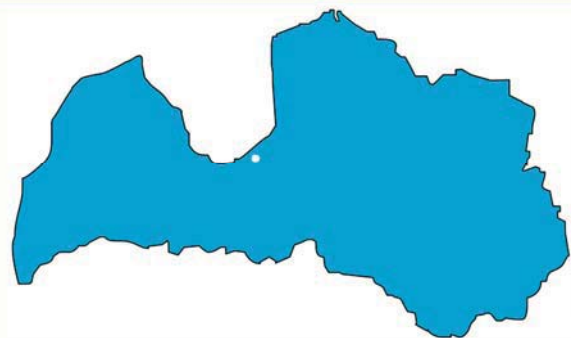




**ECNP**

european college of  
neuropsychopharmacology

# BALTIC REGIONAL SEMINAR IN NEUROPSYCHOPHARMACOLOGY



**Baltezers, Latvia**

**15 - 17 May, 2013**



# 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 and is considered to be the largest event in neuropsychopharmacology in Europe.

ECNP also supports on an annual basis participation of 100 young psychiatrists and researchers in an intensive three-day Workshop in Nice. Other activities of ECNP include the journal *European Neuropsychopharmacology* that promotes scientific knowledge along with publishing consensus statements. These consensus statements are products of an annual meeting with delegates from the scientific community in neuropsychopharmacology (scientists and clinicians), European regulators and industry in which discussion about issues such as use of placebo, guidelines for long-term maintenance are discussed. In addition, since 2009 ECNP organises a summer school of neuropsychopharmacology in Oxford, since 2012 a school of child and adolescent neuropsychopharmacology in Venice and since 2013 a school of old age neuropsychopharmacology in Venice.

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, Slovak Republic, Hungary, Czech Republic, Moldova, Romania, Greece and Russia. 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](http://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 Latvia!

**Celso Arango, MD**  
Chair ECNP Educational Committee

# Programme

## ECNP Seminar in Neuropsychopharmacology

15-17 May 2013, Baltezers, Latvia

### WEDNESDAY 15 May 2013

Arrival of participants and experts

19.00 Welcome and dinner

### THURSDAY 16 May 2013

09.00 – 09.15 Introductions to the programme

Celso Arango, Spain

09.15 – 10.00 Updates in the treatment of acute psychoses

Celso Arango, Spain

10.00 – 10.45 Serotonin and glutamate regulation of hippocampal synaptic pathology: novel mechanisms of neuropsychiatric disorders and avenues for treatment

Sven Ove Ögren, Sweden

10.45 – 11.30 Coffee break

11.30 – 12.15 Phenomenology of bipolar disorders: impact on our clinical practice and therapeutic choices

Daniel Souery, Belgium

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	<i>Celso Arango and Elmārs Rancāns</i> <b>Group 1</b>	<i>Sven Ove Ögren and Robertas Bunevicius</i> <b>Group 2</b>	<i>Daniel Souery and Jaanus Harro</i> <b>Group 3</b>
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15.00 – 15.15 Break

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

16:00 – 21.00 Excursion and dinner

**FRIDAY 17 may 2013**

<b>Presentations participants in 3 groups in 3 parallel workshops</b>			
Round 2 08.30 – 10.00	<i>Celso Arango and Elmārs Rancāns</i>  <b>Group 2</b>	<i>Sven Ove Ögren and Robertas Bunevicius</i>  <b>Group 3</b>	<i>Daniel Souery and Jaanus Harro</i>  <b>Group 1</b>
10.00 – 10.30 Coffee break			
Round 3 10.30 – 12.00	<i>Celso Arango and Elmārs Rancāns</i>  <b>Group 3</b>	<i>Sven Ove Ögren and Robertas Bunevicius</i>  <b>Group 1</b>	<i>Daniel Souery and Jaanus Harro</i>  <b>Group 2</b>
12.00 – 14.00 Lunch and preparation for plenary session			
Plenary 14.00 – 15.00	14.00 – 14.20	<b>Group 1</b> Presentation	
	14.20 – 14.40	<b>Group 2</b> Presentation	
	14.40 – 15.00	<b>Group 3</b> Presentation	

15.00 – 15.15 Preparation of awards ceremony  
 15.15 – 15.30 Short break  
 15.30 – 15.45 Awards ceremony  
 15.45 – 16.00 Concluding remark and thanks  
 Celso Arango, Spain

# Venue

## Hotel Baltvilla

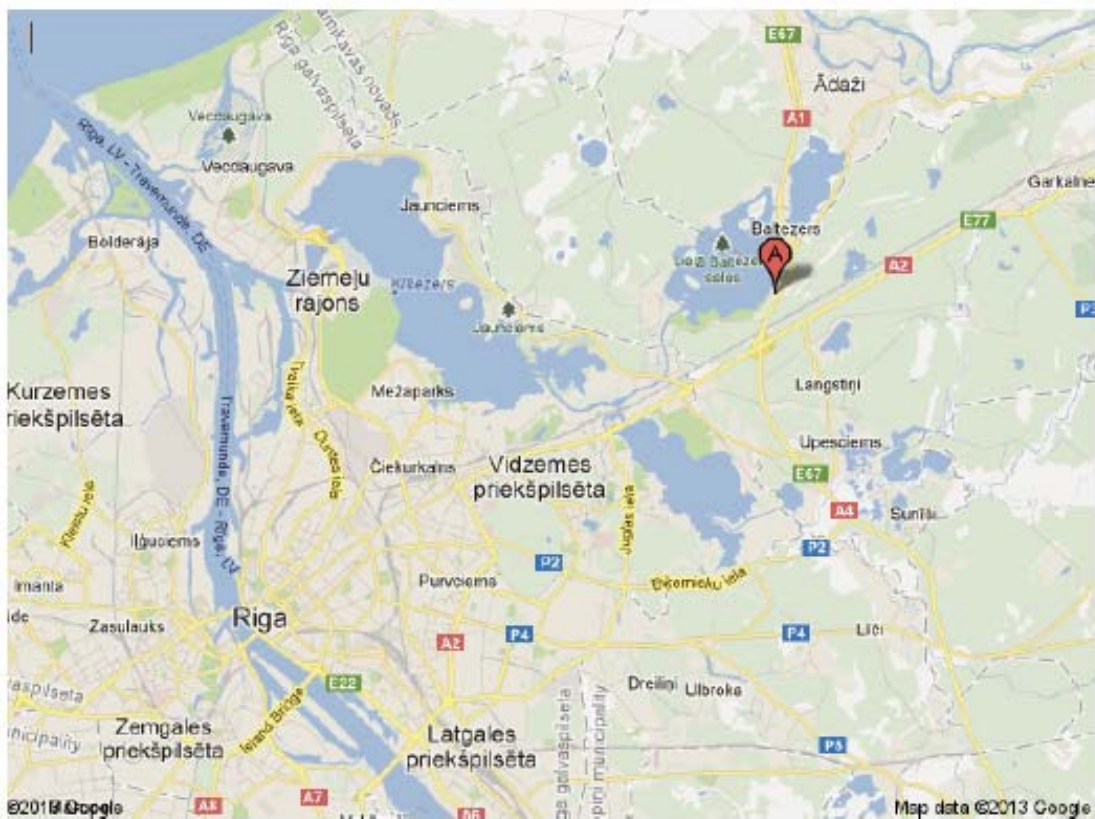
Address: Sencu pr. 45, Baltezers, Riga region, Latvia

Post code: LV-2164

phone: +371 67840640

e-mail: [info@baltvilla.lv](mailto:info@baltvilla.lv)

[www.baltvilla.lv](http://www.baltvilla.lv)





## **Celso Arango, MD, PhD**

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

Celso Arango MD, PhD is a psychiatrist and Associate Professor of Psychiatry at the University of Maryland in Baltimore and Full Professor of Psychiatry at the Universidad Complutense in Madrid. He is also Head of the Child and Adolescent Department of Psychiatry at Hospital General Universitario Gregorio Marañón.

Dr. Arango is the Scientific Director of the Spanish Psychiatric Research Network with 25 centers and more than 400 researchers. He is also Coordinator of the Child and Adolescent First-Episode

Psychosis Study (CAFEPS) funded by the Spanish Ministry of Health (with eight centers in Spain) and the Child and Adolescent Neuropsychiatry Network funded by the European College of Neuropsychopharmacology (ECNP). He has written more than 240 peer-reviewed articles, 6 books, and more than 35 book chapters. Many of his articles and book chapters have focused on the neurobiology of early-onset and first-episode psychoses as well as the safety of psychiatric medications in pediatric patients. In addition, his group has shown how patients with a first psychotic episode experience greater losses of gray matter than expected and a correlation of gray matter loss with antioxidant status.

Dr. Arango has participated in more than 62 competitively funded research projects, as Principal Investigator in 46 of them, including projects with international funding (Stanley Foundation, NARSAD, European Commission, etc.) and several clinical drug trials. He is also coordinator of several multicenter projects that assess multiple prognostic factors and treatment in early-onset psychosis, and is currently participating in five EU projects funded by the VII Framework.

## **Abstract: Treatment of acute psychoses**

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



Hospital General Universitario  
Gregorio Marañón  
Comunidad de Madrid

# Treatment of Acute Psychoses

Celso Arango

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

Latvia, May 2013

**cibersam**

Centro de Investigación Biomédica En Red  
de Salud Mental



## Index

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



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

**Placebo-Controlled First-Episode Maintenance Trials**

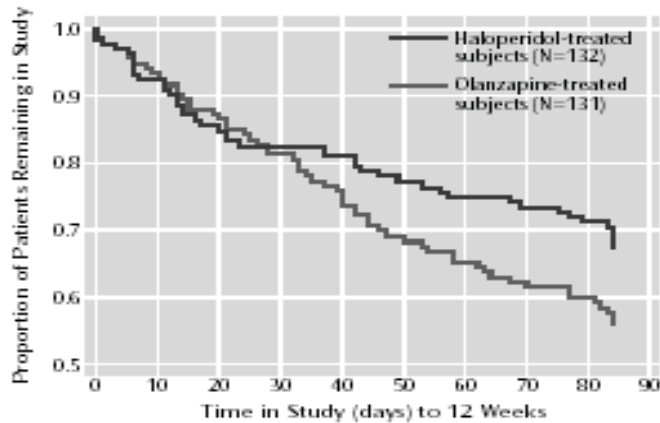
	Relapse Rate (%) Placebo	Relapse Rate (%) Antipsychotic	<i>P</i> -value
Kane et al, 1982	41 (7/17)	0 (0/11)	<0.01
Crow et al, 1986	62 (41/66)	46 (25/54)	0.002*
McCreadie, et al (Scottish Schizophrenia Research Group), 1989	57 (4/7)	0 (0/8)	NS
Hogarty and Ulrich, 1998	64	43	N/A

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

Kane JM et al. 1982;39:70; Crow TJ et al. 1986;148:120;  
McCreadie RG et al. 1989;80:597; Hogarty GE, Ulrich RF. 1998;32:243

## Olanzapine vs haloperidol

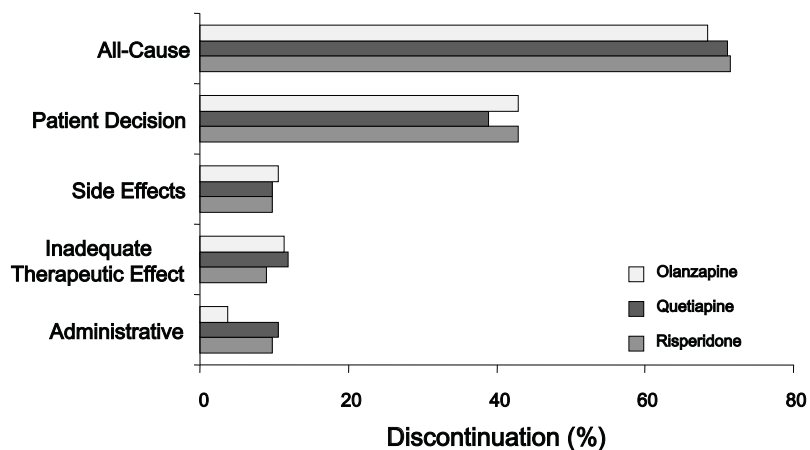
FIGURE 1. Time to Study Discontinuation for Any Reason of Subjects With First-Episode Psychosis in the 12-Week Acute Treatment Phase of a Long-Term Comparison of Olanzapine and Haloperidol<sup>a</sup>



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

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

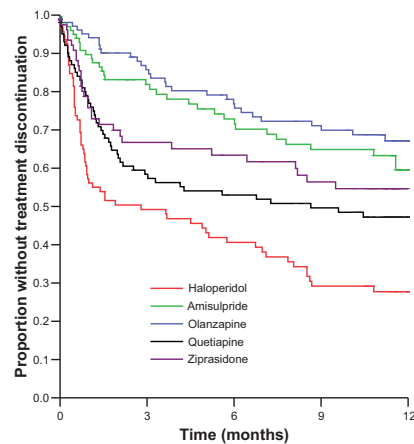
## Primary Outcome: All-Cause Treatment Discontinuation



