The beautiful land of Moldova welcomes ECNP Seminar in October 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
**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 Summerschool 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!**

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

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celso Arango and</td>
<td>Michael Davidson and</td>
<td>Alessandro Serretti and</td>
</tr>
<tr>
<td>Anatol Nacu</td>
<td>Grigorii Zapuhlih</td>
<td>Ludmila Bumacov</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Round 2</th>
<th>08.30 – 10.00</th>
<th>Celso Arango and Anatol Nacu</th>
<th>Michael Davidson and Grigori Zapuhlih</th>
<th>Alessandro Serretti and Ludmila Bumacov</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 2</td>
<td>Group 3</td>
<td>Group 1</td>
<td></td>
</tr>
<tr>
<td>10.00 – 10.30</td>
<td>Coffee break</td>
<td></td>
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</tr>
<tr>
<td>Round 3</td>
<td>10.30 – 12.00</td>
<td>Celso Arango and Anatol Nacu</td>
<td>Michael Davidson and Grigori Zapuhlih</td>
<td>Alessandro Serretti and Ludmila Bumacov</td>
</tr>
<tr>
<td></td>
<td>Group 3</td>
<td>Group 1</td>
<td>Group 2</td>
<td></td>
</tr>
</tbody>
</table>
### Program Overview

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.00 – 14.00</td>
<td>Lunch and preparation for plenary session</td>
</tr>
<tr>
<td>14.00 – 14.20</td>
<td>Group 1 Presentation</td>
</tr>
<tr>
<td>14.20 – 14.40</td>
<td>Group 2 Presentation</td>
</tr>
<tr>
<td>14.40 – 15.00</td>
<td>Group 3 Presentation</td>
</tr>
<tr>
<td>15.00 – 15.15</td>
<td>Time to fill out the evaluation forms and preparation of awards ceremony</td>
</tr>
<tr>
<td>15.15 – 15.30</td>
<td>Short break</td>
</tr>
<tr>
<td>15.30 – 15.45</td>
<td>Awards ceremony</td>
</tr>
<tr>
<td>15.45 – 16.00</td>
<td>Concluding remark and thanks, Celso Arango, Spain.</td>
</tr>
</tbody>
</table>
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.
How to prepare a manuscript

Celso Arango

Categories

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

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

Sequence

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

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

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
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

Discussion

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

Discussion

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

Local Organizer: Dr. Sinita Eugenia
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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

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
Title

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

Keywords

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

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

The context

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

Introduction

- Context
- Study question
- Relevant knowledge on issue
Major findings

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

Formal aspects

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

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

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
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......

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
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

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
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

Peer Review

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

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!)
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

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!)
“Scientists are rated by what they finish, not by what they attempt”
How to prepare a scientific presentation

Celso Arango

Before you start

• What does the audience already know about your topic?

• What are their interests?

• Why are you giving presentation?
Before you start

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

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
Organizing a Presentation

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

Making slides

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

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

Start broad, get specific, and end broad

The middle is your original contribution

Start with the biggest questions and get progressively more specific
Focus now on conclusions
Introduction

- Context
- Study question
- Relevant knowledge on issue

Major findings

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

Conclusion and Recommendations

- Key points
- Implications
- One slide for each message
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)

Formal aspects

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

Be consistent!
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!

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.*
And do not forget to…….

Relax
Listen to what you are saying
Pace and time yourself

And do not forget to…….

Face the audience
Never underestimate your audience!
With time you will enjoy…….
How to prepare a scientific presentation

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

Treatment of Acute Psychoses

Celso Arango
Hospital General Universitario Gregorio Marañón,
Madrid, Spain
carango@hggm.es

Moldova, October 2011
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

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

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


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## 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

- **Haloperidol-treated subjects (N=132)**
- **Olanzapine-treated subjects (N=131)**

Discontinuation rates and reasons among patients

![Graph showing discontinuation rates and reasons among patients.]


Time to treatment discontinuation for any cause

![Graph showing time to treatment discontinuation for any cause.]

