

in Neuropsychopharmacology
29-30 November 2014
Lopota, Georgia





#### 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 is an independent, non-governmental, scientific association dedicated to the science and treatment of disorders of the brain. Founded in 1987, its goal is to bring together scientists and clinicians to facilitate information-sharing and spur new discoveries. The objective of ECNP is to serve the public good by stimulating high-quality experimental and clinical research and education in applied and translational neuroscience. It seeks to do this by:

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

To fulfil this aim ECNP organises, amongst others, yearly the ECNP Congress that comprises of 6 plenary lectures, 28 symposia and 7 educational update sessions. The annual meeting attracts more than 6,000 participants and is considered to be the largest event in neuropsychopharmacology in Europe. ECNP organises seminars, as the one you have been invited to participate, in areas of Europe where there are less opportunities for psychiatrists to participate in international meetings. Interaction is the keyword at these meetings and they have proved very successful both for the participants and for the experts. During the seminar we discuss clinical and research issues that the local organisers feel that are needed to be covered and using these topics as a model for teaching how to ask a research question and how to plan an effective study. Leading ECNP experts





that are also talented speakers will facilitate mutual discussion in small groups allowing you to present your abstract and get feedback from your colleagues and local mentors. So far, ECNP has organised this meeting in Poland, Estonia, Turkey, Bulgaria, Slovak Republic, Hungary, Czech Republic, Moldova, Romania, Greece, Russia, Latvia and recently in Macedonia, Armenia, Georgia and Serbia. In some countries we have organised it more than once.

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

This year we start with a pilot of a new initiative, The ECNP Research Internship. This is a new collaborative initiative of ECNP and the ECNP Junior Member Advisory Panel (JMAP) that aims to provide short-term research internship opportunities for junior researchers. Senior researchers from the list of ECNP Fellow members offer unpaid 2 week exploring research internship in their institutions. Please see the ECNP website (www.ecnp.eu) where you can find information about all the above initiatives and additional information and look for the activity that fits you.

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

Gil Zalsman
Chair ECNP Educational Committee





Joseph Zohar is a professor of Psychiatry at the Sackler Faculty of Medicine, Tel Aviv Universality. Dr. Zohar is the immediate past-President of the European College of Neuropsychopharmacology (ECNP), Currently the Chair of the Expert Platform, Chair of the Israeli consortium on PTSD, and Chair of the Israeli Brain Council.

Dr. Zohar is a board member for the International Master in Affective Neuroscience, a visiting Proffesor at the University of Maastrich (Nederland's), and an immediate past-Chair of the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS).

Dr. Zohar has been honored with several awards, including the Fogarty International Research Fellowship Award (1984), the A.E. Bennet Award for Clinical Research (1986 and 2002), ECNP – Lilly Neuroscience Award for Clinical Research (1998), and the WFSBP Award for Excellence in Education (2001).

Dr. Zohar has authored 300 papers, has written or edited 15 books focusing on refractory depression, OCD and post-traumatic stress disorder, and was the founding associate editor of CNS Spectrums and of the World Journal of Biological Psychiatry.

Dr. Zohar is considered a world expert on posttraumatic stress disorder, and has recently received funding from the American National Institute of Mental Health (NIMH) to explore the potential of hydrocortisone in the immediate aftermath of trauma, as a preventive measure against the development of PTSD.

Dr. Zohar was advisor to DSM – IV and 5 in OCD and cochair with Dr. Hollander at the Sub-Workgroup of preparing the research agenda on OCD for DSM-5.

Currently Dr. Zohar Chair an international collaboration (joint venture of ECNP, ACNP, CINP and AsCINP) on developing new nomenclature for CNS drugs along with being a Director at the Division of Psychiatry at Chaim Sheba Medical Center, Israel.







Michael Davidson has obtained his MD degree form the State University in Milan and continued his postgraduate training in Cardiology in Tel Aviv, Israel. In 1980, he started training in psychiatry at the Mount Sinai School of Medicine and Medical Center, in New York, where he has remained until 1995, and where he still holds a Professorship.

In 1995, he was appointed head of Neuroscience Research Center at the Sheba Medical Center, in Tel Aviv, Israel, and later Director of the Psychiatry at the same Medical Center and Chairman of The Department of Psychiatry at the Tel Aviv University Medical School. He is an active member of ACNP and ECNP and the Editor of European Neuropsychopharmacology.

Professor Davidson has published over 300 articles in the most prestigious peer-reviewed journals, including Lancet and Science, and has been the Principal Investigator on research grants funded by the US National Institute of Health and other European governmental agencies. Since the late 1980s he was one of the pioneering investigators who, in collaboration with the pharmaceutical industry, have brought to market the currently available drug treatments for Alzheimer's disease and for Schizophrenia.

Professor Davidson sits on the CNS advisory boards of many of the major pharmaceutical companies, and is an invited speaker at the most prestigious meetings of his profession.







Francesc Colom, PsyD, MSc, PhD is currently the Head of the Psychoeducation and Psychological Treatments Area at the Barcelona Bipolar Disorders Program (IDIBAPS- Hospital Clinic University of Barcelona) and a researcher at the CIBERSAM (Spanish Network of Research in Mental Health).

The Barcelona Psychoeducation Program, designed by Dr. Colom and co-workers is nowadays the strongest evidence-based psychoeducational program for bipolar patients. His book "Psychoeducation Manual for Bipolar Disorder" has been published in several languages including English, Spanish, Italian, French, Japanese, Chinese. Turkish and Polish.

He has lectured all over the world and published over 130 scientific articles, with an H index of 43 and more than 6000 quotations. Dr. Colom has also written 12 books and a number of book chapters. He has been a member of the Board of Councilors of the International Society for Bipolar Disorders, a member of the Nomenclature Committee and Chair of the Website Education Committee of the same society, and is currently a member of the Scientific Advisory Pannel of the ECNP and Chair of the Psychological Interventions Taskforce of the ISBD. In June 2007, Francesc Colom was awarded with the prestigious "Mogens Schou Award" for the excellence of his research.







**Eka Chkonia** is an ECNP ambassador for Georgia. She is an associate professor of psychiatry at Tbilisi State Medical University and a clinical director of the central university hospital "Tbilisi Mental Health Centre".

Since 1999, she has carried out and leaded many collaborative research projects with German, Swiss and Britain colleagues in clinical and social psychiatry and published more than 20 scientific articles in the high ranked medical journals as Schizophrenia Bulletin.

She has been awarded with JFDP Junior Faculty Development Program Fellowship at Rutgers University (US, 2010) and Alberto Vilar Medical Internship at the General Hospital (AKH) in Vienna in 2003 and 2012. She has received research grants from the Royal society, Volkswagen Foundation, Swiss Federal Institute of Technology in Lausanne (EPFL), The National Centre of Competence in Research (Swiss National Science foundation) and from other national and international foundations.

Dr. Eka Chkonai is a president of the Society of Georgian Psychiatrists.







Nino Okribelashvili is a professor of psychiatry, head of chair of Psychiatry & Medical Psychology at the Faculty of Medicine and member of the Representation Council, Iv.Javakhishvili Tbilisi State University. Dr. Okribelashvili also runs an acute psychiatric department at Sun Stone Medical LTD.

Dr. Okribelashvili has been awarded by Junior Faculty Development Program (funded by the USA Department of State, coordinated by ACCELS/ACTR) in 2000/2001 at George Washington University (USA), Alberto Vilar Medical Program (American-Austrian Foundation in 1997, 2001, 2003), Health System Management (Oxford Policy Management, 2007), International Training program on Pension Reform (coordinated by BICON/SIDA in Stockholm, Sweden) and etc.

Since 1988 she carried out research studies in the field of schizophrenia, PTSD, suicide, social and transcultural psychiatry and published more than 30 articles in medical journals, such as World Cultural Psychiatry Research Review, NATO Security through Science Series, Comprehensive Psychiatry, etc.

Dr. Okribelashvili served as an expert for Council of Europe, Department of Health and of the Partial Agreement in the Social and Public Health Field (Strasbourg, France). In 2004-2009 she was a member of State Council for Accreditation of High Education Institutions of Georgia, member of Pension Reform Group at Parliament of Georgia, the Committee of Healthcare and Social Affairs.

At present she is a Board Member of Georgian Society of Psychiatrists, Mental Health Advisory Board member of the Healthcare and Social Issues Committee at Parliament of Georgia and a member of the Mental Health Policy Board at the Ministry of Labour, Health and Social Affairs of Georgia.







Manana Bokuchava is a head of the department of scince and research at the Asatiani psychiatric Institute of the Mental Health and Narcology Prevention Center and a professor of psychiatry at Tbilisi Medical Academy.

Scince 2003 she has been leading the residency program and continuing medical education in psychiatry in Georgia. Under her supervision and coordination national clinical recommendations for psychiatrist and other mental health professionals has been developed and implemented in the practice.

Manana Bokachava is a board member of the Sociaty of Georgian psychiatrists.





#### **Programme**

## ECNP Seminar in Neuropsychopharmacology 29-30 November 2014, Georgia

#### **SATURDAY 29 NOVEMBER 2014**

09.30 – 09.45 Introductions to the programme. Joseph Zohar, Israel 09.45 -10.30 Science and nomenclature - Could infusion of neuroscience change an outdated psychotropic classification? An update. Joseph Zohar, Israel

10.30 – 11.15 Bipolar disorder; clinical & therapeutic update Francesc Colom, Spain

#### 11.15 - 12.00 Coffee break

12.00 – 12.45 How to interpret results of published trials using treatment resistant schizophrenia as an example. Michael Davidson, Israel

12.45 – 13.00 How to give a talk. Joseph Zohar, Israel

#### 13.00 - 14.00 Lunch

Presentations participants in 3 groups in 3 parallel workshops

Round 1	Joseph Zohar	Francesc Colom	Michael Davidson
14.00 -	Nino Okribelashvili	Manana	Eka Chkonia
15.30	Group 1	Bokuchava	Group 3
		Group 2	_

#### 15.30 - 16.00 Break

Round 2	Michael Davidson	Joseph Zohar	Francesc Colom
16.00 -	Eka Chkonia	Nino	Manana
17.30	Group 1	Okribelashvili	Bokuchava
	-	Group 2	Group 3

#### **SUNDAY 30 NOVEMBER 2014**

Round 3	Francesc Colom	Michael Davidson	Joseph Zohar
9.00 - 10.30	Manana	Eka Chkonia	Nino
	Bokuchava	Group 2	Okribelashvili
	Group 1	-	Group 3

#### 10.30 - 11.30 Coffee break

Plenary 11.30 –	Group presentations 15 min for each group
13.00	

#### 13.00 - 13.45 Lunch

13.45–14.20 Time to fill out evaluation forms, awards ceremony, concluding remark and thanks. Joseph Zohar, Israel





#### **Award Winners**

Maka Malania

Cezar Goletiani

Tamar Aladashvili

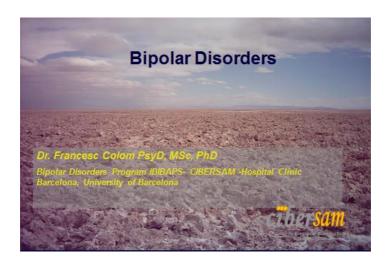
Ia Adamia

Eka Berdzenishvili





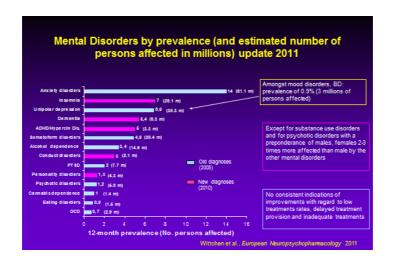


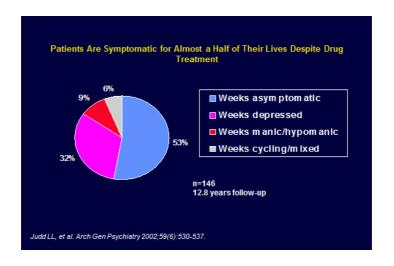


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Company	Speaker	Advisor
BMS	X	
Eli-Lilly	X	
MSD-Merck		x
Astra Zeneca	X	x
Sanofi	X	
Pfizer	X	
GSK	X	
Sanofi	X	
Tecnifar	X	
Shire		х
Lundbeck	X	
Otsuka	X	
Adamed	X	







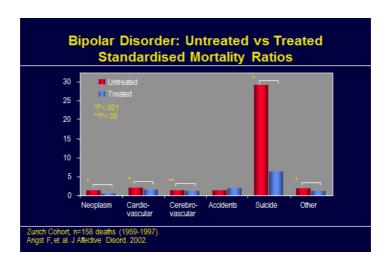






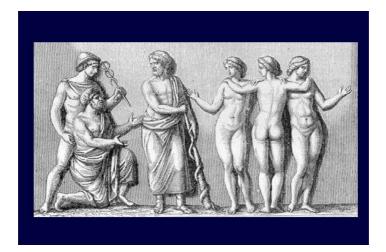
Disorder	Relative risk	Suicide rate	Lifetime risk	
		% per year	%	
Bipolar disorder	28	0.39	23.4	
Severe major depression	21	0.29	17.4	
Substance abuse	20	0.28	16.8	
Severe anxiety disorder	11	0.15	9.0	
Moderate depression	9	0.13	7.8	
Schizophrenia	9	0.12	7.2	
Personality disorder	7	0.10	6.0	
Cancer	2	0.03	1.8	
General population	1	0.014	0.8	

Harris EC et al. Br J Psychiatry 1997;170:205-28. Tondo L et al. CNS Drugs 2003;17:491-511.