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

McEvoy et al 2007

## European first episode (EUFEST ) Study



### Time to treatment discontinuation for any cause

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

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

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

## **Treatment goals in the emergency setting**

**Reducing acute symptoms**

**Minimising risk of harm**

**Calming agitation**

**Improving role functioning**

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

Arango & Bobes 2004

## **Patient requirements and preferences in the acute setting**

**Receive a rapid and accurate diagnosis**

**Be offered a choice of treatment**

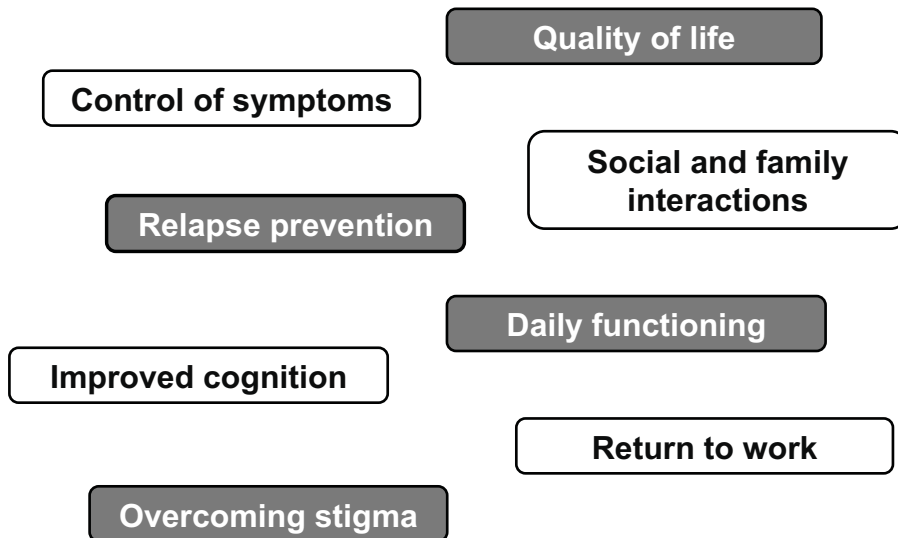
**Benefit from a good therapeutic alliance**

**Receive verbal rather than physical interventions**

**Receive oral medication**

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

## Recovery is a multidimensional process

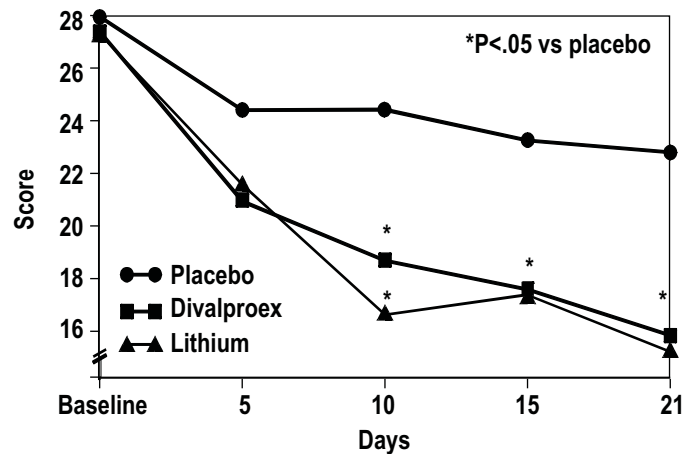


Fenton et al 1997; Lacro et al 2002

## Treatment Options for Acute Mania

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

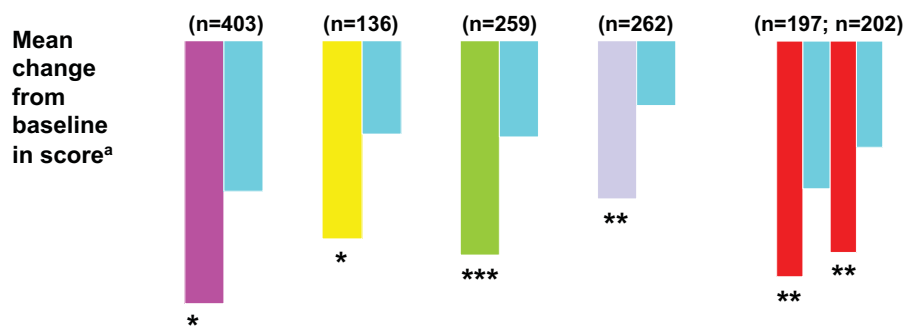
## Divalproex vs Lithium vs Placebo



Bowden CL, et al. *JAMA*. 1994;271(12):918-924.

## Efficacy of atypical antipsychotics: improvement in manic symptoms

Data from 6 selected monotherapy studies

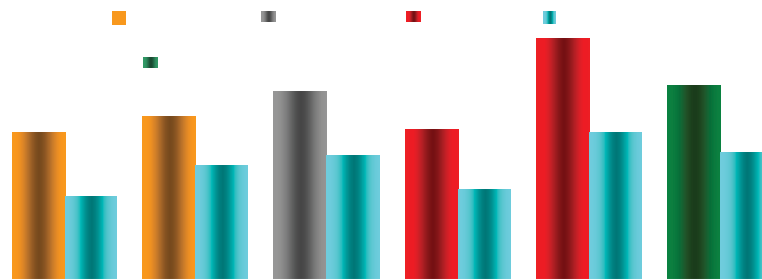


<sup>a</sup>  
\*p<0.05; \*\*p<0.01; \*\*\*p<0.001 vs placebo

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

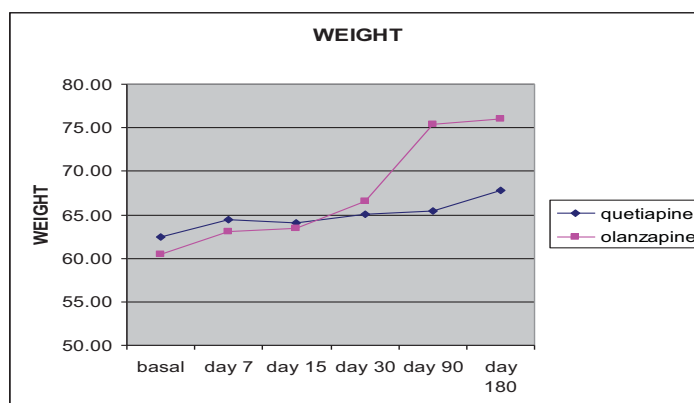
## Atypical Antipsychotics As Adjunct to Mood Stabilizers Vs. Mood Stabilizer Monotherapy

Response Rate ( $\geq 50\%$  Reduction YMRS)



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

## Change in weight over time by treatment group olanzapine/quetiapine



Arango et al, 2009

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

### At risk for adverse health outcome

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

At risk adverse	Baseline	6 month
<b>RIS</b>	<b>22.7%</b>	<b>36.4%</b>
<b>OLZ</b>	<b>15.0%</b>	<b>60.0%*</b>
<b>QTP</b>	<b>12.5%</b>	<b>20.8%</b>
* p < 0.05		

### Significant weight gain

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

**RIS: 50%**

**OLZ: 75%\***

**QTP: 29%**

\*p < 0.01

- increased in patients receiving olanzapine (p=0.047) and quetiapine (p=0.016).

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

Fraguas et al, J Clin Psychiatry 2008

## SATIETY study design

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

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

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

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



## **Treating first-episode patients**

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

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

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





## Sven Ove Ögren, MD, PhD

Prof., Dept. of Neuroscience, Karolinska Institutet  
S-171 77 Stockholm, SWEDEN, Phone: + 46 - 8 - 524 87074  
Fax: + 46 - 8 - 30 28 75  
E-mail: [Sven.Ove.Ogren@ki.se](mailto:Sven.Ove.Ogren@ki.se)

### Professional (academic) preparation

Medical Doctor of Science (Ph.D.) at the Department of Neurobiology and Histology, Karolinska Institutet (1985).  
Associate Professor (Docent) of Neurobiology (1986), Department of Histology, Karolinska Institutet, Stockholm.

Professor (Adjunct Professor) of Neurobiology (1987), Department of Neuroscience, Karolinska Institutet.

Head of the Division of Behavioral Neuroscience (1998), Department of Neuroscience, Karolinska Institutet.

### Professional (industrial) experience

Vice President of Preclinical Research, Senior Scientific Adviser and Senior Director at Astra Alab AB (now AstraZeneca), (1979).

Preclinical project leader of the development of zimelidine (1972-1982), the first serotonin reuptake inhibitor (SSRI) launched in the world (1982).

Inventor and project leader of antipsychotic drugs (1978-1986), resulting in the D2 receptor antagonist remoxipride (launched in 1992) and the resorcydamides raclopride, FLB 463 and FLB 457. These compounds are widely used as PET ligands.

### Patents

30 international patents granted for new chemical entities and new treatment possibilities in depression and schizophrenia.

### Supervision of PhD students (year of dissertation)

P. Schött (2000) J. Sandin (2000), H. Razani (2001), M. Luttgen (2004), E. Elvander-Tottie (2006), E. Kuteeva (2007), S. Beraki (2008), T. Wardi (2010), T. Eriksson (2012)

### Comission of trust

Counselor of the Executive Board of ECNP 2002-2005 and since 2010 Secretary of ECNP.

Chairman of the Scientific Program Committee (SPC) of ECNP 2006-2009 and of the Award Committee 2005-2008. Invited chairman at 46 International Congresses.

Invited lecturer at 85 International congresses. Fellow, American College of Neuropsychopharmacology (ACNP),

### Prizes and Awards

Swedish American Foundation, one year scholarship at Towson State College, Baltimore, 1964.

The Hilda and Alfred Erikssons Prize, Swedish Academy of Sciences, 1995.

Oswald Schmiedeberg's medal, Department of Pharmacology, University of Riga, Latvia, 1998.

Gold medal, University of Medical Informatics and Technology, Tyrol, Innsbruck, Austria, 2004.

Honorary member of the Austrian Society for Neuropsychopharmacology and Biological Psychiatry, Vienna, Austria, 2004.

### Publications

Author of 370 original papers and book chapters as well as 35 review articles.

# **Abstract: Serotonin and glutamate regulation of hippocampal synaptic pathology: novel mechanisms of neuropsychiatric disorders and avenues for treatment.**

Sven Ove Ögren, Therese Eriksson, Oliver Stiedl and Per Svenningsson  
Karolinska Institutet, Department of Neuroscience, Karolinska Institutet, SE-17177 Stockholm, Sweden. [sven.ove.ogren@ki.se](mailto:sven.ove.ogren@ki.se)

The past two decades has given accumulated evidence that disorders of the brain involve multiple dysfunctions in neuronal plasticity and that drugs used to treat these disorders can act via readjustments of mechanisms which involve neuronal plasticity and cognition. Of particular interest in this context is the link between the monoamine transmitter serotonin, which is associated with depression and a target for the most currently used antidepressant drugs, the SSRIs, and the excitatory transmitter glutamate which serves a major role in cortical and hippocampal plasticity and cognition (Eriksson TM, Delagrè P, Spedding M, Popoli M, Mathé AA, Ögren SO, et al., *Mol Psychiatry* 17:173-84 2012). Evidence for a link between depression and mechanisms for cognition was demonstrated by the observation that acutely changing glutamatergic transmission with treatment of the noncompetitive NMDA receptor antagonist ketamine resulted in a rapid and persistent antidepressant effect in treatment-resistant patients (Zarate CA, Singh JB, Carlson PJ, Brutsche NE, Ameli R et al. *Arch Gen Psychiatry* 63:856-64 2006). However, our knowledge about how dysregulation of 5-HT- dependent synaptic activity may interact with glutamate in domains of cognition and emotion is still limited. Recent studies in rodents have demonstrated that 5-HT- dependent signalling is an important regulator of hippocampal glutamate and mechanisms associated with hippocampal emotional and declarative (spatial) learning (Ögren SO, Eriksson TM, Elvander-Tottie E, D'Addario C, Ekstrom JC et al. *Behav Brain Res* 195:54-77 2008). The regulatory actions are mediated by some of the key serotonin receptors implicated in depression e.g. inhibitory 5-HT<sub>1A</sub> receptors and the excitatory 5-HT<sub>7</sub> receptors (Eriksson et al., 2012). Importantly, 5-HT<sub>1A</sub> receptors are colocalized with NMDA receptors on the dendritic spines of hippocampal pyramidal neurons and on GABAergic interneurons (Ögren et al., 2008). Of particular interest is the evidence for important interactions between 5-HT<sub>1A</sub>/5-HT<sub>7</sub> receptors in vivo involving hippocampal-dependent emotional memory. When the SSRI citalopram was examined in the presence of 5-HT<sub>1A</sub> receptor blockade, contrary to citalopram alone, the combination resulted in an enhancement of emotional learning mediated by stimulation of excitatory 5-HT<sub>7</sub> receptors. These results indicate that increased knowledge of how key serotonin receptors impact on glutamatergic hippocampal functions may open new avenues for understanding of synaptic pathology and reveal clues for novel treatment.

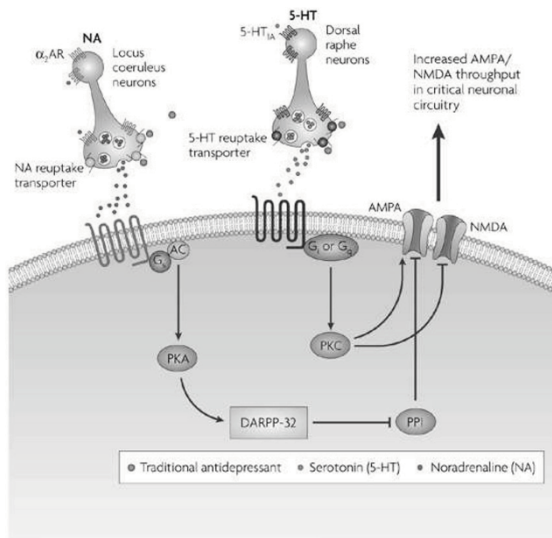
Serotonin and glutamate regulation of hippocampal synaptic pathology: novel mechanisms of neuropsychiatric disorders and avenues for treatment

Sven Ove Ögren,  
Department of Neuroscience,  
Karolinska Institute

### Human Depression and cognition

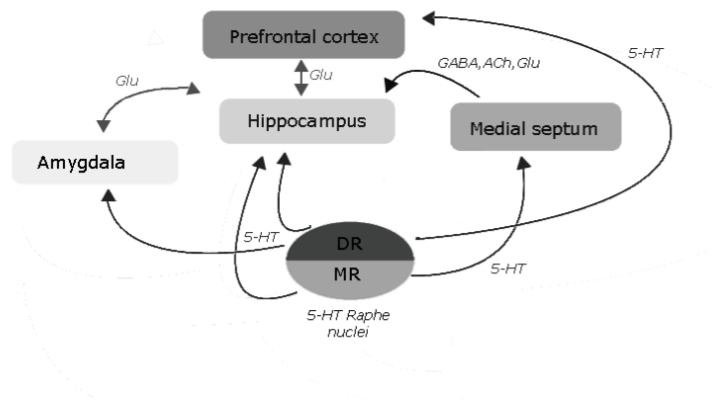
- The traditional symptoms of depression – besides depressed mood (melancholia) and inability to experience pleasure (anhedonia) – also include multiple domains of cognitive disturbances, e.g. impaired attention and executive functions and short- and long-term declarative memory deficits (DSM IV; Clark et al., 2009; Millan et al., 2012).
- In addition, depressed patients are characterized by alterations in neuronal processing of emotional stimuli (negative attentional bias) as well as deficits in emotional memory (Harmer, 2008).
- Currently used antidepressant drugs such as the SSRIs which act primarily by blocking the SERT do not usually improve cognitive dysfunctions in depressed patients but sometimes even impair (Millan et al., 2012).