Local Organizer: Dr. Sinita Eugenia
tomtit_bird@mail.ru
First-Episode Patients: Lower Medication Doses Than Multi-Episode Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Modal Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lieberman et al 2005</td>
<td>Haloperidol: 4.4</td>
</tr>
<tr>
<td></td>
<td>Olanzapine: 9.1</td>
</tr>
<tr>
<td>Schooler et al 2005</td>
<td>Haloperidol: 2.9</td>
</tr>
<tr>
<td></td>
<td>Risperidone: 3.3</td>
</tr>
<tr>
<td>Robinson et al 2006</td>
<td>Olanzapine: 11.8</td>
</tr>
<tr>
<td></td>
<td>Risperidone: 3.9</td>
</tr>
<tr>
<td></td>
<td>Quetiapine: 506</td>
</tr>
<tr>
<td></td>
<td>Risperidone: 2.4</td>
</tr>
</tbody>
</table>


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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

Arago & 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.’

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

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

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

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

Placebo
Haloperidol
Olanzapine

Wright et al 2002

Risperidone reduces agitation in acute schizophrenia

Mean PANSS agitation score

Oral risperidone (2 mg) + oral lorazepam (2 mg)
IM haloperidol (5 mg) + IM lorazepam (2 mg)

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
Recovery is a multidimensional process

- Quality of life
- Control of symptoms
- Social and family interactions
- Relapse prevention
- Daily functioning
- Improved cognition
- Return to work
- Overcoming stigma

Fenton et al 1997; Lacro et al 2002

Treatment Options for Acute Mania

- Classical antipsychotics
- Atypical antipsychotics
- Lithium
- Valproate
- Carbamazepine
- Combinations
- Benzodiazepines
- ECT
### Metanalysis of Atypicals in Mania (Caparapey & Vieta, 2005)

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>N</th>
<th>Mean (SD)</th>
<th>Control</th>
<th>Mean (SD)</th>
<th>SMD (moder)</th>
<th>95% CI</th>
<th>Weight %</th>
<th>SMD (pooled)</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Lithium</td>
<td>Lithium</td>
<td>123</td>
<td>3.10 (1.83)</td>
<td>122</td>
<td>2.60 (1.83)</td>
<td>0.50 (0.06)</td>
<td>0.34 (0.1)</td>
<td>0.10</td>
<td>0.10 (0.47)</td>
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<td>Valproate</td>
<td>Valproate</td>
<td>226</td>
<td>2.90 (1.22)</td>
<td>220</td>
<td>3.10 (1.83)</td>
<td>0.13 (0.05)</td>
<td>0.35 (0.1)</td>
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<td>0.10 (0.47)</td>
<td>0.01</td>
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<td>Subtotal (Gp 2)</td>
<td>Subtotal (Gp 2)</td>
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<td>2.91 (1.20)</td>
<td>342</td>
<td>2.90 (1.83)</td>
<td>0.14 (0.05)</td>
<td>0.35 (0.1)</td>
<td>0.10</td>
<td>0.10 (0.47)</td>
<td>0.01</td>
</tr>
<tr>
<td>CGI</td>
<td>CGI</td>
<td>91</td>
<td>40 (1.83)</td>
<td>90</td>
<td>40 (1.83)</td>
<td>18 (0.06)</td>
<td>0.34 (0.1)</td>
<td>0.10</td>
<td>0.10 (0.47)</td>
<td>0.01</td>
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<tr>
<td>OLZ</td>
<td>OLZ</td>
<td>24</td>
<td>12 (1.83)</td>
<td>23</td>
<td>12 (1.83)</td>
<td>50 (0.06)</td>
<td>0.34 (0.1)</td>
<td>0.10</td>
<td>0.10 (0.47)</td>
<td>0.01</td>
</tr>
<tr>
<td>OLZ + Valproate</td>
<td>OLZ + Valproate</td>
<td>122</td>
<td>2.80 (1.22)</td>
<td>120</td>
<td>2.80 (1.83)</td>
<td>0.13 (0.05)</td>
<td>0.35 (0.1)</td>
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<td>0.10 (0.47)</td>
<td>0.01</td>
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<td>Total (Gp 2)</td>
<td>Total (Gp 2)</td>
<td>364</td>
<td>2.91 (1.20)</td>
<td>352</td>
<td>2.90 (1.83)</td>
<td>0.14 (0.05)</td>
<td>0.35 (0.1)</td>
<td>0.10</td>
<td>0.10 (0.47)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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

