ECNP neuroscience applied

ECNP Seminar in Neuropsychopharmacology

7-9 October 2016

Óbuda, Hungary

Introduction

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

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

To fulfil this aim ECNP organises, amongst others, yearly the ECNP Congress that comprises of 6 plenary lectures, 28 symposia and 7 educational update sessions. The annual meeting attracts around 5,000 psychiatrists, neuroscientists, neurologists and psychologists from around the world and is considered to be the larges congress on applied and translational neuroscience.

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, Serbia and Lithuania. 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 and since 2012 a school of child and adolescent neuropsychopharmacology in Venice. This autumn the second Workshop on Clinical Research Methods will take place in Barcelona, Spain.

ECNP will also continue the successful pilot of the ECNP Research Internships. A selected group of senior researchers will offer a short two-week exploratory experience in their institutions. The hosting scientist is encouraged to establish a long-term relationship with the applicant and teach a basic translational research method that the participant can use at home when he/she returns.

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 hope you have a fruitful and inspiring meeting in Hungary!

Gil Zalsman
Chair ECNP Educational Committee

Programme
ECNP Seminar in Neuropsychopharmacology
7-9 October 2016, Budapest, Hungary

FRIDAY 07 OCTOBER 2016

Arrival of participants and experts
19.00 Welcome and dinner (Xenia Gonda & Gil Zalsman)

SATURDAY 08 OCTOBER 2016

09.00 – 09.15 What is ECNP? Introductions to the programme
Speaker: Gil Zalsman

09.15 – 10.00 Introduction to research methods: How to phrase a research question? The case of gene environment interaction in mood disorders
Speaker: Gil Zalsman

10.00 – 10.45 Animal model for social cooperation: implications in PTSD as a model for research plan and design
Speaker: Avi Avital

10.45 – 11.30 Coffee break

11.30 – 12.15 Bipolar disorder research as a model for research plan and design
Speaker: Andrea Murru

12.15 – 12.30 How to give a talk
Speaker: Gil Zalsman

12.30 – 13.30 Lunch

Presentation participants in 3 groups in 3 parallel workshops			
Round 1 13.30 – 15.00	*Gil Zalsman* *and* *Viktor Voros* **Group 1**	*Andrea Murru* *and* *Gyorgy Bagdy* **Group 2**	*Avi Avital* *and* *Janos Rethelyi* **Group 3**

15.00 – 15.15 Break

15.15 – 15.45 Panel discussion: How to prepare a clinical research project and how to publish it
Chair: Gil Zalsman

Panel members: Andrea Murru / Avi Avital

16:00 – 21.00 Social activity, group photo and dinner

SUNDAY 09 OCTOBER 2016

Presentations participants in 3 groups in 3 parallel workshops *(Experts rotate between the groups)*			
Round 2 08.30 – 10.00	*Gil Zalsman* *and* *Viktor Voros* **Group 1**	*Andrea Murru* *and* *Gyorgy Bagdy* **Group 2**	*Avi Avital* *and* *Janos Rethelyi* **Group 3**
10.00 – 10.30 Coffee Break			
Round 3 10.30 – 12.00	*Gil Zalsman* *and* *Viktor Voros* **Group 1**	*Andrea Murru* *and* *Gyorgy Bagdy* **Group 2**	*Avi Avital* *and* *Janos Rethelyi* **Group 3**
12.00 – 14.00 Lunch and preparation for plenary session			
Plenary 14.00 – 15.00	14.00 – 14.20	**Group 1 Presentation**	
	14.20 – 14.40	**Group 2 Presentation**	
	14.40 – 15.00	**Group 3 Presentation**	

15.00 – 15.30 Break and faculty selection of awards winners. Completion of feedback forms

15.30 – 16.00 Awards ceremony, concluding remark and thanks
Gil Zalsman & Xenia Gonda

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

Prof. Zalsman graduated from the Hebrew University and Hadassah Medical School in Jerusalem, Israel. He completed his psychiatry residency at the Geha Mental Health Center and Tel Aviv University and the Child Psychiatry residency at Geha and Yale Child Study Center in Yale University, Connecticut, USA with the late Prof. Donald J Cohen. He completed a two years Post-Doctoral Fellowship with Prof. J John Mann, in the Division of Molecular Imaging and Neuropathology, Department of Psychiatry, Columbia University and New York State Psychiatric Institute, New York City, USA, where he holds an ongoing position as an Associate Research Scientist. He also holds a Master degree in health administration (MHA. summa cum laude) from Ben Gurion University, Israel. His academic research focuses on gene-environment interactions in childhood depression and suicidal behavior and other psychiatric disorders in adolescence.
Prof. Zalsman has published more than a 200 papers, of them more than 100 original papers, dozens of reviews, book chapters, two edited books and actively participated in more than a 200 scientific meetings. Currently he is the CEO and Medical Director of Geha Mental Health Center near Tel Aviv in addition to being the director of the Adolescent Day Unit. He is an Associate Professor in Psychiatry at Sackler School of Medicine and former director of psychiatry continuing education program.
Prof. Zalsman is the past board member and president of the child psychiatry section at the Association of European Psychiatry (EPA). Currently he a counselor and chair of education at the executive committee of the European College of Neuropsychopharmacology (ECNP) and the president of the Israeli Society of Biological Psychiatry (ISBP). He served as the deputy editor of the Israel Journal of Psychiatry and recently chaired the 14th European Symposium for Suicide and Suicidal Behavior (ESSSB), held in Tel Aviv.
He is married with two children and resides in Tel Aviv suburb, Israel.

Zalsman@post.tau.ac.il

Avi Avital PhD

Avi (Avraham) Avital is assistant professor in the Faculty of Medicine, the Technion - Israel Institute of Technology, and Emek Medical Center. As a board member The Israeli Society for Biological Psychiatry (ISBP), Avi is also the head of the young basic science leadership program, operating as part of the ISBP activities.
Avi serves as a member of the ECNP education committee.

In his behavioural Neuroscience Lab, they study the effects of life circumstances on emotional and cognitive processes. Specifically, the research is focused on attention processes and social cooperation. On the translational aspect, the lab studies Schizophrenia and PTSD in animal models and clinical researches. Both basic and clinical studies are nurturing and being nurtured by each other. The entire research in the lab is involving technological equipment including software and hardware that are custom-made.

Andrea Murru MD PhD

Andrea Murru finalized his Medicine Degree at University of Cagliari, Italy, and specialized in Psychiatry cum laude in the same University.
After completing a Master in Neuroscience, he achieved an International Doctorate in Medicine, cum laude, in the University Of Barcelona, Spain.
He currently works as a post doc researcher of the Spanish Network of research in Mental Health (CIBERSAM), in the Bipolar Disorders Unit of the Hospital Clínic, Barcelona, led by prof. Eduard Vieta.

He is author of several scientific books and chapters on the treatment of bipolar disorders, as well as about 50 peer reviewed scientific articles. He focuses his research on long-term treatments, on implementation of clinical guidelines in daily practice, long-term treatments tolerability and adherence to treatment in patients affected by bipolar disorders and schizoaffective disorders. He actively collaborates with patients' associations.

György Bagdy MD PhD DSc

Prof Bagdy is Head of the Department of Pharmacodynamics at Semmelweis University and of the MTA-SE Neuropsychopharmacology and Neurochemistry Research Group of the Hungarian Academy of Science and Semmelweis University.
Prof. Bagdy graduated from Semmelweis University with a diploma in Pharmacy in, completed his doctorate in Pharmacology and Toxicology in 1981, and his PhD in Medicine in 1992. He became doctor of sciences in 1999. During this time he held various positions as research fellow, visiting fellow and research consultant both in Hungary and the United States at the National Institute of Mental Health. He was chief of the Laboratory of neurochemistry and Experimental Medicine in the National Institute of Psychiatry and Neurology in Budapest from 1994, and he became scientific director of the Institute in 2002. From 2007 he worked as research professor at the Department of Pharmacology and Pharmacotherapy at Semmelweis University and in 2008 became head of the Department of Pharmacodynamics at Semmelweis University. Since 2010 he also serves as full professor at the Department of Pharmacodynamics. He is core and council member at the Mental Health Sciences Doctoral School and Supervisor in the Szentágothai János Doctoral School of Neurosciences and Doctoral School of Pharmaceutical Sciences at Semmelweis University. Prof Bagdy is member of the Expert Committee on Medical Sciences of the Hungarian Accreditation Committee and the Committee on Medicine and Health Science of the Hungarian Rectors' Conference. He has won several Hungarian and international research grants and several honours and awards. Prof Bagdy authored more than 200 journal articles attracting more than 5000 citations, has a cumulative impact factor of over 550, and a Hirsch index of 43. His research specialty includes serotonergic mechanisms in neuroendocrine regulation, endocrine side effects in Neuropsychopharmacology, neuronal and functional damage associated with NMDA, sleep regulation, and genomics and systems approach in depression and anxiety.

János Réthelyi MD PhD

János Réthelyi is associate professor and chair of Semmelweis University Department of Psychiatry and Psychotherapy. He graduated at Semmelweis University Faculty of Medicine in 1999. Between 1996-2003 he worked under the supervision of the late Professor Mária Kopp at the Institute of Behavioral Medicine. His doctoral thesis, titled The epidemiological and clinical investigation of chronic pain syndromes and depression was defended in 2003. From 2003 he is a faculty member at the Department of Psychiatry and Psychotherapy, where besides clinical activities he teaches psychiatry and psychotherapy in Hungarian, English and German. He received board certification in psychiatry (2007) and clinical genetics (2015). His research interests include the genetics of schizophrenia, ADHD, and bipolar affective disorder, gene-environment interactions, and induced pluripotent stem cell based in vitro disease modelling. In 2005 he initiated psychiatric genetic studies together with Professor István Bitter and international partners and established the molecular psychiatry research group and laboratory of the department. Between 2014-2016 he received funding from the Hungarian Brain Research Program to carry out studies using induced pluripotent stem cells. In 2006 he worked in Utrecht, Netherlands as a postdoctoral fellow, in 2012-2013 he was a visiting sceintist at Salk Institute for Biological Studies (La Jolla, California, USA). He is the author of 51 scientific papers, among others he wrote the chapter about psychiatric genetics in the Hungarian Textbook of Psychiatry (5th edition, 2015).

Viktor Vörös MD PhD

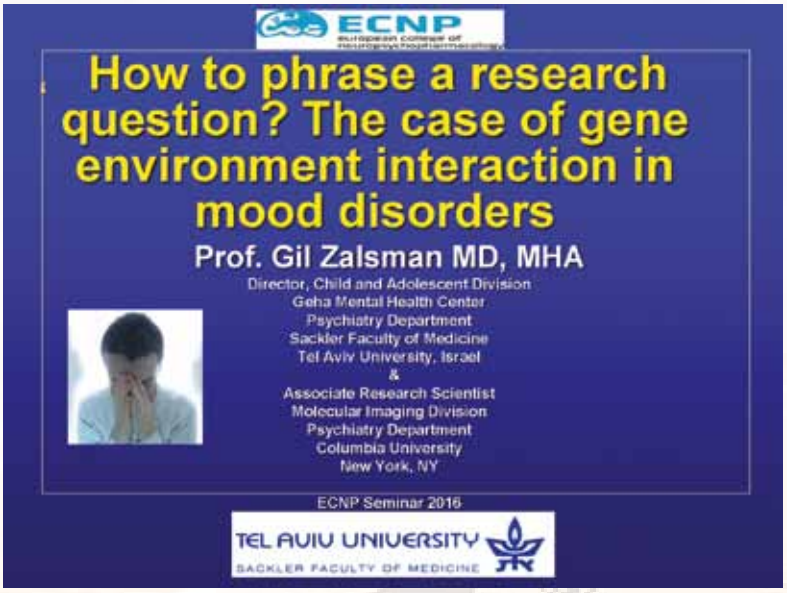
Viktor Voros MD, PhD is a Clinical Psychiatrist, an Associate Professor at the Department of Psychiatry and Psychotherapy, University of Pecs, in Pecs, Hungary. He is also a consultant for Global Genomics Group, Atlanta, GA, USA, a life sciences company focused on a mission to discover novel therapeutic and diagnostic targets.
Dr. Voros received his medical degree from the University of Pecs, Hungary, and completed his training at the Department of Psychiatry and Psychotherapy, where he also served as Chief Psychiatric Resident. After completion of the Board Exam in Psychiatry (2005), he continued to work in the University Clinic in Pecs, and developed his research interest in suicidal behavior. He received his PhD degree in 2011 for his thesis entitled 'The Stress-Diathesis Model of Suicidal Behavior'.
Besides in-patient and out-patient care and extensive clinical activity, he is also a Senior Lecturer in the gradual and post-gradual education at the University of Pecs, Hungary. He was a participant in many national and international collaborative research and studies in the field of Psychiatry (WHO-EURO study, CASE study, MONSUE program, etc.). His major scientific interest is suicidal behavior and affective disorders. He published his research in different scientific journals, books and congresses.
He is a member of many regional and international scientific societies, including the Hungarian Psychiatric Association, the American Psychiatric Association, the Hungarian Association of Psychopharmacologists, and the Brief Dynamic Psychotherapeutic Association. He is also the board member of the scientific journals Psychiatria Hungarica and the World Journal of Psychiatry. As an investigator, he is particiating in several clinical trials in the field of dementias and affective and psychotic disorders. As a collaborator, he is currently participating in a European Union's funded project (H2020 - ICT4Life), which aim is to provide integrated ICT services for life improvement for elderly.

How to phrase a research question? The case of gene environment interaction in mood disorders

Gil Zalsman
Child and Adolescent Division
Geha Mental Health Center
Psychiatric Department
Sackler Faculty of Medicine
Tel Aviv University, Israel

Associate Research Scientist
Molecular Imaging Division
Psychiatric Department
Columbia University, New York, NY

How to move from a research question to an hypothesis and then to an experiment that proves your hypothesis? Prof. Zalsman will bring his own story on 'gene by environment by timing interaction' hypothesis and how we can learn from it for our own questions in research.