Current hypotheses of antidepressant action focus on brain mechanisms for synaptic plasticity



- Antidepressants converge to regulate AMPA- and NMDA-mediated synaptic plasticity in critical neuronal circuits
- [Sanacora G. et al., Nature reviews. Drug discovery, 2008](#)

Neuronal networks of the brain involved in cognitive, emotional processes of importance for depression and several other mental disorders

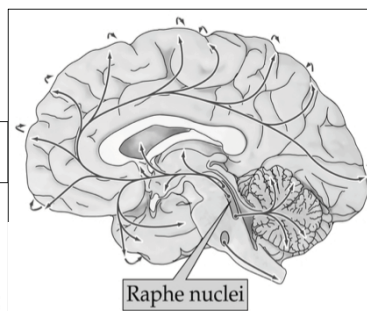
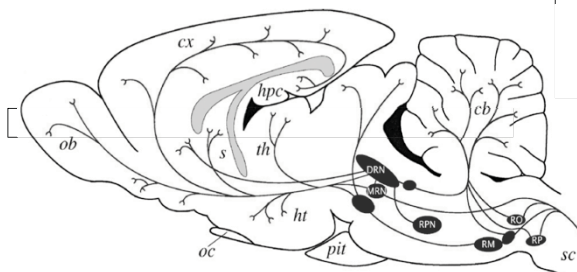


## Hippocampal serotonin in cognition and mood disorders.

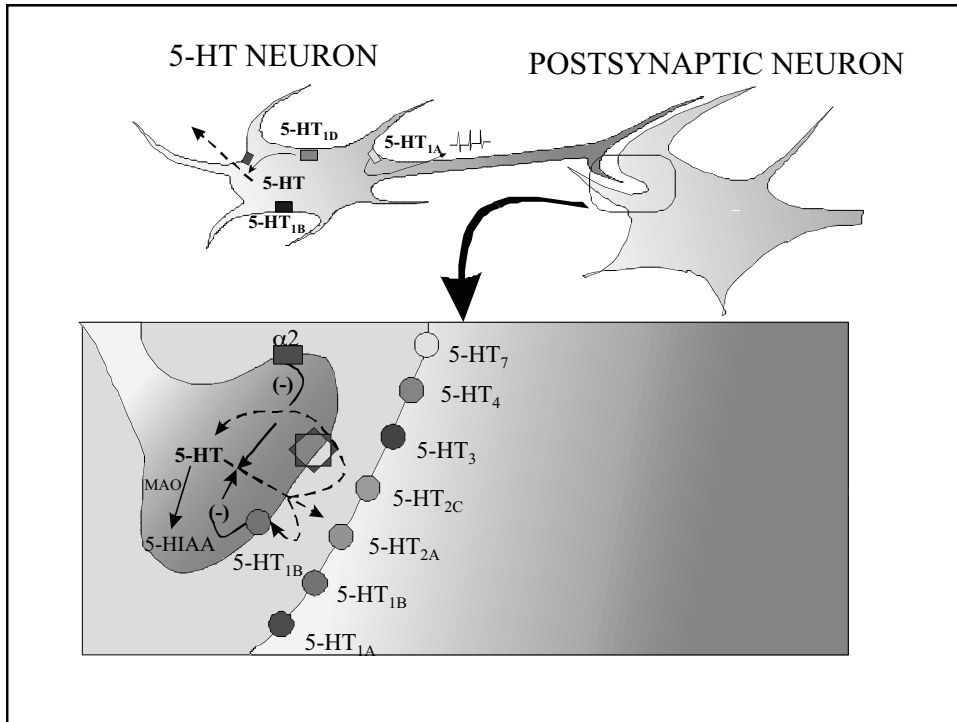
- Serotonergic (5-HT) raphe pathways densely innervates corticolimbic structures (hippocampus, amygdala, septum, frontal cortex) implicated in stress, mood regulation and emotional memory (Ögren et al., 2008).
- Disturbances in the activity of hippocampal 5-HT systems, and in particular dysfunctions of the 5-HT<sub>1A</sub> receptor, have been linked to the pathogenesis of anxiety and depression.
- Multiple 5-HT receptors such as the 5-HT<sub>1A</sub> receptors are expressed in glutamatergic neurons as well in different GABA interneurons in the CA1 and CA3-regions in the hippocampus as well as in the dentate gyrus.
- Recent rodent studies have shown that serotonin is a potent regulator of hippocampal functions involving emotional memory and depression-like behavior.

## The serotonergic system in the mammalian brain

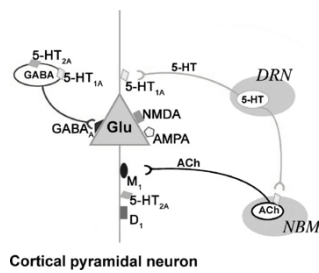
Ascending 5-HT projections from the dorsal and median raphe nuclei



Ögren, Eriksson, Svenningsson  
et al., 2008



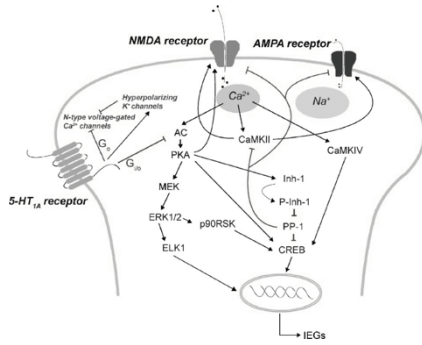
**Schematic illustration of the proposed mechanisms by which 5-HT<sub>1A</sub> receptor ligands can affect glutamatergic signaling in cortical pyramidal neurons.**



Ogren SO, Eriksson TM, Elvander-Tottie E, D'Addario C, Ekström JC, Svenningsson P, Meister B, Kehr J, Stiedl O., 195(1):54-77. Behav Brain Res. 2008



## Signaling cascades regulating the phosphorylation states of glutamate receptors and transcription factors by 5-HT<sub>1A</sub> receptor activation in hippocampal neurons.

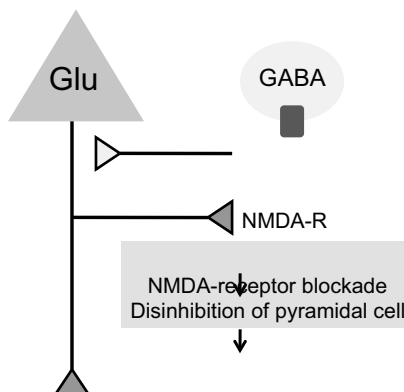


Signaling cascades regulating the phosphorylation states of glutamate receptors and transcription factors by 5-HT<sub>1A</sub> receptor activation in hippocampal neurons. 5-HT<sub>1A</sub> receptors are coupled to G<sub>o</sub> and/or G<sub>i</sub> proteins. Activation of 5-HT<sub>1A</sub> receptors leads to inhibition of N-type calcium channels, activation of hyperpolarizing potassium channels, and reduced activity of calcium-dependent adenylyl cyclase/reduced formation of cAMP/less activity of protein kinase A (PKA). PKA directly phosphorylates NMDA and AMPA receptors as well as inhibitor-1 (Inh-1). Upon phosphorylation by PKA, Inh-1 becomes a potent inhibitor of protein phosphatase-1 (PP1), which dephosphorylates NMDA and AMPA receptors. PKA also directly phosphorylates the transcription factor CREB and promotes gene expression. In addition, PKA indirectly via a MEK1/2/ERK1/2/p90RSK pathway regulates CREB phosphorylation. The PKA/MEK1/2/ERK1/2 pathway also regulates the phosphorylation state of the transcription factor ELK-1. Because of its ability to phosphorylate PP1, PKA indirectly regulates the PP1-dependent dephosphorylation of CaMKII. CaMKII, in turn, regulates the phosphorylation states of NMDA as well as AMPA receptors and their abilities to regulate Ca<sup>2+</sup> and Na<sup>+</sup> influxes. Red arrows indicate inhibition. Black arrows indicate stimulation.

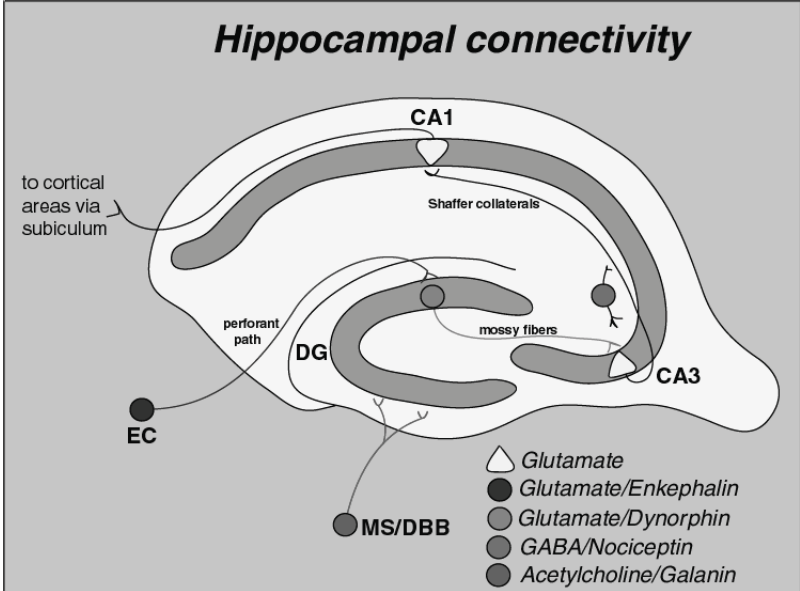
Ogren SO, Eriksson TM, Elvander-Tottie E, D'Addario C, Ekström JC, Svenningsson P, Meister B, Kehr J, Stiedl O., 195(1):54-77. Behav Brain Res. 2008

## Modulators of NMDA-receptor function and depression

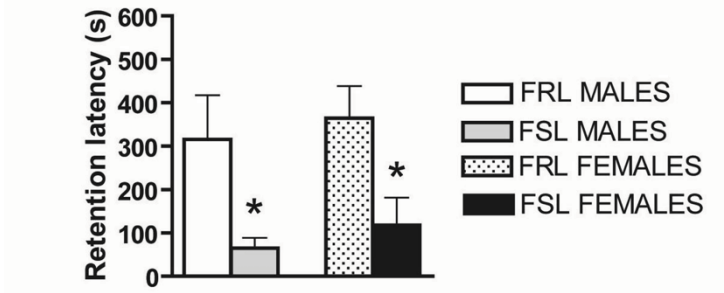
- Ketamine produces a rapid antidepressant response in therapy resistant depressed patients (Zarate et al., 2006). It blocks the glutamate NMDA receptor at the phencyclidine site within the ionotropic channel. This glutamatergic hypostate results in a disinhibition of GABAergic inputs enhancing excitatory transmission and stimulation of AMPA receptors. Disinhibition of depressed memory circuits?
- Ketamine increases glutamate release, facilitates NMDA/AMPA receptor function, activates the rapamycin (mTOR) pathway (mTOR kinase, a serine-threonine kinase) resulting into increased synaptic signalling proteins (Li et al., 2010) and antidepressant effect?



