants etc.
- Antidepressant + Mood Stabiliser; Antidepressant + Atypical Antipsychotic (AAP); SSRI + low-dose AAP (short term only)
- *antidepressant treatment can provoke rapid cycling*

Pharmacological approach

- **Depend on: acute, maintenance or prophylactic psychopharmacological treatment;**

- *Pharmacodynamics* - biochemical and physiological effects of drugs on the body (what the drug does to the body)
  - mechanism of action, (on, neuromodulator receptors, neurotransmitter receptors, Interaction with ion channels etc.)
  - pharmacological and clinical effects,
  - indications, clinical contraindication
- *Pharmacokinetics* : what the body does to the drug
  - absorption,
  - distribution,
  - T1/2 - A drug will accumulate in the body when the dosing interval is less than the time needed for the body to eliminate a single dose.
  - metabolisation,(some of drugs induce hepatic enzymes, thus lowering plasma levels and requiring an upward dose titration;
- -excretion – renal, biliary, and fecal

- *Benefit /risk* -*Clinicians must assure that the amount of benefit clearly outweighs the amount of risk. Only if there is favorable risk benefit ratio, a treatment may be considered apropriate.* Specific side effects and treatment complications should determine the choice.
- *Length of the treatment*: (short or long-term: The therapeutic effect of antidepressants is evident after at least two weeks and therapy should be administered over the course months; Maintenance treatment, can last for decades)
- *Dose* (How much drug) *Dosage regimen* (How often will be the drug given) according to the therapeutic window (the amount of a medication between the amount that gives an effect (effective dose) and the amount that gives more adverse effects than desired effects)
- *Empirical* Employed when the serum levels is not proportional to the clinical outcome.

Pharmacological approach

- *Kinetic /* therapeutic & toxic effects are proportional to the plasma conc. of drug at the receptor sites or amount of drug in the body
- The maximum dosage recommended by regulatory authorities)
- *Route of administration*
- *Switching drugs* (If a patient does not respond to the prescribed treatment after 3-4 weeks, a change of treatment is necessary).
- *Options* include the following:
- a. Increasing the dosage to the highest tolerated or permitted by labeling
- b. Switching to another drug within the same pharmacologic class (antidepressants) .
- c. Switching to another agent from a different class
- *d. Combining drugs from different classes*

Drug-interaction

- *Drug-drug interaction (DDI) occurs when the effectiveness or toxicity of one medication is altered by the administration of another medicine that is*
- *Patients on > 6 drugs have an 80% chance of a drug interaction. (The elderly are more prone to drug interactions)*
- *High risk drugs include drugs with a narrow therapeutic index (*antidepressants, carbamazepine, Lithium)
- *Pharmacodinamic* (due to competition at receptor sites)
- *Pharmacokinetic* (one drug affects the absorption, distribution, metabolism or excretion of another drug.
- (Combinations of psychotropic drugs, *contraceptive,* OTC etc.). *Eg. Significant interactions valproic acid / carbamazepine + tricyclic antidepressant; Lithium + SSRI both increase serotonin levels; carbamazepine /macrolides; Lithium + thiazide diuretics (increases toxcity of lithium)*

Drug monitoring efficacy and inoffensivety criteria

- Relationship of the therapist with the patient and family members
- Measurement of medication concentrations in blood - Its main focus is on drugs with a narrow therapeutic range, i.e. drugs that can easily be under- or overdosed: mood stabilisers (antiepileptics and Li; antipsychotics (if possible)
- *It identifies :* patient noncompliance, the effect of drug interactions
- *Helps* to tailor dosages to fit the current needs of the specific patient.
- *Clinical observation* - efficacy, side effects (patient tolerability)
- Tests such as BUN, creatinine, and liver panel to check kidney and liver function

Acute seisure's structure in neurological emergency service of National Scientific and Practical Emergency Medicine Center

Neurologist E. Vâlcu, Ph.d. in neurology St. GROPPA

Epilepsy is a major health problem in Moldova, but the incidence studies are rare. This study was undertaken to determine the structure of acute seizures in Chisinau. The study was conducted according to appeals to the neurologist in the Emergency Medicine Department (EMD) of NSPEMC, during the years 2008-2010. A total of 1856 cases were detected during this period, from 186,587 patients that were served in the EMD. The study resulted in a higher proportion of the age group 41-50 years. This rate was higher than many developed countries, but lower than in developing countries. Metabolic causes were most commonly observed factor presented. There was a weak variation rate of acute seizures during the study period.