#### Features to consider when treating BD

Lifetime history: StagingLifetime history: Polarity

Syndromal recovery

Functional recovery





#### 1° AXIS: POLARITY

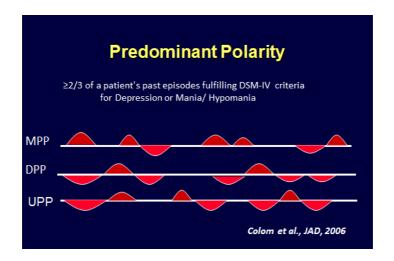
#### **Predominant Polarity**

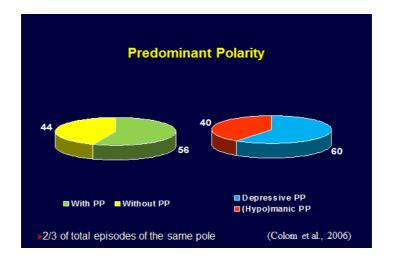
- Operational description of a clinical impression
- 2/3 of past episodes of a given polarity
- Validated with more than 1000 patients<sup>1, 2, 3</sup>
- Included in ISBD Nomenclature Taskforce recommendations<sup>4</sup>
- ...But neglected by DSM-5 despite all its clinical and therapeutic implications

1. Colom et al., 2006; 2. Rosa et al., 2008; 3. Yang et al., 2013; 4. Tohen et al., 2009



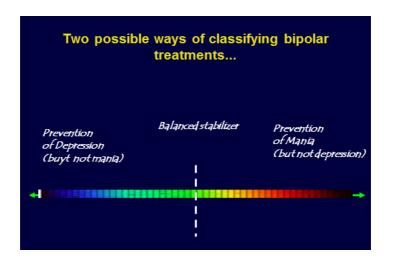


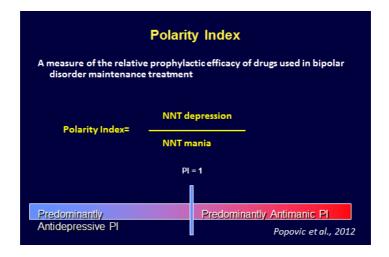






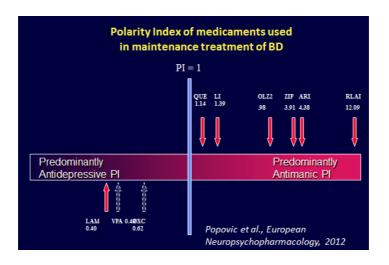










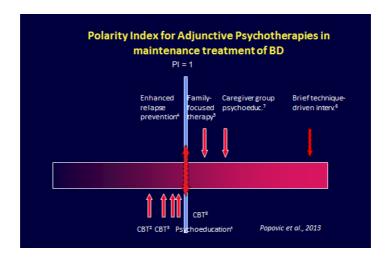


	NNT Mania	NNT Depression	NNT Any episode	Polarity Index
Psychoeducation <sup>1</sup>	7.5	5.5	4.6	0.73
CBT <sup>2</sup>	9.6	3.2	4.8	0.33
CBT <sup>3</sup>	5.7	3.6	4.9	0.63
CBT <sup>4</sup>	19	5.4	4.8	0.89
	Pop	oovic et al., 2013; <sup>1</sup>	Colom 2003: 2	?Lam 2003:
	3La	m 2005; <sup>4</sup> Meyer, 2	011	





	NINIT	BIBIT	AIAIT	D-1-de-
	NNT Mania	NNT Depression	NNT Any episode	Polarity Index
Enhanced relapse prevention <sup>4</sup>	40	40	20	1
Family-focused therapy <sup>3</sup>	4	5.6	5.3	1.40
Brieftechnique-driven interventions <sup>6</sup>	3.9	13.1	11.3	3.36
Caregiver group psychoeducation <sup>7</sup>	5.0	8.9	4.2	1.78
		t al., 2013; <sup>4</sup> Lo rry 1999; <sup>7</sup> Reir		Miklowitz







#### 2° AXIS: SEVERIGY

### Two possible ways of classifying bipolar treatments...



Stage 4: Paliative care:

Diminish impact and alleviate some
symptoms

Stage 3: Remediation & rehabilitation:
Reduce burden, improve functioning

Stage 2: Maintenance treatments:

Reduce # episodes & # days spent ill

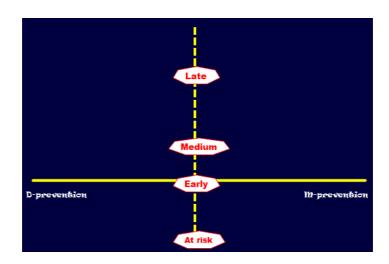
Stage 0/1: Preventive treatments:

Specific for offspring or for cyclothymia



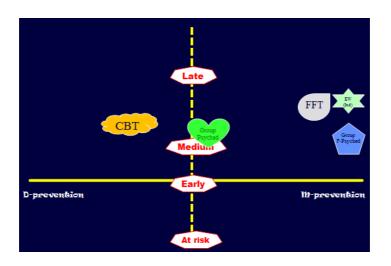


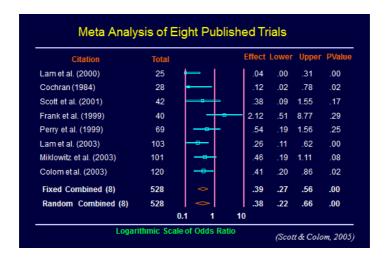
Stage	Clinical features	Biomarkers	Cognition	Pharmacological & Psychotherapy	Prognosis
1	Well defined periods of euthymia in the inter- episodic period	† inflammatory markers	No impairment	Mood stabilizer monotherapy Psychoeducation	Good with careful prophylaxis
II	Symptoms in inter- episodic periods related to comorbidities or mild cognitive impairment	Subtle changes in neuroimaging or normal BDNF inflammatory markers	Transient or mild impairment	Combination of mood stabilizers of mood stabilizer and atypical antipsychotic Psychoeducation + CBT	Prognosis depends on how well comorbidities can be managed. Worse than stage I
III	Marked impairment in functioning	Ventricular enlargement or white matter hyperintensities   BONF   inflammatory markers	Clear cognitive impairment corresponding to 2 grades of decline in general IQ as compared to previous IQ	Combination of mood stabilizer and atypical antipsychotic Clozapine / maintenance ECT Family therapy	Reserved prognosis Rescue therapy needed
īv	Unable to live autonomously due to cognitive and functional impairment	Ventricular enlargement or white matter hyperintensities   BDNF   inflammatory markers	Similar pattern to the mild cognitive impairment found in early stages of Alzheimer's disease	Palliative Daycare center	Poor prognosis





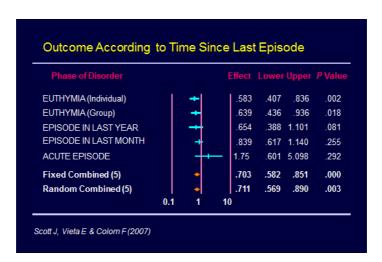


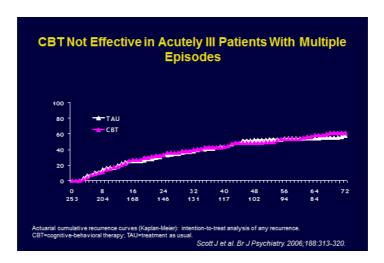






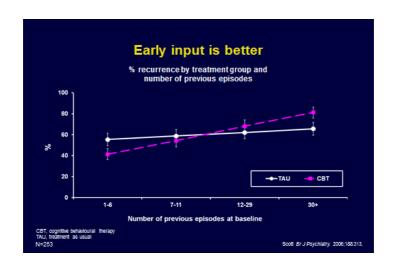


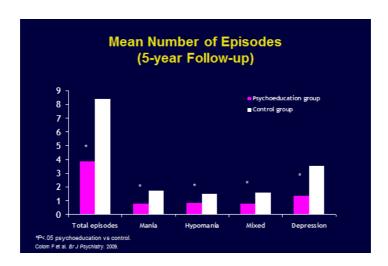






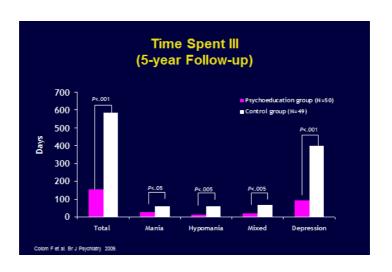


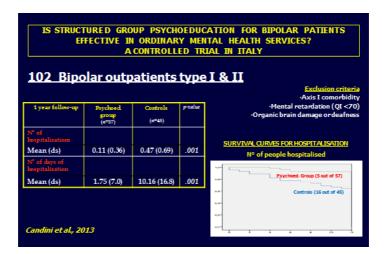






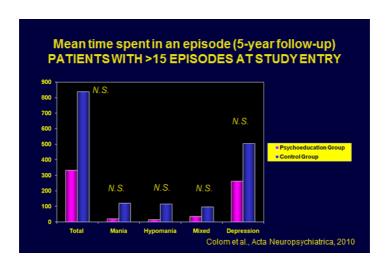


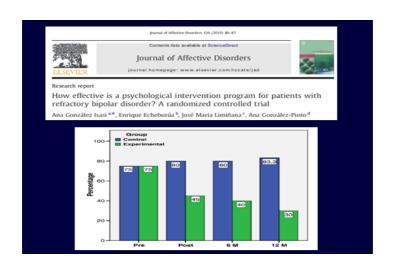








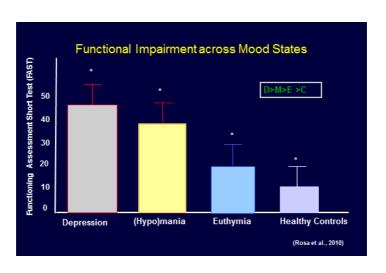






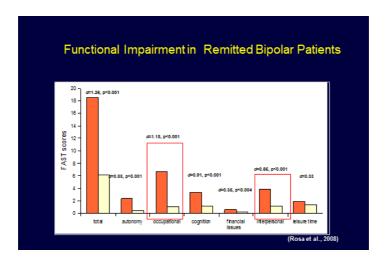


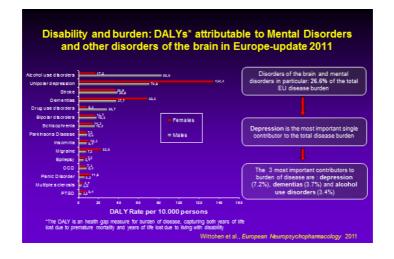
# Syndromal <u>and</u> Functional Recovery Should Be the Goal of <u>Integrative</u> Treatment













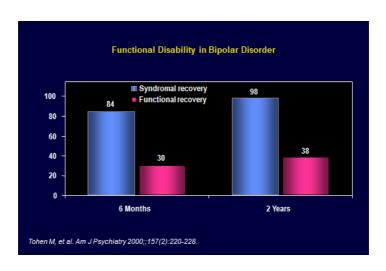


#### Cognitive Impairment in Bipolar Disorder



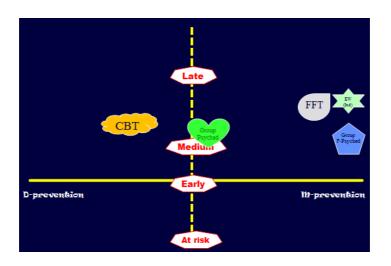
- Bipolar patients show cognitive dysfunctions across different mood states, including remission
- Patients with history of psychotic symptoms, bipolar I disorder, longer duration of illness and a high number of manic episodes are the ones who are more likely to show neuropsychological disturbances
- Cognitive impairment has a strong impact on functioning
- Early diagnosis and treatment would most likely be the best way to prevent cognitive dysfunctions and their impact on psychosocial outcome

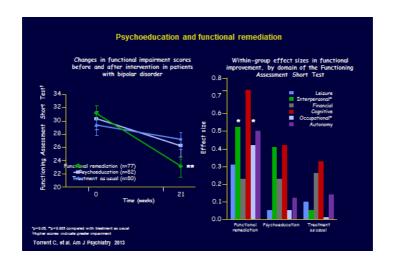
Martinez-Arán, et al. Am J Psychiatry, 2004;161:262-270.















#### **Predictors of outcome**

- Insight
- Adherence/compliance
- Treatment response
- Habits (lifestyle, substance use)
- Age of onset
- Diagnostic delay
- Diagnostic subtype (BPI vs BPII) is NOT a predictor of outcome

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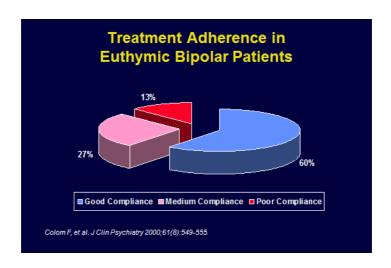


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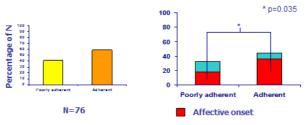






#### Adherence to oral treatment in bipolar SZA

Affective onset and a low number of purely psychotic episodes have been found to positively relate with treatment adherence.

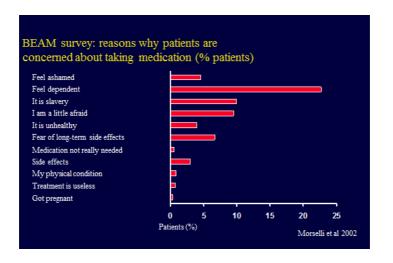


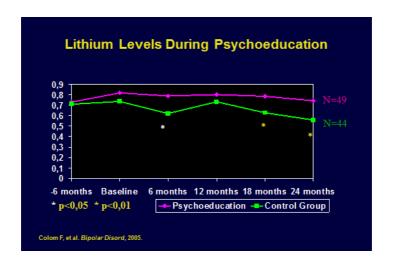
The more affective the clinical course of the illness, the better the adherence to treatment.