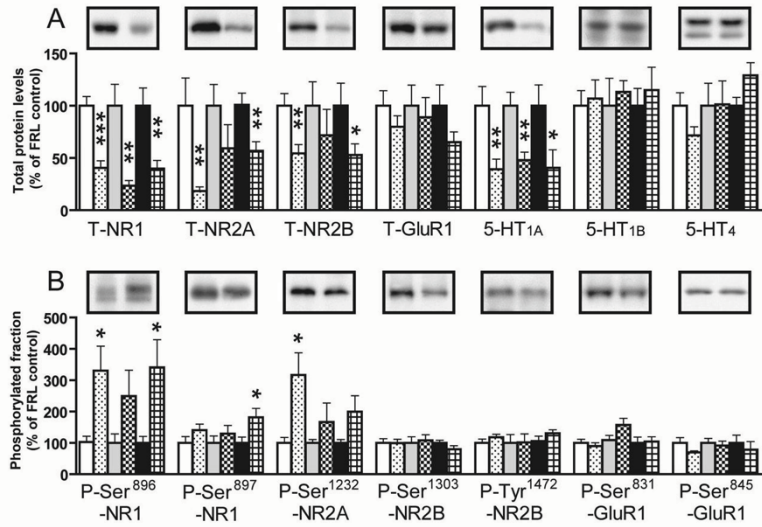
### Hippocampal connectivity



### Impaired long-term memory performance of FSL rats in the Passive Avoidance task

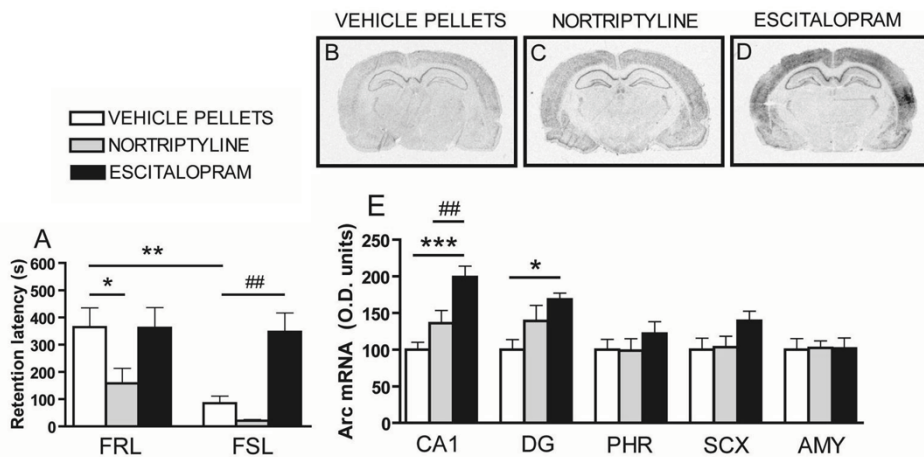


## Dysfunctional regulation of glutamatergic NMDA receptors and 5-HT<sub>1A</sub> receptors



Eriksson et al., 2012

## Memory normalization and increased Arc mRNA by the SSRI but not TCA antidepressant



Eriksson et al., 2012

### Mechanisms beyond elevation of monoamines

- Several actions of antidepressants are mediated by BDNF/TrkB regulation of AKT, PLC and MAPK intracellular cascades (Duman *et al.* 2007; Rantamäki *et al.* 2007).
  - The MEK/MAPK pathway also regulate ionotropic receptors, structural remodeling and consolidation of fear memories (Eckel-Mahan *et al.* 2008).
  - BDNF, PKA, PKC and MEK/MAPK induces expression of Arc, an effector protein enriched in hippocampal dendritic spines (Steward and Worley, 2001; Bramham *et al.*, 2010).
  - Blockade of 5-HT<sub>1A</sub> receptors augments the effect of an acute dose of paroxetine on increasing transcription of Arc mRNA (Tordera *et al.* 2003).
-



## Daniel Souery, MD

Centre Européen de Psychologie Médicale - PsyPluriel, Brussels

Dr Daniel Souery, MD, graduated in June 1991 from the Faculty of Medicine, Université Libre de Bruxelles. His clinical work has mainly focused on the management of unipolar and bipolar affective disorders, including psychopharmacological treatments and treatment resistance. He launched the COPE-Bipolar programme (Clinical Outcome and PsychoEducation for Bipolar disorders) in Belgium, consisting of a computerized tool for the diagnosis and follow-up of bipolar disorders and a psycho-education programme for bipolar patients and their families. COPE-Bipolar is now available in different centers throughout Belgium. He is the author of "comprendre et traiter les troubles bipolaires" (Eds Vivio 2012), a brochure for bipolar patients and their families. He has also been actively involved in launching research projects in different areas such as multi-centric studies in psychiatric genetics, bipolar disorders, pharmacogenetics, and treatment resistant depression. He is widely published on the subject of genetics of bipolar and unipolar affective disorders. He recently published scientific papers on clinical aspects of mood disorders (Phenomenology of psychotic mood disorders: lifetime and major depressive episode features (J Affect Disord. 2011 Dec;135(1-3):241-50). His research interests also include the genetic causes of suicidal behaviour and treatment response to psychotropic drugs (pharmacogenetics).

Dr Daniel Souery is the coordinator of an international group of experts on treatment resistant depression. He is a member of the Belgian College of Neuropsychopharmacology and Biological Psychiatry (BCNBP). He is a member of the Collegium Internationale Neuro-Psychopharmacologicum (CINP) and an active member of the scientific program committee of the European College of Neuropsychopharmacology (ECNP). He is member of the task force on the use of psychotropic drugs at the Belgian Ministry of Health (Conseil Supérieur de la Santé).

He is Scientific Secretary of EACIC (European Accreditation Committee in CNS). He is now running a multidisciplinary psychiatric center in Brussels (PsyPluriel-Centre Européen de Psychologie Médicale).

### **Abstract: Phenomenology of bipolar disorders: impact on our clinical practice and therapeutic choices**

Modern classification of the mental disorders are mainly based on a categoriel model, very useful to improve the reliability of diagnostic categories. This approach facilitates communication in clinical practice and research and has the advantage to be applicable through various cultures. However it has some limitations and dissatisfactions when applied to complex psychiatric disorders such as bipolar disorders. Clinicians often complains about the "reductionism" and rigidity of the use of the DSM-IV.

The presentation will address the unmet needs of modern classification systems when applied to bipolar disorders. We will discuss the concepts of spectrum and dimensions in bipolar disorders and how to better understand and include the phenomenology of bipolar disorders in our diagnostic concepts. Which dimensional « phenomena's » are of clinical interest and/or can contribute to improve our therapeutic approaches? As example, we will present the value of predominant polarity in diagnosing and treating bipolar disorders.

Local Organizing Committee

# Phenomenology of bipolar disorders: impact on our clinical practice and therapeutic choices



Dr Daniel SOUERY  
PSYPLURIEL  
Bruxelles



## Agenda

- Discussion around the concepts of SPECTRUM and DIMENSIONS in bipolar disorders
- To better understand and include the phenomenology of bipolar disorders
- How to integrate these « phenomena » in the diagnostic categories
- Which dimensional « phenomenas »?
- Clinical interest and therapeutic approaches

**Bipolar disorders:  
Unmet needs and dissatisfactions**

- Reductionism and rigidity of the use of the Patient DSM-IV
- “not classifiables”, vaguely classified in the category NOS
- Excess of comorbidities (anxiety, substances,...)
- “Invention” of intermediate categories as only response to the debate of the “diagnostic borders” (Schizo-affect, mixed states)

**Bipolar disorders:  
Unmet needs and dissatisfactions**

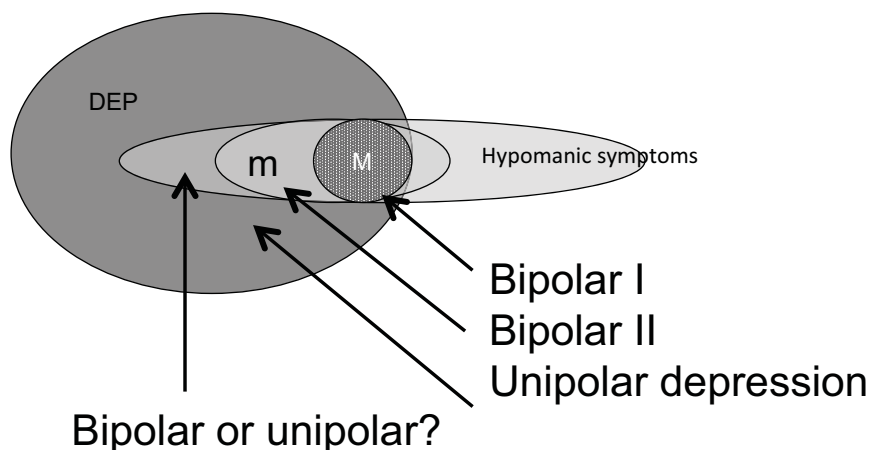
- Categorical model independent of etiologic knowledge, absence of bio-markers, relative validity
- Poor correlation between suggested categories and the pharmacological recommendations for treatment (exceptions? Rapid cycling)

**Table 3. Limitations of Current Diagnostic Criteria for Bipolar Disorder**

- Psychotic symptoms are common in mania and may also happen in depression, but they are not part of the diagnostic criteria, reinforcing the idea that psychosis is a core feature of schizophrenia but not bipolar disorder
- Mood-congruent vs mood-incongruent psychotic symptoms are not well defined
- Bipolar depression is undistinguishable from unipolar major depression
- Recurring depressions are not recognized as a potential precursor to bipolar disorder—may be diagnosed as a depressive disorder
- Mixed symptoms are not sufficiently characterized, and mixed episodes are too narrowly defined
- Cognitive symptoms are not included
- Drug-induced mania and hypomania are excluded: problems in judging what “direct physiological consequence of a drug, medication, or somatic treatment” means
- No account is taken of family history and biological markers
- Four-day duration required for diagnosis of hypomania and 1 week for mania may be too long
- Bipolar disorder not-otherwise-specified may include the majority of cases, particularly in children and adolescents

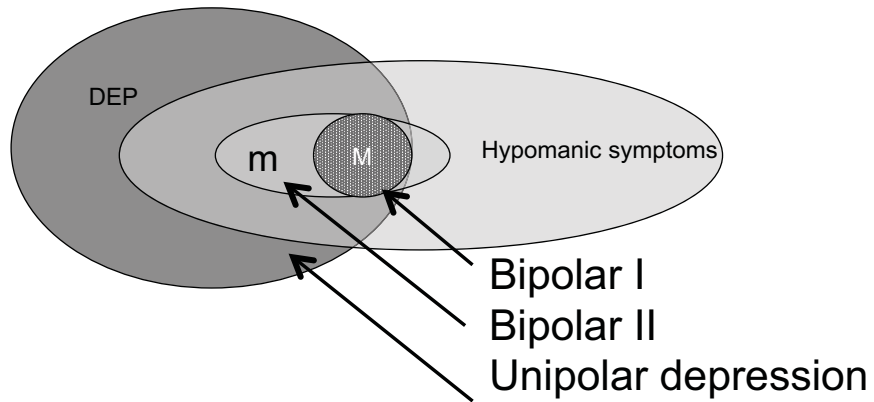
Vieta and Philips. Schizophrenia Bulletin vol. 33 no. 4 pp. 886–892, 2007

## The bipolar phenotype including the spectrum

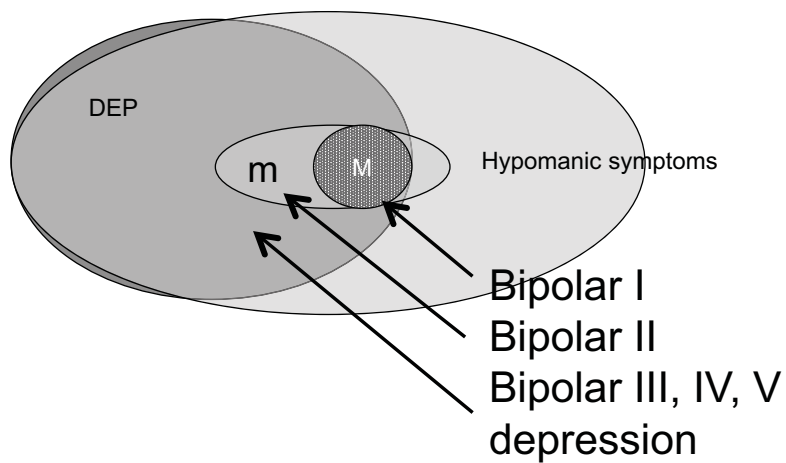




## The bipolar phenotype including the spectrum



## The bipolar phenotype including the spectrum

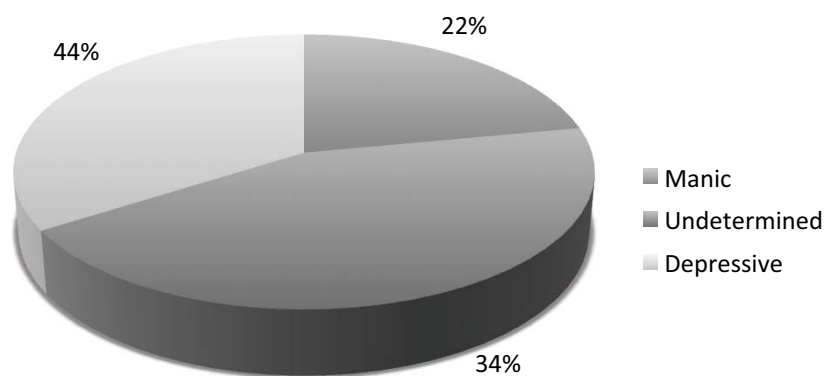


## Exemples of such dimensions

- Predominant polarity
- Psychotic symptoms
- Behaviors: Inhibition/activation
- Emotional reactivity
- Bipolar depression
- Episodes, impulsivity/suicidality/substance abuse/cognitif impairments

Adapté à partir de Vieta and Phillips 2007, Henry and Etain 2010,

## Predominant polarity in clinical practice



Colom F et al. J Affect Disord 2006

**Table 1.** Predominant Polarity Correlates

Depressive Polarity	Manic Polarity
60% bipolar patients	40% bipolar patients
More bipolar II	More bipolar I
More depressive onset	More manic onset
More seasonal pattern	Younger and earlier onset
More suicide attempts	More substance misuse
Better long-term response to lamotrigine	Better long-term response to atypical antipsychotics
More antidepressant use	

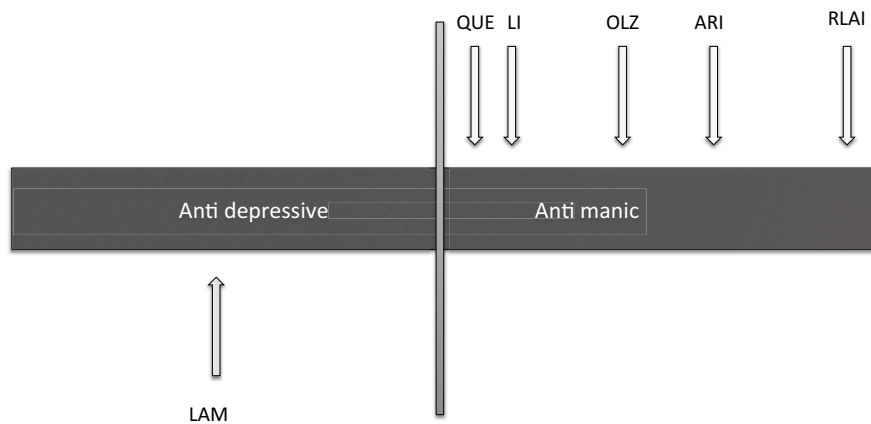
Vieta and Philips. Schizophrenia Bulletin vol. 33 no. 4 pp. 886–892, 2007

## Polarity index for medications used in relapse prevention

Medications	NNT mania	NNT depression	NNT mood episode	Polarity index
Aripiprazole	8.81	38.5	6.6	4.38
Lamotrigine	50.4	20.2	11.6	0.40
Lithium	4.4	6.1	3.5	1.39
Olanzapine	4.7	14	3.5	2.98
Quetiapine	3.5	4	2.8	1.14
Rispéridone LAI	4.4	53.2	4.5	12.09
Valproate	21.3	10.5	7	0.49

Popovic et al. Eur Neuropsychopharmacol, 2012 May;22(5):339-46.