"Psychotherapy in the complex treatment of neurosis at children and adolescents"

Leasoc Tatiana

The study is based on the clinical-pathopsychological, catamnestic and statistic research of 140 patients (105 boys and 35 girls) aged from 5 to 17 (10,83 ± 0,26) with a large scale of neurotic disorders (psychosomatic disorders – 41 patients, anxious-phobic, obsessive and depressive disorders – 25 patients, behavioural – motor disorders - 74 patients). The clinical peculiarities of the neurosis were investigated at the various stages of its appearance and development including the prenosological stage and the symptoms in the catamnesis (17,5 ± 2,3 months). There were applied the methods of psychoanalytically oriented psychotherapy that were applied individually - 47 (33,6%) patients, in family therapy - 44 (31,4%) patients and in a group with elements of Gestalt therapy, psychodrama, cognitive-behavioural (feedback) psychotherapy - 15 (10,7%) patients. The methods of psychotherapy were applied in accordance with personality, capacity of autoanalysis of the patients. The data analysis of the clinical-pathopsychological investigations of the patients (pattern method, the Eysenck H. survey, Eydemiller E.G. survey), the data of psychotherapy of the patients established at the basis of the neurotic symptomatology the intrapsychic conflict and psychological benefits caused by the disorder that have tracked the close connection with the peculiarities of the family functioning, education and the parent personalities. While comparing the effect of the different types of treatment such as complex treatment (psychotherapy and pharmacotherapy) – 78 (55,7%) patients; psychotherapy – 22 (15,7%) patients; pharmacotherapy (test group) – 40 (28,6%) patients, there were identified the increase of the effect stability in the differential use of the psychology methods. The combination of individual, group and family psychotherapy increased the efficiency of the treatment of the patients as it is facilitated the analysis of the psychological aspect of the neurotic disorder in the family environment and intrapersonal relationships. The pharmacotherapy administration was expedient in cases of acute neurotic symptomatology at the stage of preparing for the psychotherapy realization. The received data allowed identifying the algorithm of the application of the complex treatment in specific psychopathological conditions and measures of psycho-prophylaxis, which includes especially family psychotherapy.

Parental rejection perceived in the childhood and its role in the development of depressive disorders in the adulthood

Vladimir Sterpu

The influence the phenomenon of parental rejection perceived in the childhood by the depressive patients was assessed. The group of 126 patients with an ICD-10 diagnosis of depressive disorders (F 32 - Depressive episode, F 33 - Recurrent depressive disorder, F 34 - Persistent affective disorder (F34.1 Dysthymia)) were studied.

Severity of depression was evaluated according to the clinical scale HDRS (Hamilton M., 1960). To assess the parental rejection perceived in the childhood the PARQ questionnaire (Rohner R., 1990) was used. Analysis of pathological traits of personality was performed by the Mini-Mult questionnaire (Kincannon J.C., 1968).

The presence of negative correlation between perceived parental warmth in childhood and pathological traits of personality such hypochondria, depression and psychasthenia. Excessive parental control perceived by respondents is correlated with paranoid personality. It was revealed the correlations between depression and some pathological traits specific for personality disorders mentioned above. A positive correlation between depression and rejective style of parenting was shown.

Latent Suicidal Behavior Becoming "Residual Negative Symptomatology" in Neurosis.