Murru et al., Acta Psychiatr Scand, 2012









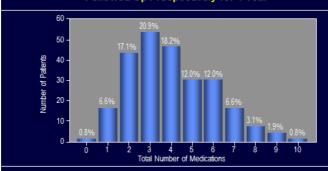




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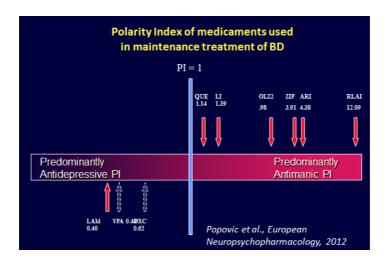
## Combination Therapy Average Number of Medications in 258 Bipolar Outpatients Followed Up Prospectively for 1 Year

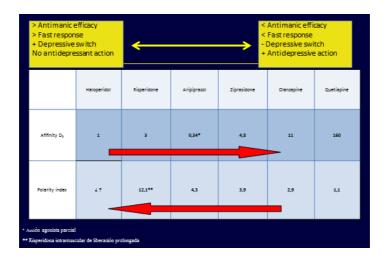


Post RM, et al. J Clin Psychiatry. 2003;64(6):680-690.













#### The International Society for Bipolar Disorders (ISBD) Task Force Report on Antidepressant Use in Bipolar Disorders

FORCE REPORT ON AMBIERD PESSORIES AND RESIDENCE AND RESIDE | Section | Sect

Am J Psychiatry. 2013 Sep 13. doi: 10.1176/appi.ajp.2013.13020185.

## Predictors of outcome

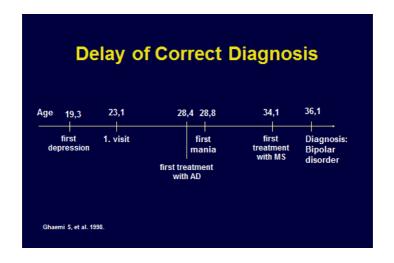
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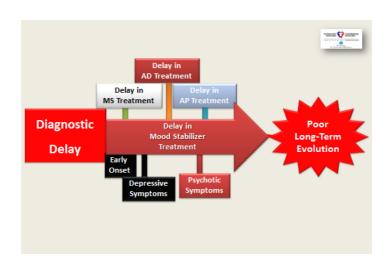
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## Thanks!

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Antoni Benabarre C Mar Bonnin Francesc Colom Mercè Comes Iria Grande José M. Goikolea Diego Hidalgo Esther Jiménez Anabel Martinez-Arán Andrea Mumu Isabella Pacchiarotti Dina Popovic María Reinares Jose Sánchez-Moreno Brisa Solé Carla Torrent Imma Torres Marc Valenti **Eduard Vieta** 







# Treatment (Rx) refractory schizophrenia:

How to understand the evidence and make rational decisions

Michael Davidson MD

I am not a pessimist, but an optimist with access to data and a lot of questions

Placebo is an ally to the clinician but a very tricky one

Constantly scrutinizing the dogma of clinical teaching and the scientific evidence # therapeutic nihilism





# Treatment (Rx) refractory schizophrenia:

How to understand the evidence and make rational decisions

## Is Rx refractoriness a matter of definition and expectations?

## Expectation of the treatment in schizophrenia

- Transient reduction of agitation
- · Reduction of psychosis
- Reduction of all symptoms (positive, negative, cognitive, behavioral) and functional improvement
- Prevent worsening (continuously and progressive or intermittent)
- Remission of illness

## Expectation of the treatment in CHF

- Transient reduction of dyspnea
- · Reduced RV pressure
- Reduction of all symptoms (dyspnea, edema, arrhythmias) and functional improvement
- Prevent worsening (continuously and progressive or intermittent)
- · Remission of illness

Totally refractory, partially refractory, domain refractory Refractory to medication, to supportive therapy, refractory to TLC





## Antipsychotics, symptom's tranquilizers or disease-centered drugs?

- The initial descriptions based on observations was consistent with a non-specific tranquilizing effect
- Subsequently, this view was replaced the Koch-like approach (pathogen-disease-treatment)\*
- Contributed to the disease-centered drug approach:
   mirage of DA hypothesis, advent of the DSM, the physician's and public quest
   for prestige and comfort, regulatory mandates, commercial considerations

## Definition of Rx refractory schizophrenia

- Non responsive to X mg/daily\* of antipsychotic drugs given for at least Y weeks with 2 different antipsychotics of 2 different classes\*\*
- Non responsive to X mg/daily of clozapine given for at least Y weeks
- Non responsive defined as lack of a decrease in PANSS by at least 20%\*\*\*
- Persistence or illness for Z years\*\*\*\*

<sup>\* &</sup>quot;the new drugs could wipe out the symptoms of psychotic patients just as internists can use insulin for the elimination of the symptoms of diabetes" president of the US Society of Biological Psychiatry Himwich, 1955, p. 421 "antipsychotic drugs help bring biochemical imbalances closer to normal" American Psychiatric Association, 1996, p. 7

<sup>\*</sup>As specified in the Summary of Product Characteristics?

<sup>\*\*</sup>What is a class?

<sup>\*\*\*</sup>Availability of metrics rather than clinical relevance?

<sup>\*\*\*\*</sup>Circular thinking?





## What is refractory?

- Is only the disease responsible for the symptoms and the aberrant behavior?
  - what about personality, cultural thresholds, family structure, the socio-economic circumstances, shortcomings of the mental health system?
- Is only the disease responsible for the poor social and vocational functioning?
  - what about education, stigma and employment opportunities
- · Mild cognitive impairment and negative symptoms
  - are they expected to be refractory to antipsychotic RX?
  - Are they specific schizophrenia?

# Are we trying to build the new men with the help of a pill?



Do we need more than one pill for the new men?





### Guidelines, recommendations, reviews and commentaries



independent or ever

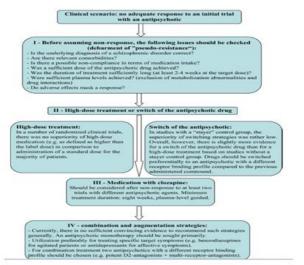
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Tokefurni Saraki <sup>1,4</sup>, Cary Remisigner <sup>6,4</sup>, Wesser H. Mahami<sup>4,5</sup>, Hinsyelis Lichela <sup>6,6</sup>, Tariti K. Raja <sup>6,6</sup> Anel Coeff Garriero <sup>6,4</sup>, Manari Minima <sup>6</sup>, Sevid C. Maria <sup>6,63</sup>

Clinical overview

The practical management of refractory schizophrenia - the Maudsley Treatment REview and Assessment Team service approach

#### Pharmacotherapy of treatment resistant schizophrenia: a clinical perspective Markus Dold, Stefan Leucht<sup>1,2</sup>

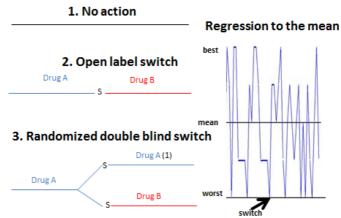






## What do I do if my patient doesn't get better?

I switched the medication and my patient got better, wow!



## Epidemiology and risks of Rx refractoriness\*

- Treatment resistance in first episode ranges between 6.5% (Crow, 1986) and 17% (Lieberman, 1993)
- Treatment resistance after multiple episodes treated ranges between 20% (Davis et al, 1980) to 50% (Essock et al, 1996)
- Percentage of responders decreases and time to response increases X3 with number of episodes \*\*\*
- Factors associated with treatment resistance
  - Early onset of disease \*\*
  - Male gender
  - Labor complications
  - Low pre-morbid functioning
  - Long duration of untreated psychosis
  - Family history of schizophrenia
  - Absence of precipitating factors
  - History of substance abuse
- \*depends on definition
- \*\* Isn't it circular thinking?
- \*\*\* Is it the same disease?





# More somatic options for Rx refractory schizophrenia

- · Benzodiazepines
- Antihistaminics
- Mood stabilizers
- Antidepressants
- ECT
- TMS
  - deep
  - superficial
  - what else needs to be investigated?
- Abracadabra

## Early Rx with clozapine

# What about non-medication options for Rx refractory schizophrenia?

- Cognitive Behavioral Therapy
- · Intensive case management
- · Environmental changes
  - move away from illicit drugs
  - get/change jobs
  - change living arrangements
  - family intervention
  - convince family and mental health providers to accept a certain level of abnormal behavior
  - win the lottery





# Treatment (Rx) refractory schizophrenia:

# How to understand the evidence and make rational decisions

## What is a Rx. related rational decision?

- A decision believed to be based on scientific evidence, with which one feels comfortable. To make such a decision one needs to ask:
  - Do I employ unbiased, relevant data or do I select data which confirm my hypothesis?
  - · Can I infer from group means to my individual patient?
  - Are the benefits and risk on the same scale and of the same magnitude?





# The solid, impeccable scientific evidence of today is the garbage of tomorrow

- Treatment of post-MI arrhythmia (CAST) trial N Engl J Med V. 324
- Beta blockers vs. Inotropic agents for CHF N Engl J Med V. 329
- · Rx of duodenal ulcer
- Hormone replacement therapy JAMA V. 288
- · The DA and the NMDA hypothesizes in schizophrenia
- · The catecholamine hypothesizes in depression

# Are there circumstances under which rational decisions might not be feasible? (I)

- · Evidence is not available
  - Unethical (ex. RCT to investigate prevention of suicide)
  - Trial design too complicated (life-long prospective cohorts)
- No commercial or political interest ( TCA or drug discontinuation in elderly schizophrenics)
- Commercial or other interests distort data interpretation (publication bias)
- Neither evidence of efficacy nor evidence of lack of efficacy is available
- · Insufficient data on rare risks





## Tricks the mind plays on us

Context and framing

Event available in the recent memory

Baserate bias

Increased sensitivity to extremes

Overweight small probabilities and underweight moderate and large

Assigning non monetary value to intangibles (e.g. pain, dyspnea, mobility, suffering or happiness) Data manipulation to address competing aims and unavailability of data

Confusion between preventing and treating

Statistical illiteracy (innumeracy) Loss aversion

The tendency to personalize and be influenced by an ecdotes

## Limitations of evidence specific to psychiatry

- Classification by diagnostic group is the result of social and behavioral constructs and not of absolute observable phenomena or markers; category)
- Multiple concomitant environmental, societal and genetic interactions of unknown relative weight making the link between intervention and outcome (causality) difficult to determine.
- If large heterogeneity exists, than empirical evidence cannot apply to all members of the group, or even the majority.
- Rx effects in RCT are driven by small minorities of patients

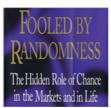




## Failure in the deduction process



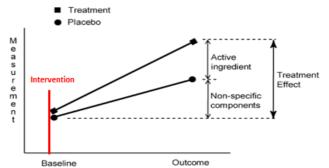
Galen (30-200 AD) said: "All who drink of this remedy recover in a short time except those whom it does not help, who all die. Therefore, it is obvious that it fails only in incurable cases."



who could afford it with bloodletting. He observed that during epidemics the poor are less likely to die than the rich, and concluded that the poor were more robust.

Antonio Durrazzini, in 1622, treated those

# Placebo is a tricky friend to the clinician and a foe to the researcher



Is judicious use of placebo the art of medicine, or benevolent deception?





## Definition

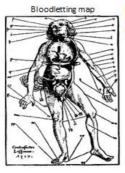
**Placebo** is any therapy that is used for its <u>non-specific</u> psycho-physiological effect or for its presumed effect

Placebo response is the degree to which a response to a placebo treatment <u>differs</u> from that of the <u>natural</u> <u>history</u>

**Placebo effect** is the beneficial effect that derives from the <u>context</u> of the encounter, the <u>rituals</u>, and the clinicianpatient <u>relationship</u> (as distinct from the rapeutic benefits, produced by the specific or characteristic pharmacological or physiological effects).

## The history of medicine is the history of placebo. What fooled Hippocrates for 2500 years?

The scientific debate dealt with methods and techniques (venesection, cupping, and leeches) rather than values and concepts.



# George Washington

- George Washington developed a sore throat on December 12, 1799
- His doctors bled him, consistent with their beliefs about the underlying physiology of his illness
- He died about midnight on December 13.









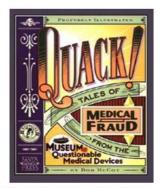
The art of medicine consists in amusing the patient while nature cures the disease." (Voltaire)



## Crooks, fakes, shams, pious frauds, voodoo, witches, or victims of innocent beliefs and misperceptions?

The \$200 analgesic Q-Ray Ionized Bracelet case





Sir Williams Osler: "one should treat as many patients as soon as possible with the new drug, while it still has power to heal".





## Is Mommy a crook?



## Why the negative attitude towards placebo?

- · Newtonian faith in material and mechanics
- Descartes' body/soul dichotomy
- Associated with "untrue", inert, nothing and with withholding "real" or "better" treatment
- Difficult to license, regulate and tax (nevertheless possible to make a profit)





## Patients' empowerment or patients' deception?

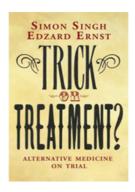
A \$34 Billion industry in the US with a large therapeutic effect size

- Acupuncture

- Mega-Vitamins
   Oriental Medicine
   Macrobiotics
   Niat
   Medical Medicine
   Macrobiotics
   Column Medical Medicine
   Column Medical Medica

- Yoga
- Positive thinking Mind-Body control Chiropractic Art therapy Mega-Vitamins Prayer therapy Prayer therapy

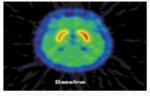
Herbal Medicine
 Acupressure
 Massage



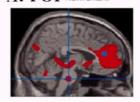
Why do they resist RCT and what happens when RTCs are conducted?

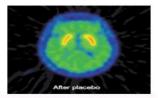
## The rehabilitation of placebo: Seeing is believing

Placebo in PD

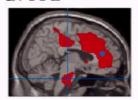


A. POP Remifentanil





B. PPL Placebo









#### Yellow pills make the most effective antidepressants, like little doses

of pharmaceutical sunshine.



#### The color green reduces anxiety, adding more chill to the pill.

20

## Red pills

can give you a more stimulating kick. Wake up, Neo.