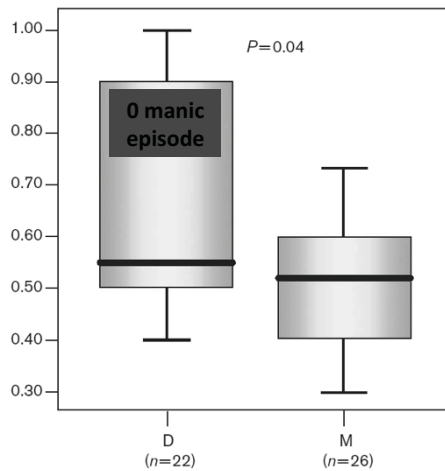
## Polarity index for medication use in relapse prevention



Popovic et al. Eur Neuropsychopharmacol, 2012 May;22(5):339-46.

**Table 2 Prediction of depressive (vs. hypo-manic, manic or mixed) polarity using logistic regression**

Variable	Estimate ( $\pm$ SE)	$\chi^2$ (Wald)	P value
Serum lithium level	6.62 $\pm$ 3.07	4.64	0.03
Diagnostic subgroup (bipolar II/not otherwise specified)	1.03 $\pm$ 1.05	0.96	0.33
Type of index episode (manic or mixed)	- 1.09 $\pm$ 1.05	1.07	0.30
Bech-Rafaelsen Mania Scale, total score	0.52 $\pm$ 0.42	1.56	0.21
Bech-Rafaelsen Depression Scale, total score	- 0.38 $\pm$ 0.33	1.29	0.26



Manic or mixed recurrences occur at lower lithium levels,  
 Depressive pole prevails in the higher range  
 Higher lithium levels are needed to prevent manic episodes than to prevent depressive episodes

Nikolaus et al. International Clinical Psychopharmacology 2007, 22:125–131

Range, quartiles and median of lithium plasma levels in patients with predominantly depressive (D) vs (hypo-) manic or mixed (M) recurrences.

**Table 2.** A proposal for dimensional classification as a further axis or module for the classification of mental disorders

Dimension/Severity	None (absent)	Mild	Moderate	Severe
Psychotic (positive) symptoms	0	1	2	3
Negative symptoms	0	1	2	3
Manic symptoms	0	1	2	3
Depressive symptoms	0	1	2	3
Cognitive impairment	0	1	2	3
Anxiety	0	1	2	3
Obsessive-compulsive symptoms	0	1	2	3
Substance misuse	0	1	2	3
Impulsivity	0	1	2	3
Suicidality	0	1	2	3
Eating problems	0	1	2	3
Sleeping problems	0	1	2	3
Sexual problems	0	1	2	3

Vieta and Philips. Schizophrenia Bulletin vol. 33 no. 4 pp. 886–892, 2007



Contents lists available at ScienceDirect

## Journal of Affective Disorders

journal homepage: [www.elsevier.com/locate/jad](http://www.elsevier.com/locate/jad)



Research report

### Phenomenology of psychotic mood disorders: Lifetime and major depressive episode features

Daniel Souery <sup>a</sup>, Leonardo Zaninotto <sup>b</sup>, Raffaella Calati <sup>b,\*</sup>, Sylvie Linotte <sup>c</sup>, Othman Sentissi <sup>d</sup>, Daniela Amital <sup>e</sup>, Ulrike Moser <sup>f</sup>, Siegfried Kasper <sup>f</sup>, Joseph Zohar <sup>g</sup>, Julien Mendlewicz <sup>h</sup>, Alessandro Serretti <sup>b</sup>

<sup>a</sup> Laboratoire de Psychologie Médicale, Université Libre de Bruxelles and "Psy Pluriel", Centre Européen de Psychologie Médicale, Brussels, Belgium

<sup>b</sup> Institute of Psychiatry, University of Bologna, Bologna, Italy

<sup>c</sup> Fonds de la Recherche Scientifique (FNRS), Laboratoire de Neurologie Expérimentale, Université Libre de Bruxelles, Bruxelles, Belgium

<sup>d</sup> Département de Psychiatrie Hôpitaux Universitaires de Genève, Faculté de Médecine de Genève, Geneva, Switzerland

<sup>e</sup> Ness-Ziona Mental Health Center, Ness-Ziona, Israel

<sup>f</sup> Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria

<sup>g</sup> Chaim Sheba Medical Center, Tel-Hashomer, Israel

<sup>h</sup> Université Libre de Bruxelles, Brussels, Belgium

## Major findings

- Our results revealed a number of robust differences in the clinical picture of Psychotic Mood Disorders (PMD),
  - 
  - 
  - 
  - 
  -of 21) of mood symptoms.
  - Thyroid dysfunction

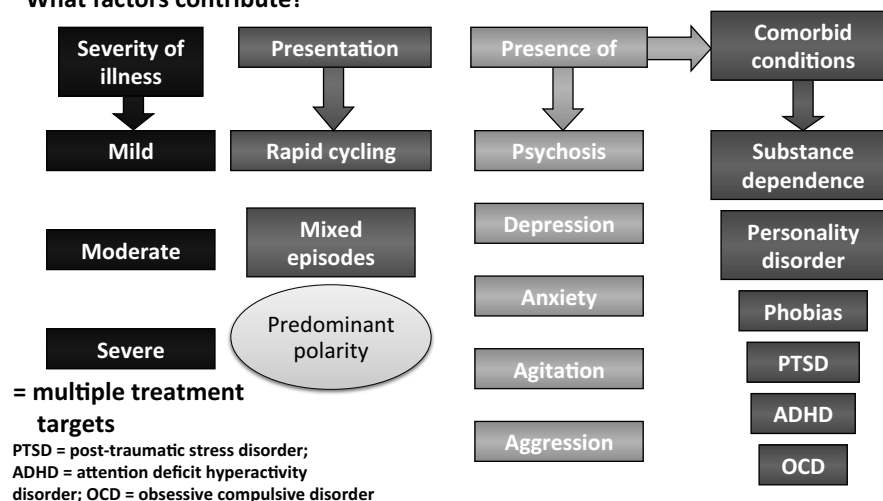
**Table 4.** Proposal for a Modular Approach to the Classification and Diagnosis of People With Mental Disorders

Module I	Categorical classification
Module II	Dimensional assessment
Module III	Laboratory data
Module IV	Medical nonpsychiatric conditions
Module V	Psychological assessment
Module VI	Social issues (environmental factors and social function)

Vieta and Philips. Schizophrenia Bulletin vol. 33 no. 4 pp. 886–892, 2007

## Dimensional approach in bipolar disorders

What factors contribute?









# 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

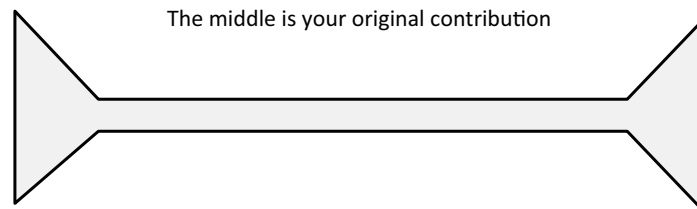


## The start

- 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



Start with the biggest questions and get progressively more specific

Focus now on conclusions



## Introduction

- Context
- Study question
- Relevant knowledge on issue

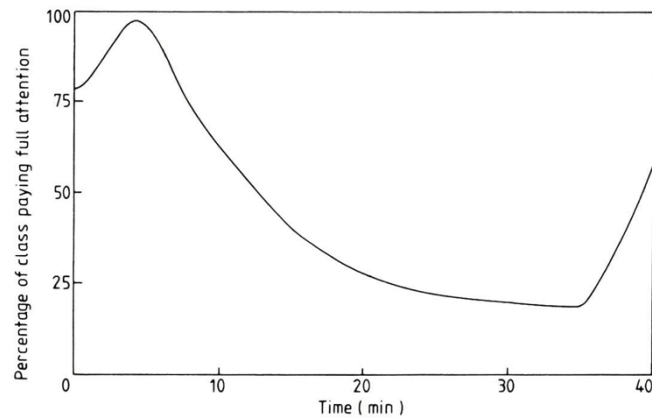


## Major findings

- 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!



## Formal aspects

Type size should be 20 points or larger:

18 point

20 point

24 point

28 point

36 point

\* References can be in 14 point font





**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”



ECNP

# How to prepare a manuscript

Celso Arango

[www.ecnp.eu](http://www.ecnp.eu)



ECNP

## Categories

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

[www.ecnp.eu](http://www.ecnp.eu)



## 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



## 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! )



ECNP

*“Scientists are rated by what they finish, not by what they attempt”*

[www.ecnp.eu](http://www.ecnp.eu)



ECNP



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

[www.ecnp.eu](http://www.ecnp.eu)



## **Elmārs Rancāns, MD, PhD**

Department of Psychiatry,  
Riga Stradins University, Latvia

Elmārs Rancāns is Professor of Psychiatry and Chair of the Department of Psychiatry and Narcology, Riga Stradins University, Riga, Latvia. Having graduated from the Faculty of General Medicine, Latvian Academy of Medicine, he completed post-graduate training in psychiatry at the Riga Psychoneurological hospital, Latvia.

Dr. Rancans has defended his PhD at the Department of Psychiatry, Umea University, Sweden on the topic of suicide research.

Dr. Rancans is currently involved in the teaching of students and he is also a Head of Residency training programme at the Riga Stradins University. He is actively lecturing nationally and internationally at different CME events for GPs and specialists.

The current clinical and research interests of Dr. Rancans are epidemiology and psychopharmacological treatment of affective and psychotic disorders. He has participated in numerous international and local trials. Dr. Rancans has published many articles and presented posters at international congresses.



## **Jaanus Harro, MD, PhD**

Dr. Jaanus Harro was trained as a medical doctor at the University of Tartu and specialised in psychopharmacology (PhD 1990 in Tartu, DMSci 1993 in Uppsala). Subsequently he held personal professorships in Tartu in neuropsychopharmacology and health promotion, and has since 1998 served as professor of psychophysiology.

In 2001 he led the establishment and became the director of the Estonian Centre of Behavioural and Health Sciences, a national alliance of research groups in medicine and social sciences focusing on regulation of behaviour. His research is on affective neuroscience and includes psychopharmacological and molecular genetic approaches in animals and humans, and population-based longitudinal studies on neurobiology of personality and health-related behaviour.

Dr Harro has authored or co-authored about 180 original articles, reviews and book chapters in broadly distributed international publications. He has served in several committees of CINP and ECNP, and is Associate Editor of *European Neuropsychopharmacology* and an Editorial Board Member of *Acta Neuropsychiatrica*. He is also a member of the WHO Expert Advisory Panel on Drug Dependence. Dr Harro is a Foreign Member of the Royal Society of Sciences in Uppsala.



## Robertas Bunevičius, MD, PhD

**Dr. Robertas Bunevičius** is a physician educated in psychiatry, endocrinology, and psychophysiology. He had run his training in Lithuania, Russia and USA. At present he holds an office of the Director and Chair of the Behavioral Medicine Institute at the Lithuanian University of Health Sciences.

Dr. Bunevičius had defeated Ph.D. thesis in 1993, and Doctor habilitus (D.Sc.) thesis in 1999. His research interest covers interaction of mental state with endocrine function and immunity, as well as reactivity to stress in psychiatric and cardiac patients. Dr. Bunevičius has published papers in medical journals with high impact factor, including first authorship in the *New England Journal of Medicine*. He made contribution for several textbooks as well as for development of new diagnostic and therapeutic methods in psychiatry and endocrinology.

For his research contributions several national and international award were presented to Dr. Bunevičius including Award of the European College of Neuropsychopharmacology (Venice, Italy, 1995), Fulbright Award (Washington, D.C, 1997), Prize of the World Federation of Societies of Biological Psychiatry (Florence, Italy, 1999), Award of the International Society of Psychoneuroendocrinology (Montreal, Canada, 2005), Scientist of a Year Award (Kaunas, Lithuania, 2009), and Lithuanian Academy of Sciences Award (Vilnius, Lithuania, 2011).

Dr. Bunevičius is involved in the activities of national and international scientific societies. He is a president of the Lithuanian Society of Biological psychiatry, a Vice-president of the World Federation of Societies of Biological Psychiatry (WFSBP), member of the Executive Committee of the International Neuropsychiatric Association (INA) and ambassador of the European College of Neuropsychopharmacology (ECNP). Dr. Bunevičius have organized several national and international scientific meetings, delivered lectures and reports as invited speaker at numerous conventions.

# Abstracts

**Alttoa, Aet**

**University of Tartu, Estonia**

Early aversive life experiences have adverse consequences that persist into the adulthood. The gaseous neurotransmitter nitric oxide (NO) has been hypothesised to play a role in regulating affective states; mice lacking the NO-synthesising enzyme neuronal NO synthase (*nNos*, also termed *Nos1*) display increased aggression/impulsivity, reduced anxiety and cognitive deficits. The aim of the current study was to investigate the effects of early life stress (by using the maternal separation paradigm) on the anxiety- and depression-related behaviour in the *Nos1*-knockout mice. The results of the study will be presented and discussed.

**Aonurm-Helm, Anu**

**University of Tartu, Estonia**

The aim of the present study is to explore whether the prenatal depression and/or blockade of SERT during the development affects the brain plasticity of adult offspring's and which is the role of NCAM/PSA-NCAM in these mechanisms. The first results of our study show that mice whose mothers were exposed to the stress or SSRI treatment during the pregnancy are more anxious, react more strongly to acute stressor and show reduction in short-term memory at the age of 2 months.

