ECNP Seminar in Neuropsychopharmacology

4th and 5th of February 2021
Slovenia (virtual meeting)

CONTENTS

WELCOME

Dear Prof. Zalsman, dr. Moreno, dr. Avital, Assoc. Prof. Gregorič Kumperščak, dr. Anderluh, Assoc. Prof. Drobnič Radobuljac and all participants,

it is my great honour of welcoming everyone on the first ECNP Seminar in Slovenia. Sadly, in the face of current circumstances, we are not able to be physically together for a long weekend full of enjoyable gatherings and exchanging knowledge. However, this opportunity is very important for our close-knit community of child and adolescent psychiatrists and residents. I think I speak in name of all participants if I say that we are all looking forward to this seminar. Experiences of foreign experts will refine our knowledge and art of prescribing pharmacological agents in child and adolescent psychiatry.

I would also like to thank people who have contributed to the organisation of this seminar. First and foremost I would like to thank prof. Drobnič Radobuljac, who had the idea of this seminar in Slovenia and helped me with organisation of it. Without her contribution, this seminar would never see the light of day. I would also like to thank ECNP office, especially Clarine Sies and Annemieke Heuvink, who guided me through the complex process of organising the seminar.

Once again welcome to Slovenia, I hope you will enjoy this seminar that is before us,

Aleksander Koroša, MD
Local Co-ordinator

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, among other things, the yearly ECNP Congress. The congress attracts around 5,000 psychiatrists, neuroscientists, neurologists and psychologists from around the world and is considered to be the largest congress on applied and translational neuroscience.

ECNP organises seminars, as the one you have been invited to, 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 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 ECNP Seminars in Armenia, Bulgaria, Cyprus, Czech Republic, Estonia, Georgia, Greece, Hungary, Latvia, Lithuania, Macedonia, Moldova, Poland, Romania, Russian Federation, Serbia, Slovak Republic, Turkey, and Ukraine. In some countries we have organised an ECNP Seminar more than once.

ECNP also supports on an annual basis participation of 100 early career scientists and researchers in an intensive three-day Workshop in Nice. Other educational activities of ECNP include the yearly ECNP School of Neuropsychopharmacology in Oxford and the yearly ECNP School of Child and Adolescent Neuropsychopharmacology in Venice, organised for 50 early career psychiatrists each, and the Workshop on Clinical Research Methods in Barcelona, Spain. In addition, the journal *European Neuropsychopharmacology* promotes scientific knowledge along with publishing consensus statements.

ECNP will also continue the successful 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 Slovenia!

Gil Zalsman
Chair ECNP Educational Committee

PROGRAMME

PRE-RECORDED LECTURES

Gil Zalsman: How to Prepare a Scientific Presentation
Gil Zalsman: Research design: introduction to research methods, how to phrase a research question, basic statistics reminder and design
Avi Avital: How to phrase a research question: Attention, Methylphenidate and PTSD, basic statistics reminder and design
Carmen Moreno: Symptoms and treatment of schizophrenia: from childhood to adulthood

THURSDAY

14.15-14.45
Welcome & Introduction by Gil Zalsman

14.45-15.45
Active discussion about the pre-recorded lectures by Gil Zalsman, Avi Avital and Carmen Moreno (3x20 minutes).

15.45-17.15
Three parallel session with one ECNP and one Local Expert. Three of the participants in each session to present and get feedback form peers and then from ECNP and local experts [5 min presentation and 25 min discussion and feedback]).

17.15-17.30
Break

17.30-19.00
Three parallel session with one ECNP and one Local Expert. Three of the participants in each session to present and get feedback form peers and then from ECNP and local experts [5 min presentation and 25 min discussion and feedback]).

FRIDAY

14:30-15:30
Lecture discussion by Gil Zalsman, Avi Avital and Carmen Moreno (3x20 minutes)

15:30-17:00
Three parallel session with one ECNP and one Local Expert. Three of the participants in each session to present and get feedback form peers and then from ECNP and local experts [5 min presentation and 25 min discussion and feedback]).