## White tablets-

particularly those labeled "antacid"—are superior for soothing ulcers, even when they contain nothing but lactose.



## Moreis

better, scientists say. Placebos taken four times a day deliver greater relief than those taken twice daily.



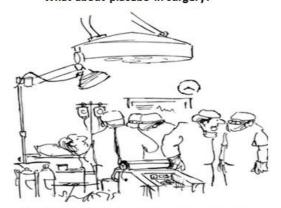
#### Branding matters.

Placebos stamped or packaged with widely recognized trademarks are more effective than "generic" placebos.



Clever names can add a placebo boost to the physiological punch in real drugs. Viagra implies both vitality and an unstoppable Niagara of sexy.

## What about placebo in surgery?



"We'll just mill around till he's asleep, and and then send him back up. This operation is actually for a placebo effect."





## **Evidence in surgery**

- RCTs declined from 14% of research articles in the British Journal of Surgery in 1985 to 5% in 1992
- Treatments in general surgery are half as likely to be based on RCT evidence as treatments in internal medicine
- 75% of "surgical trials" are actually of medical treatments in surgical patients
- · Only a third of surgical trials have adequate blinding
- In a study of 10 international journals from 1988 to 1994, less than half included objective methods for assessing outcome.

## What do they all have in common?

- · Ligation of the internal mammary artery for angina
- · Extracranial / intracranial artery connection
- · Radical mastectomy
- · Sympathectomy for peripheral vascular disease
- · Spinal fusion

## The mechanistic logic and the drama.

Doesn't psychiatry deserves a little bit of drama too?

- ECT
- TMS
- VS





## AMA position on placebo in clinical practice

... MDs are prohibited from providing "a substance that the physician believes has no specific pharmacological effect upon the condition being treated"...

### Nevertheless

More than 60% of MDs in the US recommend placebo and believe it to be ethical (saline or sugar pills 20%, vitamin 38%, analgesics 41%, antibiotics 13%).



**BMJ** 

RESEARCH

Prescribing "placebo treatments": results of national survey of US internists and rheumatologists

(on C Tiburt, staff scientist," Essive) Emanuel, director," Ted) Kaptchuk, associate director," Farr A Curlin, assistant professor of medicine, "Financia G Miller, director, research ethics programme"

## To blindly trust RCT, you have to believe that Michael Davidson and Michael Jordan are equal at basketball.

Most of what EBM has demonstrated is that when subjected to rigorous statistical review treatments believed by clinicians to be different (better) then placebo were actually not different

- MD vs. MJ -- 7 free trials each
- MD 3/7, MJ 7/7
- P = .07 (NS, Fisher Exact test)
- Conclusion: there was no difference between MD and M1.

Vickers A, Medscape 2006. Michael Jordan Won't Accept the Null Hypothesis: Notes on Interpreting High P Values

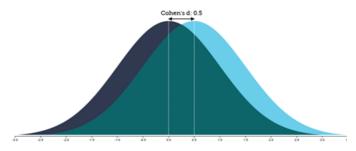




## Effect Sizes and Meta-Analysis

- Meta-analyses calculate sthe mean of several studies on the same topic
- They present p-values to indicate the probability of whether difference between two interventions is only a chance finding.
- The p-value depends in part on the sample size.
- Therefore, meta-analyses also present effect sizes which are measures of the magnitude of the difference between two intervention
- Effect size is a measure for the magnitude of the difference between interventions
- Effect size = (mean A mean B)/pooled standard deviation
- Example (PANSS total score):(90 80)/20 = 0.50

## Ilustration of the meaning of effect size

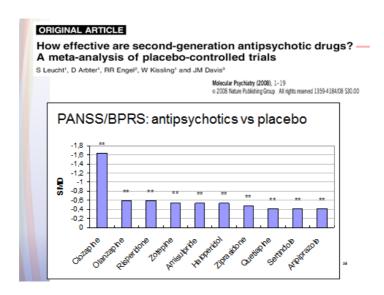


Standardised mean difference ("effect size") of:0.20 = small, 0.50 = medium, 0.80 = large

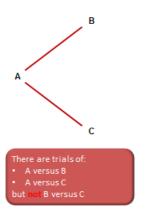
source: http://rpsychologist.com/d3/cohend/







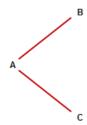
# Latest development: Network meta-analysis Principle





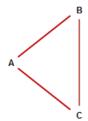


# Principle of network meta-analysis continued



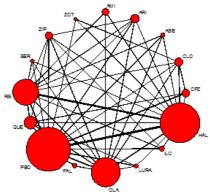
There are trials of:

A versus C
 but not B versus C



B vs C can be estimated from A vs B and A vs C

Network meta-analysis of 15 antipsychotic drugs in schizophrenia (212 studies, 43,049 participants)

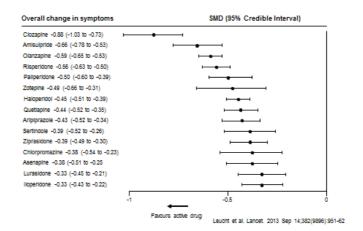


Leucht et al. Lancet. 2013 Sep 14;382(9896):951-62

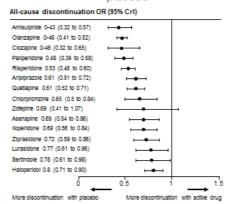




## Overall efficacy of antipsychotic drugs vs placebo



# All-cause discontinuation of antipsychotic drugs vs placebo

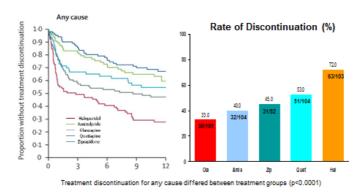


OR=odds ratio





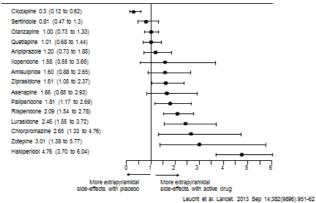
# Time To & Rates of All-Cause Discontinuation Within 12 Months



Kahn R.S. et al. Lancet 2008;371:1085-97

## EPS (use of antiparkinson medication): Antipsychotic drugs vs placebo

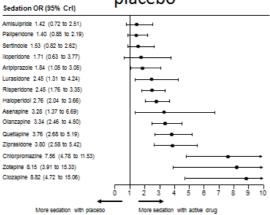
### Extrapyramidal side-effects (use of antiparkinson medication) Odds ratio (95%CrI)







# Sedation: Antipsychotic drugs vs placebo



Leucht et al. Lancet. 2013 Sep 14;382(9896):951-62

# Are we using off-label polypharmacy to solve the placebo dilemma?

- The dirty word
  - Polypharmacy
  - Cocktail therapy
  - Serendipity therapy
- · The politically correct
  - Multi-target approach
  - Symptom targeted therapy
  - Broad spectrum therapy
- The paradox
  - the 2 most effective antipsychotics are one non-selective (Clozapine) and the other very selective (Sulpiride)





## Off-label use

- Twenty percent of all prescriptions, and 31% of prescriptions for psychotropic drugs are for offlabel use (Radley et al, 2006)
- Over 66% of antipsychotic prescriptions are for off-label uses (Weiss et al, 2000)
  - Almost exclusively prescribed for off-label indications in the elderly
- Over 70% of atypical antipsychotic prescriptions are for non-schizophrenic conditions (Buckley, 1999)

## Risks underlying off-label use

- Assessment of efficacy/safety is based on shortterm use even for indications requiring prolonged treatment
- Sample size is limited, therefore infrequent, but serious events may be missed
- Use in high risk population without full exploration of potential safety issues
- Non-standard reporting of efficacy and safety results
- Use in elderly/BPSD is characteristic of this issue





## Should RCT of polypharmacy be conducted?

- · Drug A alone
- · Drug B alone
- Drug A first than add Drug B
- · Drug B first than add Drug A
- An alternative combination C + D
- Placebo
- At least 2 doses of each arm?

## At least 6 and up to 18 arms trial!

## And the future?

"A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die and a new generation grows up that is familiar to it...."

Max Planck





I hope I have not affected your views on evidence, placebo, or any other matter related to your practice.



Any questions?





## **ECNP SEMINAR**

## **REPORT GROUP 1**

LOPOTA, GEORGIA 2014

## **GROUP MEMBERS**

CEZAR GOLETIANI
DAVID TSINTSADZE
NINO NEBIERIDZE
NATIA GULIASHVILI
MAKA MALANIA
KHATUNA PARKOSADZE
MAYA ROINISHVILI
MANANA BERUCHASHVILI
GELA BESELIA
MARINA KUNCHULIA
NATO KOTARIA







## SESSION 1

### SESSION INSTRUCTORS:

JOSEPH ZOHAR AND NINO OKRIBELASHVILI

### TOPICS OF PRESENTATIONS:

- TRANSLATIONAL NEUROSCIENCES
- CASE REPORT ABOUT OCD
- SOCIAL PSYCHIATRY REPORT ABOUT QUALITY OF LIFE IN PSYCHOTIC PATIENTS



Speaker: C. Goletiani



Topic: Astrocyte-based approaches for TBI treatment



The work concerned the treatment strategies for the model of traumatic brain injury in organotypic cultures of hippocampus. Uric Acid (the agent helping increase amino acid transporters on the Astrocyte membranes) and MRS2179 (purinergic antagonist) were used in the study. Morphologically was shown neuroprotective effects Of the drugs. Electrophysiological recordings showed specific changes Depended on the dosing and therapeutic window.

Conclusion: Uric acid and MRS2179 are neuroprotective drugs and to get that effect they change physiological properties of the neural tissue.



Questions: Can these drugs be used for other pathological diseases?

Answer: Yes, they can be used in all pathologies, where excitotoxicity plays inportant role.

Question:



What are future plains?

Answer: To develop in vivo model and test these drugs for posttraumatic epilepsy.





SPEAKER: DAVID TSINTSADZE

TITLE: (F42) OBSESSIVE-COMPULSIVE DISORDER

#### DEMOGRAPHIC DATA:

PATIENT LV. AGE-25, REFERRED FROM PSYCHIATRIC HOSPITAL FOR TREATMENT

#### ANAMNESIS

- THE PSYCHOPATHOLOGICAL PICTURE WAS PRESENTED WITH MULTIPLE FEARS: FEAR OF LIGHT, FEAR OF FOAM, FEAR
  OF SHARP OBJECTS.
- . LATER HE HAD THOUGHTS OF CONTAMINATION, AND WASHED HANDS AND BODY MANY TIMES DURING A DAY.
- INTRUSIVE THOUGHTS WERE PRESENTED BY THE FEELING HE WOULD SCARE SOMEONE IN PUBLIC, SPENDING ALL DAY AT HOME.
- NEVER USED THE PSYCHOACTIVE SUBSTANCES
- . NO FAMILY HISTORY OF MENTAL DISORDER

#### OUTCOME

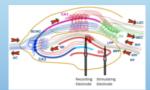
- HE WAS TREATED AT THE HOSPITAL FOR SEVERAL DAYS WITH CLOMIPRAMINE, RISPERIDONE AND QUETIAPINE.
- CONTINUED TAKING THE SAME MEDICATIONS AT HOME FOR SOME ADDITIONAL TIME AND REPORTED A MARKED IMPROVEMENT IN THE FOLLOWING. THE INTURVISE THOUGHTS AND COMPUSIONS WELL RADICTLY DECREASE MARKED IMPROVEMENT IN MOOD, SPENDING MODE TIME OUTSIDE AND HAVING A DESIRE TO PREPARE FOR EXAMS.

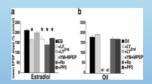
### SPEAKER: NINO NEBIERIDZE

### TITLE: β-ESTRADIOL AND SYNAPTIC PLASTICITY

MAIN GOAL: UNDERSTANDING THE MECHANISMS OF ACTION OF EB AS IMPORTANT ISSUE FOR COGNITIVE FUNCTION.

QUESTION: IS RELATED DECLINE OF ESTROGEN LEVEL WITH SCHIZOPHRENIA?

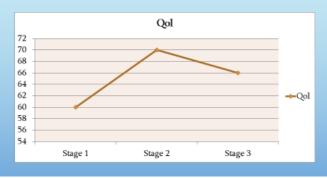








# SPEAKER: NATIA GULIASHVILI TITLE: CHANGES IN QUALITY OF LIFE IN PATIENTS WITH FIRST-EPISODE PSYCHOSIS



## SESSION 1 DISCUSSION

- · PERSPECTIVES OF FUND RAISING
- QUESTIONS ON INDIVIDUAL PRESENTATIONS





## SESSION 2

### SESSION INSTRUCTORS:

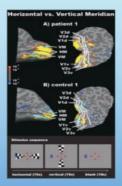
MICHAEL DAVIDSON AND EKA CHKONIA

### TOPICS OF PRESENTATIONS:

- AGING RESEARCH AND AGE-RELATED EYE DISEASES AND VISUAL FUNCTIONS
- VISUAL PERCEPTION IN PSYCHOTIC PATIENTS
- DRUG USE PATTERNS AND RISK BEHAVIOR OF NEW PSYCHOACTIVE SUBSTANCE USERS

# SPEAKER: MAKA MALANIA TITLE: AGE RELATED MACULAR DEGENERATION AND CORTICAL PLASTICITY



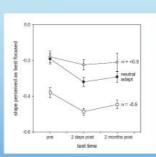






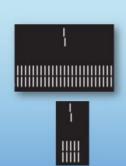
# SPEAKER: KHATUNA PARKOSADZE TITLE: BLUR ADAPTATION IN CATARACT PATIENTS BEFORE AND AFTER CATARACT SURGERY

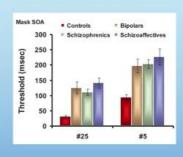




#### **SPEAKER: MAYA ROINISHVILI**

# TITLE: SHARED BACKWARD MASKING DEFICITS IN PATIENTS WITH FUNCTIONAL PSYCHOSES









#### SESSION 2 DISCUSSION

- QUESTIONING ABOUT RESULTS
- RECOMMENDATIONS ABOUT STUDY DESIGN

#### SESSION 3

SESSION INSTRUCTORS:

FRANCESC COLOM AND MANANA BOKUCHAVA

#### TOPICS OF PRESENTATIONS:

- NEUROPSYCHOPHARMACOLOGY
  - NICOTINE ADDICTION
  - SPATIAL MEMORY AND LEVEL OF NEUROTRANSMITTERS
  - CHOLINERGIC SYSTEM -GENETIC VARIATION STUDY





#### Speaker -G. Beselia

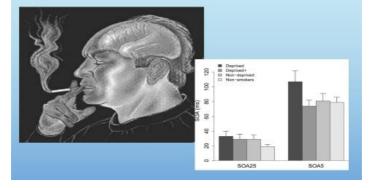
Topic: Spacial working memory and extrcellularhippocampal glutamate and GABA levels in memantine/saline treated rats

The following investigation was conducted to determine the effect of chronic memantine (NMDA antagonist) treatment on hippocampalGlu and GABA release prior to, during and after spontaneous alternation test; Also, the effect of chronic treatment on basal and KCI-stimulated release of neurotransmitters.