**At risk for adverse health outcome**
- **BMI ≥ 30.0**
- **BMI ≥ 35.0**
- Hypertension > 140/90
- Fasting cholesterol > 220 mg/dL
- LDL cholesterol > 130
- HDL cholesterol < 40
- TG > 150
- Hyperglycaemia ≥ 110 mg/dL

**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%

**At risk adverse**
- **Baseline**
- **6 month**

<table>
<thead>
<tr>
<th>Drug</th>
<th>At risk adverse</th>
<th>Baseline</th>
<th>6 month</th>
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</thead>
<tbody>
<tr>
<td>RIS</td>
<td>22.7%</td>
<td>36.4%</td>
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</tr>
<tr>
<td>OLZ</td>
<td>15.0%</td>
<td>60.0%*</td>
<td></td>
</tr>
<tr>
<td>QTP</td>
<td>12.5%</td>
<td>20.8%</td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Age</th>
<th>Sex</th>
<th>Soc. status</th>
<th>Marital status</th>
<th>Stressful life events</th>
<th>Major life changes</th>
<th>Loss of support</th>
<th>Health habits</th>
<th>Medication history</th>
<th>Social support</th>
<th>Researcher</th>
<th>Age</th>
<th>Sex</th>
<th>Soc. status</th>
<th>Marital status</th>
<th>Stressful life events</th>
<th>Major life changes</th>
<th>Loss of support</th>
<th>Health habits</th>
<th>Medication history</th>
<th>Social support</th>
<th>Researcher</th>
<th>Age</th>
<th>Sex</th>
<th>Soc. status</th>
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<th>Stressful life events</th>
<th>Major life changes</th>
<th>Loss of support</th>
<th>Health habits</th>
<th>Medication history</th>
<th>Social support</th>
<th>Researcher</th>
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<tbody>
<tr>
<td>Primary episode</td>
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<tr>
<td>Westen et al(^{1})</td>
<td>n = 150 women, ≤ 1 previous episode</td>
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<tr>
<td>Joensu et al(^{1})</td>
<td>n = 10 potential women, non-chronic</td>
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<tr>
<td>Paykel et al(^{1})</td>
<td>n = 80 in or outpatients with primary depression</td>
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<td>Fagin et al(^{1})</td>
<td>n = 87, new or chronic</td>
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<tr>
<td>O’Leary et al(^{1})</td>
<td>n = 100, 74% first episode, younger</td>
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<td>Chronic or recurrent</td>
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<td>Kupfer, Spitzer(^{1})</td>
<td>n = 76 inpatient</td>
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<tr>
<td>Joyce et al(^{1})</td>
<td>n = 84, SAE respondents</td>
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<tr>
<td>Zobenzo et al(^{1})</td>
<td>n = 300, separation, 60% treatment</td>
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<tr>
<td>Hersfield et al(^{1})</td>
<td>n = 623, chronic</td>
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</tbody>
</table>

\(^{1}\) Prioritization of negative responses; ++ no effect for outcome 'response' of variable was not assessed in this study.

---

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

*A Comparison Between the STAR*\(^{\text{D}}\) 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.**