17.00-17.15
Break

17.15-17.45
Group presentations parallel sessions (3x10 minutes) + discussion

17.45-18.00
Closing

FACULTY

PROF. GIL ZALSMAN M.D., M.H.A. (SEMINAR LEADER)

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 then at 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 Adjunct 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 suicidal behavior, gene-environment interactions in childhood depression and suicidal behavior and other psychiatric disorders in adolescence.

Prof. Zalsman has published more than 250 papers, of them 125 original papers, dozens of reviews, book chapters, three edited books and actively participated in more than a 250 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 a full 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 is a counselor and past chair of education at the executive committee of the European College of Neuropsychopharmacology (ECNP) and the past president of the Israeli Society of Biological Psychiatry (ISBP). He chaired the 14th European Symposium for Suicide and Suicidal Behavior (ESSSB), held in Tel Aviv and Co-Chaired the IASR/AFSP annual suicide summit in Las Vegas, November 2017.
Prof. Zalsman served as an invited speaker in the major psychiatric congresses worldwide including APA, EPA and ECNP.

He is married with two children and resides in Tel Aviv suburb, Israel.

Email: zalsman@tauex.tau.ac.il

Website: www.zalsman.org
Wikipedia: https://en.wikipedia.org/wiki/Gil_Zalsman

DR. CARMEN MORENO, MD, PHD

Dr. Carmen Moreno (MD, PhD) is a Child and Adult Psychiatrist at the Hospital Gregorio Marañón in Madrid and Associate Professor at Complutense University School of Medicine, Madrid, Spain. Dr. Moreno completed her MD and PhD degrees at Autónoma University and Complutense University in Madrid, followed by a Research Fellowship in Child and Adolescent Psychiatry at Columbia University/New York Psychiatric Institute, New York, USA.

Dr. Moreno has been focusing her career on severe early-onset psychiatric disorders, mainly psychotic and affective disorders, and autism and other neurodevelopmental disorders. She is actively involved on multinational research projects exploring key biological aspects of first-episode psychotic disorders, including multimodal neuroimaging, intermediate mechanisms such as inflammation and oxidative stress, and metabolomics. Her efforts are also focused on exploring secondary effects of psychopharmacological interventions and towards development of new treatment interventions in young patients. Dr. Moreno is actively involved on the development of clinical psychopharmacology in children and adolescents. She has served as consultant for the European Medicines Agency (EMA) and is currently serving as Co-chair of the ECNP Adolescent Child and Adolescent Neuropsychopharmacology Network, and the ECAPN, integrated in the EmprEMA. She has previously served in the ECNP Membership Committee.

Dr. Moreno has published more than 70 peer-reviewed original publications and book chapters and has presented numerous scientific communications. She has participated in more than 25 research projects, including 7 with European Union funds. She has been awarded the ECNP Research Fellowship Award, and the Awards for Young Scientists and Senior Scientists of the Spanish Association of Biological Psychiatry.

ASSOC. PROF. AVI AVITAL, M.A, B.A.

Avi Avital, M.A, B.A., graduated in Psychology and Statistics and cum laude in Psychobiology from the Haifa University in Haifa, Israel.
He was a visiting scientist at the Stanford Institute for Neuro-Innovation & Translational Neuroscience (SINITN) and US Army Research Laboratory (ARL), Stanford University, CA, USA

He has worked as a Scientific consultant Neurobiology at the Weizmann Institute of Science and held positions as Head of the Center for Psychobiological Psychiatry and as a Board member of the Israeli Society for Biological Psychiatry.
Avraham Avital is currently an Assistant Professor in the Faculty of medicine at the Technion – Israel Institute of Technology, and vice director of research authority in the Emek Medical Center.

As a Ph.D student with Prof. Gal Richter-Levin, they discovered the effects of exposure to juvenile stress on emotional and cognitive coping abilities in adulthood.
He then moved to the Weizmann Institute of Science and together with Prof. Menahem Segal, he continued his research on stress and found the unique role of mineralo- and Gluco-corticoid system in the mechanism of neural plasticity following stress. Starting his interest in translational neuroscience, he also studied and found blood markers for the severity of Schizophrenia symptoms.