Research evaluation of memantine reveals that changes in KClstimulated Glu and GABA release after chronic memantine treatment did not affect working memory in adult rats assessed in spontaneous alternation task.

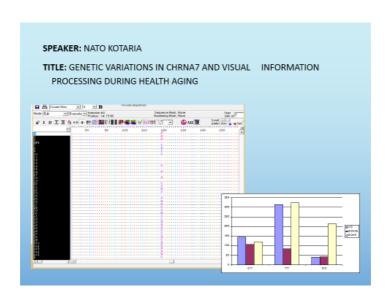
SPEAKER: MARINA KUNCHULI

TITLE: SHORT-TERM NICOTINE DEPRIVATION AFFECTS VISUAL TEMPORAL PROCESSING BACKWARD MASKING









# SESSION 3 DISCUSSION

- QUESTIONING ABOUT RESULTS
- RECOMMENDATIONS HOW TO IMPROVE PRESENTATION
- RECOMMENDATIONS HOW TO MAKE YOUR PAPER PUBLISHABLE





### **Group II Presentation**



ECNP Seminar in Neuropsychopharmacology Georgia, 2014

Presenter: Tamar Aladashvili

# Introduction

## 16 Participants:

- 10 Clinicians
- 5 Residents
- 1 Scientist

#### Affiliations:

- "Center for Mental health and Prevention of addiction – Tbilisi"
- "Centre of Experimental Biomedicine" - Tbilisi
- "Center for Mental health" – Rustavi
- · "Sunstone Medical"
- "Center for Mental health" – Tbilisi, Gldani





### Methods

- Presentations
- Interaction
- Evaluation
- Discussion
- · Recommendations, notes and suggestions

Language of communication generally English.

# 11 Cases 1 Scientific presentation(English)

- · Diagnoses discussed in cases:
- · Mainly Paranoid Schizophrenia
- · 1 case of Bipolar disorder
- · 1 case of Depressive disorder
- 1 case of Somatophormic disorder
- · 1 case of Vascular Dementia
- 1 case of Acute and transient Psychotic disorder
- AEP Drug Therapy and EEG in Epileptic Children











# **Recommendations and Notes**

- · More discussion of differential diagnosis
- · Perform more scales and analysis
- · Specify diagnoses according to ICD or DSM
- Use generic names of medications instead of trade names

- · Face to face contact
- Use body language
- · Amount of words on one slide
- Letter sizes
- No statistics





# Results

- To combine clinical study and scientific research
- · Learn how to perform presentations
- Exchange experience
- Extend skills

# Take message at home

- Disseminate information gained from seminars to our departments
- Share with colleges and residents
- Encourage young generation to participate in future ECNP meetings





# Our evaluation

- · Tutors helpful and kind
- · Participant friendly
- Meeting place beautiful
- Social and cultural events wonderful

P.S. Our group spent coffee breaks like this ©











III group presentation

# **ECNP** SEMINAR IN GEORGIA

- Experts Presentations
- Workshops
- Plenary Session

INTRODUCTION





- New information from experts
- Exchange new ideas
- Communication
- Expressing ourselves

#### **OPPORTUNITIES**

- New nomenclature
- Presentation skills
- New data
- New diagnostic and treatment approaches

**LECTURES** 





- Cases on different topics
- Research statistical data
   about victim of torture
- 2. Clinical case presentations

# **WORKSHOPS**

- Skills of making presentation
- Necessity of differential diagnosis
- Importance of evidence based treatment

CONCLUSION





#### **Abstracts**

## Bipolar Disorders Francesc Colom

Bipolar disorder (BD) is a chronic condition affecting approximately a 4% of the general population. Several studies report BD as one of the five most disabling illnesses and it is associated to a high morbility, mortality and functioning problems. Despite proper treatment, bipolar patients spend almost half of their life presenting acute symptomatology. Moreover, less than 40% of bipolar patients reach functional recovery in areas such as family life, autonomy, and occupational functioning two years after admission. These functioning problems –usually linked to cognitive impairment- may appear early in the illness course but worsen with each relapse, accounting for important socioeconomic costs. Suicide is 15 times more likely to occur amongst people suffering from BD compared to the general population. Bipolar disorder has a biological aetiology and its treatment is primarily pharmacological. Lithium salts are still the gold-standard in the maintenance treatment of BD, but in the last 20 years several atypical antipsychotics and anticonvulsants have also shown its efficacy.

However, external factors may also play a crucial role by triggering newer episodes and by causing chronification of subthreshold symptomatology. Monitoring and managing these factors has been shown to play a major role in both the syndromal and functional recovery. This could be reached by means of several psychological interventions being psychoeducation and family-focused treatments the two techniques showing more evidence-based efficacy.

The lecture will give a general overview of the current clinical and therapeutic knowledge regarding bipolar disorder.

How to interpret results of published trials using treatment resistant schizophrenia as an example.





#### Michael Davidson

In clinical practice treatment refractory, treatment resistant, partial response are all expressions of treatment disappointment and apply to the majority of patients with schizophrenia seen in the outpatient and inpatient services. This is not surprising considering that despite administration of antipsychotic medication 15% to 30 % of the patients remain actively psychotic, almost all manifest either negative symptoms or/and depression, or/and a-volition and only 5% to 10% are employed in a real-life job. Treating psychiatrists, under pressure from patients, family, staff and driven by the therapeutic activism embedded in medical education, turn to the medical literature for solutions. The medical literature is made up by few trails sponsored by the pharmaceutical industry conducted for regulatory or marketing purposes and by hundreds and thousands of trials conceived by individual researchers in academia and funded by governments or foundations.

Since neither the pathophysiology of schizophrenia nor the mechanism of action of currently administered drugs is known, "plausible hypothesis worth testing" includes almost any CNS active compound. For reasons of availability and convenience, pharmaceutical companies generally test new chemical entities while investigators in academia mostly test drugs already available on the market for other indications or combinations of drugs.

Because the potential for bias associated with the profit drive reporting of trial results by the pharmaceutical industry is closely scrutinized and highly regulated by statutory bodies. This is not always the case regarding schizophrenia treatment trials conceived and sponsored by academic investigators for the purpose of advancing science. Despite genuine self-policing efforts by professional organizations, journal editors and others





(ex. <u>ClinicalTrials.gov</u>) and the peer review process, it is not feasible to scrutinize the plethora of trials submitted for publication. Yet the overwhelming majority of trials which report positive results subsequently fail to replicate. Nevertheless, these positive results are met with hope and often enthusiasm by the public and implemented by prescribers, and the lack of replications is often missed or ignored. Furthermore, the only proven remedy for treatment refractory schizophrenia, clozapine is highly under-utilized while polypharmacy or unproven strategies are over-utilized.

The presentations will discuss clinical and research example and propose remedies.





#### la Adamia Tbilisi mental health centre

Patient B. T. 43 years old, female, Georgian, married, lives in Tbilisi. Chief Complaint:

"My mother is not my mother, she is changed."

"Scary things are happening here, scary faces are coming up to me." History of present illness:

After the last discharge from the hospital patient quit taking the medicines, she could not sleep, she had convulsion, which lasted nearly 15 minutes "she was like a statue."

Past Psychiatric history:

Since childhood, the patient has diagnosis of Partial Epilepsy. Last few years manifested signs of psychosis with tendency to aggression. She was admitted to our hospital twice. Last time discharged on 08.10.13. Past medical history:

Complicated pregnancy and delivery. At age 1,5-2 she had febrile convulsions, night enuresis until 13. Five times, she had generalized tonic-clonic seizure. She has taken Carbamazepine for many years. In 1983 she was diagnosed with systemic allergic vasculitis. Since 1992, she is under supervision of neurologist and since 2010 she has diagnose of partial epilepsy with complex partial and secondary generalized seizures.

No family history of mental disorders.

Physical examination normal.

Mental state:

She says: "There is an evil in my home, it wanted to eat me, they were scary, their faces are changing, the teeth are seen." "The police will come and they will take all of you into prison I know." "This man is not my husband my husband is not so old, sometimes my husband comes back, and sometimes that other man is coming with my husband's face."

Mood is dysphoric, cognitive functions impaired (poor memory, attention, concentration)

Diagnosis: F06.2 Organic delusional [schizophrenia-like] disorder





# Tamar Aladashvili Center for Mental Health and Prevention of Addiction

Participating in psychopharmacological researches is always a great opportunity to enlarge practical experience. Previously I've taken part in the following research: Using Ketilept (Quetiapine) in ambulatory treatment of patients with Schizophrenia.

Research showed that Ketilept (produced by Egis) by its antipsychotic activity is not a bit inferior to other traditional antipsychotics and is widely used for both acute and chronic forms of schizophrenia.

Effective influence on both positive and negative psychopathological symptoms and minimum number of side effects make this medicine especially attractive and promising for ambulatory therapy. In future I would like to be involved in clinical research of Using Aripiprazole in the treatment of schizophrenia with minimal hormonal side effects.

### Nino Babunashvili Mental Health Center

47, male, Georgian, military person, married, lives in Tbilisi.

Chief Complaint: Overweight (gained 70 kg within two years), high blood pressure, shortness of breath, acute headache, low mood, loss of energy and ability of work, hypersomnia.

History of Present Illness: Low mood, loss of energy and ability to carry out his official duties, hypersomnia, interpersonal difficulties with others, impaired cognitive functioning, personality changes: loss of sense of shame, respect, overeating, low hygiene, enuresis (no concern), anxiety, and restlessness.

Past Medical History: In 1992 diagnosis of concussion. In 2008 diagnosis of cardiac ischemic disease, unstable stenocardia, hypertension II stage, over-weight (+ 70 kg), perspire, nodular goitre- euthyreosis, Cushing's syndrome, hypertensive encephalopathy.

Family History: No family history. Father and brother – military service personnel, mother – military nurse.

Habits: Chain-smoker.

Physical Exam: (CT) – Lacunar infractions nodes (chronic) in bilateral basal nuclear, to the right side in the frontal lobe on the level of semi-oval center. Pituitary microadenoma. (MRI) – Local lacunar chronic





dyshemical nodes in white substance of both hemispheres, moderately depicted internal hydrocephalia. Cortical atrophy. Electrocardiography, Echocardiography, Selective coronarography, Ecoscopy of thyroid gland.

Medications: Valproate (Deprexor), Medazepam, Cytoflavin,

Memantine (alceba), Dostinex, Euthyrox, bolus-khuato.

Mental Status Exam:

Appearance – over-weight, structural dysplasia

Behavior – indifferent, unceremonious, low self-control, during the visit had spontaneous urination (without sense of concern), goes up and down in the room, picks up the certain things without asking, hums during the conversation.

Orientation – orientation in time, place, surroundings and oneself – partially preserved.

Cognitive functions – impaired memory.

Speech – dysarthria (because of Facial nerve peripheral neuropathy, Bell's palsy in 18.02.2014).

Associative process – delayed, sometimes disconnected.

Mood - labile.

Emotional status – apathy.

No insight

Diagnosis: Subcortical vascular dementia. F 01.2

Treatment, medication: Lorazepame, Memantine, Cytoflavin.

#### Levan Baramidze

# Department of Health Management, Policy and Economics; Tbilisi State Medical University

Vulnerability to Mental Health Problems, Chronic Stress, and chronic diseases

Problem statement: Chronic stress can lead to serious health problems and can affect nearly every system of the human body, as suggested by physical, cognitive, affective and behavioral symptoms.

Aim: Investigation of the interrelations between insufficient coping skills under chronic stress and impaired physical and mental health.

Target population: 200 Students aged 18-24 years of Tbilisi State Medical University (100), Batumi Shota Rustaveli State University (100)

Method: Random sampling, Interviews with Structured questionnaire





# Tamar Bazgadze Gudushauri National Medical Centre, Department of Psychiatry

Male, 15, Georgian

Chief Complaint: Obsessions – distressing thoughts about contamination, becoming ill, not being able to perform at school, etc. against these thoughts, he developed multiple rituals. He can't get up in the morning if someone does not enter his room and takes his blanket. He must touch any subject several times before taking them or type each letter for several times before writing whole word, etc. He has tics – stretches his legs and exhales and inhales loudly.

His obsessions started when he was 13. He needed to touch his books certain times otherwise he could not study lessons. He believed that, if someone left home before him, this day would be dreadful. He developed exhausting repetitive behaviours.

His social life worsened and interpersonal contacts diminished. He rarely leaves home, only for school.

Previous Treatment: Diazepam, Clomipramine, Risperidone.

Treatment was effective, but prolactin level had increased and he applied to another psychiatrist.