Sinita Eugenia

Clinical and psychological research of a lot of 30 patients suffering diverse psychic non-psychotic pathology (neurosis, stress-related, depression, adaptation trouble with depression and anxiety, organic cerebral pathology, epilepsy), refering to the life quality index, motivational level and the importance of necessities subjective appreciation by the patients, allows to name three cathegories of persons performing latent suicidal behavior: (a)„lack of motivation for life itself" – I don't want and I can not"; (b) „escapism – I want, but I can not", (c) „capricious latent suicide behavior – I can, but I do not want". Latent self – distructive behavior becomes a major factor of handicap increase in non – psychotic disorders, determining poor life quality, low life expectancy, high rates of accidental deaths (mostly caused by the lack of the motivation for life) among the chronic out-patients suffering various neurotic conditions. The prospective observational study design is presented. Its realization would allow to study the latent suicide phenomena, its typology, clinical manifestations, diagnostication criteria and thus would allow to determine possible therapeutical interventions.

Correlation analysis of anatomical localization of epilepsy and cognitive – intellectual functions in children."

Dr. Saracuta Victoria,

The clinical observational study was performed in 2008-2010 on a group of subjects: 82 children with epilepsy or epileptic syndrome in public health institution Clinical Hospital of Psychiatry Chisinau, revealing the dependence of cognitive and intellectual functioning in children suffering epilepsy, such as attention , memory, associative processes and general intelligence, possible mental retardation and dementia caused by the psychiatric condition on epilepsy activity localization. As a result, all the patients in the study lot have been established with normal or decreased one or more intellectual functions. Correlation between the anatomical localization of epileptic cortex activity and the affected intellectual and cognitive function were highlighted. The study has also revealed the relationship between the pathology duration and the intensity of cognitive decrease.

THE COMPLEX PROPHYLAXIS OF THE EARLY ALCOHOLDEPENDENCE RELAPSES

Cosciug Ion , Deliv Inga

In this study, which included 299 patients, it has been studied the relation between early alcoholic relapses in patients in therapeutical remission and the structure and depth of the affective, hormonal disturbances and grade of pathologic attachment towards alcohol; the influence of acupuncture in combination with oxytocin upon the dynamics of the psycho-endocrine disturbances and pathologic attraction towards alcohol in dependence upon the functional status of the hypothalamic - hypophyseal - suprarenal system; the possibility of prediction of early alcoholic relapses by means of the application of stepwise cluster analysis of the factors, which provoke disease relapses.

To achieve this aim, clinical methods have been used, along with clinical-psychological tests of anxiety, depression, dysphoria levels, and radioimmunological methods of adrenocorticotropine, prolactin, cortisol blood levels measurement and other methods.

There has been revealed that the development of early alcoholdependence relapses is determined by the structure and depth of affective disturbances, by the patient's hormonal status and by the degree of pathologic attachment towards alcohol.

There has been shown for the first time, that in the case when affective disturbances of the anxietal and depressive type prevail, without correlation with their degree, the function of the stressogenic system is damaged, whereas when dysphoric disturbances prevail, both stressogenic and antistressogenic systems are damaged.

There has been elaborated a method of psycho - endocrine changes correction and of early alcoholic relapse prophylaxis, by means of a combined use of acupuncture and oxytocin.

There has been proposed an original and simple method of an early prognosis of alcoholic relapses.

EFFICIENCY OF TREATMENT IN SCHIZOPHRENIA.

Garaz Grigore

The need of objectification in the treatment efficiency was always a challenge for psychiatrists; the following study (which included 41 patients, with the Diagnose of F20 – Schizophrenia, monitored from the first 72 hours till 2 weeks) highlights the way and the practical advantage of the scales (PANSS, BPRS, CGI-S) as efficient and valid tools in achieving this goal. Thus it was possible to prove the need of psychotherapeutic work after achieving a score of 30-40% reduction in the PANSS dynamics and discovering the dilemma of difference in treatment efficiency of patients from different backgrounds (rural vs urban). The hypothesis that abusive consume of alcohol impacts the dynamic of clinical recovery is indirectly confirmed, thou there is need in more research.