After joining the Technion and Emek medical Center, he has established the Behavioral Neuroscience lab. Since then he has been investigating the regulation and dysregulation of attention and social cooperation processes in health and disease, combining state-of-the-art behavioral technologies with molecular and physiological tools. During these studies he has developed a fully computerized social cooperation maze, currently enabling to decipher the genetics of social cooperation and also subserving a groundbreaking collaborative research on the dysregulation of sociability in Autism (with Prof. Alejandro Sosnik and Prof. Herman Wolosker).

His ongoing translational research on attention dysregulation has led to a newly EMG-based instrument (patent reg. #63524) and the establishment of a startup company (Mindtension, ltd) that further the R&D and implementing this technology to better diagnose and treat ADHD, ‘circumstantial’ ADHD (e.g. medical residents and combat pilots, following workload), and the involvement of the attention system in stress (i.e. PTSD).

Avital’s research along the years has been extensively funded by the Israeli ministry of defense, US army/NIH and the ISF.

ASSOC. PROF. HOJKA GREGORIČ KUMPERŠČAK, MD, PHD

Assoc. Prof. Hojka Gregoric Kumperscak, MD, PhD was born in Maribor, Slovenia in 1970. She finished Faculty of Medicine in Ljubljana, Slovenia in 1996. She was trained in child and adolescent psychiatry in Slovenia and abroad (Italy, UK, Germany and Switzerland). She has held the Chair of the Department of Psychiatry in the Faculty of Medicine, University of Maribor in Slovenia, since January 2017, and has been Head of the Child and Adolescent Psychiatry Unit, University Clinical Center in Maribor since 2008. She is a President of Slovenian Association for Child and Adolescent Psychiatry.

She is also the National Coordinator – Training Director for Child and Adolescent Psychiatry in Slovenia and UEMS-CAP secretary since 2020. She is member of editorial board for WPA- CAP Journal.

Her clinical work is mainly with adolescents with personality and psychotic disorders. The research work is focused in genetic of developmental disorders and early onset schizophrenia. She is Adolescent Identity Treatment psychotherapist and trainer. She has written many scientific articles and book chapters on different CAP topics.

DR. MARIJA ANDERLUH, MD, PHD

Dr. Anderluh has been working as a consultant in child psychiatry at the University Children's Hospital since 2004. Since 2016 she has been a head of Child Psychiatry Unit at the University Children's Hospital, leading inpatient and outpatient services with multidisciplinary teams and a specialist autism service, as well as newly established Center for evidence based early interventions. She has been leading a successful pilot study of introduction of parenting programs from the well-researched Incredible Years series to Slovenia. Based on this work funded through the Norwegian Financial Mechanisms, the permanent funding was obtained from the National Insurance Agency. Today, there are 11 centers delivering the program in seven different regions across the country in three different sectors, mental health services, local social work services, as well as municipality of Ljubljana. She has been dedicated to support schools in supporting children's emotional and social well-being for more than a decade. In 2019 a parallel program from the Incredible Years series for teachers in primary schools and kindergartens has started to be introduced to Slovenian schools to promote emotional and social development as a matter of general prevention. She is currently working with the Ministry of Education to support sustainable funding and delivery of the early evidence based interventions in Slovenian schools.

Apart from being clinically active she has been a dedicated mentor to the trainees in child & adolescent psychiatry and paediatrics for more than 15 years.

In 2018 she took an active role in preparation of the Resolution on National Mental Health 2018-2028 in Slovenia at the Ministry of Health. In 2018, the Resolution has been confirmed by the Slovenian parliament. She has been part of the working group responsible for the implementation of the National Mental Health Plan 2018-2028 to support the mental health of children & adolescents since then. In the last two years ten Child & adolescent outpatient multidisciplinary teams – out of 26 planned – have been established as part of the implementation of the National Mental Health Plan in Slovenia.

She has been trained in psychiatry at the University Psychiatric Hospital in Ljubljana and at the Institute of Psychiatry and Maudsley Hospital in London, where she has been on a 15 months contract as clinical researcher at the Eating Disorders Unit. The clinical and research work had been done under the supervision of prof. Janet Treasure and prof. Ulrike Schmidt.