ECNP
How to phrase a research question? The case of gene environment interaction in mood disorders
Prof. Gil Zalsman MD, MHA
Director, Child and Adolescent Division
Geha Mental Health Center
Psychiatry Department
Sackler Faculty of Medicine
Tel Aviv University, Israel
&
Associate Research Scientist
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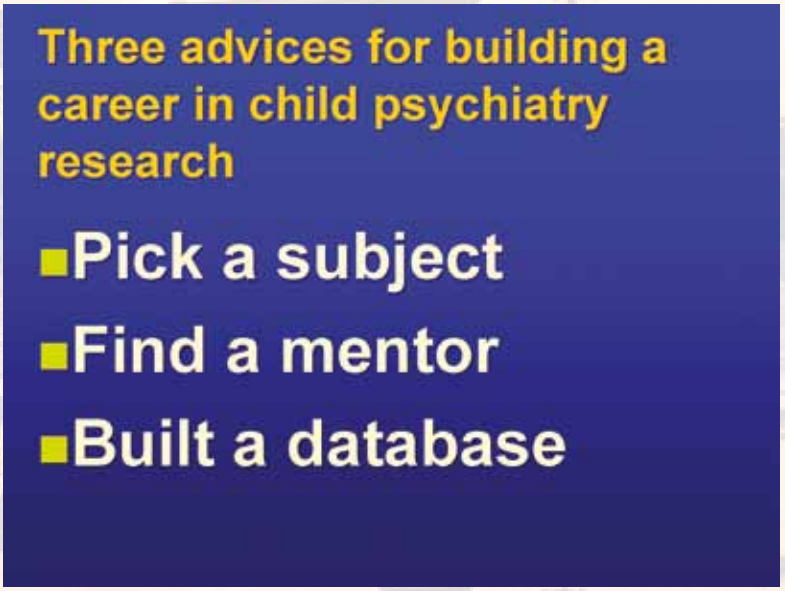
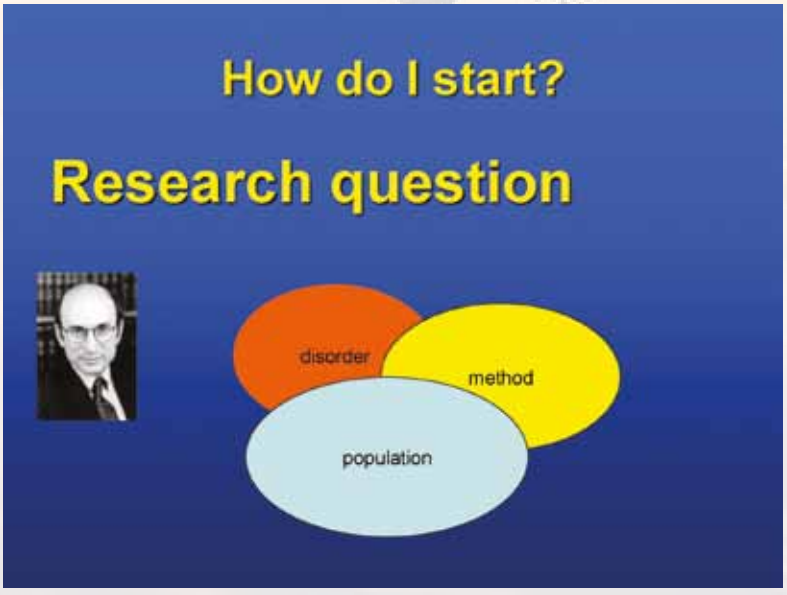
Columbia University
New York, NY
ECNP Seminar 2016
TEL AVIV UNIVERSITY
SACKLER FACULTY OF MEDICINE


Three advices for building a career in child psychiatry research
Pick a subject
Find a mentor
Built a database


How do I start?
Research question
disorder
method
population

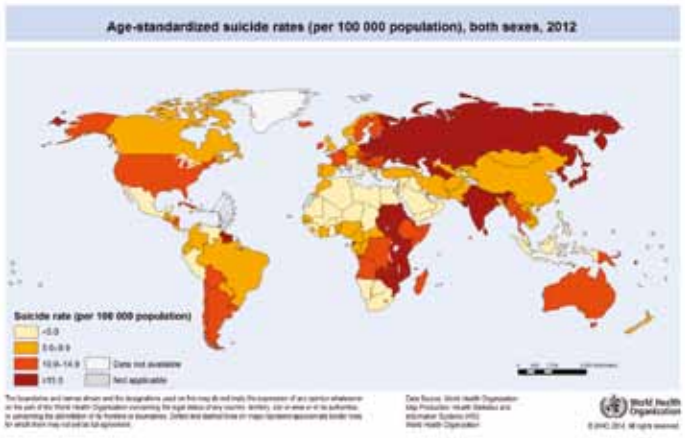
Create your own DATA BASE!!!

The phenomena

SUICIDE

- 1,000,000 people a year worldwide
- Over 150,000 in Europe
- About 65,000 in the EU countries
- Males 5 times more
- Attempts X10. Mostly females

World Suicide Rates (WHO)



If you don't ask you don't know

- 90% of suicide victims suffered from a mental disorder
- 60% of suicide victims met their primary care physician in the month prior to suicide

  Mann et al., JAMA, 2005

- Asking is not dangerous

  Gould et al., JAMA 2006

Definitions

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

Risk Assessment

Risk Assessment

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

Risk Assessment

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

Evaluation after a suicide attempt

- Timing and location
- Letter (SMS/email)
- Violence and irreversibility of method
- Medical lethality (note: potential)
- Access to means
- Support system
- Collaboration with therapist
- Personal connection

Treatment

Tx of the suicidal patients

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

Evidence- Based Psychotherapies for Depression and Suicidal Behavior

- CBT, CBT-A
- DBT- specifically for BLPD NSSI
- IPT, IPT-A
- MBCT

Basic Research

Neurobiology

Familial Transmission and Gene-Environment Interaction

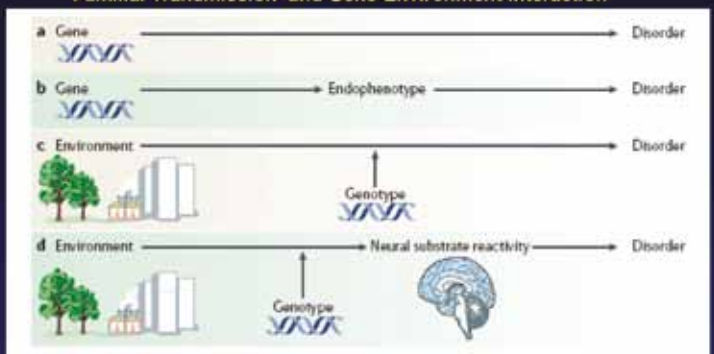


Figure 1 | **Approaches to psychiatric genetics research. a** | The gene-to-disorder approach assumes direct linear relations between genes and disorder. **b** | The endophenotype approach replaces the disorder outcomes with intermediate phenotypes. **c** | The gene–environment interaction approach assumes that genes moderate the effect of environmental pathogens on disorder. **d** | Neuroscience complements the latter research by specifying the proximal role of nervous system reactivity in the gene–environment interaction.

Caspi and Moffitt, Nature Reviews Neuroscience, July 2006, with permission

GWAS

A pilot genome-wide association and gene expression array study of suicide with and without major depression

Zalsman et al., The World Journal of Biological Psychiatry, 2011

GxE → D

Childhood Adversity

Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

Avshalom Caspi,[1,2] Karen Sugden,[1] Terrie E. Moffitt,[1,2*] Alan Taylor,[1] Ian W. Craig,[1] HonaLee Harrington,[2] Joseph McClay,[1] Jonathan Mill,[1] Judy Martin,[3] Antony Braithwaite,[4] Richie Poulton[3]

In a prospective-longitudinal study of a representative birth cohort, we tested why stressful experiences lead to depression in some people but not in others. A functional polymorphism in the promoter region of the serotonin transporter (5-HTT) gene was found to moderate the influence of stressful life events on depression. Individuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events than individuals homozygous for the long allele. This epidemiological study thus provides evidence of a gene-by-environment interaction, in which an individual's response to environmental insults is moderated by his or her genetic makeup.

5-HTT-LPR- serotonin transporter linked polymorphism region

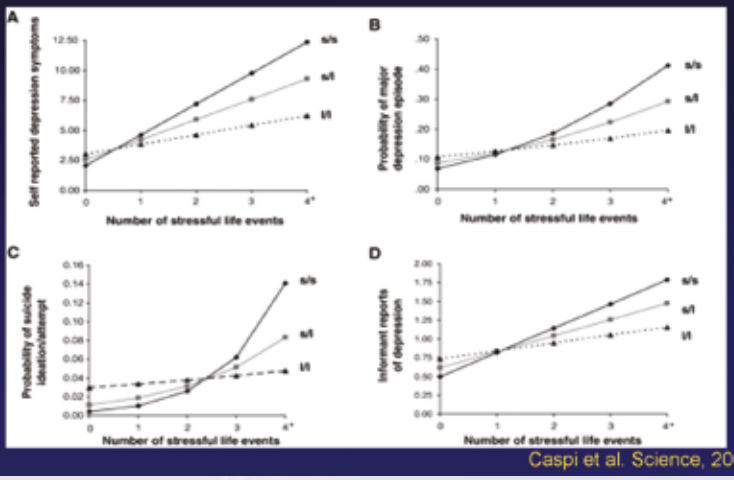
promoter

A functional polymorphism consists of two common alleles, a short (S) and long (L) variants, differing by 44 bp

S<<L

Lesch et al. 1994, Heils et al. 1996

5HTTLPR
Gene X Environment Interaction
Caspi et al. 2003

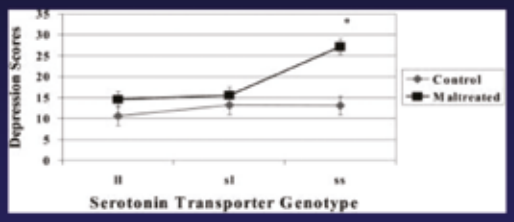


Caspi et al. Science, 2003

Social supports and serotonin transporter gene moderate depression in maltreated children.

Kaufman J et al. **Proc Natl Acad Sci USA 2004; 101:17316-17321**

(N=101)



Maltreated children (57 age 10-15; were removed from their parents' care) with the s/s genotype and no positive supports had the highest depression ratings.

Positive supports reduced risk.

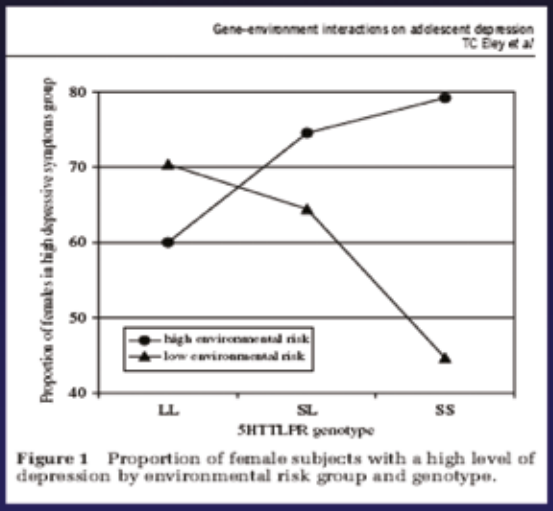
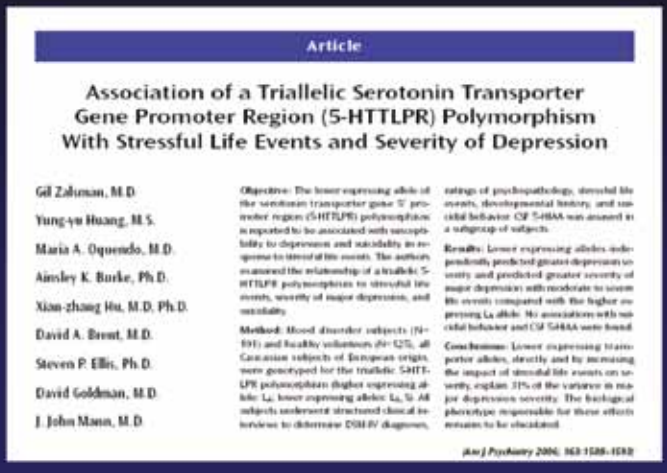


Figure 1 Proportion of female subjects with a high level of depression by environmental risk group and genotype.

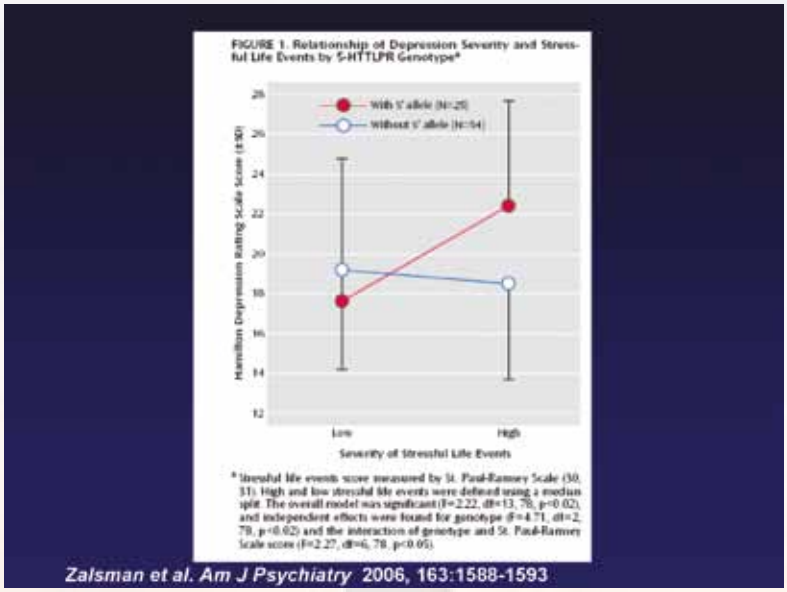
N=1990, age 10-20 Eley et al., Mol Psychiatry 2004



Article

Association of a Triallelic Serotonin Transporter Gene Promoter Region (5-HTTLPR) Polymorphism With Stressful Life Events and Severity of Depression

Gil Zalsman, M.D.
Yung-yu Huang, M.S.
Maria A. Oquendo, M.D.
Ainsley K. Burke, Ph.D.
Xian-zhang Hu, M.D., Ph.D.
David A. Brent, M.D.
Steven P. Ellis, Ph.D.
David Goldman, M.D.
J. John Mann, M.D.



OOPS!!!!

- Risch N et al. JAMA, 2009;302:492

Meta-analysis of 14 studies found no significant association (OR=1.05)

Karg et al. 2011

META-ANALYSIS

ONLINE FIRST

The Serotonin Transporter Promoter Variant (5-HTTLPR), Stress, and Depression Meta-analysis Revisited

Evidence of Genetic Moderation

Katja Karg, BSc; Margit Burmeister, PhD; Kerby Shedden, PhD; Srijan Sen, MD, PhD

Arch Gen Psychiatry.
Published online January 3, 2011.

Data Synthesis: We included 54 studies and found strong evidence that 5-HTTLPR moderates the relationship between stress and depression, with the 5-HTTLPR *s* allele associated with an increased risk of developing depression under stress ($P=.00002$). When stratifying our analysis by the type of stressor studied, we found strong evidence for an association between the s allele and increased stress sensitivity in the childhood maltreatment ($P=.00007$) and the specific medical condition ($P=.0004$) groups of studies but only marginal evidence for an association in the stressful life events group ($P=.03$). When restricting our analysis to the studies included in the previous meta-analyses, we found no evidence of association (Munafò et al studies, $P=.16$; Risch et al studies, $P=.11$). This suggests that the difference in results between meta-analyses was due to the different set of included studies rather than the meta-analytic technique.

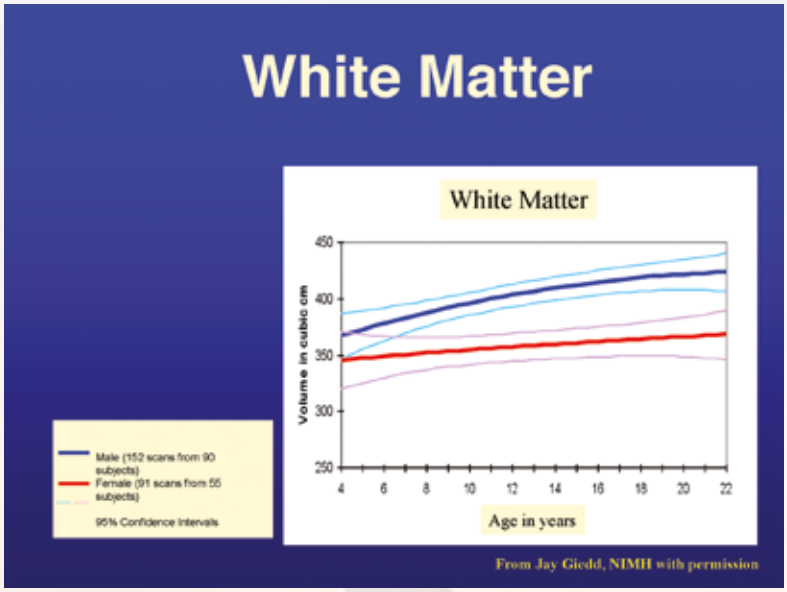
Are brains of children and adolescents different?