ORGANIC PERSONALITY DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER: SIMILARITIES AND DIVERGENCES

D. Paladiciuc, N. N. Oprea, V. Şveţ, Gh. Cărăuşu.

The ultimate goal of this research is to analyze the factors that precede and have common behavioural symptoms (impulsiveness, hyperactivity, inattention) in organic personality disorder and attention-deficit/hyperactivity disorder (ADHD), in children hospitalized in the Juvenile wards of Psychiatry Clinical Hospital. In this research are analysed and explored heredity, family relationships, personal pathological history, paraclinical changes and complex therapeutic approaches (medications and psychotherapy). To highlight these factors were used data from the literature of these pathologies and analyzed a group of 7 children from the ward with a complex symptomatic taking in consideration the hardness of nosology description in growing children and teens. Approaching Attention Deficit Hyperactivity Disorder with its increased co morbidities and Organic Personality Disorder which involves a neurological symptomatic, both first and second case meet the diagnosis of Minimum Cerebral Dysfunction. Study data analysis highlighted on the one hand that these children require care, and on the other hand that they get tired quickly, which confirms organic elements involvment.

CANNABIS USE IMPACT AMONG PATIENTS AT THE FIRST EPISOD OF PSYCHOSIS

Alisa Cretu

The aim of the present study was to investigate the relationship between cannabis use and psychosis onset; to study the psychosis clinical characteristics and the evolution of psychotic symptoms in cannabis users. In odder to achieve this purposes, we have investigated and observed, both at the hospitalization, on the 10-13th day and as well on the 20-23-th day of treatment, 22 patients, aged from 25,7 ± 1,8 years, diagnosed with the first episode of psychosis, 13 (59,0%) of them were patients with a history of cannabis consumption and 9 (69,2%) patients never used cannabis. The study showed that as a result of cannabis consumption the onset age of psychosis it is earlier, the clinical manifestation are more severe, showing mainly negative symptoms as well as slightly depressive symptoms. The decrease of psychotic symptoms is much slower for cannabis users.

Giant intracerebral aneurysm of basilar artery: presentation of a clinical case

Stanislav Groppa[1], Valeriu More[2],Vitalii Cozac[3]

The importance of cerebral aneyrisms pathology dramatically increased with the progress of accesability to modern diagnostics' methods. Cerebral aneurysm is considered giant if it is 25 mm and more in size. We present a case of 5 years' term outcome of unrupted giant intracerebral aneurysm of basilar artery at a male patient aged 47. The findings and a review of literature suggest that these types of cerebral aneurysm often present as mass effect lesion and thromboembolic complications rather than with ruptures.

Nonepileptic seizures under levetiracetam therapy.

Ignatenco A, Arzy S, Ghika J, Genoud D, Kaplan PW, Groppa S, Seeck M.

We describe two patients with epilepsy who presented with nonepileptic seizures (NES) when started on levetiracetam (LEV), which disappeared or significantly decreased when LEV was discontinued. NES are traditionally attributed to psychic trauma often after physical or sexual abuse, whereas the psychiatric side effects of levetiracetam largely encompass depression, hallucinations, and psychosis. We conclude that NES are a rare side effect of LEV treatment and part of the spectrum of behavioral changes observed with LEV treatment.

Melatonin – the future of psychopharmacology?

Mitu Violeta

Clinical investigations held recently have revealed a lot of data concerning the structure of melatonin, its synthesis, metabolism, excretion processes and of course, its impact in biological systems. These data are presented in current scientific work of synthesis, while the analysis of these data would allow us to find the answer to the following question: is melatonin, being the main neural and endocrine regulatory factor, a universal therapy remedy of the future?

The specific of clinical psycho-diagnostic for adults

Gabriela Popenco

Clinical psycho-diagnostic means not only to collect relevant information about a person, specially from pathology, but means recognition of a desease, strating from the description of the doctor and other professionals. Denotes an activity of knowledge and refers specifically to the knowledge of psychological factors of the human subject, with relevance to health and disease. Clinical evaluation is the process through which clinical psychologist obtain relevant information about the patient's mental status after performing a clinical psychological examination.

Psychological and clinical examination offers the information and psychological understanding of the functioning of a subject by focusing on emotional state, emotional, cognitive, IQ measurement, behavioral, anxiety, psychological evaluation of the degree of discernment, etc.

All together the results of psycho-diagnosis means, implicitly or explicitly required for intervention and corrective solutions.

Paranoid schizophrenia debute: evaluation and prognosis.

Igor Nastas, Larisa Boronin.