She participated in the Workshop Professional Development of Young Psychiatrists in 2000 lead by prof. Norman Sartorius, as well as two research seminars organised by ESCAP, in 2001 and 2002. She participated in the first ECNP workshop on Neuropharmacology in Child Psychiatry in Venice in 2012.

She lectured at different scientific and professional meetings nationally and internationally. In 2018 and 2019 she contributed as temporary advisor to WHO on workshops on Reduction of Child Maltreatment, organised by the Nordic Council of Ministers and WHO in Riga and Vilnius.

She has participated in two international research projects and has led two multicentric research projects funded by Slovenian Ministry of Health in 2017-2019 and 2020-2023, supporting further implementation of IY parenting programs.

She is an author or co-author of more than 15 well recognised scientific papers, which have been cited in more than 1200 independent scientific papers.

ASSOC. PROF. MAJA DROBNIČ RADOBULJAC, MD, PHD

I am a 44-year-old consultant child and adolescent psychiatrist and an associated professor for psychiatry. Currently I'm in charge of an 18-bed open adolescent psychiatric department and a 10-bed child and adolescent secure unit, a tertiary outpatient clinic and a 24-hour outpatient emergency clinic.

I received my medical degree at the University of Ljubljana in 2002, worked as a resident and young researcher at University Psychiatric Hospital Ljubljana from 2003 and completed EU certified training in child psychiatry in 2012. I'm specialized in working with adolescents with emerging personality disorders, depression, anxiety disorders and psychosis. I also completed systemic family therapy training and Child Attachment Interview training.

I spent a part of my education and research abroad (3 months as an honorary clinical research fellow at the Acorn Lodge Children's Unit in Bethlem Royal Hospital, Maudsley in London, UK; 2-month elective in Royal Melbourne Hospital in Australia).

Since 2015 I have been lecturing in the field of child and adolescent psychiatry in Medical Faculty, University of Ljubljana where I was nominated an associated professor of psychiatry in December 2019.

At the moment I'm a part of a large research project on the impact of psychological stress in juvenile diabetes, as well as other ongoing projects (attitudes of health workers toward adolescent NSSI, evaluation of an indicated prevention program for mental disorders in children, phenomenology of autism vs. psychosis, antipsychotics' side effects in children).

I'm a member of national and international societies, have national and international publications and conference attendances. Please refer to the CV and Bibliography for further details.

PRESENTATIONS

“GENERAL ECNP INTRODUCTION”

- More than 50 scientific meetings held every year
- 400 early career scientists trained every year

The ECNP Congress

Annually attracts more than 5,000 of the world's neuroscientists, psychiatrists, neurologists and psychologists

For early career scientists:

- Registration discounts
- Special reduced with-a-member rate
- Free registration for abstracts accepted for publication in the congress supplement
- ECNP Excellence Awards for the best abstracts
- ECNP Poster Awards for the best posters
- Career Development Sessions, Science-on-the-Rocks

ECNP

European Neuropsychopharmacology

- IF 3.853
- 12 issues per year
- 500,000 downloads annually
- Top 10% of psychiatry and pharmacology journals

ECNP

ECNP Networks

- Nineteen multicenter European collaborations
- Funded by ECNP
- Covering major psychiatric diseases and platform technologies
- Important springboard for European grants

ECNP Networks & Thematic Working Groups

Developing early career scientists

- ECNP Workshop
- Research Methods Workshop
- ECNP Research Internship
- ECNP School
- ECNP Child and Adolescent School
- Seminars
- Grants and awards

All participants at ECNP early career scientist meetings **supported by ECNP** for registration and accommodation

ECNP neuroscience applied

Stay tuned . . .

- Join us on social media – www.facebook.com/myecnp and @ECNPtweets
- Sign up for the ECNP newsletter

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GIL ZALSMAN: “HOW TO PREPARE A SCIENTIFIC PRESENTATION”

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How to prepare a scientific presentation

Prof. Gil Zalsman MD, MHA
ECNP

ECNP Seminar

EC ECNP

Learning

- Definition of *any* kind of learning?