Current Treatment: Fluvoxamine 100 mg, aripiprazole 10 mg, lorazepam 1mg

Diagnosis: F42.2 Mixed obsessional thoughts and acts

## Natia Beitrishvili Ministry of Corrections of Georgia , Department N 6

40 years old man, first time is admitted to hospital. Five days that he became aggressive, could not sleep at night, and had rapid associations and absurd ideas: "I have a business of timber, these are unique trees, each tree grows up for two meters a month. For this business I have bought a car (Jeep), which is in front of the bank and I have to take this car and supply workers with foods." The First diagnose was: mania without psychosis F30.1. The serological analyses of blood showed (RPR+). After consultation by Venerologist the patient was diagnosed with organic affective disorders F06.3 and neurosyphilisis A52.3.





# Shorena Bekauri Center for Mental Health and Prevention of Addiction

23, male, married, Georgian by nationality, lives in Terjola Chief Complaint: Phobias "voices"

History of Present Illness:

His state started with restlessness, agitation, inadequate behavior, insomnia, ideas of persecution, megalomaniac thoughts, misperceptions, and beliefs of having "subjective doubles". Treatment in outpatient setting: Risperidone 4–6 mg, Haloperidol 0,5%–2ml – i/m, only once;

Symptoms became polymorphic and acute. After two weeks he was admitted to hospital.

Past Psychiatric History: No history of psychotic state Past Medical History: No history of somatic complications

Family History: Grandfather committed suicide

Habits: Smokes cigarettes,

Physical Exam: without complication

Medications and Allergies: Acute extra-pyramidal side effects due to Haloperidol injection.

Mental Status Exam:

Wears big black sunglasses; He is agitated, restless, sometimes aggressive, smiles pointlessly, touches others; orientation in time, space, place and self sometimes deteriorates; concentration and attention impaired, speech clear and incoherent. He has ideas of reference, persecution and control, megalomaniac thoughts, misperceptions of others and self, "subjective double" phenomenon. Unstable mood, euphoric or sometimes dysphoric, anxious or frightened. No insight.

Diagnosis: F23.0 Acute polymorphic psychotic disorder without symptoms of schizophrenia

Treatment, medication: Trifluoperazine (Thriphtazin) 0,2% - 9 ml, Trihexyphenidyl (Cyclodol) 4-6 mg, Levomepromazine (Tisercin) (50-100 mg), Clozapine (50 -200 mg), Amisulpride (Soliani) 400-800 mg, Valproate (Depakine –Chrono) 500-1500 mg.





## Ekaterine Berdzenishvili Ltd Acad. O. Ghudushauri National Medical Center, Psychiatric Department

My clinical practice revealed that one of the challenges in treating patients with schizophrenia is maintaining systematic and continuous medication treatment. Patients often stop taking medicines spontaneously, at will, which leads to aggravation of psychotic symptoms. I suggest that among the major reasons for the termination of treatment are patients' subjective feelings and experiences which they have when on medication, and after discontinuation of treatment. Experiences during these two periods of time (with treatment and without treatment) differ greatly. I think that collecting data based on the patients' narratives will help better understand whether these two different subjective mental states have an impact on treatment process, and, if so, what kinds of subjective experiences that patients have may prompt them to stop the treatment.

Research participants: 10 patients with schizophrenia, 5 women and 5 men, who have at least a 2-year history of illness, are treated with non-conventional antipsychotics, and frequently and arbitrarily stop the treatment. Age range: 20 to 35 years old.

Research procedure: Qualitative research, namely, phenomenological. Patients will be interviewed during stationary treatment after psychotic symptoms have been substantially reduced

Research materials: Patients' description of their direct experience during receiving and stopping the treatment. Narratives will be recorded during nondirective interviews. The patient tells about his condition, feelings, emotions, bodily sensations, desires, attitudes towards others, self-esteem etc. during the period of time when he/she receives medications and when he/she stops receiving medications.





## Magda Berianidze Ministry of Defense, department of psychological assessment and monitoring

26 years old man, has mental problems for two years. Diagnosed by: paranoid schizophrenia F20.0

He had positive psychosis symptoms: persecutory ideas, imperative auditory hallucinations. Was aggressive towards his mother. Treatment started with Haloperidol 2ml a day, cyclodol (4mg a day). After several days, because of increase anxiety we changed medication (gave Risperidone - Rispolux 4mg a day), but he developed acute dystonia. We stopped giving antipsychotics for two days and then started with aripiprasole (Aripegis) 10mg a day and increase dose to 15mg a day and added Olanzapine (Olzap) 10mg a day. Patient's mental state improved: delusions deactualized, hallucinations disappeared and relationship with mother improved.

### Manana Beruchashvili LEPL Drug Addiction and Mental Health Policy and Programmes Management Center

Clinical Features, Drug Use Patterns and Risk Behavior of New Psychoactive Substance Users

Aim: To study Biological, psychological and social consequences of NPS use.

Hypothesis: Mental health problems will be more prominent than somatic and behavioural consequences

Importance of the study: Clinical experience shows that NPS users are mainly young people who due to the NPS use are suffered by multiple health problems: acute intoxication, sudden death, mental disabilities Target population: Patients involved in OST; detox programs and harm reduction services; patients treated in narcology clinic; all suspicious cases from intensive care units having experience of NPS use

Spatial working memory and extracellular hippocampal glutamate and GABA levels in memantine/saline treated rats

G. Beselia1, T. Naneishvili2, M. Demurishvili2, S. Mataradze2. 11.Beritashvili Center of Experimental Biomedicine, Behavior and Cognitive Function, Tbilisi, Georgia.





2St.Andrew the Firs-Called Georgian University of Georgian Patriarchate, Neuroscience, Tbilisi, Georgia

For over a decade intensive research have been dedicated to search for NMDA receptor antagonists as a potential neuroprotective treatment for both acute (e.g., stroke) and chronic neurodegenerative diseases. Although only very few such agents reached late stages of clinical development because of side effects, it was discovered that several compounds currently in clinical use such as memantine, amantadine and others have NMDA blocking properties which likely play a role in their therapeutic efficacy. It is still not clear, however, as to how memantine produces its symptomatological improvement of memory in demented patients. The effects of memantine on in vivo hippocampal glutamate levels have not been examined. Analysis of neurotransmitters and related substances in the dialysates from probes inserted into discrete brain areas has been extensively used to monitor extracellular levels of neurotransmitters, yielding a great deal of information about functional interactions of endogenous neurotransmitter systems.

The following investigation was conducted to determine the effects of chronic memantine treatment on hippocampal Glu and GABA release prior to, during, and after spontaneous alternation test. Also, we have investigated the effects of chronic treatment with memantine on basal and KCI-stimulated release of GLU and GABA in the hippocampus. A total of 18 male Wistar rats (Department of Animal Care, I. Beritashvili Center of Experimental Biomedicine) were used in the present study. All experiments were approved by the Animal Care and Use Committee of the Center and were in accordance with the principles of laboratory animal care. Two groups of rats were treated either with memantine (2,5 mg/kg/day; i.p. Sigma Chemical Co., St. Louis, MO) or with vehicle (saline) for a period of 4 weeks. To allow extrapolation of animal data to the clinical situation therapeutically relevant doses should be used in animal experiments. Rats were trained in a four-arm plus-shaped maze.\ Memantine-treated rats, relative to saline rats, had a significantly lower level in the number of arms entered during the testing session. However, the groups did not differ in the level of alternation behavior.

The results indicate that memantine treatment produced decreased locomotor (exploratory) activity (p<0,05) but did not affect spatial working memory in adult rats assessed in spontaneous alternation task (p>0,05).





Glu release during the 10 min samples taken at the time of the behavioral testing of memantine or saline treated animals increased during behavioral testing but were not significantly different (p>0,05) from those seen immediately before and after testing. We found increase in KCl-stimulated glutamate and GABA release in the hippocampus of memantine treated rat compared to the saline treated rat. This difference in KCl response between memantine treated and control rat was statistically significant (p<0,05). Our evaluation of memantine reveals that changes in Gluergic neurotransmission after chronic memantine treatment did not affect working memory in adult rats assessed in spontaneous alternation task.

Treatment approach to mental health outcomes of torture among former prisoners.

# Khatuna Chkoidze Tbilisi Mental Health Center

GCRT – The Georgian Centre for Psychosocial and medical rehabilitation of torture victims has worked with former prisoners after their release from prison. Since 2012, the center has served 564 victims in 4 regions of Georgia. The team has offered multidisciplinary approach, medical and psychological assistance, diagnosis of mental and somatic disorders and pharmacological and psychological treatment. The obtained data have been used to study: 1) The common mental problems among victims of torture falling into different crime categories, 2) Relation between torture methods and developed mental disorders, 3) Treatment efficiency with medication in comparison with treatment using medication and psychotherapy together.

Results: The most frequent psychiatric diagnoses were depressive conditions with various severity (31.2%), stress related and anxiety disorders (14.3%), personality and behavioral disorders due to brain disease (7.8%), damage and dysfunction, personality disorders, mental and behavioral disorders due to psychoactive substance abuse. Comorbidity and dual diagnosis with drug addiction were common (29.5% of all cases). Imprisonment length and torture intensity correlated with severity of mental state (Pearson correlation, p= 0.007). The treatment efficacy was very low for both combination treatment and





psychopharmacological treatment alone without significant statistically differences.

## Nino Dzagania Rustavi Mental Health Center, Crisis Intervention Department

My clinical interest concerns two spheres:

To use Naltrexone (a competitive opioid antagonist used in abstinence maintenance therapy) in treatment of schizophrenia;

Combination of psychopharmacotherapy with psychotherapy in treatment and psychorehabilitation of Generalized Anxiety Disorder(GAD) and Obsessive-compulsive disorder(OCD).MM

Some reasons of frequent hospitalization

**Evidence Based Practice Center** 

A.Abashidze, N.Abdushelishvili, G.Geleishvili, M.Nikolaishvili, S.Oragvelidze,

N.Chirgadze, I.Menteshashvili, S.Getsadze, E.Gamreklidze, G.Cheishvili, A.Mgeladze

After 23 months of Assertive Community Treatment Program (ACT-program) in Tbilisi provided to 44 patients it is possible to make some conclusions, which seem valuable for identifying reasons of frequent hospitalizations psychiatric clinics. Here are some of them:

- 1.Bad compliance to medication administration (on its turn due to various reasons);
- 2.Unfair financing of outpatients. Misbalance in financing of in-patient and out-patient treatment programs;
- 3.A gap between hospitals and outpatient facilities;
- 4. High level of expressed emotions;
- 5. Nonexistence of any other 24 hour psychiatric services except hospitals;
- 6. While there are no community based services, duration of hospitalizations are too short;
- 7. During voluntary hospitalizations patients can dictate to psychiatrists what treatment they "need" and avoid what is better from doctor's standpoint;
- 8. Absence of housing programs;
- 9. Sometimes family members arrange frequent hospitalizations via specially provocating patient;
- 10.Untreated hypertension.





### Salome Gogava Ltd. Center for Mental Health and Prevention of Addiction

33-year-old woman from Gardabani, Georgia. Single.

Complaints: The unpleasant taste in the mouth, the smell and uncomfortable feeling in her body, changing appearance, auditory hallucination inside the head.

Disease statred with dismorphophoa, delusions of reference and poisoning. Soon she developed delusions of control, auditory pseudohallucinations, passivity phenomena (made emotions and movement).

Hospitalized for the first time.

Mother has diagnose of schizophrenia.

No allergies on food and medication.

Appeared bored, tired, cooperative, interested in treatment. She is oriented to place, time and space. Intelligence fits to level of education and knowledge. Speaks clearly and emotionally. Associations are consistent, with clear communication. She has dismorphophobic, delusional thoughts of reference, control and poisoning. Depressed mood, anxiety, no insight.

Ds: F20.0

Treatment: Haloperidol 15mg. Amisulpride (Solian) 800mg.

Risperidone 6mg, Clomipramine (Anafranil) 200mg.

Astrocyte-based approaches for traumatic brain injury(TBI) treatment.

## Cezar Goletiani Institute of Cognitive Neurosciences, Agricultural University of Georgia

Excitotoxicity is one of the causes of delayed cell death and neurodegeneration during TBI.

Uric acid (UA) is the drug regulating level of excitatory amino acid transporters on the astrocyte membranes.

We were using UA against excitotoxicity in the equibiaxial model of neurotrauma in the hippocampal organotypic cultures of the rat.

Neuroprotective effect of UA was shown morphologically with propidium iodide fluorescent method.





Protective effect was shown on the functioning of neural tissue in the electrophysiological study with recordings of input-output currents and paired-pulses measuring short-term synaptic plasticity. Electrophysiological effects of UA were depended on the dosing and therapeutic window.

### Natela Guliashvili Ilia State University

The aim of the research was to investigate the quality of life of patients with first psychotic episode and the follow up changes within the 2 years and the impact of psychopathological symptoms. The patients with first episode psychosis participated in the study with the intervals of six months within 2 years. The study showed that during 2 years general indicator of the quality of life in patients with first-episode psychosis (at the initial stage - 60.39) increased (70.17), and then - decreased (66.01). However, statistically significant differences were observed only in domains of psychological well-being (p = 0.027) and environmental conditions (p = 0.001). The negative symptoms slightly worsened and severity of positive symptoms decreased. The result of the study revealed statistically significant negative correlations between physical well-being and psychopathological symptoms; and psychological well-being and positive symptoms. Quality of life of patients is lower compared to healthy population. Relation among psychopathology and quality of life is obvious

### Sopio Gurashvili Mental Health Center

26 male, single, Azidi, lives in Tbilisi

Chief Complaint: Insomnia, aggression towards his mother, feeling of being possessed by the negative force. Inability to control his emotions. History of Present Illness: Last one month he could not sleep, moved to another flat. Thinks that his trouble started after conflict with his friend. He came to an appointment with his brother.

Past Psychiatric History: - three years ago had episode of depressed mood, with loss of appetite and weight. Did not take any medication or get any treatment.

Past Medical History: No complaints





Family History: No family history of mental disorders.

Lives with his mother

Physical Exam: No complications Medications and Allergies: None

Mental Status Exam: tidy, well groomed, polite, orientation preserved. Concentration and attention moderately deteriorated, intellectual ability in accordance with education and knowledge. Speech clear, incoherent, tangential. Mood labile. do not have insight.