The performed study is based on the identification of several criteria selected statistically, including two groups of pacients (the first including 100 patients with schizophrenia debute at the age before 25 years, the second including 100 patients with schizophrenia debute at the age older than 40 years). 135 statistic items have been analyzed, among them statistically important: exaggerate effort during military service, insomnia, psychiatric genetic conditions, maternal psychiatric conditions, paternal psychiatric pathology, sense of lack of vital tonus, cranio-cerebral trauma with consciousness loss, personality type (impulsive, schizoid, anancast, hypertimic), stress during working activity in other countries, including migration, thoracic cenestopathy. The discriminant function (F) was calculated, that confirm the phenomena of residual estates apparition based on the selected criteria in 78.26% cases in 3 year old period after de paranoid schizophrenia debute.

Catatonia with oneiroid estates: differential diagnosis and psychopharmacology

Lucia Carp

The clinical case of a young woman suffering catatonic schizophrenia, and passing through different estates that are very hard to differentiate: oneiroid, neuroleptic syndrome, catatonic sub-stuporous estates. The psychopharmacological approach used was a complex one, passing from typical first generation antipsychotics to Clozapine, as well as other treatments (mood stabilizers, antidepressants, ECT discussion in hospital conference dedicated to this difficult clinical case).

COMPULSORY OUT – PATIENT TREATMENT IN PATIENTS WITH PARANOID SCHIZOPHRENIA.

Catrinici Carolina

Anti-social behavior of the patients, suffering mental disorders, remains one of the most important issues for general and forensic psychiatry, and for the society as a whole, and it is particularly important in terms of prevention of the illicit behavior presented by the psychiatric patients, who have manifested it in their anamnesis. For preventing the accomplishments of such offences, the analysis of leading psychopathologic symptoms in of high necessity, as well as the analysis of the motivational side of the behavior of the subject, and evaluation of macro-and micro-social factors, that might become determining for the social dangerous acts. The combination of the significant changes in social interactions during the last period of time, as well as in the social structure, and other complex factors, that are involved in the formation of

socially dangerous motivation and behavior in patients with schizophrenia, should be analyzed in their correlation with the natural evolution of the disease and the main psychopathological syndrome. It is universally-adopted that the system of prevention of socially dangerous acts of mentally disordered patients is mainly realized by compulsory treatment in special institutions, and the organization of therapeutic- rehabilitative work outside the hospital, with application of a compulsory dispensary observation and treatment is in the process of implementation in Republic of Moldova. Today it is necessary to perform the study and analysis of social-situational factors, social functioning of the patients, who committed repeated illicit social dangerous acts, study of the influence of macro-and micro-social sphere, that could become cause of disadaptative behavior and accomplishment of antisocial actions or facilitating conditions. This complete multilateral approach would allow to develop practical recommendations, Protocols, legislative acts modifications, and as the result if would become possible to achieve the reduction of repeated social dangerous acts, that is very important both socially and medically.

"Multilateral approach in the therapy of autistic children (4 -7 years old)",

Jana Chihai

Today, we got more and more families with autistic children asking for help. Autism is part of a larger group of disorders that is referred to as autism spectrum disorders. The symptoms of autism can range from very mild to quite severe. Children who are diagnosed with autism often see numerous specialists several times a week for various types of therapy. Very little is known about effective treatments for autism.

Traditional therapies use behavioral therapy, such as ABA, and intend to address outward behaviors and to teach concrete skills. Most practitioners recommend that treatment for autism should also include additional therapies as necessary, including Social Skills Therapy, Play Therapy, Occupational Therapy and Psychoanalysis.

Psychoanalysts see autistic children from two to four times a week, typically with a parent in the room. They also counsel parents once a week separately to keep them abreast of progress. In a nutshell, the analyst serves as a sensitive translator who attempts to decode what the child is thinking, feeling and doing. .

Most specialists offering something called "play therapy" to children with autism are actually providing something akin to Floor time Therapy. Floor time is a play-based technique which builds on autistic children's own interests or obsessions to develop relationships and social/communication skills. The therapist will get down on the floor with your child and truly engage him through the medium of play.