ECNP

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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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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Organising 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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Introduction

- Context
- Study question
- Relevant knowledge on issue

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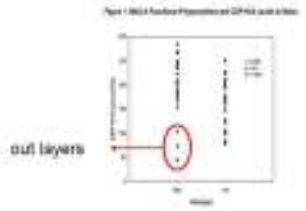
Major Findings

- 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 *(Continued)*

- 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 Slides *(Continued)*

- 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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Making Slides *(Continued)*

- Best contrasts

Yellow on Blue

or

Black on White

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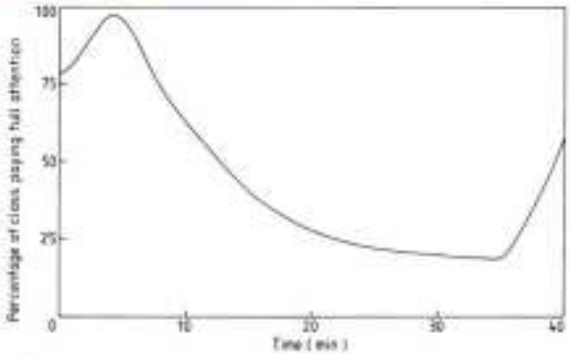
Audience Attention Curve



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The TED Style

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

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The Learning Rule

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

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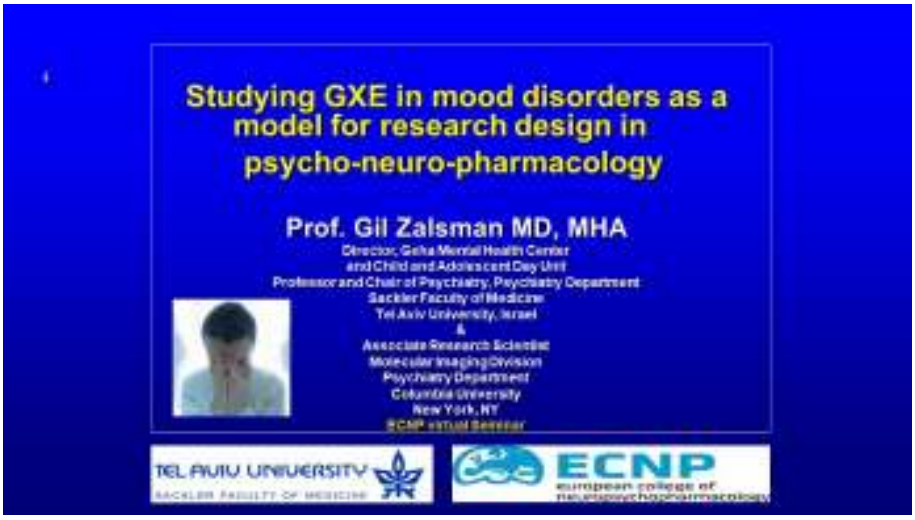
GIL ZALSMAN: "RESEARCH DESIGN: INTRODUCTION TO RESEARCH METHODS, HOW TO PHRASE A RESEARCH QUESTION, BASIC STATISTICS REMINDER AND DESIGN"



How do I start?

Neurobiology of adolescent suicide

Three advices for building a career in psychiatry research

- Pick a subject
- Find a mentor
- Built a database

Create your own DATA BASE

e.g. Neurobiology of Pediatric Depression and suicide

A birth of an hypothesis

- Depression runs in families
- GxE interaction seems logical but failed replication
- New data on brain development appeared
- A new hypothesis needed a proof
- Animal model proved GxExT interaction

Facts about pediatric depression

- Depression is common
- Depression runs in families
- Depression is different before & after puberty

1. Prevalence
2. Gender ratio
3. Treatment efficacy

Depression in Children & Adolescents

Early Childhood:

- looks sad

- tearful
- slow movements or **irritability**
- monotone voice
- hopeless
- self in negative terms
- school problems
- **somatization!!**

Late childhood and adolescents:

- low self esteem
- apathy
- irritability

- **anxiety**
- low concentration
- **suicide attempts**

Familial Transmission and Gene-Environment Interaction

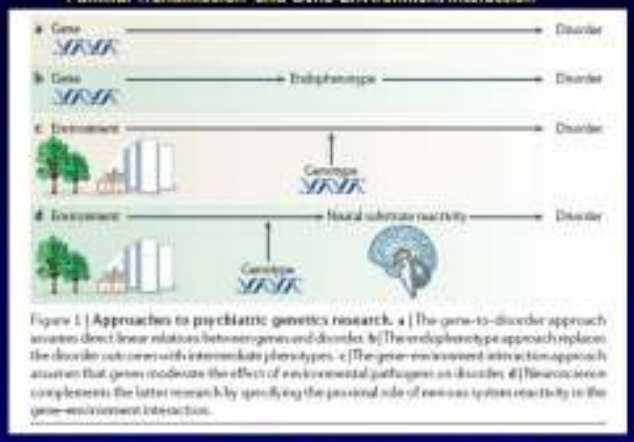


Figure 1 | **Approaches to psychiatric genetics research.** a | The gene-to-disorder approach assumes direct linear relations between genes and disorder. b | The endophenotype approach replaces the disorder outcome with intermediate phenotypes. c | The gene–environment interaction approach assumes that 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

Suicidal Behavior Runs in Families

Direct main effect approach

- TPH1
- SERT
- COMT
- MAO
- 5HT's
- DR
- NET
- BDNF
- Wolfram (WFS1)
- Etc……
- TPH2….

→ Equivocal results
→ MZ>DZ but far from 100%

G X E Interaction

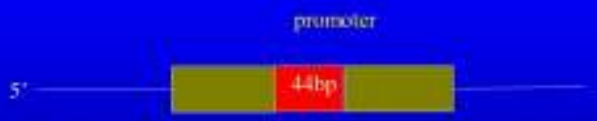
Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

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,[2] 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.

Caspi et al., Science 2003

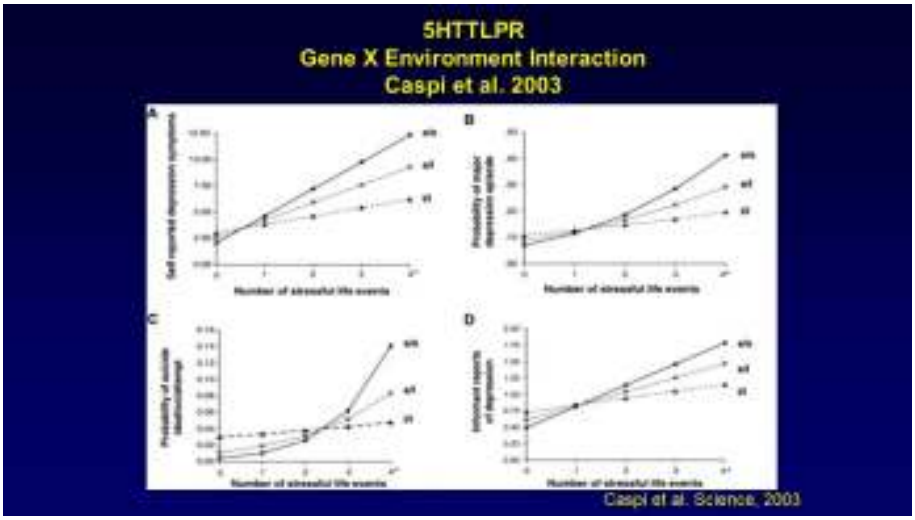
5-HTT-LPR - serotonin transporter linked polymorphism region