Local Organizer: Dr. Sinita Eugenia
tomtit_bird@mail.ru
# Examples of PGx: FDA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Effect measure</th>
<th>Gene-allele</th>
<th>FDA guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab</td>
<td>Colorectal cancer</td>
<td>Disease-free survival</td>
<td>EGFR+</td>
<td>Required</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Breast cancer</td>
<td>Disease-free survival</td>
<td>Her2 overexpression</td>
<td>Required</td>
</tr>
<tr>
<td>Lapatinib</td>
<td>Breast cancer</td>
<td>Disease-free survival</td>
<td>Her2+</td>
<td>Required</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Childhood leukemia</td>
<td>Myelotoxicity</td>
<td>TPMT Variants</td>
<td>For information only</td>
</tr>
<tr>
<td>6MP</td>
<td></td>
<td>Disease-free</td>
<td>Philadelphia chromosome +</td>
<td>For information only</td>
</tr>
<tr>
<td>Busulfan</td>
<td>Myelogenous leukemia</td>
<td>Ejection fraction; survival</td>
<td>β1-AR (arg389)</td>
<td>none</td>
</tr>
<tr>
<td>Carvediol</td>
<td>Heart failure</td>
<td>HDL and total cholesterol levels, atherosclerosis progression</td>
<td>CETP-Bi</td>
<td>none</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Dyslipidemia</td>
<td></td>
<td>HMGCR (HAP7)</td>
<td>none</td>
</tr>
<tr>
<td>Donepezil</td>
<td>Alzheimer's Disease</td>
<td>Improvement in ADAS-Cog</td>
<td>ApoE4+</td>
<td>none</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>Alzheimer's Disease</td>
<td>Improvement in ADAS-Cog</td>
<td>ApoE4-</td>
<td>none</td>
</tr>
</tbody>
</table>

## Graph

**HAMD DECREASE DURING FLUOXAMINE TREATMENT**

5-HTTLPR variants in psychotic and non-psychotic subjects

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>L and l subcategory</th>
<th>Size L</th>
<th>Size l</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
<th>OR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. Gheorghe 2004</td>
<td>49/167</td>
<td>24/62</td>
<td></td>
<td>95.56 [1024, 32.21]</td>
<td>95.56</td>
<td>95.56 [1024, 32.21]</td>
</tr>
<tr>
<td>K. K. 2006</td>
<td>21/51</td>
<td>19/49</td>
<td></td>
<td>10.99 [1.58, 0.61]</td>
<td>1.58</td>
<td>1.58 [1.58, 0.61]</td>
</tr>
<tr>
<td>Total</td>
<td>304/490</td>
<td>88/246</td>
<td></td>
<td>100.00 [2.22, 0.21]</td>
<td>2.22</td>
<td>2.22 [0.21, 0.21]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 3.33, df = 5, p = 0.76, I² = 0%
Test for overall effect: Z = 4.19, p = 0.0001

Favorable response s/s genotype
Favorable response l/l and l/s genotype

FEATURES MODULATED BY SERT PR

<table>
<thead>
<tr>
<th>Neuroanatomic Sites</th>
<th>Positive and Negative Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampal volume</td>
<td>++</td>
</tr>
<tr>
<td>Amygdala response</td>
<td>++</td>
</tr>
</tbody>
</table>

ANXIETY PERSONALITY TRAITS

<table>
<thead>
<tr>
<th>Infants</th>
<th>+++</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (l/l)</td>
<td>+++</td>
</tr>
<tr>
<td>Adults</td>
<td>++++++++T+T+T+T+T+T+T</td>
</tr>
<tr>
<td>Cluster C diagnosis</td>
<td>-</td>
</tr>
</tbody>
</table>

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 | - |
| Embryonia                     | - |

Local Organizer: Dr. Sinita Eugenia
tomtit_bird@mail.ru
## FEATURS MODULATED BY SERTPRL

<table>
<thead>
<tr>
<th>MOOD DISORDERS</th>
<th>POSITIVE AND NEGATIVE STUDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depressive Disorder</td>
<td>+ **</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>+ **</td>
</tr>
<tr>
<td>Total depressive symptomatology</td>
<td>-</td>
</tr>
<tr>
<td>Psychic anxiety symptomatology</td>
<td>+</td>
</tr>
<tr>
<td>Depression, Mania, Delusion and Disorganization symptomatological factors</td>
<td>+</td>
</tr>
<tr>
<td>Early age at onset</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Lower illness recurrence</td>
<td>+</td>
</tr>
<tr>
<td>Rapid cycling (I or s allele)</td>
<td>+</td>
</tr>
<tr>
<td>Antidepressant induced mania</td>
<td>+ + +</td>
</tr>
<tr>
<td>Better response to serotoninergic treatments (l allele)</td>
<td>+ + +</td>
</tr>
<tr>
<td>Better response to total sleep deprivation (l/l)</td>
<td>+</td>
</tr>
<tr>
<td>Side effects (nausea)</td>
<td>-</td>
</tr>
<tr>
<td>Stressful life events</td>
<td>+ + + +</td>
</tr>
<tr>
<td>SUICIDE</td>
<td>+ + + +</td>
</tr>
</tbody>
</table>