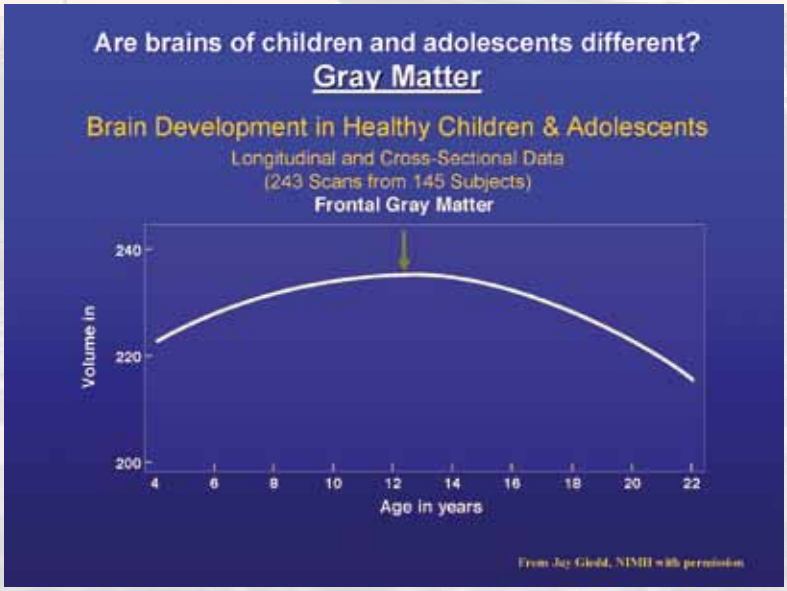
**Almost no suicides under 10

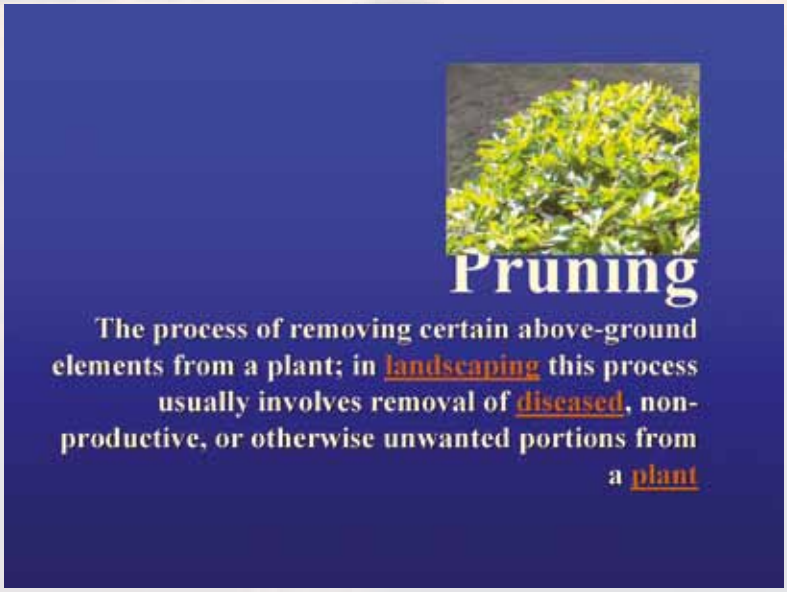
Normal Brain Development

243 Scans from 145 healthy children

1. Giedd JN, et al., Child psychiatry branch of the NIMH longitudinal structural MRI study of human brain development. Neuropsychopharmacology. 2015
2. Giedd JN. The amazing teen brain. Sci Am. 2015


White Matter
White Matter
Volume in cubic cm
450
400
350
300
250
4
6
8
10
12
14
16
18
20
22
Age in years
Male (152 scans from 90 subjects)
Female (91 scans from 55 subjects)
95% Confidence Intervals
From Jay Giedd, NIMH with permission

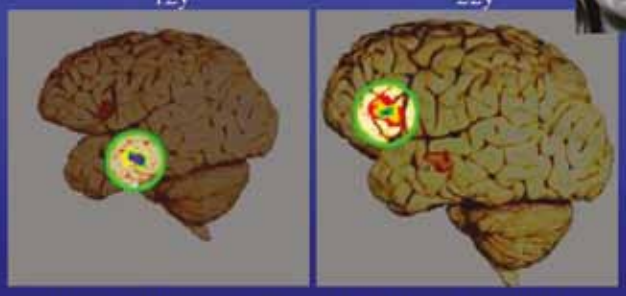

Are brains of children and adolescents different?
Gray Matter
Brain Development in Healthy Children & Adolescents
Longitudinal and Cross-Sectional Data
(243 Scans from 145 Subjects)
Frontal Gray Matter
Volume in
240
220
200
4
6
8
10
12
14
16
18
20
22
Age in years
From Jay Giedd, NIMH with permission


Pruning
The process of removing certain above-ground elements from a plant; in landscaping this process usually involves removal of diseased, non-productive, or otherwise unwanted portions from a plant

Are brains of adolescents and adults are different?

**Pick of suicidality during in adolescence

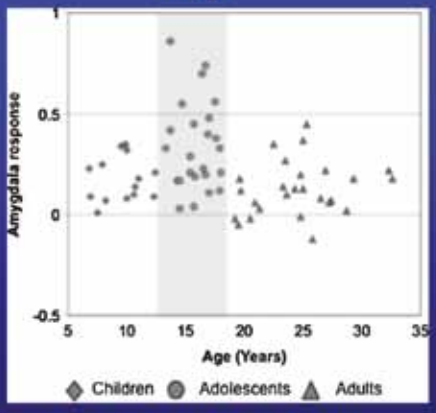
Reading Emotions Differently



When reading emotion, teens **(left)** rely more on the amygdala, while adults **(right)** rely more on the frontal cortex.

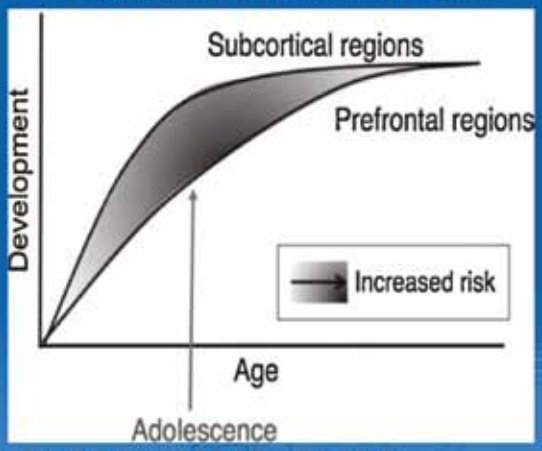
Deborah Yurgelon-Todd, 2000

Amygdala response to fearful faces as a function of age.



Casey et al., Dev Psychobiol 52: 225–235, 2010.
Hare et al., Biological Psychiatry 63:927-934, 2008.

later development
of prefrontal regions relative to subcortical
regions involved in emotional processes.



Casey et al., Dev Psychobiol 52: 225–235, 2010.


European Neuropsychopharmacology (2015) 25, 2075–2085

ELSEVIER

www.elsevier.com/locate/euroneuro

Genetic vulnerability, timing of short-term stress and mood regulation: A rodent diffusion tensor imaging study

Gil Zalsman[a,b,e], Avihay Gutman[c,d], Liat Shbiro[d], Ruth Rosenan[d], J. John Mann[b], Aron Weller[d]

Zalsman et al., Eur Neuropsychopharmacology 2015

WKY

WKY

The Wistar Kyoto (WKY) rat, is stress-reactive, and is considered as a "genetic animal model of depression" with anxiety-like behaviors

(Exposure to stress) at different developmental windows

G x E x Gender x T

T1 (27)

T2 (44)

T3 (58)

WKY

Stress manipulations

Elevated maze .1
Restrains .2
Wet cage .3

Elevated maze

Wet cage

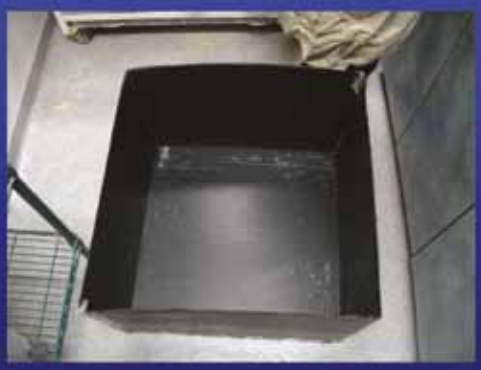
Restrains

Behavioral tests for "depression"

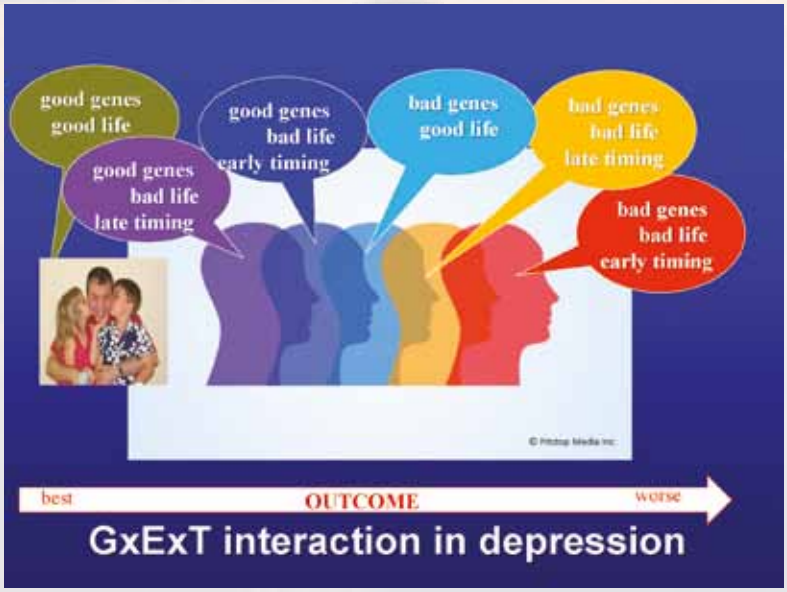
1. Forced Swim Test X2
2. Saccharine test
3. Open field with novel object

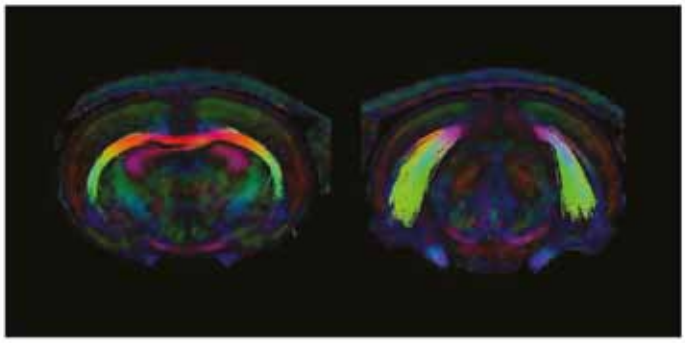
Saccharin test for anhedonia

Open field



Fiber tracking





Corpus Callosum (CC)

My Message

- Suicidal behavior is not rare after puberty
- Complete suicide is rare and hard to predict
- Risk assessment and recording is essential
- Pharmacotherapy include SSRIs, Lithium, Clozapine, ECT and maybe Ketamine
- SSRIs do not cause more completed suicides
- Animal model prove GxExT interaction
- Prevention in the national level is effective
- Connection and Compassion are critical

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www.zalsman.org

Animal model for social cooperation: implications in PTSD as a model for research plan and design

Avraham Avital
Behavioral Neuroscience Lab
Department of Physiology
The Bruce Rappaport Faculty of Medicine

Social cooperation is defined as a joint action for mutual benefit that depends on the individual and the counterparts' behaviors. To gain valid evidence for social cooperation behavior in rodents, in our maze the partners achieve equal rewards in a fully automated non-conditioned apparatus.

In a series of experiments we depicted three major findings: (i) During 18 days of social cooperation learning, the rats showed a progressive learning curve as well as latent social learning; (ii) Examining the perceptual communication between the cooperating partners, we found a correlation between the available perceptual modalities and the social cooperation performance; and (iii) Investigating contextual learning as a competing process to the social cooperation, we found that additional contextual cues impaired the social cooperation performance.

In conclusion, our automated cooperation maze is designed to further our understanding of social cooperation under normal conditions, such as decision-making. In addition, a variety of neuropsychiatric disorders are characterized by disruptions in social behavior, including depression, autism spectrum disorders, and PTSD. Thus, on the pathological end, our automated maze can contribute significantly to the investigation of a wide range of social cooperation impairments in a rodent model and the effects of suggested treatments.

Animal model for social cooperation: implications in PTSD as a model for research plan and design

Avraham (Avi) Avital, Ph.D
Behavioral Neuroscience lab,
The Bruce Rappaport Faculty of Medicine, Techion– Israel Institute of Technology

Introduction

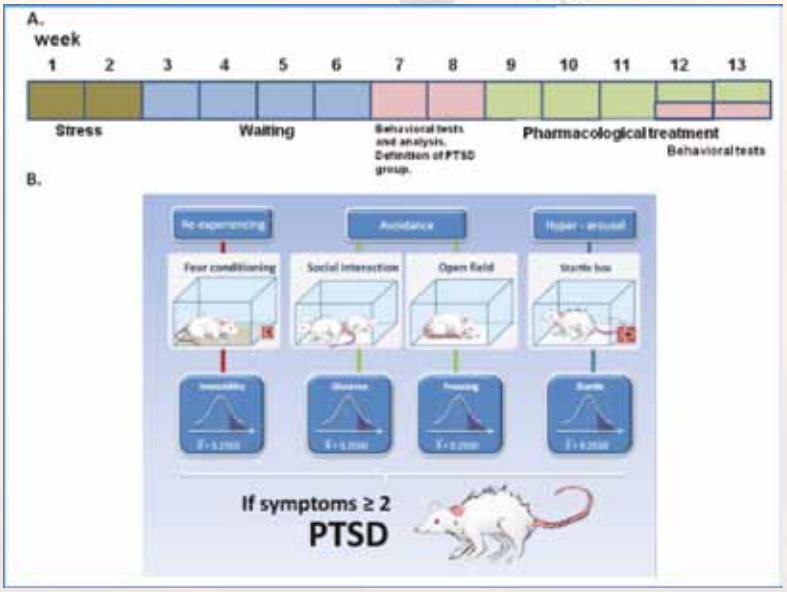
Methylphenidate and Desipramine Combined Treatment Improves PTSD Symptomatology in a Rat Model

The characteristic symptoms of post-traumatic stress disorder (PTSD) include: re-experiencing, avoidance and hyper-arousal.

Nowadays, the common treatment for PTSD includes various antidepressants. However, these treatments focus on the anxiety, depression, flattened affect or detachment symptoms and less on attention problems.

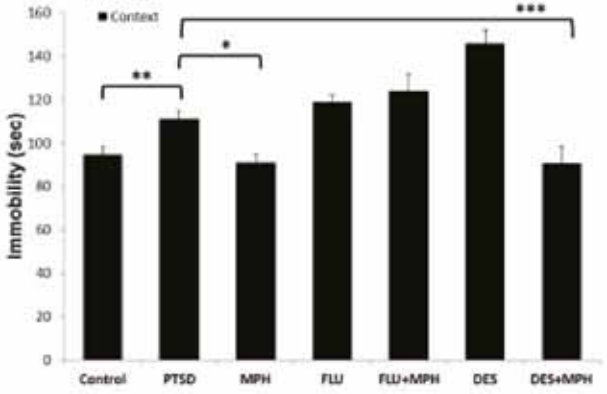
To determine whether, in addition to the common antidepressants, Methylphenidate (Ritalin) treatment will affect PTSD core symptoms.