**Kaasik, Kadri**

**University of Tartu, Estonia**

Modeling the relationship between serotonin transporter gene promoter region polymorphism (5-HTTLPR), adverse life events, neuroticism, anxiety, and eating disorder symptomatology. The aim of this study is to show associations between 5-HTTLPR, adverse life events, neuroticism, anxiety, and eating disorder symptomatology in a large non-clinical female population. This study is based on ECPBHS (Estonian Children Personality, Behaviour and Health Study) data. The main finding of the current study is that the influence of neuroticism and adverse life events on eating disorder symptomatology (bulimic symptomatology, drive for thinness) is mediated by trait anxiety. Trait anxiety can be seen as a stable trait predisposing people toward higher levels of eating disorder symptomatology.

**Vaht, Mariliis**

**University of Tartu, Estonia**

In a population-representative birth cohort study, 5-HTTLPR genotype had a significant effect on subjects' alcohol consumption when birth cohort (representing environmental changes) and gender were also taken into account. Subjects with s/s genotype appeared to be most affected by environmental changes and the effect differed between male and female subjects. These results indicate that expression of

genetic vulnerability for alcohol use in children and young adults is influenced by cohort effects and also depends on the gender.

**Bezborodovs, Nikita**

**Riga Stradins University, Latvia**

We have conducted an audit of the patterns of use, effectiveness and side effect profiles of antipsychotic medication in CAP inpatients with schizophrenia spectrum disorders, treated by CAP services in Riga, Latvia. We found that antipsychotics are widely used in aforementioned population, but the rate of side-effects (hyperprolactinaemia, weight gain and QTc elongation) is high. We would like to extend this study by conducting a prospective cohort study, enrolling in an open cohort all patients presenting with psychotic symptoms to Riga's CAP services, and following them up to the age of 18, paying special attention to side effect monitoring. This could both yield important insights and improve the standards of care.

**Bušs, Jānis**

**Riga Centre of Psychiatry and Addiction disorders, Latvia**

The word stigma is used to define the feeling of shame or failure which makes the individual different from other people. Disease symptoms, side-effects of the treatment and psychiatric diagnosis as such can be a reason for negative and stigmatizing attitude from other people. 30 outpatients with depression and 30 outpatients with schizophrenia were questioned about the characteristic signs of psychiatric stigma in a previous study. It was found that patients undoubtedly experienced psychiatric stigma and that depressive patients experience less psychiatric stigma than schizophrenia patients. Aims: to study the stigmatization of hospitalized depressive and schizophrenia patients and compare the results obtained with the results of outpatients. Methods: The Link's Devaluation and Discrimination Scale will be used and patients with schizophrenia and depression will be questioned on the last day of hospitalization.

**Grauda, Liēna**

**Riga Stradins University, Latvia**

Portrayals of Psychiatry in the Internet Environment: the Role of Online News Media Background: Internet has become an important environment for communication and online news sites are an easy, fast and widely-used media for getting the latest news. Thus the impressions created by these media have a profound impact on the public. Aim: to study the portrayal of psychiatry, psychiatrists and psychiatric patients in Latvian online news media. Hypothesis: portrayal of psychiatry, psychiatrists and psychiatric patients in Latvian online news media are mostly stereotypical, stigmatising, distorted and exaggerated and the mentally ill are commonly portrayed as frightening and dangerous.

**Jumtiņa, Elina**

**Rīga Stradins University, Latvia**

It is estimated that approximately 130 million people are infected with chronic hepatitis C virus (HCV) worldwide. According to the guidelines on treatment of HCV issued by the Latvian Centre of Infectology (LIC), first choice treatment for HCV patients is co-administration of pegylated interferon and ribavirin. As reported in research papers, around 19-44% of patients treated with interferon developed symptoms of depression. The objective of the first phase of the envisaged study is to identify and assess patients treated with interferon at LIC, also receiving any group of antidepressants. The second phase will involve multifactor analysis of the data obtained.

**Pudāns, Matīss**

**Rīga Stradins University, Latvia**

It is estimated that approximately 130 million people are infected with chronic hepatitis C virus (HCV) worldwide. According to the guidelines on treatment of HCV issued by the Latvian Centre of Infectology (LIC), first choice treatment for HCV patients is co-administration of pegylated interferon and ribavirin. As reported in research papers, around 19-44% of patients treated with interferon developed symptoms of depression. The objective of the first phase of the envisaged study is to identify and assess patients treated with interferon at LIC, also receiving any group of antidepressants. The second phase will involve multifactor analysis of the data obtained.

**Rusaka, Marija**

**Rīga Stradins University, Latvia**

**Personality profile of patients with first episode acute and transient psychotic disorder**

Introduction: Acute and transient psychotic disorder (ATPD; F23, ICD-10) has been described as an acute psychosis with brief onset and polymorphous symptomatology. Methods and materials: A prospective follow-up study of all first-time hospitalised patients from the Rīga Centre of Psychiatry and Addiction Disorders (RCPAD) in Latvia who fulfilled the ICD-10 criteria.

Results: 102 patients were hospitalized with first-episode ATPD. Over an average 26.5-month follow-up period, 59.8% (61) of patients were not re-hospitalised. 72.6 % had elevated scores of the personality profile.

Conclusions. A large portion of ATPD patients showed deviations from the norm in personality profiles.

**Sprūģe, Ilona**

**Riīga Stradins University, Rīga Centre of Psychiatry and Addiction Disorders, Latvia**

Chemotherapy has severe and persistent physical and psychosocial symptoms which worsens quality of life (QoL) and requires a new adaptation. A research project which I would like to do is to study how depression prior to first chemotherapy cycle



influences QoL of oncologic patients (two comparable groups) depending on haematology value – haemoglobin (Hb). Correlations what I am planning to investigate: Does depression influence QoL and in what grade? Is low Hb concentration is contributing factor of depression for poorer QoL? Have the characteristic features of patients (family status, level of education, employment status, health behaviour) involved severity of depression and scoring of QoL?

**Štāne, Laura**

**Riga Stradins University, Latvia**

My research topic is: schizoaffective disorder- nosological, diagnostic and therapeutic issues in Riga Centre on Psychiatry and Addictions. The aim of the research is to analyse schizoaffective disorders' nosology, diagnostics and treatment in different periods of time in our country and to compare it with literature data. I use the literature about different aspects of the disorder: epidemiology, demography, genetic, visual diagnostic, symptomological, ect. It is a retrospective, longitudinal research, I am analysing the medical documentation of patients, and it is a random study. The hypothesis of the study is that schizoaffective disorder is undiagnosed in Riga Centre Psychiatry and Addictions and that disturbs to reach the aims of treatment.

**Vāvers, Edijs**

**Latvian Institute of Organic Synthesis, Latvia**

**Sigma-1 receptor as a novel CNS drug target**

Accumulating evidence suggests that the sigma-1 receptor plays an important role in the pathophysiology of many neurological and psychiatric disorders, such as Alzheimer's disease, amnesia, pain, depression, schizophrenia, stroke and addiction. Dementia is a serious loss of global cognitive ability which includes learning and memory impairments. A novel 4,5-disubstituted derivative of piracetam E1R possesses positive sigma 1 receptor modulatory activity and significant cognition enhancing properties. The effects of E1R will be evaluated in behavioural experiments (passive avoidance test with scopolamine-induced cognitive deficits). E1R might serve as a novel pharmacological agent for improving affected cognition processes in neuropsychiatric disorders.

**Vrublevska, Jelena**

**Riga Stradins University, Latvia**

**Screening for depression in primary care in Latvia**

Mood disorders are highly prevalent and undiagnosed in primary care in Latvia. Only recently the first data on the prevalence of depression in Latvian population was obtained, however, at the same time no studies on prevalence of depression in primary care have been conducted before. In the research project is planned to select 8 general practices by stratified random sampling and quota methods. During 2-week period all patients will be invited to fill in PHQ-9 paper-and-pencil questionnaire. Screening positive respondents will be interviewed as a standard using MINI and will be asked for demographic data.

**Zālītis, Pēteris**

**Riga Stradins University, Latvia**

Initial drug therapy appointment tactics and evaluation of the efficacy of hospitalized schizophrenic spectrum patients over the last 30 years. New onset of medical treatment tactics of the past 30 years has been different from the present day. The study would look at the possibility of differences in the effectiveness of treatment approaches for several decades back and make a comparison. A class of medications and dosages. Duration of hospitalization, and time to the second hospitalization adverse event profile

Aim: Compare treatment tactics and effectiveness of first-time RPNC (Riga's Psychiatry and narcology center) F2 hospitalized patients sphere months of September and March 1986th, 1996. and 2006. year.

Hypothesis: Closer to the present day observed effective initial treatment of patients.

- Relatively decreased drug therapy due to side effects of medication dose levels.

The last years of treatment compared to the previous tactic enhances the patients' clinical condition, reduce symptoms.

- Closer to the present day due to the different treatment tactics decreased the number of days of hospitalization and rehospitalisation rate of patients discharged from the hospital.

Methods and Materials: Research would be made as retrospective study. Data collection will be using RCPAD archive of patient records and will analyse the medical history of patients RPNC archive dividing the respective disease groups according to ICD - 10 classification. For data collection would be made the protocol, after that database creation. Pooled data - patient received therapy specificity for the year, syndrome, remission, rehospitalisation frequency and time between them, processing and analysis. For making happen evaluation of the tactics for neuroleptic therapy would be use using neuroleptics equivalent table to convert working process of neuroleptic dose. Data processing with SPP20 program would be done to do comparison of treatment history, duration of remission, the frequency of hospitalization and syndromology.

**Antonova, Ingrida**

**Vilnius University, Lithuania**

**Visual event-related potentials in schizophrenic patients and the impact of treatment to visual perception**

It is known that the visual perception is affected in schizophrenia but there are few studies researching visual perception changes in people with mental disorders using event-related potentials (ERP) technique.

The goal of this research is to find differences in visual ERPs before and after the treatment of schizophrenia when different pharmaceuticals are used for the treatment.

Healthy controls and schizophrenic patients (two groups: with hallucinations and without hallucinations) participate in this research.

Three tasks for eliciting visual ERPs P300 are used:

1. Stroop task
2. Figure recognition task
3. Visual odd-ball task

Coloured words are visual stimuli in the 1st task, and five different geometric shapes (square, circle, parallelogram, diamond, and triangle) are stimuli in the 2nd and the 3rd tasks.

It is scheduled to perform ERP recordings before the treatment, during the treatment period, and after the treatment with neuroleptics. Comparison of data between healthy subjects and patients will be done, and differences before and after the treatment will be defined.

Changes of visual ERPs could demonstrate the effectiveness of certain pharmaceuticals on cognitive functions. Such studies are very important, because the better methods of treatment, better medication for each patient is chosen, the healthier and more sustainable life the patient can lead.

**Burkauskas, Julius**

**Lithuanian University of Health Sciences, Lithuania**

**Effect of Beta-blockers on Cognitive Functions in Coronary Artery Disease Patients**

### **Introduction**

Recent study has been stipulating inverse association between beta-blockers usage for hypertension and dementia [1]. Little is known about what specific cognitive functions are affected by beta-blockers usage. The aim of our study was to determine the effect of beta-blockers on cognitive functions in non-demented coronary artery disease (CAD) patients.

**Methods.** A 3-year study included CAD patients two weeks after acute myocardial infarction or unstable angina attending cardiac rehabilitation program. In sum, 539 patients were enrolled to the study; 386 (72%) men and 153 (28%) women; mean age of 59 years (SD=9). Patients were evaluated for demographic and clinical characteristics including, medication plan, cardiovascular functional status according to the New York Heart Association (NYHA). Left ventricular ejection fraction (LVEF) was evaluated quantitatively by cardiologist by the means of echocardiography. Digit Span Test and Digit Symbol Test were used to assess auditory attention, mental flexibility, psychomotor performance and incidental learning. Trail Making Test A and B was used to measure perceptual speed and task switching. Participants were considered impaired in the specific cognitive performance if their scores fell below the 25<sup>th</sup> percentile of the study population. Multiple logistic regression models were used to evaluate beta-blockers risk for impairment in each of the cognitive tests.

**Results.** Controlling for potential confounders such as age, gender, education, NYHA class and LVEF, beta-blockers usage was associated with a 3.56-fold increase (95% confidence, 1.360 to 9.335) in risk for impairment in incidental learning as measured by Digit Symbol Test. There was no significant effect of beta-blockers to other measured cognitive functions.

**Conclusions.** In CAD patients two weeks after acute cardiac events beta-blockers usage is associated with a selective impairment in incidental learning.

**Diržius, Edgaras**

**Lithuanian University of Health Sciences, Lithuania**

### **Oppel-Kundt illusion manifestation peculiarities for patients with schizophrenia**

Background: Oppel-Kundt illusory pattern can be described as an observable path which is divided by a number of equally spaced markers and is usually perceived longer than an undivided path of the same length (1). This illusion manifestation for schizophrenia patients was investigated once in 1974 (2).

Methods: Subjects were patients at HLUHS Kaunas Clinics in the clinic of psychiatry. Approval of LUHS bioethics centre was acquired, all participants agreed to take part in the study on a free will. The experiments were carried out in a darkened room with stimuli presented on a monitor. Subjects were asked to adjust the length equality in the two stimuli intervals. The number of the filling spots varied from 0 to 19 in the referential intervals. Each subject repeated experiments for 10 times. Symptoms were gathered from patients history. Anti-psychotic drug doses were converted to chlorpromazine equivalents and benzodiazepine drug doses were converted to diazepam equivalents. ANOVA and T-Test criteria were used for data analysis.

Results: Study group consisted of 11 individuals with diagnoses: F20.0 (N=3), F25.1 (N=5), F20.6 (N=2), F23.11 (N=1). Control groups consisted of 11 matched individuals (no mean age or sex difference between groups  $p < 0,05$ ). No illusion manifestation difference was found between two groups, except with 0 filling spots. Statistically significant difference was found when comparing dependence on: anti-psychotic drug dose, diagnoses, psychotic episodes and symptoms (confusion and disorganization).