Personality profile of the patients' family members affected by schizophrenia

Vadim Aftene, *Anatol Nacu*

The statistical analysis of the СМОЛ questionnaire (В. П. Зайцев, 1981) data on the patients' family members affected by schizophrenia revealed certain specific features of character. The study was performed on a group of 48 persons, members of schizophrenic patients' family, both from urban and rural areas. The data show significant deviations in profile of the patients' family members (the schizoid scale values above the limit of normality). Patients' father personality pattern presents passive,

withdrawn attitude (scales of depression, hysteria and paranoia values beyond of normality). Identifying characteristics of psychopathology in family members allows the recognition of patterns of behavior involved in family conflict situations with repercussions on the evolution of the disease.

CLINICAL RESEARCH PROJECT: COGNITIVE PROCESSES PARTICULAR FEATURES IN CHILDREN WITH AUTISM.

Anna Albu

Autism in children – is a variant of a psychophysical disontogenesis, that manifests itself by lack of harmony in psychic development, characterized by the combination of a rapid development of some psychic functions and features, as well as by the retardation in the development of the other functions in the same time. Autism in children can be diagnosed in early childhood, starting with birth, when the unproportional psychic development can be observed.

Actuality of the research. Revealing the influence of autism on cognitive processes manifestation in children, in order to create a correct selection of methods of psychological correction for these children and to evaluate the efficacy of selected psychocorrectional programs.

The object of the research. Cognitive processes in autistic children with retardation.

Methods and research process steps. The research takes place in Clinical Hospital of Psychiatry, Chisinau, starting with February, 2010 – estimated end: 2012.

The research includes:

- Children diagnosed with autism, aged 7 – 10, divided in 2 groups: experimental and control groups.
- As a structure: 20 patients, 10 males and 10 females aged 7 – 10.

Practical Methods:

1. Wechsler Test
2. Seguin boards
3. Method "Learning 10 words" A. R. Luria
4. Method Rossolimo
5. Simple analogies
6. Comparison of notions

The role of regional infiltrations in pain management of Thoracic Outlet Syndrome

I. Andronati[1], S. Plesca[1], M. Sangheli[2], L. Chetrari[1]

Background. The aim of this study was to establish the role of regional injections in processing of evoked pain and muscles tension in patients with neurogenic type of thoracic outlet syndrome TOS.

Material and Methods. In this study were selected 28 patients who suffered from neurogenic type of TOS and were resistant to standart treatment with drugs and physiotherapy. All patients underwent X-ray, EMG and MRI exams in order to make differential diagnosis with other underlying medical

conditions that may be confused with TOS. Adson's maneuver, Wright test, Roos stress test and palpation of scalenus were used in this study.

Results. Manual examination before the treatment reveled cervical muscle spasm, tenderness of brachial plexus in the supraclavicular area and shoulder region. The selection of points for injections was made based on anatomical peculiarities of brachial plexus and muscles insertion. The course of infiltrations with lidocaine and steroids included 3-5 procedures starting with the anterior scalene muscle, followed by supraspinatus muscle (block of the suprascapular nerve) and the place of the inseration of the pectoarlis minor and long head of biceps brachii muscles. Results evaluation (Visual Analog Pain Scale, McGill Pain Questionnaire) showed: in 75% of patients occured stable remission, 18% - pain episodes of lower severity; 7% - without results.

Conclusions. These results appear to demonstrate that the treatment by regional infiltrations may be helpful in alleviating symptoms in patients with TOS being necessary to study previously the pain pattern, to reveal the secondary involved muscles.

Video-EEG monitoring in epilepsy and epileptic syndromes.

Bunduchi Andrei

Aim of the study: To detect epileptic activity with appreciation of seizure type and form of epilepsy.
Materials and method: 600 consecutive ambulatory and stationary patients with suspicion or diagnosis of epilepsy or epileptic syndromes, age 3 months to 60 years, underwent video-EEG monitoring on a computer system ,,Nicolet One'' USA, with 48 channels using 23 surface electrodes according to international system "10-20", with duration 1-12 hours (mean – 4 hours).
Results and Discussion: Epileptic activity was detected in 403 cases (67,2%) from 600 patients. In 197 cases (48,9%) it was detected in functional state of wakefulness, while in 206 cases (51,1%) epileptic activity was detected only during sleep. In 152 cases (37,7%) epileptic activity was generalized, while in 251 cases (62,3%) it had regional character.