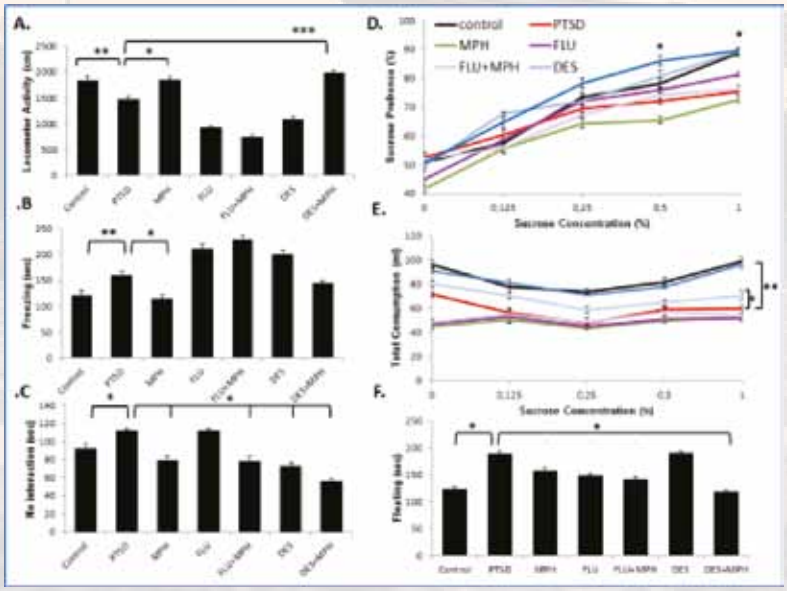
Translational Psychiatry, 2014



Results

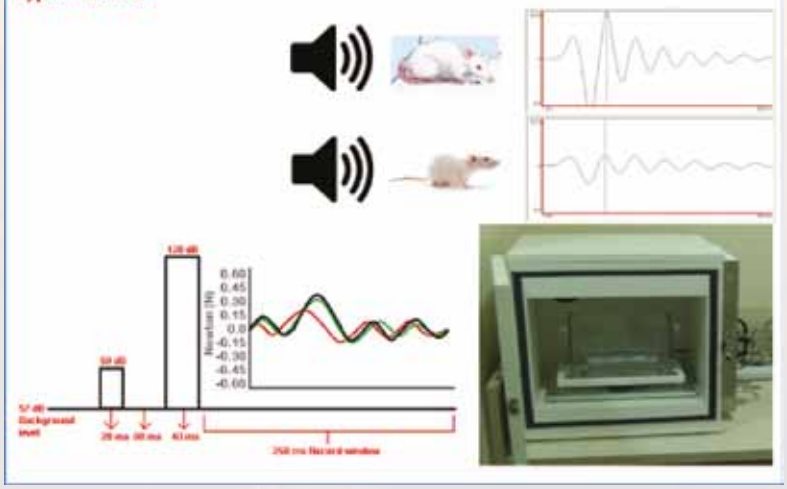
Re-experiencing





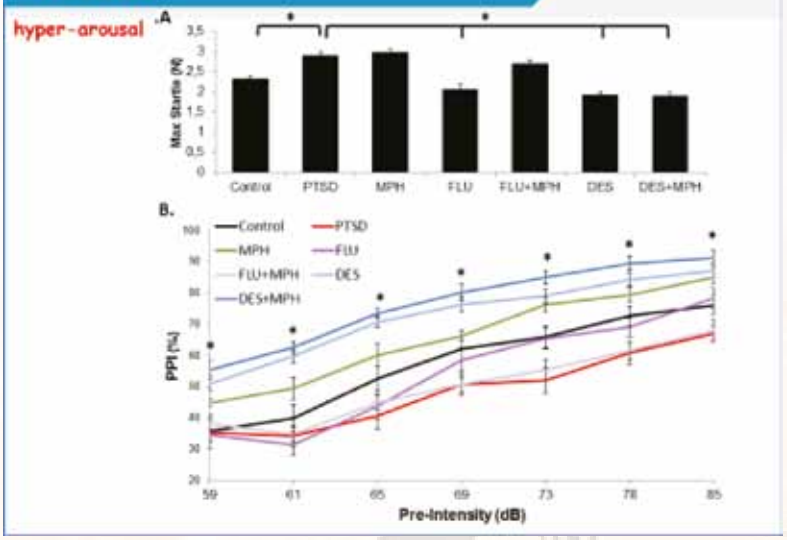
Methods

hyper-arousal



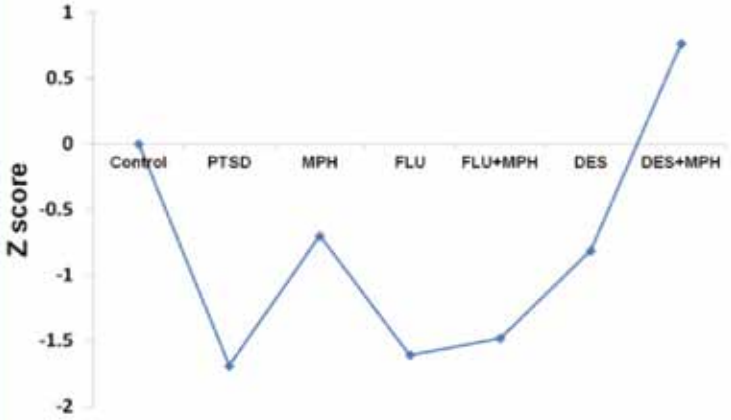
Results

hyper-arousal

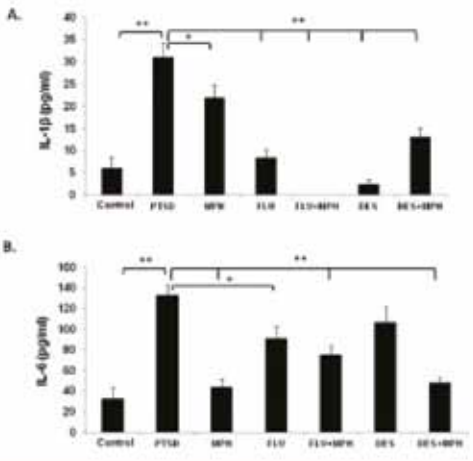


Results

Aim 2



Results



Conclusions

Considering the versatile emotional and cognitive symptoms of PTSD, our results suggest a new duo-treatment for PTSD comprised of antidepressant (desipramine) and psycho-stimulant (methylphenidate) that partially share norepinephrine-reuptake-inhibition mechanism.

PTSD as well as many other diseases/disorders accompanied by poor social abilities.

One answer leads to a new question

Introduction:

- Social cooperation underlies coordination toward a shared goal \ reward.

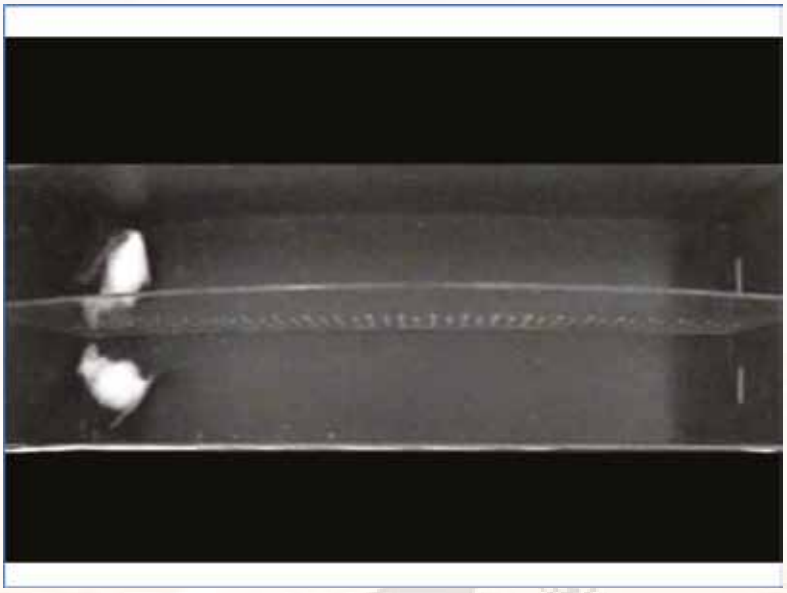
- Social cooperation is considered to be a trait shared by cognitively advanced organisms.

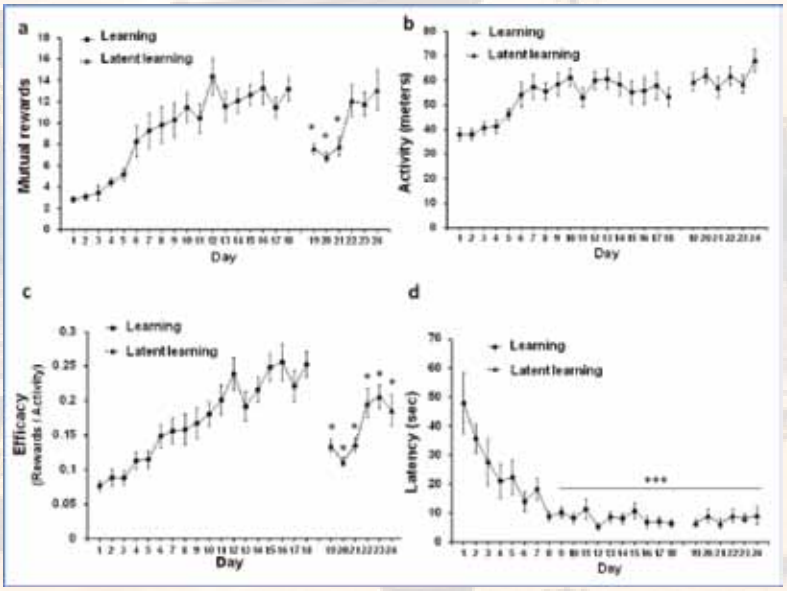
Exp. controlled environment

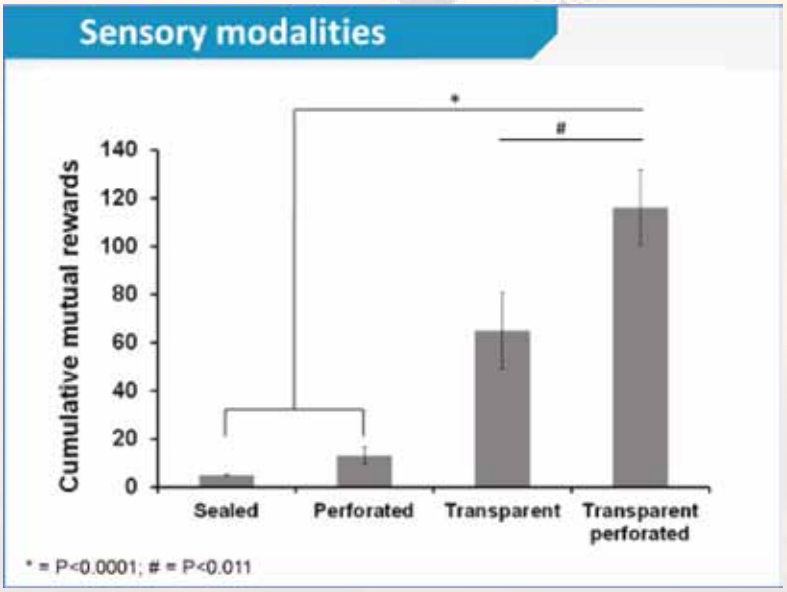
Pulling one end resulted in failure because the rope came unthreaded

Plotnik et al., 2011 (PNAS)

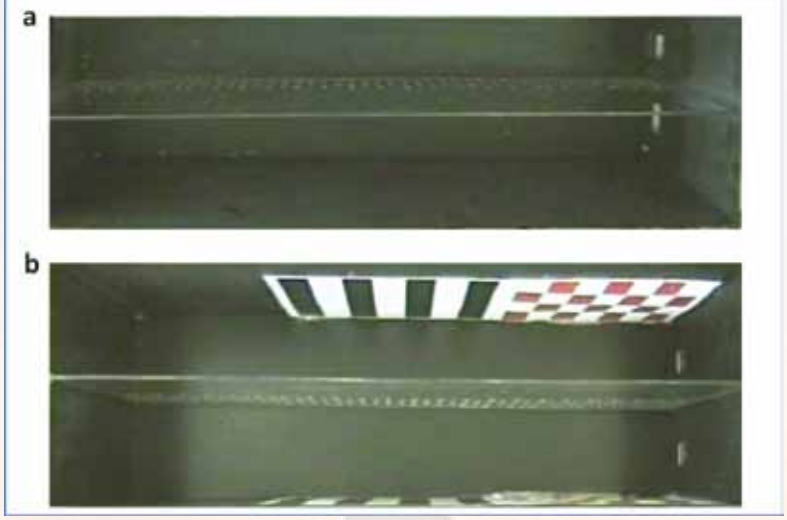
Hare et al., 2007 (Current Biology)

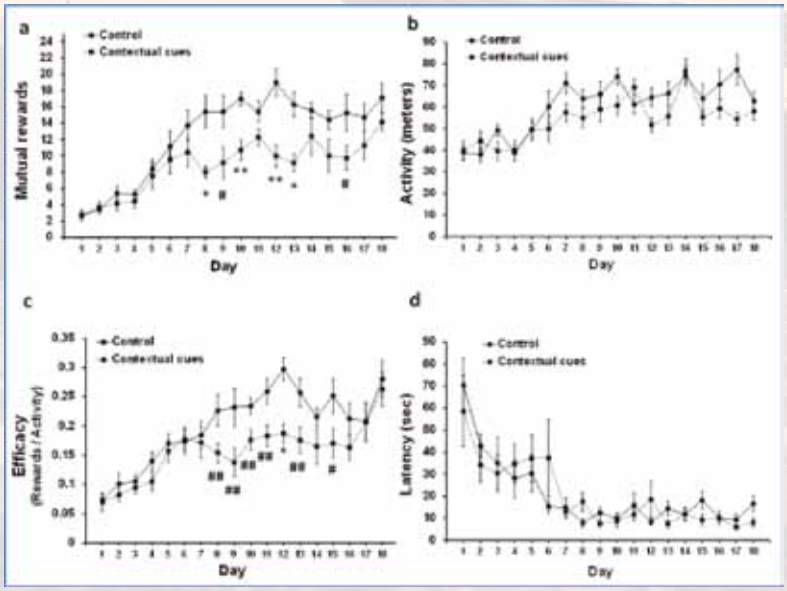



a
Learning
Latent learning
Mutual rewards
Day
b
Learning
Latent learning
Activity (meters)
Day
c
Learning
Latent learning
Efficacy
(Rewards / Activity)
Day
d
Learning
Latent learning
Latency (sec)
***
Day

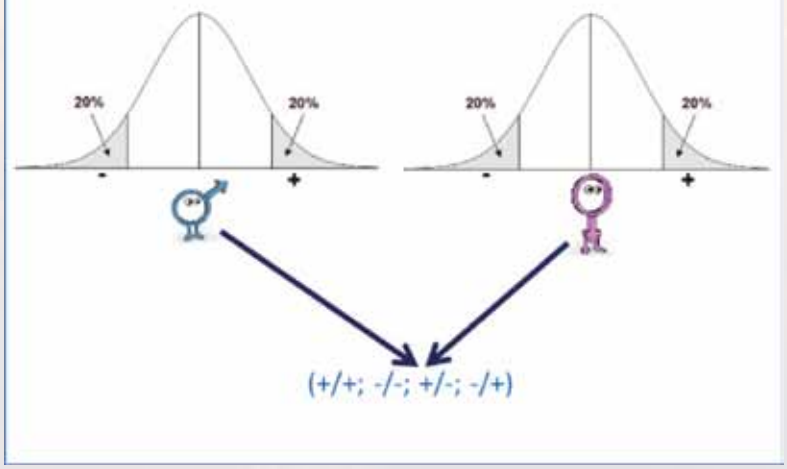

Sensory modalities
*
#
Cumulative mutual rewards
140
120
100
80
60
40
20
0
Sealed
Perforated
Transparent
Transparent perforated
* = P<0.0001; # = P<0.011

Attentional competition: Contextual versus Social

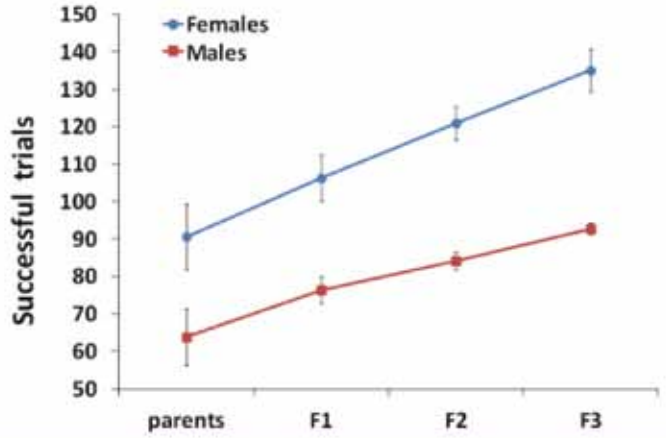




Counterbalanced breeding



Trans-generational effect



Conclusions

Our suggested cooperation maze is designated toward wide range of rodent models characterizing behaviors missing social cooperation and communication such as autism spectrum disorders , Down syndrome, Prader-Willi syndrome and last but not least, the neural basis of social cooperation.