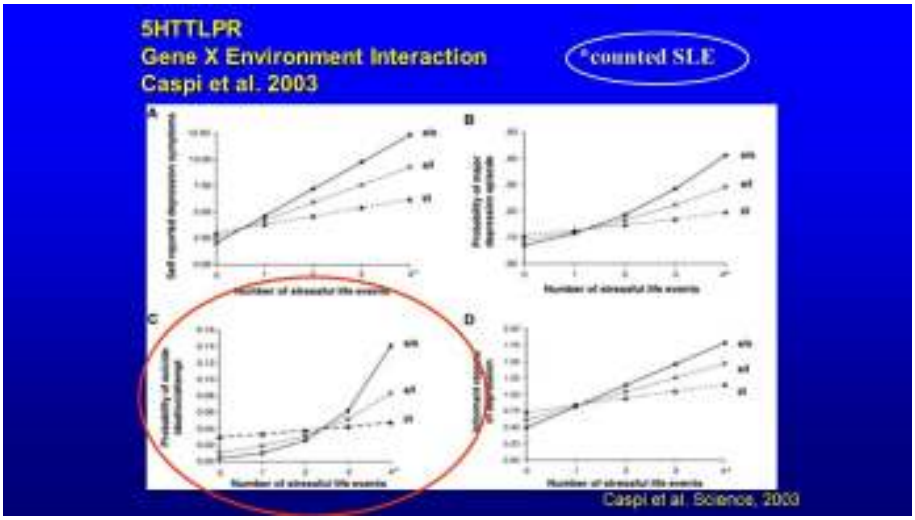


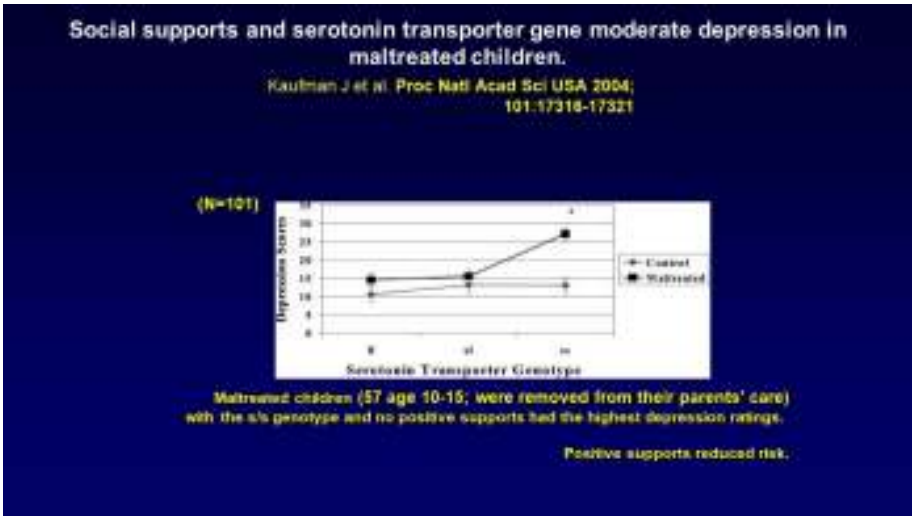
A functional polymorphism consists of two common alleles, a short (S) and long (L) variants, differing by 44 bp