RISK FACTORS FOR HEADACHE CHRONIFICATION: MEDICATION OVERUSE AND DRUG PHOBIA

Angela Jelihovschi

Together with medication overuse drug phobia could play a role in headache chronification. Several factors as age, female gender, obesity, medication overuse, anxiety and depression have been described in the literature as risk factors for headache chronification. The aim of the study was to elucidate the potential risk factors for headache chronification and to analyze the clinical features of medication overuse and phobia in chronic migraine patients. Some clinical features as young age, earlier disease onset, shorter disease duration and higher pain tolerance could help to differentiate chronic migraine patients with drug phobia from chronic migraine with medication overuse.

The specific of clinical psycho-diagnostic for pre-school children (4 – 7 years old)

Cornelia Iacubovschi

Clinical psycho - diagnostic for pre – school children provides guidelines for diagnosing a spectrum of childhood disorders. The detailed coverage provides students and professionals with important research findings and practical tools for a correct and easy diagnosis.
Here we got classification methods that and categorical methods of diagnosis. It then highlights this research is related to clinical psychology and specific diagnosis. The remainder of the text covers constructs and core symptoms of interest, diagnostic standards, assessment methods, interpretations of findings, and case studies for all of the major childhood disorders.

Subacute degeneration caused by deficiency of folic acid

Author: Surucean Gabriela

Hereby is presented a case of a 28-year old female patient, hospitalized in the Institute of Neurology and Neurosurgery with complaints of weakness and tension in the legs, gait instability and emotional lability. The disease began in 2007, by weakness in the right leg. The evolution was slowly progressive. The neurological examination detected: diminished muscular strength at the legs level - 3/5 points, hypertonus, diminished vibration sensitivity, walking stance – spastic, positive signs of Rossolimo, Bechterev, Jucovscki. Laboratory investigations were normal, except the Folic Acid which was low (2,94; N 4,5-45,8 ng/ml). At electromyography were determined the signs of the axonal damage. Cerebral MRI revealed multiple pathological findings of different sizes (0,2-0,4 cm), placed anterior to the right semioval centre. Cervical and thoracic MRI revealed a diffuse narrowing of the spinal cord. Therefore, were established the following neurological syndromes: 1) upper motor neuron syndrome (spastic paraparesis, pathological reflexes, pyramidal hypertonus); 2) lower motor neuron syndrome (diminished patellar reflexes, characteristic changes on EMG); 3) sensitivity impairment syndrome (diffuse reduction of vibration sense); 4) gait disorder syndrome (spastic gait + sensory ataxia); 5) MRI's changes syndrome.

Particularities of diagnosis of mitochondrial encephalopathy

Authors: Catherine Chele, Buducea Rodica, Angela Jelihovschi

Objectives : To appreciate clinical manifestations for suspecting diagnosis of mitochondrial encephalopathy and to implement of a diagnostic algorithm.
To achieve the objectives we have outlined the following tasks:
1. Evaluation of main clinical manifestations of mitochondrial encephalopathies.

2. Approval of a plan for a diagnosis in accordance with clinical symptoms and with proposed diagnostic algorithm.

Encephalopathies are multy-systemic disturbances characterized by mitochondrial and genetic defects with hereditary transmition. The disturbances are due to respiratory oxido-reduction chain and affect internal mitochondrial membrane.

In this study were investigated 5 children with mitochondrical encephamiopathies (MELAS, NARP, MERRF, Kearns-Sayre) with different clinical forms, treated in IMSP ICSOSMC. Children were between 1-10 years. Complex neurological examination was performed in neuropediatrical clinic.

There were performed laboratory tests, including: serum creatinine, creatinine kinase, serum lactate, EMG, brain CT, MRI brain. Cerebral MRI was performed to confirm the presence of extensive demyelination process – signal that are affecting both substances as well as subcortical and the white matter of the brain. The study was based mainly on clinical characteristic signs plus MRI and muscle biopsy.