Acknowledgments

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Inon Maoz 

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Mr. Salman Zubedat

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המכון הלאומי לפסיכוביולוגיה בישראל
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US-Army Research Office (ARO)

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Spanish Network of research in Mental Health (CIBERSAM),
Bipolar Disorders Unit
Hospital Clínic, Barcelona

Bipolar disorder (BD) is a severe, chronic and recurrent disorder characterized by fluctuations in mood state and energy. It affects more than 1% of the world's population, irrespectively of nationality, ethnic origin, or socioeconomic status. BD represents one of the leading causes of disability among young people, and it often leads to significant cognitive and functional impairment as well as an increased mortality, both for somatic correlates and consumed suicide. In recent years, a global effort has been conducted to identify genetic and biological correlates of the disorder. Its complex multifactorial nature partially justifies BD's pleomorphic presentation and eludes a clear biological characterization of the illness. Currently, no valid biomarkers for BD have been identified. Nonetheless, a great bulge of genetic, biological and clinical correlates is being increasingly produced, this underlying a complex interaction of different anatomical and physiological systems.

ECNP

Bipolar disorder research as a model for research plan and design

Andrea Murru, MD, PHD

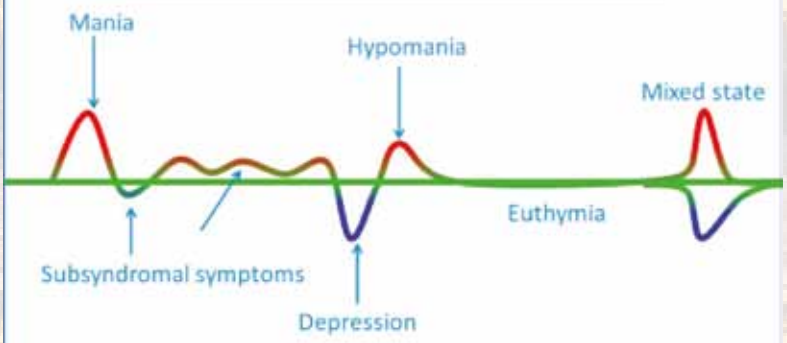
Budapest, 8th October 2016

CLÍNIC BARCELONA Hospital Universitari

IDIBAPS

cibersam

What is bipolar disorder?



Genes: Vulnerability

Neurons: Connectivity

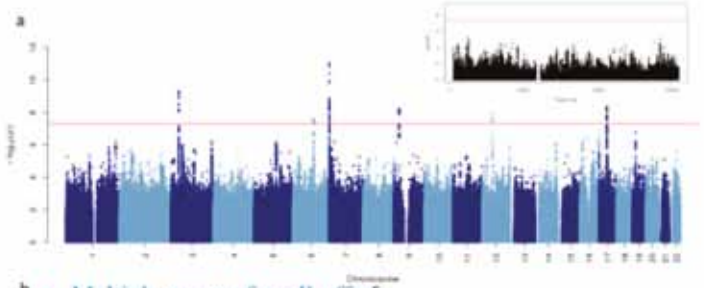
Brain: Anatomical and functional changes

Subject: Emotional and behavioral changes

Society: Functioning and efficiency

Vieta E. 2013.

Genetic perspective



- Multiple genes of small effect
- GWAS with >40.000 patients
- replicate different risk loci previously described (ANK3, TRANK1 and ODZ4…)
- 2 new risk loci for BD

Hou et al, Hum Mol Genet. 2016 Jun 21.

The bipolar brain: animal models

• Healthy mouse

• Depressed mouse

• Manic mouse

• Rapid cycling mouse

DSM for Mice (mDSM-I)

core signs

- "anhedonia" (↓ drinking of sucrose solution)
- "giving up" (learned helplessness)
- "despair" (Porsolt swim test)

associated behavioural signs

- anxiety & neophobia (elevated O-maze, dark-light-box)
- psychomotor behavior (activity boxes, open-field-test)

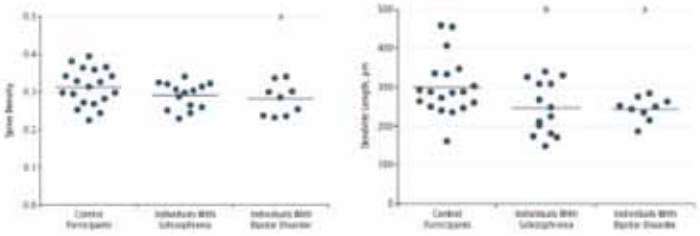
vegetative signs / biological markers

- sleeping, feeding and sexual behavior
- Hypothalamus-Pituitary-Adrenals - System

Gass et al., Physiol. & Behav., 2001

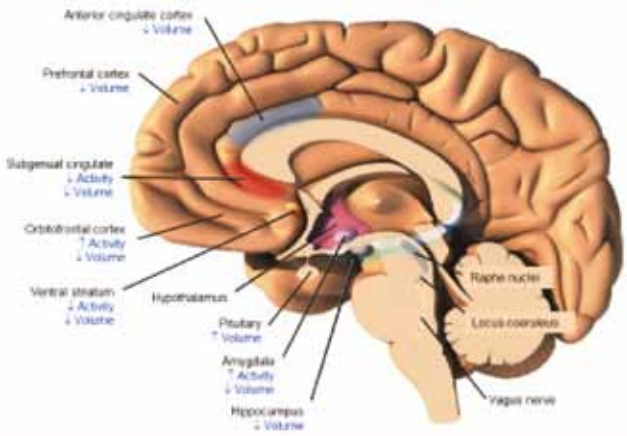
The bipolar brain: Post-mortem studies

Prefrontal Cortical Dendritic Spine Pathology

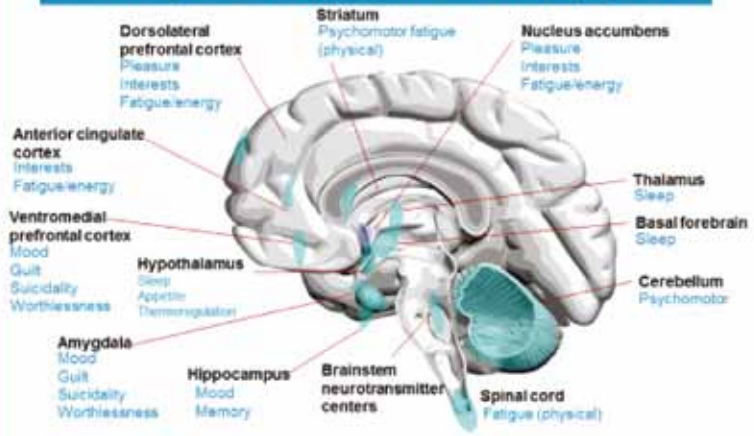


Konopaske, JAMA Psychiatry, 2014

The Bipolar Brain: Neuroanatomy

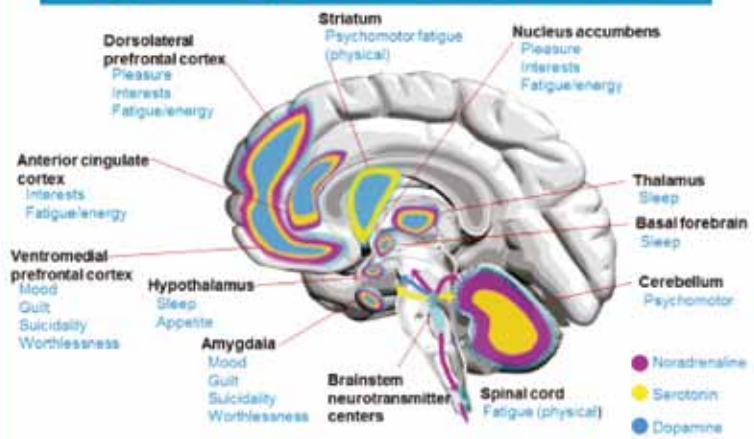


Brain Regions and Associated Function/Symptoms



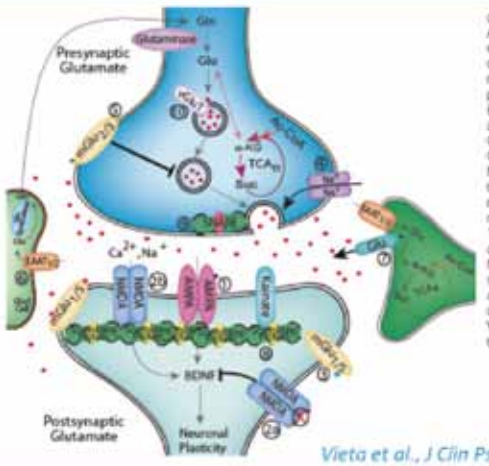
Stahl SM., 2008;
Nutt D, et al. J Psychopharmacol. 2007;
Vieta E. Acta Psychiatrica Scand. 2014.

Hypothetically associated neurotransmitters



Stahl SM., 2008;
Nutt D, et al. J Psychopharmacol. 2007;
Vieta E. Acta Psychiatrica Scand. 2014.

The Glutamatergic System as a target

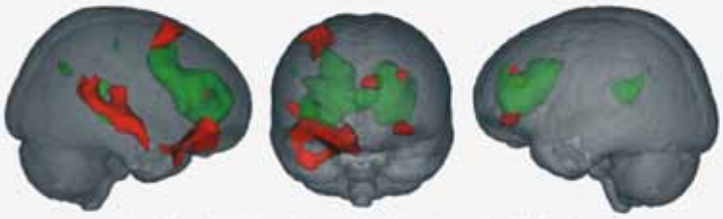


α-KG= α-ketoglutarate; Ac-CoA=acetyl co-enzyme A; AMPA = α-amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid receptor; EAAT = Excitatory amino acid transporter; Gln = Glutamine; Glu = Glutamate; mGlu = Metabotropic glutamate transporter; NMDA = N-methyl-D-aspartate receptor; TCA = Tricarboxylic acid cycle; SNARE = Soluble N-ethylmaleimide sensitive factor attachment receptor complex; VGLUT = Vesicular glutamate transporter.

Vieta et al., J Clin Psychiatry 2014

Brain changes in BD

Diffused axonal pathology
Loss of cortical gray matter
Subcortical dysfunction
Loss of volume and / or alterations in membrane permeability
Mitochondrial dysfunction vs. neuroinflammation



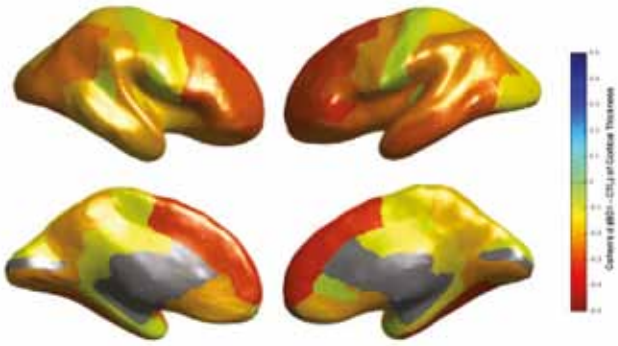
whole-brain high angular resolution molecular diffusion imaging

Gray matter
White Matter

Canales Rodriguez et al, Biol Psychiatry 2013

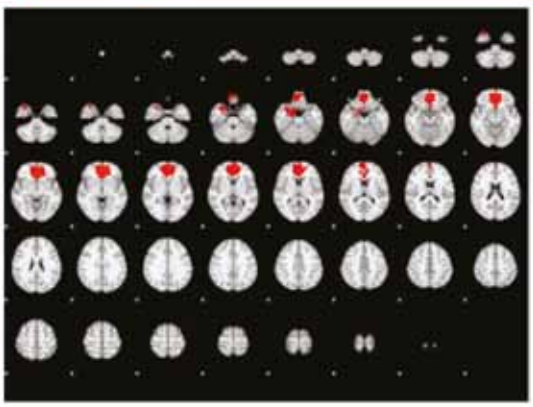
Structural neuroimaging

1.017 BD patients and **2.451** healthy controls



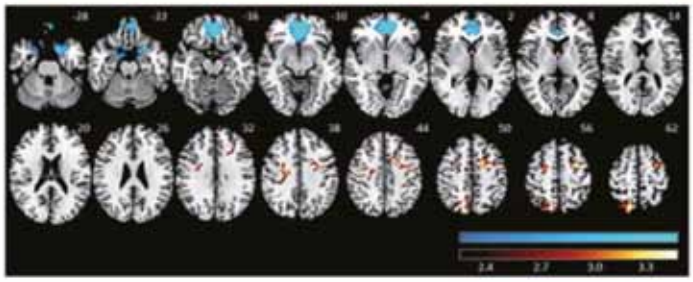
Hibar et al., Mol Psychiatry, 2016

Default mode network during a working memory task in bipolar depression



Fernández-Corcuera et al, JAD 2012

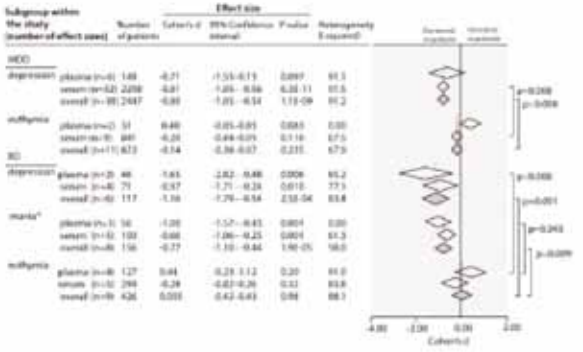
Failure to deactivate the default mode network in mania



Pomarol-Clotet et al, *World J Biol Psychiatry* 2012

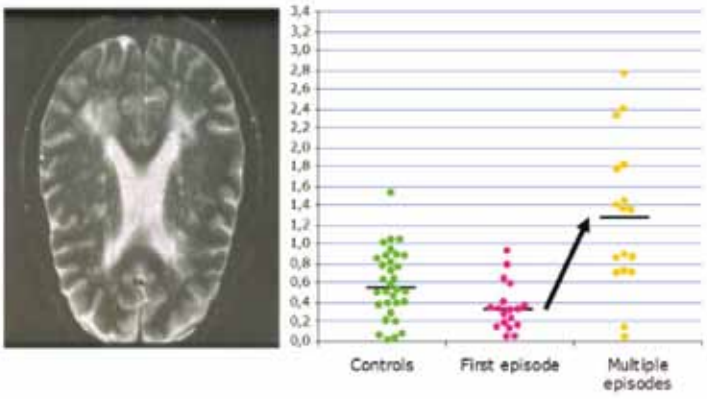
Structural neuroimaging

BDNF as a biomarker for successful treatment of mood disorders



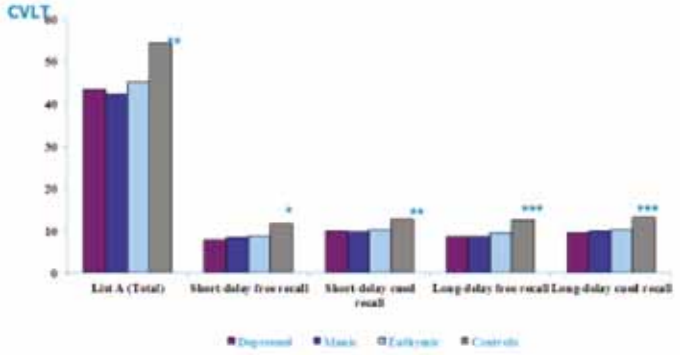
Polyakova et al., 2015 JAD

Ventricular Volume in Bipolar Disorder



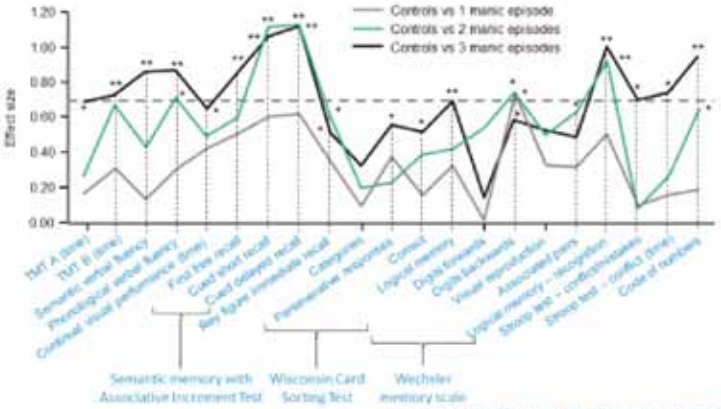
Strakowski SM et al, Am J Psychiatry. 2002.