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### 5-HTTLPR variations

**Broad influence of a single gene on a range of aspects**

**Poor serotonin pathway plasticity**

- Anatomical change
- Stress reactivity
- Temperament
- Response to antidepressants
- Mood disorders
Main replicated genes

◆ HTT
◆ 5-HT1A
◆ 5-HT2A
◆ BDNF
◆ COMT
◆ MAO-A
◆ NET
◆ Gβeta3
◆ FKBP5
◆ PGP

Less replicated genes

◆ TPH1
◆ TPH2
◆ ACE
◆ CRHR
◆ CLOCK
◆ APOE
◆ NR3C1
◆ PDE
◆ GSK-3β
◆ GRIK4
### Preliminary findings

<table>
<thead>
<tr>
<th></th>
<th>5-HT1B</th>
<th>5-HT3A</th>
<th>5-HT3B</th>
<th>5-HT5A</th>
<th>5-HT2C</th>
<th>5-HT6</th>
<th>DAT</th>
<th>DRD2</th>
<th>DRD3</th>
<th>DRD4</th>
<th>ADRB1</th>
<th>ADRA2A</th>
<th>GRM2</th>
<th>GRM3</th>
<th>CACNA1C</th>
<th>FGF</th>
<th>RGS4</th>
<th>p75NTR</th>
<th>MCR1</th>
<th>MCR2</th>
<th>PPGAL</th>
<th>GNB3</th>
<th>CHRBP</th>
<th>OPRM1</th>
<th>SIGMAR1</th>
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### Pharmacogenetics: problematic issues... and possible solutions

- Low variance explained by polymorphisms (HTTLPR=2.8%, TPH=2.7%, Gβ3=1.2%) → Other variables influence drug response: Life events, social support, temperament, hormones... *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

<table>
<thead>
<tr>
<th></th>
<th>Responders N (%)</th>
<th>Non-responders N (%)</th>
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<tbody>
<tr>
<td>L/L Non-exposed</td>
<td>(n=26) 22 (85%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>L/L Exposed</td>
<td>(n=30) 24 (80%)</td>
<td>6 (20%)</td>
</tr>
<tr>
<td>S-carriers Non-exposed</td>
<td>(n=31) 22 (71%)</td>
<td>9 (29%)</td>
</tr>
<tr>
<td>S-carriers Exposed</td>
<td>(n=72) 49 (68%)</td>
<td>23 (32%)</td>
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</tbody>
</table>

The first G x E Pgx study

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 he 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 has 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

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

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Alzheimer’s disease</th>
<th>Vascular dementia</th>
<th>Diffuse Lewy body</th>
<th>Fronto-temporal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychomotor agitation</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Aggressive behaviour</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Delusions</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Depression</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Anxiety</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Apathy/retardation</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Sleep changes</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Appetite Changes</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Sexual disinhibition</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
</tbody>
</table>
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

Other dementias:
- Frontal lobe dementia
- Creutzfeldt-Jakob disease
- Corticobasal degeneration
- Progressive supranuclear palsy

Vascular dementias:
- Vascular dementia
-Binswanger's disease

Mixed Vascular dementias and AD

Dementia with Lewy bodies:
- Parkinson's disease
- Diffuse Lewy body disease
- Lewy body variant of AD

AD and dementia with Lewy bodies

50-60.6%

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 on 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 Testing
- LP: Suspicion of metastatic CA, CNS infections, neurosyphilis, 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