Mitochondrial diseases may occur at any age. They evolve varied, in most cases are complicated with death in first months of life or during childhood sometimes over several years, benign sometimes. Clinical phenotype can have very important elements for diagnostical orientation.

Neurological and neuromuscular disturbances that are caused by dysfunction in respiratory mitochondrial chain, were discovered in the past 30 years with increasing frequency. Mutations in mitochondries or in nuclear genome, produce an error in synthesis that is essential for energy production and metobolism. This brings to a big variety of problems in clinico-functional and diagnostical problem. The diagnosis of mitochondrial diseases is complicated with their heterogen presentation and the lack of some screening procedures or diagnostic biomarkers that are sensible and specific. Often the diagnosis is a long process and bigins with the general clinical evoluation, followed by mitobolical and imagistical screening and finally by genetic tests and more invasive biochemical and histological analisys.

Neuromyelitis Optica: Pathogenetic, Clinical and Diagnostic Aspects Review, A Case Report

Cucovici Aliona

Background: Neuromyelitis optica (NMO, Devic's disease) is a severe, inflammatory, immune-mediated and disabling disease that affects primarily young women (relapsing NMO) but either sex can develop monophasic NMO, and NMO rarely occurs in adolescents. The disease principally attacks the optic nerves and spinal cord causing blindness and paralysis. The recent discovery of a serologic auto-antibodies against aquaporin-4 (AQP-4) antigen, which is the main channel that regulates water homoeostasis in the central nervous system, has allowed early diagnosis and specific treatment of patients with NMO.

Aim: To highlight the pathogenesis, diagnosis and management of NMO based on the current scientific literature. Presenting of this case report to point out the clinical and imaging features of monophasic NMO.

Case Report: In October 2008, a 49-year-old Caucasian woman had an acute episode of severe transverse myelitis that led to tetraplegia. The patient was admitted to the hospital with progressive weakness in upper and lower limbs, numbness on the right side of the body, paresis of the right hand. In December 2008, MR imaging from the inferior third of the cerebellum to cervical spine C5 showed an intradural, intramedullary, isointense focus (9, 5 cm) with gliotic peripheral changes. MR imaging of the cervical spine showed an expanded spinal cord with signal abnormalities from C1 to C7 and heterogeneous postcontrast enhancement between C1 and C7. In January 2009, MR imaging with contrast of the cervical spine showed an intramedullary massive tumor with expanding from the medulla oblongata to the thoracic spine T1. Analysis of cerebrospinal fluid revealed a clear Colour, 3 WBC'S per mm ^{3}, protein 0,168 g/l and sugar 3, 16 mmol/l, chloride 127, 4 mmol/l. The HIV/AIDS test was negative. In March 2010, she presented with impaired vision in her left eye that worsened over the course of a few days. Ten days later, she lost vision in her right eye, so the patient has developed a bilateral blindness. The dilated fundus examination showed: narrow arteries, dilated veins, altered macular reflex, bilateral optic atrophy. The treatment with corticosteroids has not proven to be effective. In December 2010, after two years of disease onset, the patient's condition worsened suddenly is installed impaired consciousness, respiratory and cardiac arrest occurred and the patient has died.

Conclusions: The severity of NMO attacks is almost always debilitating and potentially fatal as in this case report. Our case illustrates the characteristics of the disease that meet the revised diagnostic criteria for NMO.

Cortexin in the treatment of cerebral pathology

Veronica Florea

For the treatment and rehabilitation of patients with various forms of cerebral vascular disease medications are used efficiently peptide structure, combining the nootropic, vasoactive, neuroprotective effects. For drugs in this group is Cortexin. Cortexin influence on functional and biochemical status of the central nervous system is carried out both by restoring the balance between excitatory (aspartate, glutamine, glutamic acid) and inhibitory (GABA, serine, glycine), amino acids, neurotransmitters, and as a result of influence contained in the preparation of mineral substances on enzyme activityregulating apoptosis, the antioxidant system and the functional state of dopamine, acetylcholine neuroreceptors [14].

The method organspecific diagnostics - determine the level of brain creatine kinase fraction (CK-BB) - shows that Cortexin has a direct effect on the metabolism of nerve cells [1].