Neurocognitive dysfunction across mood states



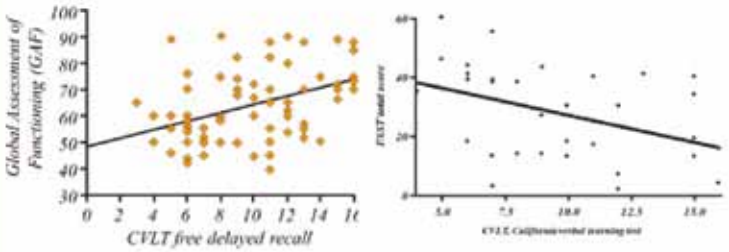
Martínez-Arán et al, Am J Psychiatry 2004

Neurocognition in 1st, 2nd, and 3rd episode patients and controls

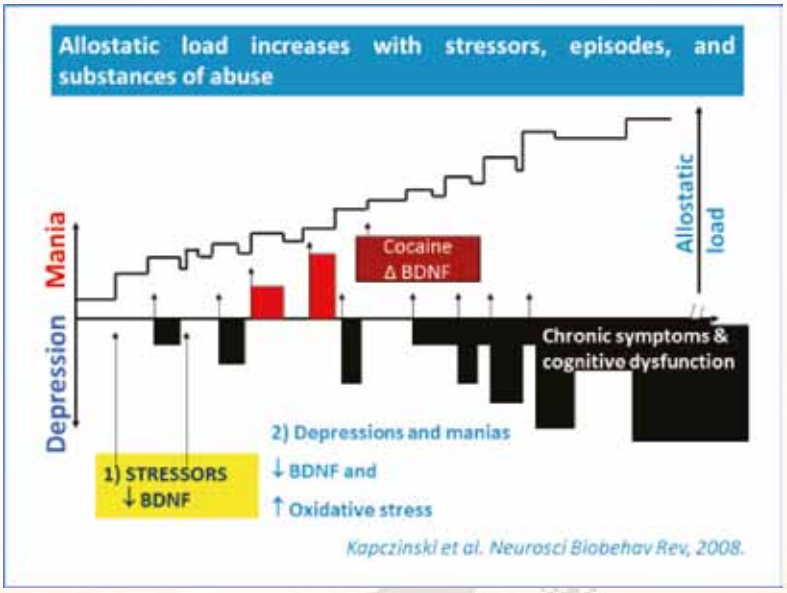


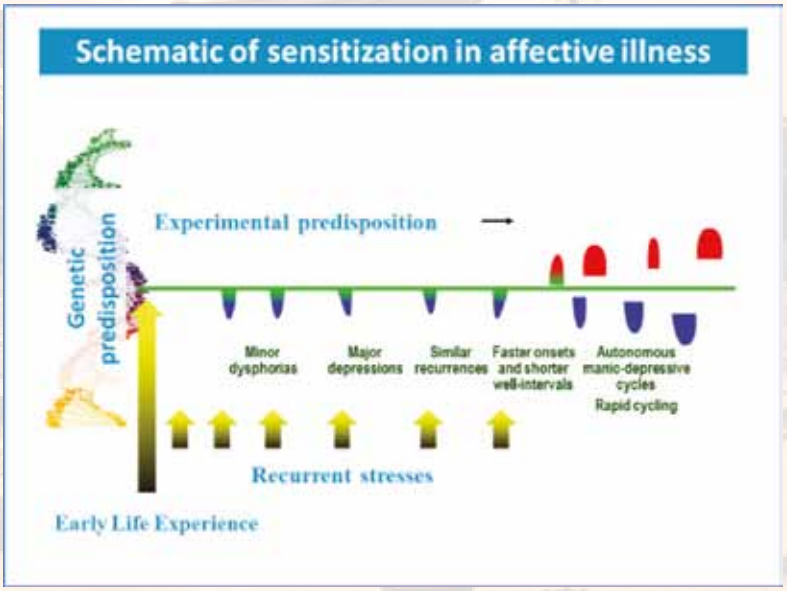
Lopez-Jaramillo et al. Bipolar Disord 2010

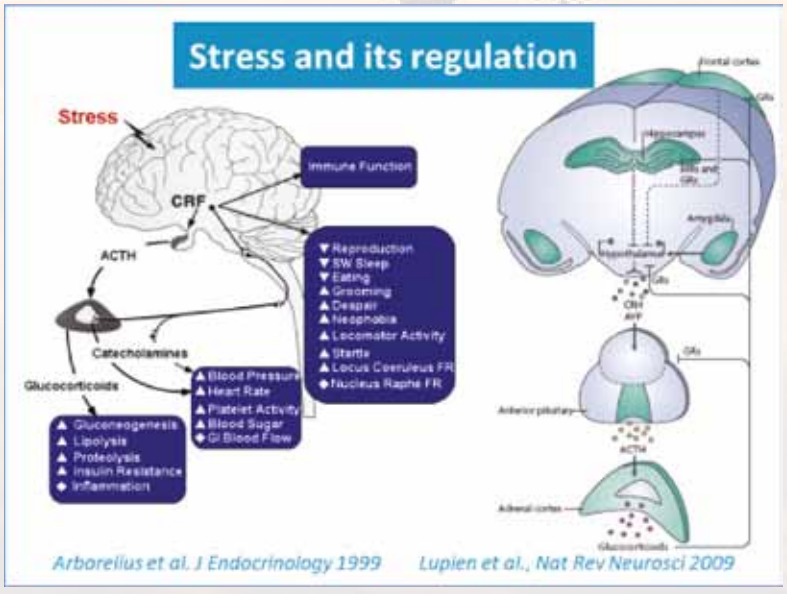
Neurocognitive and psychosocial functioning in bipolar disorder



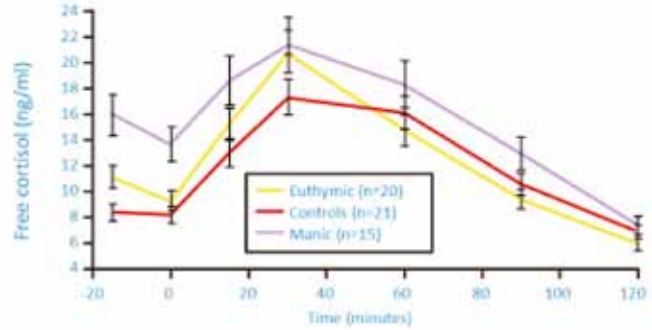
Martínez-Arán et al, Bipolar Disord 2007
Bonnin et al, J Affect Disord 2010


Allostatic load increases with stressors, episodes, and substances of abuse
Mania
Depression
Allostatic load
Cocaine
Δ BDNF
Chronic symptoms & cognitive dysfunction
2) Depressions and manias
↓ BDNF and
↑ Oxidative stress
1) STRESSORS
↓ BDNF
Kapczinski et al. Neurosci Biobehav Rev, 2008.


Schematic of sensitization in affective illness
Genetic predisposition
Experimental predisposition
Minor dysphorias
Major depressions
Similar recurrences
Faster onsets and shorter well-intervals
Autonomous manic-depressive cycles
Rapid cycling
Recurrent stresses
Early Life Experience

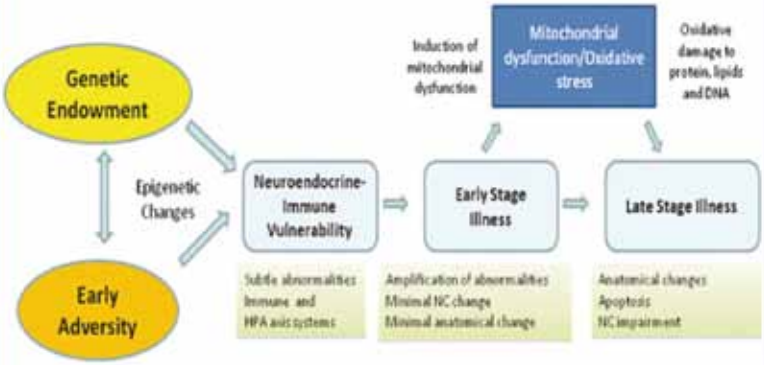

Stress and its regulation
Stress
CRF
ACTH
Immune Function
Catecholamines
Glucocorticoids
Arborelius et al. J Endocrinology 1999
Lupien et al., Nat Rev Neurosci 2009

The Bipolar Brain: HPA Axis



Vieta et al, Psychol Med 1999

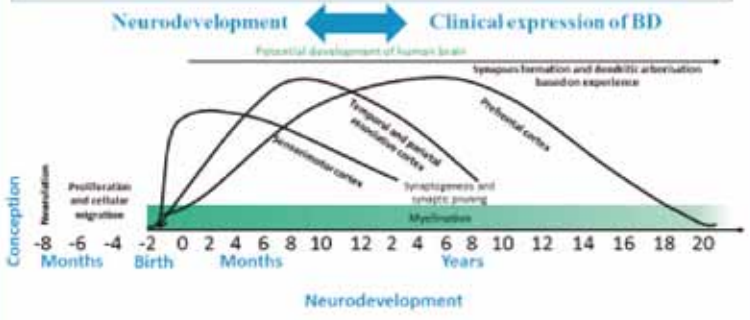
Biological indicators of illness in BD



Duffy et al., Early Int Psych 2011.

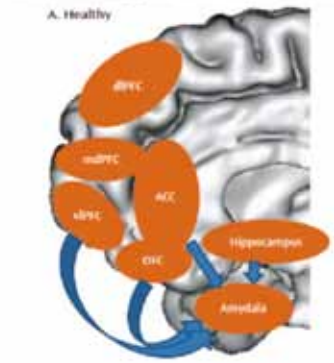
Myelination and neurodevelopment influence clinical expression

Neurodevelopment and BD: complex and bidirectional interaction changes. BD symptoms interfere with neurodevelopment / neurodevelopment with manifestations across ages.



Abnormal emotional reactivity .1

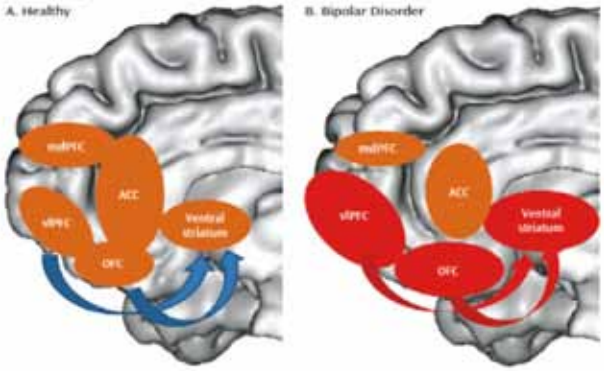
Emotion-Processing and Emotion-Regulation Circuitry[a]



Phillips & Swartz, Am J Psych, 2014

Abnormal emotional reactivity .2

Reward-Processing Neural Circuitry[a]



Phillips & Swartz, Am J Psych, 2014

Sleep and circadian rhythm disturbances

Sleep and circadian disturbances induce mood episodes

Evidence suggests weak coupling of circadian system to external environment

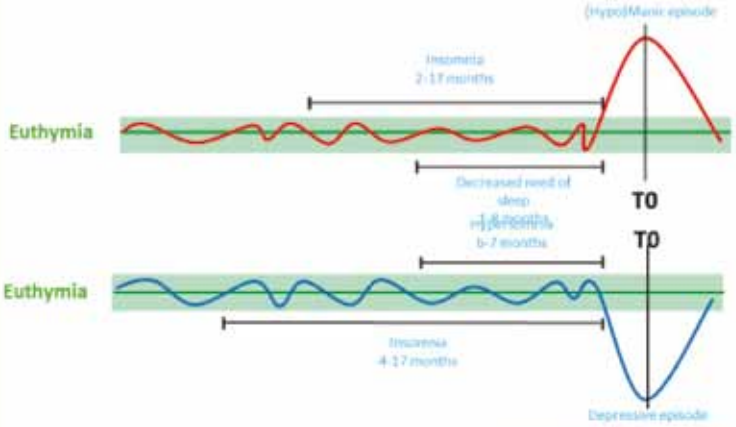
Euthymic bipolar patients show
- variability in sleep duration
- circadian rhythm instability
- low and delayed melatonin peak

Several genes important in sleep and circadian systems have been linked to bipolar disorder (TIMELESS, CLOCK, ARNTL)

Sleep and circadian rhythm disturbances should be assessed throughout course of illness and treated to prevent relapse

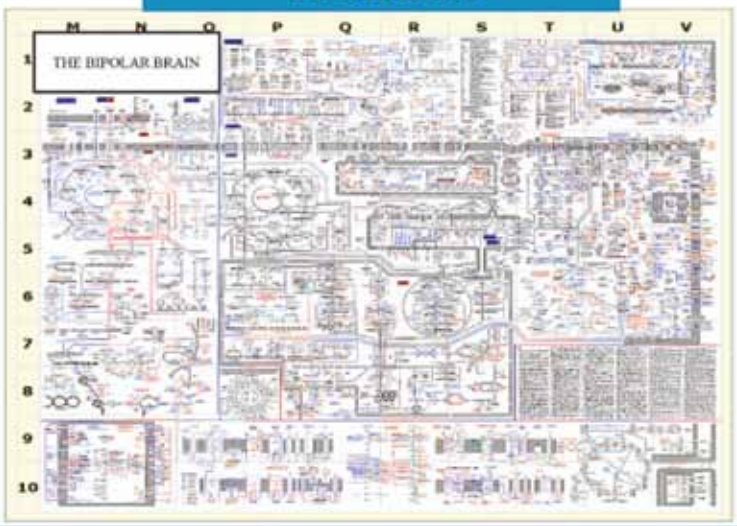
Harvey et al 2005
Mansoeur et al 2005
Harvey 2008
Lebayer & Kupfer 2010

Sleep alterations anticipate BD onset



Pancheri et al., submitted

Conclusions



Thank you

amurru@clinic.ub.es

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How to prepare a scientific presentation

Seminar Leader
15 minutes

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Learning

- Definition of *any* kind of learning?