Local Organizer: Dr. Sinita Eugenia tomtit_bird@mail.ru
Risk Factor *(why me?)*

*a life-long endeavor starting with the choice of genes*

<table>
<thead>
<tr>
<th>Factor (Reliability)</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Follow-up, y</th>
<th>Association With Cognitive Decline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat (s)</td>
<td>1</td>
<td>2600</td>
<td>5-6</td>
<td>Inadequate evidence*</td>
</tr>
<tr>
<td>Total metals (g-11)</td>
<td>2</td>
<td>62851</td>
<td>3-3</td>
<td>Copper: no association except in subgroups</td>
</tr>
<tr>
<td>Mediterranean diet (12-13)</td>
<td>2</td>
<td>3386</td>
<td>4-5</td>
<td>Decreased risk</td>
</tr>
<tr>
<td>Fruits and vegetables (14-15)</td>
<td>2</td>
<td>17 036</td>
<td>2-5</td>
<td>Decreased risk (vegetables) no association (fruits)</td>
</tr>
<tr>
<td>Medical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (16-27)</td>
<td>12</td>
<td>47 629</td>
<td>2-25</td>
<td>Possibly increased risk</td>
</tr>
<tr>
<td>The metabolic syndrome (19-28-30)</td>
<td>4</td>
<td>5513</td>
<td>1-8</td>
<td>Increased risk, except for age &gt;80 y</td>
</tr>
<tr>
<td>Hypertension (19-21-24-40)</td>
<td>19</td>
<td>64 300</td>
<td>1-8</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Hypoalbuminemia (7-17)</td>
<td>6</td>
<td>70 184</td>
<td>3-6</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Homocysteine (48-63)</td>
<td>5</td>
<td>43 079</td>
<td>2-10</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Obesity (18, 19, 54)</td>
<td>3</td>
<td>8479</td>
<td>4-5</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Depression (16, 24, 56)</td>
<td>13</td>
<td>12 969</td>
<td>5-5</td>
<td>Probably increased risk</td>
</tr>
<tr>
<td>Anxiety (16, 25, 56)</td>
<td>4</td>
<td>6297</td>
<td>6</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resilience</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental health</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social, economic, or behavioral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childrenhood exposure (9-27)</td>
<td>3</td>
<td>6981</td>
<td>2-4</td>
<td>No association</td>
</tr>
<tr>
<td>Occupation (11, 23-70)</td>
<td>14</td>
<td>43 202</td>
<td>1-11</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Social engagement (19, 27, 71, 80, 81-90)</td>
<td>16</td>
<td>7271</td>
<td>4-13</td>
<td>Individual studies showed possible decreased risk, but exposure were too heterogeneous to synthesise</td>
</tr>
<tr>
<td>Other leisure activity (89, 90, 99)</td>
<td>3</td>
<td>9099</td>
<td>1-5</td>
<td>No consistent association</td>
</tr>
<tr>
<td>Alcohol (18, 19, 100-105)</td>
<td>7</td>
<td>19 081</td>
<td>1-5</td>
<td>No association</td>
</tr>
<tr>
<td>Tobacco (18, 19, 37, 38, 100, 105)</td>
<td>14</td>
<td>13 685</td>
<td>2-7</td>
<td>Increased risk</td>
</tr>
<tr>
<td>Toxic environmental exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pesticides</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Genetic

- Apolipoprotein E allele (19, 21, 23)

- 15

- 8059

- 1-14

- Increased risk

---

**Using CSF Biomarkers to Predict Progression from MCI to AD***

<table>
<thead>
<tr>
<th>Measure</th>
<th>Cutoff Value</th>
<th>Sensitivity/ Specificity</th>
<th>Hazard Ratio†</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-Tau</td>
<td>&gt;350 ng/L, &lt;530 ng/L</td>
<td>95% / 83%</td>
<td>17.7 (p&lt;0.0001)</td>
</tr>
<tr>
<td>P-Tau</td>
<td>&gt;60 ng/L, &lt;530 ng/L</td>
<td>95% / 81%</td>
<td>16.8 (p&lt;0.0001)</td>
</tr>
<tr>
<td>T-Tau</td>
<td>&gt;350 ng/L, &lt;6.5</td>
<td>95% / 87%</td>
<td>19.8 (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

*4-6 year follow up

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

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**How clinically relevant is it?**

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Local Organizer: Dr. Sinita Eugenia
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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

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
  - Neuroprotection
  - Decreased amyloid deposits

The occasional irrationality of the current Rx

Real life
- Persistent delirium
- Add a benzo to Rx agitation

No improvement
- Rx of apathy with antidepressant or antipsychotic
- Increase the dose or add a second drug
- Sedation, confusion, agitation
Drug Development for AD

Enzymes Inhibitors
Anti-amyloid vaccine
Neuro-protection?