Diagnosis: F23.0 Acute polymorphic psychotic disorder without

symptoms of schizophrenia

Treatment, medication: Risperidone 4mg, Valproate (Depakine-

chrono) 750mg

### Shorena lashvili Center for Mental Health and Prevention of Addiction

During my work at the clinic, I participated in several studies on certain medications (olanzapine risperidone, quetiapine). I have studied the practical use of these drugs for a variety of mental disorders and introduced the results. I would like to investigate cases with religious delusions and efficacy of atypical antipsychotics for treatment such cases. Particularly, I am interested to study efficacy of Amisulpride injection.

### Baia Kachkachishvili Rustavi Mental Health Centre

I am interested in pharmacological management of agitated behaviors in patients with dementia. I have gained a practical experience in this field. The mean age of the patients is 70 years, average number – 335. Most of them meet criteria Alzheimer Disease, others for mixed AD and vascular dementia, Target symptoms include excitement, aggressiveness, pacing, increased motor activity, insomnia... Typical and atypical antipsychotic drugs, antidepressant are generally well tolerated by them, but narrow therapeutic window, excessive sedations, paradox effects, progressive cognitive impairment cause certain limitations in their use.

I am interested in effectiveness of Trasodone in these cases.





Genetic variations in CHRNA7 and visual information processing during health aging

Nato Kotaria1, Marina Kunchulia2, Adam Kotorashvili1 H. Herzog3 1Genome Center, National Center for Disease Control and Public Health (NCDC&PH), Tbilisi, Georgia. 2Institute of Cognitive Neurosciences, Agricultural University of Georgia, Tbilisi, Georgia.3Laboratory of Psychophysics, Brain Mind Institute, School of Life Sciences, EcolePolytechniqueFederale de Lausanne (EPFL), Switzerland.

A genetic variation of the cholinergic nicotine receptor gene, alpha-7 subunit (CHRNA7) has been shown to be associated with stronger backward masking deficits in schizophrenic patients. Given the pivotal role of CHRNA7 in backward masking in schizophrenia, the aim of the current project to study the polymorphisms of this gene in elderly with different masking performance, that could help to identify genetic factors that play role in individual variation in backward masking performance during health aging.

Three-dimensional architecture of hippocampal neuron treated with pentylentetrazole. Atomic force microscopic study M. Ksovreli1, M. Zhvania1,2 1Institute of Chemical Biology, Ilia State University, 2I. Beritashvili Center of Experimental Biomedicine

Using atomic force microscope, Bioscope II, Veeco, we observed the three-dimensional architecture of chemically fixed and living hippocampal neuron treated with epilepsy-produced drug – pentylententrazole. Postnatal hippocampi from 1- to 5 day old mice were used. Neuronal culture was prepared using conventional procedure. Cells were fixed with 2.5% glutaraldehyde. For living cells the glasses treated with polyethylenglicole were used. The cells were imaged using tapping mode. The architecture of normal and pentylentetrazole-treated neuron was described. Different parts of neurons, including processes were visualized and the nanomodifications that have been developed as a result of pentylentetrazole treatment were revealed.





# Olgha Kukhianidze Center for Mental Health and Prevention of Addiction

I participated in the following studies:

Evaluation of clinical effectiveness of Sedarex (Risperidon)
Evaluation of clinical effectiveness of Olzap (Olanzapine)
Evaluation of clinical effectiveness of Ketilept (Quetiapine)
There are several important for me practical nuances in
psychopharmacology, which I would like to draw particular attention. I
would like to take part in the study to overcome treatment resistance
within the treatment of delusion in schizophrenia and schizoaffective
psychoses, particularly resistant ideas of reference, delusions of love,
religious ideas. I am interested in the problem of resistance to the
treatment of insomnia. I am extremely interesting to know the opinion
of leading experts about real clinical benefits of certain selective
serotonin reuptake inhibitors in the complex therapy of obsessivecompulsive disorder, especially if it contains a component of sexual
perversions.

# Nino Kukuladze LTD Center for mental health and prevention of addiction

The patient is a 50-year-old, male, Georgian, Single, from Telavi Resistant insomnia, lack of energy, suicidal thoughts. His psychiatric problems started with insomnia that worsened the mood. He had an unpleasant, suicidal ideas feeling of worthlessness and low self esteem. Medication – Haloperidol, Valproate (Depakin-chrono). He was brought to hospital by his brother.

First time he was hospitalised in 1998 with diagnosis of mixed affective episode. In 2000-2006 had 2 episodes a year, and then - 3-4 episodes a year. Medication - lithium carbonate, Amitriptilin, Haloperidol, Valproate (Depakin-chrono).

He had brain injury, coma.

No bad habits

No allergiesa

Slow movements, correctly oriented, no cognitive impairment, normal flow of associations, depressive mood and ideas. The most difficult time experiences in the morning; formal insight.

Short-term nicotine deprivation affects visual temporal processing





Marina Kunchulia1, Karin S. Pilz2, Michael H. Herzog3 1Institute of Cognitive Neurosciences, Agricultural University of Georgia, Tbilisi, Georgia. 2School of Psychology, University of Aberdeen, Scotland, UK.3Laboratory of Psychophysics, Brain Mind Institute, School of Life Sciences, EcolePolytechniqueFederale de Lausanne (EPFL), Switzerland.

Nicotine is an important stimulant in the human brain that is involved in modulating many neuronal processes, including those related to vision. In this study, we tested visual backward masking in healthy smokers and non-smokers to further understand the effects of nicotine on spatio-temporal vision. We investigated 48 participants: One group of non-smokers (n=12) and three groups of regular smokers that were either cigarette deprived (n=12), non-deprived (n=12),or deprived but were allowed to smoke directly before the start of the experiment (n=12).Our results showed stronger effects of masking for deprived smokers.

### Nino Kvaratskhelia Tbilisi Mental Health Center

Ch. G. male, 47, Georgian, combat, participant of Abkhazian war, married.

Over-Weight (within last two years put on weight 70 kg), high blood pressure, short breath, splitting headache, low mood, loss of energy and ability of work, hypersomnia.

Personality change, lack of energy and capacity for official duties, hypersomnia, loss of sense of shame, respect, overeating, likes cartoons, poor hygiene, enuresis (without sense of concern), anxiety, restlessness. In 1992-1993 participated in Abkhazian War and got brain injury twice. Since 2008 had had headaches, asthenia, hypertensia (260/160 – 160/100 mm Hg) and other cardiovascular complaints.

In 1992 diagnosis of concussion. In 2008 diagnosis of Myocardial ischemia, hypertension, over-weight (+ 70 kg), Cushing's syndrome, Hypertensive encephalopathy

Diagnosis: Subcortical vascular dementia. F 01.2 Treatment: Lorazepam, cytoflavin, memantine.

Maka Malania1, Megi Sharikadze1,2, Eka Chkonia1,3, Gregor Volberg4 1 Institute of Cognitive Neurosciences, Agricultural University of Georgia, Tbilisi, Georgia





2 Institute of Clinical Chemistry an Laboratory of Medicine, University Hospital of Regensburg, Regensburg, Germany, 3 Tbilisi State Medical University, Tbilisi, Georgia, 4 Institute of Experimental Psychology, University of Regensburg, Regensburg, Germany Brain abnormalities and recognition of emotions in depression Depression influences perception of facial emotions that at the end lead to inability of managing social relations. Auditory mismatch negativity (MMN) is widely used paradigm in such psychiatric studies as schizophrenia and considered to be a reliable cognitive marker for different mental illnesses. Our aim is to investigate the face/emotion recognition in context of visual MMN during the depressive episode as well as in the remission phase and compare it with non-depressed controls. This way we will find out if difficulties in preattentive emotional processing found in depression can help to distinguish different types of depression and predict treatment resistance.

#### Mariam Menteshashvili Ltd. Center for Mental Health and Prevention of Addiction

75-year-old-man, Georgian, widower, from Surami.

Apathy, loss of interests, irritability.

In 2011 year, after the death of his wife, high blood pressure, low mood, lost interests, suicide ideas, 3 suicide attempts during the last month.

Hospitalized first time. He was treated by psychiatrist during 2 years: trifluoperazine (Triptazin), Benzhexol, Amitriptyline, Chlorprotixene (Truxal).

Patient's mother had the symptoms of depression. Brother and son committed suicide.

T/A - 160/90 mmHg.

NO Food and medication allergies.

Mental state: Normal Appearance, sits silently, looks down. Low mood, sits still, in one pose. No cognitive impairment, oriented in place, time and space. Poverty of speech, suicidal thoughts, formal insight.

Ds: F33.1

Trifluoperazine (Triptazin) 20mg, Fluvoxamine (faverin) 50mg





# Ekaterine Mgaloblishvili Center for Mental Health and Prevention of Addiction

Previously I have participated in the following clinical trials:

Effectiveness of Rispaxol(Risperidone ) in treating positive symptoms of schizophrenia.

Clinical research about efficiency of Ketilept (Quetiapin) in treating positive symptoms of schizophrenia and affective disorders in patients with younger age group.

In the future I would like to take part in research about treatment of resistant depression with modern psychopharmacological drugs. Preventive care (medication) of cognitive deficiency developed during dementia.

# Nana Narimanidze Mental Health Centre of Rustavi

58 years-old, female, Georgian, married. Rustavi.

Chief Complaint: Low mood, loss of appetite, lack of energy, constipation, urinary retention, believes to have cancer.

History of Present Illness: Stopped treatment, became passive, mainly lays in the bed, not take care of herself, eats and speaks little.

Husband brought her to our hospital on 23.04.2014.

Past Psychiatric History: She was hospitalized twice in 19.07-15.08.2012 and 08.10-15.12.2012 . Treated with: Tab.Amisulpride (Soliani) 800mg/d;

Tab. Venlafaxine (Velaxini) 150mg/d; Tab. Chlorprothixene (Truxal) 50mg/d; Tab. Mexibat 500mg/d; Escitalopram (Cypralex)10mg/d;

Imipramine (Melipramin) 400mg/d; Past Medical History: Hypothyroidism Family History: No family history

Physical Exam: Healthy

Medications and Allergies: No

Mental Status Exam: Disorganized, passive, orientated in space, place and time, poverty of speech, depressive, anhedonia, hypochondriac

delusion, no insight Diagnosis: F 33.3

Treatment: Agomelatine (Melitor) 50mg/d; Olanzapine (Olzap) 10mg/d;

Lamotrigine (Latrigal) 100mg/d; Lorazepam (lorafen) 2mg/d;

Chlorprothixene (Truxal) 25mg/d; L.tiroxini100mkg/d.





N.Nebieridzea,e, L.Veliseka,c,d, J.Veliskovaa,b,d aDepartment of Cell Biology & Anatomy, bDepartment of Obstetrics & Gynecology, cDepartment of Pediatrics, dDepartment of Neurology, New York Medical College, Valhalla, NY, USA, eAgricultural University of Georgia, Institute of Cognitive Neurosciences, Tbilisi, Georgia -estradiol and synaptic plasticity

Estrogen, besides reproductive function, has an important influence on cognition as well. During normal aging or in a case of surgical ovariectomy, declining level of estrogen is accompanied by impaired memory in women, which can be prevented by estradiol replacement. Using long-term potentiation (LTP), we investigated the effects of EB on synaptic plasticity in the rat dentate gyrus.

Female Sprague- Dawley rats were ovariectomized (OVX) and treated subcutaneously with EB or oil, daily for 4 days. Transversal slices containing entorhinal cortex-hippocampus were prepared for extracellular recording. We used different drugs. At medial perforant path-dentate granule cell synapses in hippocampal slices of OVX female rats EB replacement was critical for an initial induction of LTP to enhance the magnitude of subsequent LTP elicited by a second high-frequency stimulation, metaplasticity, which was not present in slices from oil-treated control animals. Understanding the mechanisms of EB action will allow for design of new pharmacological interventions to directly target these mechanisms.

# Rusudan Nozadze Tbilisi Center for Mental Health

41 years old male, Georgian, divorced, Tbilisi

Chief Complaint: Mood impairment, insomnia, pulling and freezing sensation in the pelvic area.

History of Present Illness: Irritability, anxiety, fear of people, loss of appetite, pulling and freezing sensation in the pelvic area.

Trifluoperazine (Triftazin) 5 mg, Cyclodol 2 mg, Clozapine 25 mg, Clomipramine (Clofranil)25 mg.

Past Medical History: Hearing impairment

Family History: No family history of mental disorders, divorced, has three years old daughter, lives with parents.

Physical Exam: Somatic condition is satisfactory.

Medications and Allergies: None

Mental Status Exam: Psychical Status





Well groomed, tidy;

Adequate behavior

Oriented in place, environment and himself

Cognitive functions, memory within normal limits. Concentration is impaired. Intellect correlates with education

Speech is legible.

Associations are understandable, successive, with elements of symbolism

Hypochondriac content, focused on his feelings

Mood is Dysphoric, impaired

Lack of insight

Diagnosis: Undifferentiated somatoform disorder F45.1?

Treatment, medication: Risperidone (Sedarex) 4 mg.; Clozapine

(Azaleptin) 25 mg, Clomipramine (Clofranil)100 mg.

### Mariam Okruashvili Ilia state university

Aim:The aim of our study was to investigate the quality of functioning in patients with first psychotic episode, its relation to the cognitive skills and psychopathological symptoms and changes in these indicators over time. Methodology: The study involved 32 patients with a first psychotic episode and 32 healthy controls. The study consisted of three phases with an interval of 6 months for patients. The diagnosis was based on DSM IV-criteria by a clinical interview, the positive and negative symptoms were evaluated for positive (SAPS) and negative (SANS) symptoms assessment scales. The study used cognitive tests(WCST, CPT,SOA) of executive functions, as the patients and the control group. Schizoid personality characteristics in the control group were evaluated by the Schizoid Personality Questionnaire – brief version (SPQ-B brief version), and social functioning of patients evaluated by Health and Outcome Scale(HoNOS).