Conclusion: Study shows, that there could be some Oppel-Kundt illusion perception differences for schizophrenia-affected people.

**Gudaitytė, Rima**

**Lithuanian University of Health Sciences, Lithuania**

### **Relationship between suicidal behavior and cognitive disorders in the elderly**

Introduction. Suicide - a major public health problem. Evaluation of European Union data, suicide per 100 000 population increases with age, it is twice more common in old age, than in the general population [1].

The aim – to evaluate the relationship of suicidal behaviour and cognitive disorders in the elderly.

Study participants and methods. The data of 184 patients, with tested cognitive functioning, was analyzed in this study.

Results. 60-70 years age group 62.5% of subjects expressed suicidal thoughts, 70-80 years - 62.3%, in 80 years - 76.9%. Among the city's population 66.0% of subjects had suicidal thoughts, in rural areas - 62.8%. More often expressed suicidal thoughts patients with somatic disease - 66.5%. Suicidal thoughts are more frequent among patients with secondary education - 71.4% or higher - 66.7%, of the original - 61.1%, basic - 55.6% or higher education - 54.2%. Patients, with mental disorders, has been established over the past 12 months, were more likely to commit suicide or expressed suicidal thoughts (73.5% of observed cases).

Conclusions. An elderly patient with cognitive disorders with the risk for suicidal behaviour commonly lived in an urban area, had a secondary education, a comorbid somatic illness and their suicidal behaviour indicated during the first year from psychiatric diagnosis.

**Jusiūtė, Raimonda Egle**

**Lithuanian University of Health Sciences, Lithuania**

### **Characteristics of violence experiences by Lithuanian health professionals in some medical institutions**

Introduction: Violence experienced by medical professionals at work is a very relevant topic. The following forms of violence are distinguished: verbal abuse, psychological violence, physical, sexual harassment [1]. There are three groups of factors, which may cause aggression or violence against employees: internal factors – mental disorders, alcohol, drugs, etc.; external factors – lack of privacy and space, overcrowded hospital wards; and interactional factors related to interaction between staff and patients [2]. There is almost no statistical data and preventive or supportive measures concerning this issue in Lithuania.

Purpose of the study: to assess prevalence and characteristics of workplace violence experienced by health sector employees in Lithuania.

Subjects and Methods: 568 health sector employees (81.5% (n=463) women and 18.5% (n=105) men) working at medical facilities of Kaunas and Šiauliai cities in Lithuania were surveyed using a questionnaire developed by the investigators and including items concerning sociodemographic and professional data as well as characteristics of experienced violence. Statistical analysis was conducted using the SPSS 16.0 software, the statistical significance level  $p < 0.05$ .

Results: 54.8% (n=311) of subjects reported experience of violence. 53.1% (n=164) reported two or more kinds of violence, 24.9% (77) verbal abuse, 17.2% (53) psychological violence, 2.3% (7) physical abuse, 3% (1) sexual harassment, 2.3% (7) all kinds of violence. 29.1% (n=90) experienced violence of the patients and their relatives, 22% (n=68) of the patients, 7.4% (n=23) of employer or a person in superior position, 3.9% (n=12) of patients relatives, 2.9% (n=9) of peers, 2.6% (n=8) of co-worker in lower position, 0.3% (n=1) other, 31.7% (n=98) experienced violence of two or more of aforementioned persons.

Conclusions: More than half of the health sector employees in Lithuania reported the violence at work – two or more kinds of violence, predominantly verbal and psychological violence. Most of subjects reported experiencing violence from patients and their relatives.

**Juškienė, Alicja**

**Lithuanian University of Health Sciences, Lithuania**

### **Mental distress and treatment interventions in myocardial infarction patients: gender differences**

Objectives: To evaluate gender differences in symptoms of depression, anxiety and Type D personality in myocardial infarction (MI) patients after conservative

treatment (CT), percutaneous transluminal coronary angioplasty (PTCA) and coronary bypass graft surgery (CABG).

Design: MI patients after revascularization procedures (PTCA or CABG) or non attending a rehabilitation program were invited to participate in this cross-sectional study.

Methods: In total 443 patients (72% men and 28% women; mean age  $59 \pm 9$  years) participated in the study. Cardiovascular functional status was assessed according to the New York Heart Association (NYHA) functional class guidelines. Symptoms of depression and anxiety were assessed with the Hospital Anxiety and Depression scale (HADS). Patients scoring on the HADS depression subscale and HADS anxiety subscale  $\geq 8$  were considered having possible clinical depression and possible clinical anxiety, respectively. The type D personality construct was measured with the Type D Personality Scale (DS14). The DS14 consists of two 7-item subscales assessing negative affectivity and social inhibition respectively. Patients were categorized as Type D using a standardized cut-off score  $>10$  on both the negative affectivity and social inhibition subscales.

Results: Prevalence of depression symptoms did not differ between men and women in CT group; however, anxiety symptoms were more prevalent in women than in men (64.1 % and 30.2 %,  $p=.002$  respectively). More women than men after PTCA had expressed symptoms of depression (22.2 % and 9.6 %,  $p=.007$ ) and anxiety (50.8 % and 30.1 %,  $p=.002$ ). In CABG group prevalence of depression and anxiety symptoms did not differ between men and women. More women than men had Type D personality (42.9% and 29.2%;  $p=.041$ ) in PTCA group. Prevalence of men and women categorized as Type D did not differ in CT and CABG groups.

Conclusions: Mental distress is more expressed in women than men after PTCA as well as women experience more anxiety symptoms than men when are treated conservatively.

**Krasauskaitė, Dovilė**

**Lithuanian University of Health Sciences, Lithuania**

**Clinical manifestations of neurosyphilis: case report**

Introduction: The classic clinical syndrome of neurosyphilis now rarely seen. The early diagnosis and adequate treatment of infectious syphilis has greatly diminished the incidence of neurosyphilis [1]. Neurosyphilis the problems are further compounded because the signs of neurosyphilis are not pathognomonic and often overlap with signs of other diseases [2]. Paretic neurosyphilis was a major cause of psychosis, dementia, mood disorders and corticospinal tract diseases. Behavioral changes can be present in up to 50%, and simple dementia in 35% of affected individuals [3]. If left untreated, 30% of patients may develop tertiary syphilis, which can manifest as neurosyphilis.

Case report: the case of 66-year-old woman, which symptoms of anxiety, lowered mood, apathy, psychomotor slowing with episodic psychomotor agitation, delusions, cognitive change was a manifestation of neurosyphilis. The diagnosis of depression with psychotic symptoms and diagnosis of light cognitive impairment were

determined. Neurological examination showed no symptoms of any disorder. Treatment with psychotropic medications such as Haloperidol, Diazepam, Citalopram, Olanzapine and Mirtazapine did not give sufficient effect. The positive blood test for syphilis provided the first hint of neurosyphilis and gave direction for further diagnosis and treatment. The treatment was supplemented with an adequate antibiotic treatment for neurosyphilis. After such combined therapy the patient showed clinically significant improvement of mental state.

Conclusion: Neurosyphilis should be part of the differential diagnosis of each patient showing the first time psychiatric disorders.

**Lapėnienė, Justina**

**Vytautas Magnus University, Lithuania**

### **The Associations between Pregnancy Self-efficacy, Pregnancy Anxiety and Health Indexes**

The aim of the study was to evaluate the associations between pregnancy specific psychological and physiological factors. The subjects of the study were 146 pregnant women.

The participants were asked about various aspects related to pregnancy. In order to evaluate pregnancy self-efficacy, Childbirth Self-efficacy Scale (CBSEI, Lowe N.K., 1991) was given. Childbirth self-efficacy is a construct, which reflects women's confidence in her ability to cope with pregnancy, labour and reflects the belief of being able to become a good mother and take appropriate care of the baby. Pregnancy anxiety (Pregnancy Anxiety Scale, Dunkel C.S., Rini C., 1999) is another construct, unique to pregnancy, which reflects the exact purport of specific to pregnancy worries. In order to evaluate biological aspects of pregnancy, questions about specific pregnancy outcomes were asked. Sleep quality, physical activity level and unfavourable to health behavior were measured in order to get a better understanding of various aspects of pregnant women's daily life and behavior.

The results of the study showed that pregnancy specific anxiety declines, when pregnancy self-efficacy enlarges ( $p=0,002$ ). The enlargement of self-efficacy is associated with decline of pregnancy complications ( $p=0,000$ ). Moreover, lower self-efficacy is associated with these complications: „the infection of kidney“ ( $p=0,002$ ), „pelvic pain“ ( $p=0,043$ ), „nausea“ ( $p=0,031$ ) and „vomiting“ ( $p=0,004$ ) and „lower fetus movement“ ( $p=0,017$ ). Major mean of pregnancy self-efficacy scale was identified in the contingent of those pregnant women, whose physical activity level was higher. The increase of self-efficacy is associated with better sleep quality ( $p=0,005$ ). Major mean of pregnancy self-efficacy scale was identified in the contingent of those pregnant women, who didn't smoke during pregnancy ( $p=0,044$ ). The analysis of pregnancy specific anxiety and its correlations with other aspects of pregnancy revealed that - major mean of anxiety level was identified in contingent of those pregnant women, who were diagnosed with „pregnancy anemia“ ( $p=0,028$ ), „low fetus movement“ ( $p=0,042$ ), „bleeding during pregnancy“ ( $p=0,047$ ). Moreover, the results of the study showed that the more active pregnant women are characterized with moderate pregnancy anxiety level. The enlargement of anxiety is

associated with decline of sleep quality ( $p=0,002$ ). Those pregnant women, who didn't drink alcohol during pregnancy were characterized with higher pregnancy anxiety level ( $p=0,038$ ).

**Liaugaudaitė, Vilma**

**Lithuanian University of Health Sciences, Lithuania**

**An association between suicidal ideation and psychiatric medication use in primary care patients**

Background: Psychiatric medication use, depression and anxiety disorders contribute to increased rates of suicidal behaviour (1). The aim of this study was to evaluate the influence of antidepressants use to suicidal ideation in primary care (PC) patients.

Methods: A sample of 998 patients from four urban PC clinics was assessed for current mental disorders and suicidal ideation using the Mini International Neuropsychiatric Interview (MINI). Information regarding management of psychiatric disorders was obtained from medical records. Binary logistic regression was used to evaluate if use of psychiatric medications controlled for socio-demographic and clinical characteristics of patients account for suicide ideation.

Results: Suicidal ideation was identified in 61 (6.1%) patients. After adjustment for socio-demographic and psychiatric factors, univariate and multivariate analysis revealed that current antidepressants use (odds ratio [OR], 5.4; 95% confidence interval [CI], 1.7 to 16.9) and current major depressive episode (MDE) (OR, 2.9; 95% CI, 1.5 to 5.8) was associated with greater chance for suicidal ideation. Excessive alcohol use (OR, 2.0; 95% CI 1.1 to 3.8) was associated with increased suicidal ideation in multivariate model only. Any anxiety disorders (OR, 3.0; 95% CI, 1.8 to 5.1) and anxiolytic use (OR, 2.2; 95% CI, 1.2 to 4.2) were associated with increased suicidal ideation in univariate analysis only. In the final analysis odds for suicidal ideation were evaluated separately for men and for women in multivariate models. In men odds of suicidal ideation were associated with current MDE only (OR, 4.7; 95% CI, 1.5 to 14.8); whereas in women apart of current MDE (OR, 3.6, 95% CI 1.9 to 7.1) it was also associated with use of antidepressants (OR, 6.7, 95% CI 2.1 to 20.9) and with excessive alcohol use (OR, 2.1, 95% CI 1.03 to 4.1).

Conclusions: In PC patients use of antidepressants as well as excessive alcohol use are associated with suicidal ideation in women, but not in men. Presence of current major depressive episode is associated with suicidal ideation in men and in women.

Key Words: primary care, suicidal ideation, antidepressants.

**Mickevičiūtė, Dalia Elena**

**Lithuanian University of Health Sciences, Lithuania**

**Prolonged Grief in Women Experiencing Child Loss**

Loss of the child is a traumatizing life experience which can lead to complicated grief. The aim of the study was to evaluate emotional state of the mothers' who have lost their child at least six months ago. It was a pilot study in which 27 women participated. 7 of them (25,9 %) had symptoms of moderate depression, 1 participant (3,7 %) had symptoms of severe depression; 16 participants (59,3 %) had symptoms of



posttraumatic stress disorder (PTSD). Symptoms of depression and PTSD correlated with somatic complaints. We can conclude that child loss is a risk factor for prolonged grief and this population needs special attention for mental health disorders.

**Noreikaitė, Aurelija**

**Lithuanian Health Science University, Lithuania**

### **Mild cognitive failure prophylaxis by food supplements in pharmacy practice**

**Objectives.** Ginkgo and vitamin E medications and food supplements could be used for the prophylaxis of mild cognitive failures (CF). Task of our study was to identify cognitive failures of patients and to evaluate patterns of food supplements use in pharmacy practice.

**Methodology.** The use of food supplements for cognitive failures therapy was evaluated by questionnaire in pharmacy. Cognitive failures: forgetfulness, distractibility and false triggering were evaluated by CFQ (The Cognitive Failures Questionnaire). 153 randomly – chosen people were asked to complete questionnaire. Statistical analysis of data was performed by using SPSS (Statistical Package for the Social Sciences) program package, 10.0 version.

**Results.** 53 study participants of 153 (34.64%) scored more than 45 points of CFQ and expressed cognitive failures. Forgetfulness, distractibility and false triggering dependence on age and is statistically significant, Spearman's correlation coefficients:  $r_s=0.85$ ;  $p<0.01$ ,  $r_s=0.79$ ;  $p<0.01$  and  $r_s=0.4$ ;  $p<0.01$  and doesn't depend on sex and education level. The results also showed that utilization of drugs and food supplements depends on age: younger population use food supplements, Spearman's correlation coefficient  $r_s = - 0.227$ ;  $p=0.005$ . 108 patients (70.59%) of 153 were using food supplements. 97 (89.81%) patients of 108 used ginkgo products, 67 (62.04%) patients used vitamin E, and only 32 (29.63%) patients used vitamin C supplements. Recommended doses of all three products were lower than that doses, used in clinical trials.