Clinical trials
Secondary prevention trials
MCI trial
Mini-AD trial

Hypothetical time course of AD
Rising Aβ oligomers, diffuse and focal Aβ deposition associated with microglial, astrocytic and PHF accumulation; super-numerary dystrophy, astrocytosis, altered APP metabolism, oxidative injury; many secondary biochemical changes but limited neuronal loss

Worsening Aβ and tau biochemistry and pathology with more neuronal loss. Atter's CSF biomarkers (e.g., Aβ), then rising tau. Subtle cognitive deficits detected only with challenging tasks. LATE PRESYMPTOMATIC AD

Worsening biochemical changes (including tau) and neuronal/neuromodulatory pathology. Mild cognitive symptoms and signs. MCI

Worsening neuromodulatory changes. Progressive cognitive defects. Mild AD

As in mid-AD, plus increasing behavioural and motor signs. MODERATE 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
Professor Anatol Nacu, Chairman, Chair of Psychiatry, Addictions and Clinical Psychology, State University of Medicine and Pharmacy “Nicolae Testemitanu”, Republic of Moldova

CLINICAL CASE. Catatonic Schizophrenia

IMSP SCP al. MS RM, Clinical Unit Nr. 14
Prof. Dr. A. Nacu
General data

- The female patient P. Iulia, 1977, mun. Chisinau,
- Inpatient, Acute Psychosis 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 patient's 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 – father's 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.
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.

Pharmacological approach to affective disorders management

Ludmila Bumacov
Chisinau
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.

How to treat?

Which are the general principle of correct drug choice

Pharmacological approach

Local Organizer: Dr. Sinita Eugenia
tomtit_bird@mail.ru
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)
- Aetiology - genetic or organic factors
- The type, phase and severity of the illness - acute, chronic; BP I, BP II, Cyclothymia, 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 UM 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 undisussed 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, inoffensivity, 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 (SSRIs)** - Fluoxetine, fluvoxamine, sertraline, paroxetine; or
- **Monoamine oxidase inhibitors (MAOIs)** - irreversible – Phenelzine, tranylcypromine, or - reversible – Mocllobemide; 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 (fluifenazine, perhenazine) all effects are moderate.
- **Butyrophenones:** Haloperidol, droperidol – very potent antipsychotic and intense extrapiramidal eff, moderate sedative or.
- Thioxanthenes – Chlorprothixene, thiothixene – there are pharmacodynamic 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.
    - metabolism, (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 appropriate. 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 toxicity of lithium)

---

**Drug monitoring efficacy and inoffensivity 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 seizure'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 – destructive 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 Diagnosis 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. Șveț, Gh. Cărăușu.

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 involvement.

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 order to achieve these 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 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 Groppa¹, Valeriu More², Vitalii Cozac³

The importance of cerebral aneurysms pathology dramatically increased with the progress of accessibility 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 unruptured 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 disease, starting 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 debut: evaluation and prognosis.**

Igor Nastas, Larisa Boronin.

The performed study is based on the identification of several criteria selected statistically, including two groups of patients (the first including 100 patients with schizophrenia debut at the age before 25 years, the second including 100 patients with schizophrenia debut 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 debut.

**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.

- 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. Andronati¹, S. Plesca², M. Sanghelii, L. Chetrari²

**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 insertion of the pectoartis 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 transmission. The disturbances are due to respiratory oxido-reduction chain and affect internal mitochondrial membrane.

In this study were investigated 5 children with mitochondrial 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 metabolism. 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 beginis 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 activity regulating 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].