Results:Cognitive functions at the initial stage of the disease were significantly impaired compared to the healthy controls. The patients did not show significant cognitive impairment within 2 years since the first psychotic episode. The social and symptomatic indicators of HoNOS of patient, whoadhered to the treatment regime improved.

Conclusion:Baseline impaired cognitive functioning has not significantly changed since the first psychotic episode. The treatment compliance improves social and symptom indicators. First psychotic episode is an





important period for prevention of cognitive and social deterioration. Supportive social environment and stable mental state are strong predictors of better outcome.

Khatuna Parkosadze1, Teona Kalmakhelidze2, Marina Tolmacheva2, Georgi Chichua2, Archil Kezeli1, Michael A. Webster3, John S. Werner4

1 Institute of Cognitive Neurosciences, Agricultural University of Georgia, University Campus at Digomi, David Aghmashenebeli Alley #240, 0159 Tbilisi, Georgia, 2 Eye Disease Clinic MZERA, 9 Tsinandali Street, 0144 Tbilisi, Georgia, 3 Department of Psychology, University of Nevada, Reno, NV, USA, 4 Department of Ophthalmology & Vision Science, University of California, Davis, CA, USA Blur adaptation in cataract patients before and after surgery We examined how perception of blur is adjusted before and after cataract surgery. Seventeen cataract patients participated in our study. Grayscale images of natural scenes were used for adaptation and testing. Results before cataract removal showed that best focused slopes were slightly negative, suggesting overcompensation for optical blur. Two days after surgery results shifted to more negative ('blurry') values, suggesting that subjects perceived the world as too sharp. This shift was not significantly changed when patients were retested at 2 months. We conclude that after cataract removal a strong adaptation persists for at least two months showing slow renormalization of spatial vision.

The work was supported by CRDF grant (GEB1-2930-TB-08)

#### Nino Paturashvili

Tbilisi State Medical University, Institute of Postgraduate Medical Education and Continuous Professional Development

Female,29; married;

Chief Complaint: Anxiety, suicidal ideas, depressed mood, inner feeling of emptiness.

History of Present Illness: - She had family conflict, tensions gradually evolved, she said that her family members made her son to be against her. Mood depressed, anxious. She has suicidal ideas, said that some "voices" tells her to kill herself. She was taking prescribed medications at home: Ketilept (quetiapine) and Depakine chrono (Valproate). Past Psychiatric History:





Hospitalisations: - November 2012, F23.3 Other acute predominantly delusional psychotic disorders.

January,2013 - depression, extrapiramidal side effects July,2013 -insomnia, paranoid thoughts about poisoning. F25.1.

Schizoaffective disorder, depressive type

November, 2013 last hospitalization.

Prescribed medications: triphtazin (Trifluoperazine) 4mg i/m, diazepam 20mg, depakin chrono (Valproate) 1000mg, olanzapin 10mg, cyclodol (Trihexyphenidyl) 2mg, amitriptilin 25mg.

Family History: Mother left family when she was 2 years old. Her brother has same diagnosis:

Diagnosis: F25.1. Schizoaffective disorder, depressive type

Maya Roinishvili 1, Eka Chkonia2, Michael h. Herzog3, Andreas Brand4 1 Institute of Cognitive Neurosciences, Agricultural university of Georgia, Tbilisi, Georgia, 2 Department of Psychiatry, Tbilisi State Medical University, Tbilisi, Georgia, 3 Laboratory of Psychophysics, Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland, 4 Klinikum Bremen-Ost, Center for Psychiatry and Psychotherapy, Bremen, Germany

Shared backward masking deficits in patients with functional psychoses

In visual backward masking, a target is followed by a blank screen (ISI) and, then, a mask which deteriorates target processing. Schizophrenic patients show strong but complex processing deficits in visual masking compared to healthy controls. Recent genetic, behavioral, and clinical studies suggest that functional psychoses (schizophrenia, bipolar disorder, schizoaffective disorder), previously thought to be distinct from each other, belong to one continuum. The shine-through masking paradigm has been proven to be a reliable endophenotype of schizophrenia with a high sensitivity and specificity discriminating between patients, their clinically unaffected relatives, and healthy controls. Hence, if schizophrenia, bipolar disorder and schizoaffective disorder belong to one common disease, strong masking deficits are expected to occur in all three diseases. Here, we examined whether the complex masking effects, we found in schizophrenic patients previously, are also found in bipolar and schizoaffective patients. 20 bipolar, 22 schizoaffective, 28 schizophrenic patients, and 20 healthy controls participated in various variants of the shine-through masking paradigm.





All 3 groups of patients showed a very similar pattern of masking deficits. First, Masking was strongly prolonged compared to controls: Schizophrenic patients needed ISIs of 110 ms, Bipolars of 125ms, schizoaffective of 130 ms and controls of only 30ms. Second, these prolonged ISIs were not caused by deteriorated spatial or temporal resolution as two additional experiments show. We suggest that schizophrenic patients as well as bipolar and schizoaffective patients suffer from similar dysfunctions in early visual processing.

#### Maia Sakhvadze Rustavi Mental Health Centre

11 years old, female, Georgian, separated from her mother, who works in Italy for 6 years.

Has frightening voices and vision of her mother and stranger man accompanying with fear.

Her mental problems started 2 years ago, with hallucinations, frequently provoked by talking on phone with her mother, gradually she became aggressive, had some difficulties with study.

Admitted to psychiatric hospital in 2013.

Since 2011 has been treated for hypothyreosis

Her father and sister have Epilepsy.

Diagnosis: F29 Unspecified nonorganic psychosis

Medication: Risperidone 3mg/d, Depacin-chrono (Valproate) 500mg/d,

Truxali (Chlorprothixeni) 25mg/d, Phenibute 500mg/d.

### Sopho Salia Mental Health Center "Mentalvita"

Female, 14. registered since May 2013.

Diagnose - F91.1 Unsocialized conduct disorder
No family history of mental disorders. Though father has been
described as a psychopathic personality, excess consumption of
alcohol and other psychoactive substances, was imprisoned several
times. Mother married at an early age, soon divorced from her
husband because of the conflicts.

in 2012, patient spent the summer holidays in his father's family. Mother doubts about incest between father and daughter. Since then the patient's attitude toward her mother changed. She became disobedient, refused to attend lessons and classes. Experienced sleep





disturnebces, nightmares, was emotionally cold toward family members, neglected hygiene and personal appearance, started smoking cigarretes and used psychoactive substances, ran away from home. In 2013 was diagnosed with F 91.1 and prescribed - Risperidon, Melitor (Agomelatine).

### Giorgi Sikharulidze Tbilisi State University

#### Objectives:

Antipsychotic augmentation is a common strategy for treatment resistant OCD. This open-label study evaluated the efficacy of adding Aripiprazole in patients whose OCD was insufficiently responsive to an adequate SSRI or SNRIs treatment.

#### Methods:

Fourteen adult outpatients, who met the DSM-IV-TR criteria for OCD and had treatment resistant OCD were evaluated in open-label trial.

The patients received Aripiprazole (7.5-10 mg/day)/SSRI-SNRIs for 10 weeks. Patients were evaluated using the Yale-Brown Obsessive Compulsive (Y-BOCS) scale.

#### Results:

This Combination therapy significantly improved Patients Condition. A significant reduction in total scores of Y-BOCS was found. Aripiprazole was generally well tolerated.

#### Conclusion:

Results of the present study indicate that Aripiprazole augmentation of SSRI/SNRIs therapy may be effective for treatment-refractory OCD.

#### Zura Sikharulidze Medical Center 'Uranti'

Substance use and Dual Diagnoses in Georgian people Background: The co-occurrence of mental and physical disorders related to substance abuse is more often a serious problem to medical services. Aim: To investigate the prevalence of dual diagnosis DD in patients with diagnosis of substance use disorder in years 2012-2013 Target groups: Patients with DD; with diagnosis of mental disorder without substance use: with diagnosis related to substance use.





Methods: The retrospective study of 200 case records of patients in years 2012-2013. The control group (n=20) will be created among patients with mental disorders and without substance abuse.

## Ketevan Silagadze Institute of Neurology and Neuropsychology

41, married male, lives in Tbilisi,

Current complaints: low mood, increased irritability, disturbed sleep and loss of appetite.

He has been experiencing these symptoms for 5 months after his conflict with his boss. His mental state worsened last month. He became hopeless, lost weight.

He has never had depression before.

No history of alcohol or drug use. Smokes cigarettes occasionally. Mental state: Apparent sadness, looks down, moves slowly, movements are restricted, speaks softly; well-oriented in time, space and place. He has impaired attention and concentration, depressed mood, pessimistic thoughts and hopeless attitude toward the future; worries about his condition.

According the Beck Depression Inventory and the Hamilton Rating Scale for Depression he has moderate depression.

Treatment: Fluvoxamine 150 mg/day – 50 mg in the morning, 100 mg in the evening

Hydroxyzine (Atarax) 25 mg in the evening

### Mariam Tarkhnishvili Tbilisi Center of Mental Health

29 years old, female, Georgian, unmarried, lives in countryside, Shilda.

The first psychotic episode occurred when she was 21, with headache, aggression, agitation; she was detached and isolated from others and did not look after herself. For three years, she had never leaved her room, refused to take medication, keep hygiene and talk with others. She talked only with her "voices". She was aggressive towards her mother, shouted at her and destroyed subject. She had delusion of reference, religious believes, auditory hallucinations. No family history of mental disorder.





She was disobedient and stubborn child. After finishing school, she never studied or had a job.

Mental State: When admitted to hospital she was dressed in dirty clothes and underweight, she did not answer the questions; refused taking medication and food. Did not use toilet and defecated in her bedroom. She had marked stereotype movements, religious delusion and auditory hallucinations.

After treatment, she started eating, taking medication and looking after herself, behavior normalized.

Treatment: Haloperidole 1 ml; Diazepam (Relanium) 2 ml; Sulpiride (Eglonil) 2 ml; Chlorpromazine injection (Aminazine) 2ml; Trifluoperazine (Triftazin) 5 mg; Chlorpromazine in tab (Aminazin) 100mg

# Eleonora Tavadze Center for Mental Health and Prevention of Addiction

Previously I have participated in the following psychopharmacological researches:

Valproate (Depakin Chrono) efficiency on affective pathologies – Treatment of type I and type II bipolar disorder.

Effectiveness of Rispaksol and Sedarex (international name Risperidone ) in treating positive symptoms of schizophrenia.

Clinical research about efficiency of Ketilept (international name Quetiapin) in treating positive symptoms of schizophrenia and affective disorders in patients with younger age group.

In future I would like to be involved in clinical research of cognitive deficit developed during schizophrenia and its medical treatment.

#### Nato Tkeshelashvili Center for Mental Health and Prevention of Addiction

I have always participated in clinical evaluations of antipsychotic and antidepressant drugs. In the clinical trials, we investigated mental and somatic states and made laboratory analyses. We have increased doses by titration and observed clinical improvement. I have been involved in several studies investigating efficacy of Valproate (Depakine-Chrono), Risperidone, Olanzaine, Fluvoxamine, Zuclopenthixol. The data were published in the journal of "Georgian Psychiatric News".





I would like to study Amisulpride effectiveness in long-term treatment perspectives.

### Nino Topchishvili Center for Mental Health and Prevention of Addiction

I have participated in the following clinical trials: 1. Efficacy of Valproate (depakine chrono) in treatment of Bipolar I, and II disorders. Effectiveness of Risperidone - Rispaxol vs Sedarex in treatment of positive symptoms of schizophrenia

Efficiency of quetiapine in treatment of positive symptoms of schizophrenia and mood disorders in young patients.

I would like to be involved in the study regarding treatment of cognitive functions in patients with dementia.

# Qetevan Vadachkoria Center for Mental Health and Prevention of Addiction

In 2011 and 2012 I participated in clinical trial that investigated effectiveness of "soliani" (amisulpride). We have tested 20 patients both inpatients and outpatients. Since that time I have been widely using this medicine in my practice. I would like to study efficacy of a novel antidepressant or antipsychotic, particularly I am interested in efficacy of aripiprazole (recently introduced drug in Georgia) for treating positive symptoms of schizophrenia and mood disorders.

### Salome Vashalomidze Regional Family Medical Center in Batumi

Male, 4 years old, Ukrainian.

Main complaint: Uneasiness, fear of darkness, wakes up at nights due to fear.

History of present illness: His fear towards flowers and grass started when he was 3 years old. He walked only on paved areas and in cases when it was necessary to walk on the grass he coerced parents to pick him up. He could sleep only with lights on and saw different fantastic scenes in his dreams, was afraid of sitting in the car and loved when his mother was reading for him about planets and space.

Past psychiatric history: He went to kinder garden when he was 2 years old and it was hard for him to adapt to the environment.





Teachers were saying that kid could stay behind his age and that he was not paying attention to people around him.

Past medical history: He had bronchitis when he was 6 months. He was born from first pregnancy. Pregnancy was passing with toxicity with anemia. Childbirth was timely but difficult, took 10 hours to deliver.

Newborn wasscored 7-8 Apgar.

Family history: Boy's uncle has mental disorders and parents are members of religious sect.

Mental status exam:

Facial expression exalted, eyes sparkling, actively gesticulates, makes theatrical poses; Orientation in time, place and environment – disrupted; He has mental retardation, tongue-tied, rhotacism, concentration difficulties, labile mood and sees fantastic scenes of different content. Diagnosis: Infant type of continuous schizophrenia. Unease phobia syndrome.

Treatment, medication:

Phenazepam – 0,0005, 1/4 tablet three times a day.

Risperidone (Rispolept)– 0,3 mg, 50% glycerin solution 1 spoon 3 times a day.

When discharged from hospital – Mental state improved. He did not see fantastic scenes anymore, intensity of fears decreased and became rare, parents noticed that the boy calm down.