**Conclusions.** Study results showed, that for mild cognitive failures prophylaxis, study participants used Ginkgo biloba products, despite the fact that evidence of its efficacy is very low and doses used were not in line with recommended from clinical trials. Taking into account the data stated in above, mild cognitive failures prophylaxis by food supplements in pharmacy practice is irrational.

**Ina Rybakova**

**Lithuanian University of Health Sciences, Lithuania**

### **Peculiarities of suicidal behavior in men and women**

**Introduction.** World Health Organization provides the following data: in every 40 seconds 1 person in the world commits a suicide, in every 3 seconds 1 person attempts suicide [1]. According to the statistical suicidal rates of the recent years Lithuania takes lead in Europe [2].

The aims of this study was to assess the characteristics and the reasons of suicidal behavioral between men and women as well as the connection with alcohol consumption.

**Methodology.** 114 patients (51,75% men (n=59) and 48,25% women (n=55)) hospitalized at the sector of the somatopsychiatry of the Psychiatry Clinic of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics after a committed suicidal attempt were surveyed. Statistical analysis was conducted; results are statistically significant when  $p < 0,05$ .

**Results.** The methods of suicide attempt: hanging - 10,17% men and 1,82% women ( $p=0,0051$ ), pharmaceuticals - 42,37% men and 83,64% women ( $p < 0,0001$ ), self-inflicted injuries - 30,51% men and 9,09% women, other methods - 16,95% men and 5,45% women. Reasons for suicide attempt: 27,12% men and 43,64% women specified family conflicts, 30,51% men and 20,00% women - conflicts with a beloved one, 5,08% men and 3,64% women - financial problems, 27,12% men and 20,00% women - other reasons, 12,73% men and 10,17% women could not identify a reason. Consumption of alcohol in anamnesis - 41,82% women and 72,88% men ( $p=0,0012$ ).

**Conclusions.** There was no significant difference noticed in reasons of suicidal attempt, although a chosen suicide method differs significantly in men and women. Men having attempted suicide statistically significantly more frequently than women were consuming alcohol.

**Šeškevičienė, Giedrė**

**Lithuanian University of Health Sciences, Lithuania**

### **The impact of parental emigration on the children's psycho-emotional state**

**Introduction:** Emigration is one of the main study objects in our country. Parental emigration and divorce affects the children's psycho-emotional state more than other separation factors, for example one of parents death [1 - 2].

The aim of this study was to compare the psycho-emotional state between children from divorced families and those whose parents emigrated.

**Material and Methods:** A total of 1292 fifth-twelfth grade school children (there were 49.2% of girls and 50.8% of boys) from five different schools in Kaunas instant answered the questionnaires consisting of five parts: 1) the demographic questions and family structure; 2) the Strengths and Difficulties Questionnaire (SDQ); 3) questions about parental emigration and divorce. SPSS18.0 software (Chicago, USA) was used for the statistical analysis.

**Results:** The study found that children from separated families were significantly much more likely to self-harm behaviour than their peers from full families. Children who are left behind because of parental (e)migration are statistically more frequently prone to have suicidal thoughts than their peers who have never experienced separation from their parents. In both groups of (e)migrated and divorced families the average cumulative values in emotional difficulties scale were statistically higher among the girls than the boys.

**Conclusions:** 1. Children from separated families more frequently experience psychosocial and emotional difficulties and have a higher risk of suicidal thoughts and self-dangerous behaviour. 2. Parental migration and divorce negatively correlate with girls' emotional state, while parental divorce negatively correlates with boys' conduct.

**Vėbraitė, Birutė**

**Lithuanian University of Health Sciences, Lithuania**

**Diagnostics of Parkinson's disease: a comparative value of transcranial sonography and single photon emission computed tomography**

Background: Single photon emission computed tomography (SPECT) is the most reliable ancillary diagnostic method for Parkinson's disease (PD). Transcranial sonography (TCS) is relatively new, but promising technique. Both these methods were recently recommended in the diagnostic work up of PD by the EFNS/MDS-ES. Up-to-date three published studies did not detect any relationship between SPECT and TCS findings, but one. The aim of the study was to determine diagnostic accuracy of these two diagnostic methods and to determine relationship.

Methods: We studied retrospectively medical documents of 84 patients, who were directed with clinically suspected PD and underwent either SPECT only (n=39) or both TCS and SPECT (n=45) imaging from Jan 2007 until Jan 2012. SPECT was performed with <sup>123</sup>I-iodoflupane radiopharmaceutical agent (General Electrics, the UK), and TCS by Voluson 730 Expert ultrasound system equipped with 2-5PA transducer (General Electrics, Austria). To determine diagnostic accuracy of both methods, TCS vs. SPECT and clinical diagnosis (CND, based on the UK PD Brain Bank criteria), also SPECT vs. CND were compared.

Results: The final CND of the patients distributed as follows: PD n=48 (55.2%), essential tremor (ET) n=30 (34.5%), PD-ET n=1 (1.1%), secondary Parkinsonism n=2 (2.3%), dementia n=1 (1.1%), 5 cases (5.7%) remained unclassified. The mean ( $\pm$ standard deviation) age of PD patients was  $66.9 \pm 10.3$  yrs, n=22 (45.8%) were male, n=39 (81.2%) were at early H&Y stages. The values of sensitivity and specificity for PD were: 1) when the threshold value of the substantia nigra on TCS was 0.20 cm<sup>2</sup> - 88% and 50% (ROC analysis, AUC=0.648), when 0.26 cm<sup>2</sup> - 75% and 60% (vs. CND); SPECT vs. CND- 97.3% and 95.6%; TCS (0.26cm<sup>2</sup>) vs. SPECT- 76.2% and 71.4%.

Conclusions: SPECT had the highest sensitivity and specificity for PD, but diagnostic accuracy

**Žukauskaitė, Gintarė**

**Lithuanian University of Health Sciences, Lithuania**

**Müller-Lyer illusion perception peculiarities among people with psychiatric disorders**

Aim: to compare the Müller-Lyer illusion perception peculiarities between schizophrenia, schizoaffective disorder affected individuals and healthy control group.

Methodology: subject group were patients at HLUHS Kaunas Clinics (clinic of psychiatry). Control group were gathered from dermatological and venereal disease clinic, LUHS lecturers and students. Approval of LUHS bioethics centre was acquired, all participants agreed to take part in the study on a free will. Patients were divided in three groups: paranoid type schizophrenia, schizophrenia simplex and schizoaffective disorder. The experiments were carried out in a dark room. The stimulus consisted of white Müller-Lyer figures in the black background. Inner

corners of figures changed from  $10^{\circ}$  to  $350^{\circ}$ . Central figures position changed randomly and subject's aim was to place figures part in the middle between outer figures. Illusion strength was evaluated as a distance (measured in arc min) between subjects chosen position and geometrical figure center. Antipsychotic drug doses were converted to chlorpromazine equivalents and benzodiazepines were converted to diazepam equivalents. ANOVA and T-test criteria were used for statistical analysis. RESULTS. Study group consisted of 10 individuals with diagnoses: F20.0 (N=6), F25.1 (N=3), F20.6 (N=1). In the control group were 10 matched individuals. Experiments showed that for the study group illusion manifestation was stronger than for the control group. When the figures corners approached to  $180^{\circ}$  the manifestation of illusion diminished and difference between subject and control groups disappeared. When evaluating smaller ( $<123^{\circ}$ ) or bigger ( $>254^{\circ}$ ) corners the statistical significance of differences had tendency to increase: subject group made bigger errors. Significant differences were found between patients who had been taking different doses of anti-psychotics. The differences were not found between patients who had been taking different doses of benzodiazepines. Perception of illusion did not differ for patients who had positive symptoms, but differed for those with negative.

**Alexandrov, Alexei**

**Minsk regional clinical center of psychiatry and narcology, Belarus**

**Preliminary results of Belarus pilot substitution treatment project**

Today in Belarus is about 10000 registered opioid addicts. More than 40% of them are HIV-positive. 2 year substitution treatment pilot project was designed for 50 HIV+ opioid addicts. We provide clinical examinations and scales at enrollment and every three months. Now we enrolled in project 18 patients (15 males). After the first three month all stay in treatment and show drug-free weekly urine screens. All participants reported better quality of life. Most important problems were depression that needs antidepressant and mood swings that need mood stabilizers. We continue this project and plan to present 6 month follow up data.

**Halubitski, Yauheni**

**Minsk regional clinic center of psychiatry and narcology, Belarus**

**A case of diphenhydramine-caused psychosis during methadone maintenances therapy**

A 43 year-old male patient with opioid dependence was included in methadone maintenance therapy. In initial period withdrawal symptoms and craving disappeared. In a month patient was admitted to hospital because of bronchial asthma worsening. In the pulmonology ward the following condition suddenly had developed: acute sedation, closed eyes, mumbling, irrelevant replies, and disturbed gait. Patient couldn't describe his inner condition at that moment.

Doctors decided that it is opioid overdose and sent him to resuscitation department. After 1-day infusion therapy patient get better and could describe his condition in details. In purpose to get high he used 50 mg of Dimedrol (difenhidramin) intravenously and developed psychotic-like experience: he felt euphoria, emotion

well-being and oneiroid. Because of feeling of having total control under situation he didn't want to describe his condition to doctors at all. He thought he looks absolutely normal and was absolutely unaware of his bad condition.

**Kruk, Nina**

**Grodno State Medical University, Belarus**

### **The Image Study**

This project is carried out under the auspices of the Association for the Improvement of Mental Health Programmes. Medical educators' attitudes towards psychiatry as a discipline, a career; psychiatric treatment, training and perceptions of psychiatric patients were measured by using 37-item Perceptions of Psychiatry survey questionnaire.

Local results are:

- perceptions of psychiatric patients is mostly stigmatized
- evaluation of psychiatric training and the importance of learning psychiatry in general are quite high

**Krupchanka, Dzmitry**

**Minsk regional clinic center of psychiatry and narcology, Belarus**

### **Insight as a mediator between stigma and depression in schizophrenia**

The "Paradox of insight" in schizophrenia is a fact of its controversial impact with both positive and negative sides. We hypothesized that correlation between level of depression in patient and stigmatizing views of their close relatives depend on patient's illness awareness. 120 patients with a diagnosis of "paranoid schizophrenia" were included in the cross-sectional, observational study. Following questionnaires were used: "The Scale to Assess Unawareness of Mental Disorder" (SUMD), "Calgary Depression Scale for Schizophrenia" (CDSS), "Mental health in public conscience". Results: We have found statistically significant differences of correlations between patients' groups with different level of insight. Conclusions: Insight mediates the link between stigma and depression in patients with schizophrenia.

**Nestsiarovich, Anastasiya**

**The Republican research and practice center of mental health, Belarus**

### **Epigenetic factors in discrimination of different psychopathological dimensions of schizophrenia**

The project that I'm planning is related to a new perspective direction in psychiatry – epigenetics. Its aim is to find out whether different psychopathological dimensions of schizophrenia are determined by specific risk alleles in the system of DNA methylation (MTHFR, DNMT1, DNMT3a) and subsequent abnormal expression of the main candidate genes (DRD2, GABRA1, COMT and others). Methods – PCR, real-time PCR; PANSS; battery of neurocognitive tests CANTAB. Expected results – detectable predictors of disease itself, of its course and outcome.

## List of Participants

### Estonia

Alttoa	Aet	aet.alttoa@ut.ee
Aonurm-Helm	Anu	anu.aonurm@ut.ee
Kaasik	Kadri	kadri.kaasik@gmail.com
Vaht	Mariliis	mariliis.vaht@gmail.com

### Latvia

Bezborodovs	Ņikita	nikita.bezborodov@gmail.com
Bušs	Jānis	janis.buss.md@gmail.com
Grauda	Liena	lienate@inbox.lv
Jumtiņa	Elīna	elina.jumtina@gmail.com
Pudāns	Matīss	matiss.pudans@gmail.com
Rusaka	Marija	rusaka.m@gmail.com
Sprūģe	Ilona	ispruge@gmail.com
Štāne	Laura	laura.shtane@gmail.com
Vāvers	Edijs	edijs@biomed.lu.lv
Vrubļevska	Jelena	vrublevska@inbox.lv
Zālītis	Pēteris	ltpa@navigator.lv

### Lithuania

Antonova	Ingrida	ingrida.antonova@gmail.com
Burkauskas	Julius	julius.burkauskas@hotmail.com
Dirzius	Edgaras	edgarasdirzius@gmail.com
Gudaityte	Rima	rimagudaityte@yahoo.com
Jusiute	Raimonda Egle	r.e.jusiute@gmail.com
Juskiene	Alicja	alicja.juskiene@gmail.com
Krasauskaite	Dovile	dkrasauskaite@gmail.com
Lapeniene	Justina	justina.lapeniene@gmail.com
Liaugaudaite	Vilma	vilma.liaugaudaite@lsmuni.lt
Mickeviciute	Dalia Elena	dalia.mickeviciute@gmail.com
Noreikaite	Aurelija	n.aurelija@yahoo.com
Rybakova	Ina	rybakova.ina@gmail.com
Seskeviciene	Giedre	giedrekmu@yahoo.com
Vebrate	Birute	biruteveb@gmail.com
Zukauskaite	Gintare	gintarezuk@gmail.com

### Belarus

Alexandrov	Alexei	a.a.alexandrov@mail.ru
Halubitski	Eugene	eugenwww@mail.ru
Kruk	Nina	dlaninki@gmail.com
Krupchanka	Dzmitry	dmitry.krupchenko@gmail.com
Nestsiarovich	Anastasiya	nestsiarovich@mail.ru