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Common Causes of Ineffective Presentations

- Failure to prepare the talk
- Cut and paste from your paper
- Gaps in logic
- Poor delivery (speaker)
- Poor time planning
- Too many slides

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Organizing a Presentation

i. Outline
ii. Problem and background
iii. Design and methods
iv. Major findings-the heart of your talk
v. Conclusion, limitations and recommendations

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Learning

- Definition of *any* kind of learning= a steady change in behavior as a result of an experience
- The change has to happen in your audience
- Effective learning is an active process

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Before you start

- **Who is your audience?**
- **What is your desired outcome?**
- **How much time do you have?**
- **What are the key messages?**
- **Is your PP presentation working?**

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Introduction

- Context
- Study question
- Relevant knowledge on issue

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Major findings

- Text and or table/graph
- One slide for each
- Message should be clear
- Figures are the best

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Conclusion and Recommendations

- What have we learnt?
- Key points
- Clinical Implications
- Clear closure (pause, high note, thanks)

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Making slides

- Main points only
- One idea per slide
- Few words (5-10 per line)
- Strong statements: active voice
- 1 slide per 1 minute

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Making slides

- Every slide should have a heading
- Lists should contain no more than 3-4 items
- Limit text blocks to no more than two lines each
- Visuals

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Making slidests

Type size should be 24 points or larger:

18 point

20 point

24 point

28 point

36 point

* References can be in 14 point font

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Best contarts:

Yellow on blue

OR

Black on White

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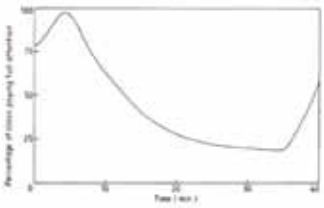
Audience attention curve



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The TED's style

- Move when possible (unexpected tract)
- Contact
- Time yourself precisely
- Change tones
- Use humor when appropriate
- Enjoy….

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The learning rule:

- **"Tell me and I will forget, show me and I will remember, involve and I will understand"**

List of selected participants

Dániel Baksa
Vktória Balla
Szabolcs Bandi
Edit Bíró
Emese Bogáthy
Bíborka Bruzsik
Tzipi Buchman Wildbaum
Nóra Eszlári
Kinga Farkas
Lili Fejes-Vékássy
Zsuzsanna Fodor
Anikó Fülöp
Bernadett Gál
Kinga Gecse
Melinda Hal
Tamás Halmai
Orsolya Hegedűs
Sara Hosseini-Nezhad
Enikő Kasos
Tünde Kilencz
Andrea Koncz
Ildikó Kovács
Zsüliet Kristóf
Emese Kruk
Dániel Kuti
Diana Martos
Christina Miskolczi
Szilvia Anett Nagy
Noémi Papp
Zsuzsanna Schnell
Sandra Stojic
Ádám Szabó
Szilvia Szalóki
Andrea Szegő
Péter Szocsics
Dalma Tényi
Estilla Zsófia Tóth
Zsuzsanna Tóth
Péter Ujma

Abstracts of the selected participants

Dániel Baksa
MTA-SE NAP B Genetic Brain Imaging Migraine Research Group, Hungarian Academy of Sciences, Semmelweis University

The genetic background of migraine in interaction with psychopathological disorders

A previous research investigated the biochemical, genetic and psychological background of depression. Thus, there is a database of Hungarian adults (n=895) with detailed phenotypic data, including depression, migraine type headaches, and genotyped genetic samples. As a continuation of this research my goal is to investigate the genetic background of migraine in interaction with psychopathological disorders (depression, hypomania, anxiety). We will collect additional data about the headache symptoms of the participants to have a more reliable and valid migraine diagnosis. A genetic association study will be carried out, first on candidate genes, then on a whole genome basis.

Viktória Balla
Department of Cognitive and Neuropsychology, Institute of Psychology, University of Szeged

Visual prediction mechanisms with biofeedback-based priming

The neural basis of the feeling of agency is considered to rely on sensory predictions that were suggested to be disrupted in disorders such as schizophrenia or obsessive-compulsive disorder. Only a few studies were investigating this phenomenon in the visual modality and none of them were using biofeedback-based priming. In this study we examined prediction-related modification of visual event-related potentials elicited by movement-evoked stimuli. We used the Myo Armband to evoke a stronger sense of ownership of the stimuli. The results of our study present experimental evidence for visual effects that might contribute to the sense of agency.

Szabolcs Bandi
Department of Personality and Health Psychology, Institute of Psychology, University of Pécs.

The Orthogonal Narcissism Concept

The aim of our study was to clarify in a trait-based dynamic system the complex concept of narcissism. In clinical practice narcissism and NPD (Narcissistic Personality Disorder) often appear as unidimensional concepts, however personality psychologist sooner proved, that narcissism at least has two different subtypes. According to the current clinical literature the grandiose and vulnerable types have both different overt and covert phenotypes. In our research we would like to offer a new dynamic dimensional framework, which can unify the (sub)clinical and normal levels of narcissism and the different typological concepts.

Edit Bíró
Department of Psychiatry, University of Szeged

Development of a new tool to assess neurocognitive symptoms of depression through their impact on everyday life

The affective and somatic symptoms are the major contributing factors to the depression related psychosocial impairment. Our major aim is to create a brief, reliable self-rating tool to identify the cognitive profile for screening and initial assessment. In the last two years our research group developed a new screening tool, named DEP-Cog. The self-administration of DEP-Cog requires 5 minutes but additional tests such as (MADRS,

MMSE, BDI, SDS, DAS, neuropsychological tests) were applied in the validation process. The current dataset is still not enough for statistical evaluation, therefore the scope and the methods are presented here.

Emese Bogáthy
Department of Pharmacodynamics, Semmelweis University

Investigation of 5-HT2C and CB1 receptors and their interaction in anxiety

The subject of my research is exploring the relationship between serotonin 2C (5-HT2C) and cannabinoid type 1 (CB1) receptors in the regulation of anxiety-related behaviours and symptoms. To investigate the short-term interactions between these receptors, we administered acute dose of SB-242084 (5-HT2C rec. antagonist) followed by acute AM251 (CB1 rec. antagonist) treatment, and examined behavioural changes of rats in social interaction and elevated plus maze tests. Applying the same treatment conditions, we also measured alterations in sleep-wake cycle and brain oscillations of rats with electroencephalographic (EEG) experiment. Namely, the EEG methods are suited to investigate the acute interactions of these receptors in a more complex level of central nervous system and a larger time interval as well.

Bíborka Bruzsik
Department of Behavioural Neurobiology, Institute of Experimental Medicine, Hungarian Academy of Sciences

The role of prefronto-hypothalamic projections in aggressive behaviour

Aggression is associated with many cognitive and emotional aspects processed by the prefrontal cortex (PFC). Although previous studies showed that the medial PFC sends direct projections to the mediobasal and lateral hypothalamus in rats (MBH and LH), the role of these projections in aggression is unknown. We found that optogenetic stimulation of the PFC-MBH pathway elevated the attack numbers, whereas activation of PFC-LH projections shifted the attacks towards vulnerable bodyparts and eliminated attack signalling. Our data implies that the PFC directly modulates the quantitative and qualitative characteristics of aggressive behaviour via its hypothalamic efferents.

Tzipi Buchman Wildbaum
Department of Clinical Psychology and Addictions, Eotvos Lorand University

Psychological factors in treatment compliance and quality of life among patients with serious mental illness

Treatment adherence plays a vital role in psychiatric rehabilitation but still, reports indicate that up to 50% of psychiatric patients do not adhere to their prescribed medications, which has severe impact on their quality of life. The first goal of the study is to understand the internal experience of mentally ill patients and how it is related to treatment compliance and quality of life. The second goal is to conduct a comparison between the different psychiatric diagnoses in the effort to understand whether there are differences in the way different patient population experience their illness and engage with their treatment.

Nóra Eszlári
Department of Pharmacodynamics, Semmelweis University

Genome-wide genetic background of depressive rumination

Several studies have discussed candidate genes in the background of depressive rumination (shortly rumination), which denotes a risk factor for numerous psychiatric and physical disorders. In our current investigation, being part of the NewMood study, we plan to explore its genetic factors in a ge-

nome-wide scan among around 1800 European adults. We seek for genome-wide significant hits at three levels: single nucleotide polymorphism (SNP), gene (the scores aggregated from those of SNPs), and gene set (the scores aggregated from those of genes). With this genome-wide analytic approach, our results may reveal completely novel biological mechanisms underlying rumination.

Kinga Farkas
Department of Psychiatry and Psychotherapy, Semmelweis University

Visual mismatch negativity in schizophrenia

According to aberrant salience theory, patients with schizophrenia have difficulties with suppression of irrelevant information, and attach more importance to irrelevant stimuli. During electrophysiological measurements when an unexpected, deviant event occurs in a regular repeating pattern of standard stimuli mismatch negativity is generated, and supposed to reflect the difference between the sensory experiences and former predictions as a prediction error. Our primary hypothesis was to find significant differences in MMN generation even to simple visual targets (Gabor patches) between patients and healthy controls. 28 patients with schizophrenia and 27 matched healthy controls participated. EEG was recorded with a 128-channel amplifier.

Lili Fejes-Vékássy
Institute of Psychology, Pázmány Péter Catholic University

Self(ie)-esteem? – A Manifestation of Adolescent Self-creating Endeavours in the Virtual Space of Facebook

In the centre of our interest stand the manifestations of adolescent self-creating endeavours in the virtual space of the social media portal called Facebook. Frequent self-photography (selfie) making, as a pronounced cultural feature of contemporary youth, and regular activity on Facebook handled as tightly connected factors; we propose that youngsters, bearing these attributes, have a different self-esteem than those adolescents who rarely or never take any photographs of themselves. In the first, quantitative part of our research the participants (N=80) filled in the Rosenberg Self-Esteem Scale and a questionnaire containing questions in connection with Facebook-usage (compiled by us). In the qualitative part of the research the participants took part in a half-structured interview, containing questions in connection with selfie -making (also compiled by us). Our hypothesis was not proven by the statistical analysis, no connection could be testified between frequent selfie-making and low self-esteem.

Zsuzsanna Fodor
Department of Psychiatry and Psychotherapy, Semmelweis University

Differentiation of Amnestic Type Mild Cognitive Impairment (aMCI) from the Non-Amnestic (naMCI) Types by Structural MRI

Altogether 62 aMCI, naMCI, and healthy control subjects underwent a routine brain MR examination and a detailed neuropsychological examination. Hippocampal volume and cortical thickness of the entorhinal cortex and the fusiform gyrus were significantly ($p<0.016$) decreased in aMCI relative to naMCI and controls. The cortical thickness of the precuneus was significantly decreased in both MCI groups compared to controls. Significant between group differences were also found in the neuropsychological test results. Memory performance in the aMCI group correlated with the thickness of the entorhinal cortex and with the volume of the amygdala.

Anikó Fülöp
Wigner Research Centre for Physics, Hungarian Academy of Sciences

Interactional model of cortical networks

Network analysis plays significant role in understanding the structural and functional organization of the brain. In the multi-level cortical network, microscopic and macroscopic levels are relatively well explored but mesoscopic organization, responsible for intra-areal and inter-areal integration, is little-known. Mesoscopic network is formed by neuronal populations via their modular connectivity as in the case of columnar organization. However, mesoscale network architecture of the cerebral cortex is not known. To answer this question we develop a network model of the macaque monkey cerebral cortex representing the interactions of cortical areas.

Bernadett Gál
Department of Psychiatry, University of Szeged

Neural correlates of nalmefene opioid antagonist in alcohol dependence

Nalmefene is an opiate receptor modulating agent which is an approved form of harm reducing intervention in alcohol dependence. It is considered to deliver its effect via influencing the impulsive-compulsive spectrum, however the exact neuronal mechanism is not profoundly known yet. In our study, we investigated nalmefene's mechanism on the neurophysiology in alcohol dependent patients (N=20) by the means of an alcohol primed Go/NoGo paradigm and EEG. The present study revealed that nalmefene influenced response inhibition, conflict detection and complex analysis of visual stimuli in the frontal region.

Kinga Gecse
Department of Pharmacodynamics, Semmelweis University

Changes in plasma endocannabinoid levels associated with pain and stress in patients suffering from migraine

The endocannabinoid system has an important role in the control of pain, and in the regulation of stress and anxiety. Recent studies reported decreased plasma levels of endocannabinoids, namely anandamide and 2-arachidonoylglycerol in patients suffering from migraine. In our study, participants – migraineurs and non-migraineur controls – were exposed to pain and stress stimuli during brain functional magnetic resonance imaging (fMRI). Blood samples were collected to observe the changes in the endocannabinoid plasma concentrations before and after the experimental tasks. We expect altered plasma endocannabinoid concentrations, and in parallel distinct brain activation pattern in migraineurs compared to controls.

Melinda Hal
Mental Health Sciences Doctoral School, Semmelweis University

Psychological factors of headache

Background: The personality of patients struggling with pain greatly affects either pain threshold or pain response.
Aims: The aim of the research was to detect the personality traits that are in the background of headaches.
Results: Individuals with tension-type headache scored significantly higher at the scales of anxiety, anger and hostility, vulnerability and persistence. Those with migraine-type headache showed significant differences at depression, assertivity and positive emotion scales.
Conclusions: We created a new headache indicator (IHI) that can be easily utilized in neurological practice. IHI is a novel and easily applicable method for the assessment of headache patients.

Tamás Halmai
Department of Psychiatry and Psychotherapy, Semmelweis University

Schizophrenia and violence: biological and psychological markers

In our study, we set out to investigate the rate and topological profile of minor physical anomalies, which may be external markers of early abnormal brain development, in patients with schizophrenia with the history of committed or attempted homicide (n=44) comparing them to patients with schizophrenia without homicide in their history (n=22) and to normal control subjects (n=21), using a list of 57 minor physical anomalies. Minor physical anomalies are more common in homicidal schizophrenia patients compared to non-homicidal schizophrenia patients and normal controls, which could support a stronger neurodevelopmental component of etiology in this subgroup of schizophrenia.

Orsolya Hegedűs
Vadaskert Child Psychiatric Hospital and Outpatient Clinic

OCD and ADHD in the background of aggressive behavior in a 12-year-old girl

The case report is about a 12-year-old female patient. She has been admitted several times to our inpatient ward for disruptive behaviour, which was first thought to belong to OCD, then later to bipolar symptomatology provoked by the SSRI. Last time, a detailed evaluation showed ADHD symptoms, which, at the time did not cause any impairment. She was discharged with the first SSRI, and has been aggression-free since then. Conclusion: the long-term fight with OCD symptoms have depleted her resources to keep ADHD symptoms under control. This, together with familial factors, have led to disruptive behaviour.

Sara Hosseini-Nezhad
Department of Clinical Psychology, Eötvös Loránd University

Mental health of Iranian Immigrants in Canada

Immigration is a movement of people from their native country to another country; in other words. People immigrate to other countries due to political, social, and economical problems in the hope for a better life circumstances. Studies have consistently revealed a high level of psychological stress among immigrants since it is very hard to adapt to new environment and culture. Exposure to different stressors will lead to psychological disorders, like anxiety, depression, and post-traumatic stress disorders (PTSD).
In my future research I would like assess the effect of immigration on the mental health of Iranian immigrants in Canada (excluding refugees) between the age 18 to 75 and will compare them to Iranians who have never experienced immigration. I will measure depression, anxiety, and PTSD level between the two groups, considering other factors like acculturation stress level, acculturation style, age, gender, social support, length of residence, experience of discrimination, self-esteem, level of education, social identity, and sociocultural adaptation

Enikő Kasos
Department of Affective Psychology, Faculty of Education and Psychology, Eötvös Loránd University,

Changes in the level of oxytocin during active-alert hypnosis

The effects of oxytocin have been the subject of contemporary research in a number of disciplines. We know it plays a significant role in interpersonal interactions and has several psychological and emotional effects. The theory of female-pattern stress management in the social environment of relationships is also based on the effects of oxytocin.

Some theorize that oxytocin can positively influence the relationship between the hypnotist and the subject, and supposedly is one of the important factors behind the fast improvement that results from hypnotherapy. The present study examines the role of oxytocin during the dyadic interaction using active-alert induction.

Tünde Kilencz
Department of Cognitive- and Neuropsychology, University of Szeged

Information processing of schizophrenic patients in the visual modality

The ability to feel agency has been associated with internal forward modelling, which is considered to rely primarily on sensory predictions. Some psychopathological symptoms are associated with these predictions' dysfunction, for example, hallucinations and the feeling of „being influenced" in schizophrenia. Although the neural correlates of this phenomenon could be relevant to understand the psychotic features, only a few results were published in the visual modality. In this research plan I will present a protocol suitable for investigating prediction-related modification of visual processing among schizophrenic patients by analysing event-related potentials over the occipital cortex elicited by images depicting hands.

Andrea Koncz
Department of Psychiatry, University of Szeged

Examining neural glucose transporters

Glucose is the primary source of energy for mammalian cells. Cells use glucose transporters (GLUT) to uptake glucose from the extracellular space. A disruption in glucose metabolism is characteristic of many central nervous system disorders, such as Alzheimer's disease, Huntington's disease, autism or attention deficit hyperactivity disorder (ADHD). Our ongoing research focuses on GLUT1 and GLUT3, which are more abundant in the central nervous system (CNS) than other isoforms.
Our research builds on recent data which found that a CNS involving GLUT3 more frequent in ADHD population. A humanized transgenic mouse model with an additional copy of the SLC2A3 gene encoding the GLUT3 protein was constructed. My task and goal is to monitor these transgenic mice for any phenotypical differences compared to the wild type. I performed behavioural tests (blinded for genotype) including Open Field, Elevated Plus Maze, Morris Water Maze and 3 Chamber Sociability Test. Genotyping is in progress, my next step is the assessment of these tests. Future plans include a closer investigation of GLUTs, as there is currently limited information in the literature regarding how the glucose transporter activation is affected by conditions outside the normal physiological range, such as fasting or high glucose feed. My long-term plans include investigating the potential effect of a changing glucose supply on the expression of GLUT1 and GLUT3 and whether the modification of GLUT expression offers any potential therapeutic options for treating diseases of the central nervous system.

Ildikó Kovács
Department of Psychiatry, University of Szeged

From behavioural addictions to substance related disorders: neurocognitive aspects of impulsivity

Impulsivity is a multifaceted factor that is crucial in understanding addictive disorders. Gambling disorder (GD) and alcohol use disorder (AUD) share common characteristics, which are represented in the recategorisation of GD in DSM-V. The altered functioning of ventral areas (particularly vmPFC and OFC) is associated with reward responsiveness and cognitive impulsivity both in GD and AUD, but the extent is yet to be ascertained.

The different aspects of impulsivity can be measured by computerized neurocognitive tasks. The aim of our study is to assess the presence and severity of gambling and measure neurocognitive functioning in alcohol dependent patients.

Zsüliet Kristóf
Árpád-Házi Szent Erzsébet Hospital

Social cognition and violence in schizophrenia

The aim of our study is to investigate the schizophrenic patient's empathic abilities and theory of mind. We examined 44 hospitalized males with paranoid schizophrenia, divided into two groups: 22 patients, whose committed violent acts against others compared with 22 patients without criminal record. To examine these abilities, we administered the Faux Pas Recognition Test, the Ekman 60 Faces Test, the Interpersonal Reactivity Index, the Impulsiveness-Venturesomeness-Empathy Questionnaire and the Anger Expression Scale. Based on the previous results, we expect that violent patients perform better on complex theory of mind tasks than their non-violent counterparts, and that they have poorer empathic abilities.

Emese Kruk
Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis University

DNA methylation analyses in a pilot study of patients with borderline personality disorder

The aetiology of borderline personality disorder (BPD) is complex, the genetic risk factors are probably interacting with each other and with environmental factors. We analyzed the DNA methylation level of the catechol-O-methyltransferase (COMT) gene alternative promoters (soluble, membrane-bound). Four different easily accessible biological samples (blood, saliva, bucca, mouthwash) were collected from patients with BPD (n=14) and from control persons (n=12). Epigenetic marks can be tissue-specific, therefore we investigated an epithelial tissue specific CpG site (PTPN7 cg18384097). The methylation level of the soluble-COMT region showed an inverse correlation to the PTPN7 CpG marker sites (R2=0.9) in mouth-related samples.

Dániel Kuti
Department of Molecular Endocrinology, Institute of the Experimental Medicine of the Hungarian Academy of Sciences

Microbiota as a supplementary therapy against chronic stress

Growing body of evidence supports an important influence of gut microbiota on emotional behaviour, brain mechanisms and hypothalamic–pituitary–adrenal axis (HPA) responsiveness. Further, these studies point out that the manipulation of this bidirectional brain-gut microbiota interaction is a possible supplementary therapy for different psychiatric disorders such as depression, chronical stress, ADH or schizophrenia.

In my research, maternal separation and chronical variable stress was performed on C57Bl6 mice. During the CVS, their microbiome, excluded the control group, was manipulated by an antibiotic. Afterwards, their behaviour, HPA response and microbiome alteration were observed.

Diana Martos
Department of Neurology, University of Szeged

Effect of kynurenine analogues in mice behavioral tests

The neuroprotective kynurenic acid (KYNA) effectively inhibits the glutamate neurotoxicity. Nevertheless, the administration of KYNA in low doses may facilitate the

learning/memory processes, as a partial agonist of glutamate receptors. Our aim was to examine the dose response effects of KYNA and its analogues (SZR72, SZR73, and SZR81), which may have abilities to affect the cognitive functions, without harmful side effects.
KYNA or its analogues or saline (2 l) was injected in 0.01, 0.05 and 0.1 M concentrations into the right lateral ventricle of C57BL6 mice. We observed their behavioural changes in open field, rotarod and ataxia/stereotype test.

Christina Miskolczi
Department of Behavioural Neurobiology, Institute of Experimental Medicine of the Hungarian Academy of Sciences

Investigating the connection between childhood social adversities, abnormal aggression in adulthood and the central serotonergic system

Childhood social adversities may lead to the development of abnormal aggressive behaviour in adulthood. To investigate this, we have developed an animal model in which rats are subjected to post-weaning social isolation. Isolated rats display abnormal aggressive behaviour in adulthood compared to socially housed controls. Since serotonin plays a crucial role in the regulation of aggression, we have studied the gene expression of the serotonin-metabolyzing enzyme MAOA, and of serotonin receptors 5HT1A and 5HT1B. We have also investigated the effects of buspiron treatment. Results show that gene expression is altered in isolated animals, and that buspiron lowers aggression dose-dependently.

Szilvia Anett Nagy
MTA – PTE, Neurobiology of Stress Research Group

Examination stress and anxiety in medical students: an fMRI study

Medical examination is perceived as being stressful and has a negative effect on cognitive functioning of students. The present study was carried out to assess examination stress and its effects on functional Magnetic Resonance Imaging (fMRI) in medical students. fMRI was carried out twice (one during the examination period and one 8 weeks after that) on 6 voluntary medical students (5 females 1 male) using a facial emotion recognition paradigm. Our results showed significant deactivation during the examination period in cingulate gyrus and precuneus. These results are discussed in relation to the effects of episodic stress, anxiety and sleeping disturbances.

Noémi Papp
Department of Pharmacodynamics, Semmelweis University

Investigation of EEG gamma oscillations in a rat model of depression

Using the alteration of brain oscillations (quantitative EEG, qEEG) as biomarker in psychiatric and neurological disorders is an intensively developing field, as qEEG as a non-invasive method provides sensitive information about the global brain activity - often preceding other signs of the disease. Beyond the well-known sleep alterations of depression (e.g. elevated REM sleep time) we could hardly found data about the alterations in gamma oscillations (which are involved in several psychiatric disorders) in depression. We aim to investigate how gamma oscillations (and their relationship with other oscillations) are altered by subchronic/chronic stress, and how antidepressant interventions can modify it.

Zsuzsanna Schnell
Department of Psychology and Department of Linguistics, University of Pécs

Social cognition and pragmatic skills - developmental and neurocognitive perspective

The focus of the lecture is twofold: we investigate the role of theory of mind in pragmatic language development, targeting different aspects of non-compositionality and indirectness (simile, metaphor, irony, humor and maxim infringement), tracking the order and cognitive difficulty of their unfolding. The study also investigates the pragmatics of irony processing and contextual effects in schizophrenia. Relying on neuroimaging (fMRI) techniques the research reveals the brain networks involved in social cognition and in non-compositional processing, and confirms theory of mind deficit, along with difficulties in irony comprehension in schizophrenia. We also attempt to identify the area of the precuneus having an integrative role as the neural correlate of the hypothesized meta-module of pragmatic meaning construction.

Sandra Stojic
Doctoral School of Psychology, Department of Clinical Psychology and Addictions/ Department of Cognitive Psychology, Eotvos Lorand University, Budapest

Impact of sex hormones on the performance of different perceptual tasks

Investigation of similarities or differences among both sexes in terms of abilities and also between human's brain hemispheres, gave a new and broad area of research due complexity and intrigue. Aim of this study would be to examine performance and to determine scored success of men and women (in different phases of menstrual cycle and (non)/contraceptive users) in different tasks. Having an opportunity to directly observe fine effects of hormonal supplements would bring an opportunity to tackle neuroendocrinological nature; clarification and restriction of hormone effects, or more specific, put the roles of estrogen and progesterone apart, what would in the end, enable to make final conclusions among numerous conducted studies and could possibly serve as a significant contribution.

Ádám Szabó
MR Research Center, Semmelweis University

Neurobiological correlates of impaired mixed emotion processing in schizophrenia: An fMRI study

Background: Schizophrenia has a negative effect on the activity of the temporal and prefrontal cortices in the processing of emotional facial expressions. However, no previous research focused on the evaluation of mixed emotions in schizophrenia, albeit they are frequently expressed in everyday situations and negative emotions such as fear are frequently expressed by mixed facial expression.
Methods: Altogether 19 patients with schizophrenia and 18 healthy control subjects were enrolled in the study. The two study groups did not differ in age and education. The stimulus set consisted of 10 fearful (100%), 10 happy (100%), and 10-10 mixed fear (70% fear and 30% happy) and mixed happy facial expressions. During the fMRI acquisition pictures were presented in a randomized order and subjects had to categorize expressions by button presses.
Results: A decreased activation was found in the patient group during fear, mixed fear and mixed happy processing in the right ventrolateral prefrontal cortex (VLPFC) and the right anterior insula at voxel and cluster level. No difference was found between study groups in activations to happy facial condition. The study group X condition interaction was found significant in the right parietal operculum and right superior temporal gyrus.
Conclusions: Patients with schizophrenia showed decreased activation in the right anterior insula, which is activated in emotional tasks with cognitive demand and in

the VLPFC, a region responsible for salience signaling. Our results indicate that fear and mixed happy/fear processing are impaired in schizophrenia, while happy facial expression processing is relatively intact.

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Examination of self-agency as a possible nosospecific feature of schizophrenia

The identification and the treatment of schizophrenia are obstructed by the lack of nosospecific markers. From neurophenomenological perspective the disturbed „minimal-self" (MS) is a specific feature of the disease. The examination of the self-agency seems to be an adequate method to investigate the MS. In our study we use a device developed by our research group, and paradigms applied in other studies in order to test the sense of agency (SoA) comprehensively. Besides we adopt the EASE scale for testing the subjective experience of the MS. We investigate SoA simultaneously in schizophrenia and bipolar disorder to verify the specificity of disturbed self-agency in schizophrenia.

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Psychotropics in emergency therapy in Hungary: a comparison with international trends

Methods: Anonymous survey questionnaires were dispatched to 210 Hungarian institutions consisting of questions related to care of an agitated patient showing psychotic symptoms. The results were compared with data from the latest international studies carried out in this field
Results: 92.9% of participants indicated haloperidol. 80.6% of participants would take a combination with benzodiazepines. 59.4% would use IV and 23.9% IM therapy, and 9% would apply the combination of these two. 7.7% of participants did not answer this question.
Conclusions: Administration of haloperidol and benzodiazepines is a widespread practice in Hungary which corresponds to international trend.
The international survey indicates that clinicians only use IM medication in 18 countries, whereas in 3 countries - like in Hungry – they regularly use IV medications.

Péter Szocsics
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Immunohistochemical investigation of the primary motor cortex in schizophrenic patients

We investigate post mortem brain tissue from the primary motor cortex (Brodmann's area 4) in control and schizophrenic subjects, using SMI32 and parvalbumin immunostaining. The density and soma size of the stained cells are measured. We found a decrease of the density and soma size of the giant motoneurons, but we did not find a similar effect neither on the other pyramidal neurons nor by the motoneurons in the animal model of the antipsychotic treatment. Our findings show a sensitivity of the giant motoneurons, but the clarification of the etiology needs further research.

Dalma Tényi
Doctoral School of Clinical Neurosciences, University of Pécs

The possible role of the insula in the epilepsy and the gambling disorder of Fyodor Dostoyevsky

Considering Dostoyevsky's neurological (ecstatic seizures) and psychiatric (pathological gambling) disease and the crossroads, these

two disciplines make regarding the underlying pathology, we would like to suggest a speculative theory that these two disorders have a common insular pathomechanism, namely, the malfunctioning of the risk prediction–risk prediction error coding system. Furthermore, based on Dostoyevsky's case, regarding gambling disorder in general, we would like to hypothesize that the three common gambling-related cognitive distortions (near-miss effect, gambler's fallacy, and the illusion of control) can be all attributed to the impairment of the anterior insular risk prediction–risk prediction error coding system.

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Expression changes of mitochondrial enzyme citrate synthase in parvalbumin-immunostained interneurons in the hippocampi of patients with temporal lobe epilepsy

Surgically removed hippocampal samples from patients with drug resistant temporal lobe epilepsy have been examined. Post mortem control samples were obtained from subjects without any sign of neurological disorders. Double fluorescence immunohistochemistry was used to assess the coexpression of citrate synthase and parvalbumin and the density changes of citrate synthase. Confocal microscopic analyses were carried out. The density of citrate synthase labelled mitochondria were measured in the hippocampal parvalbumin-positive interneurons. Citrate synthase-immunostaining was present in only part of the mitochondria.

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Relationships between cortisol changes and brain activation during fMRI in migraineurs and medication overusers

Stress response is controlled, among other physiological processes, by the hypothalamo-pituitary-adrenocortical axis. Acute stress could activate this system and result in increased cortisol secretion. In our study cortisol levels were measured during brain functional magnetic resonance imaging (fMRI). Saliva samples were collected from migraineurs, medication overusers and controls 5 times: in the evening before the scan day, in the morning of the scan day, before and after the fMRI. Our aim is to investigate the saliva cortisol concentration changes in the study groups and determine how cortisol changes and brain activation pattern to fearful faces are correlated.

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Reduced cortical ageing in high IQ individuals: evidence from sleep

Slow wave activity in deep NREM sleep is an index of cortical plasticity. Slow wave activity is greatly reduced even in healthy ageing, mirroring age-related changes in cognitive abilities. High IQ has been shown to be protective against many detrimental effects on health, including overall mortality, cancer and cardiovascular mortality and psychiatric as well as neurological illness, even when correcting for other risk factors. In a cross-sectional study of 159 healthy subjects we demonstrated that the age-related reduction in slow wave activity is significantly smaller in high IQ (120+) subjects, indicating more preserved cortical plasticity.