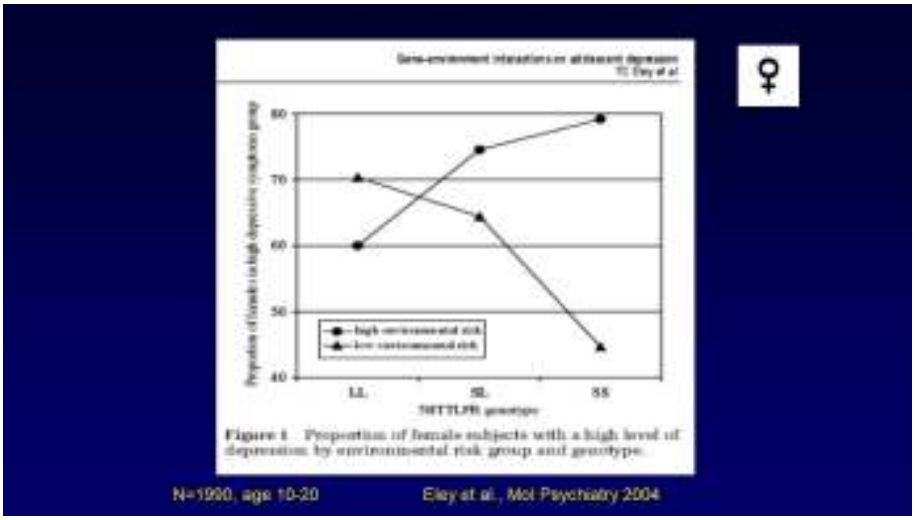
S<<L

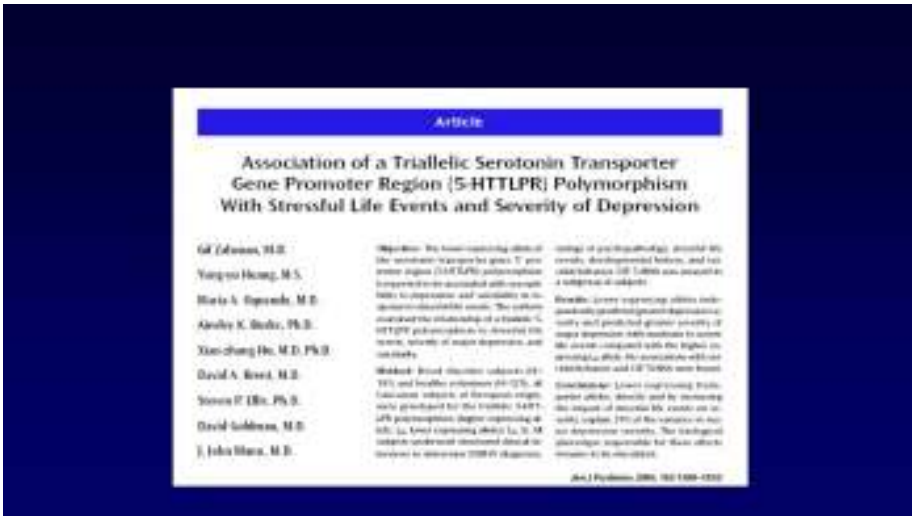
Lesch et al. 1994, Heils et al. 1996

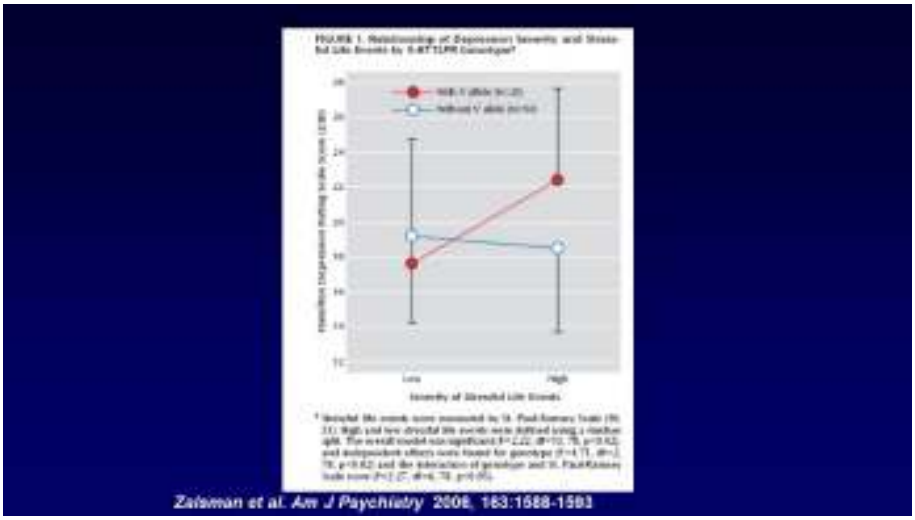

5HTTLPR
Gene X Environment Interaction
Caspi et al. 2003
Caspi et al. Science, 2003


5HTTLPR
Gene X Environment Interaction
Caspi et al. 2003
*counted SLE
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)
Depression Score
Control
Maltreated
Serotonin Transporter Genotype
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.


♀
LL
SL
SS
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


Zalsman et al. Am J Psychiatry 2006; 163:1588-1593

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; Kirby 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 ($P=.00017$) 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.

One sleepless night hypothesis

- G X E X T Interaction

Review

Timing is critical: Gene, environment and timing interactions in genetics of suicide in children and adolescents

G. Zalsman

Zalsman G., Eur Psychiatry, 2010

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

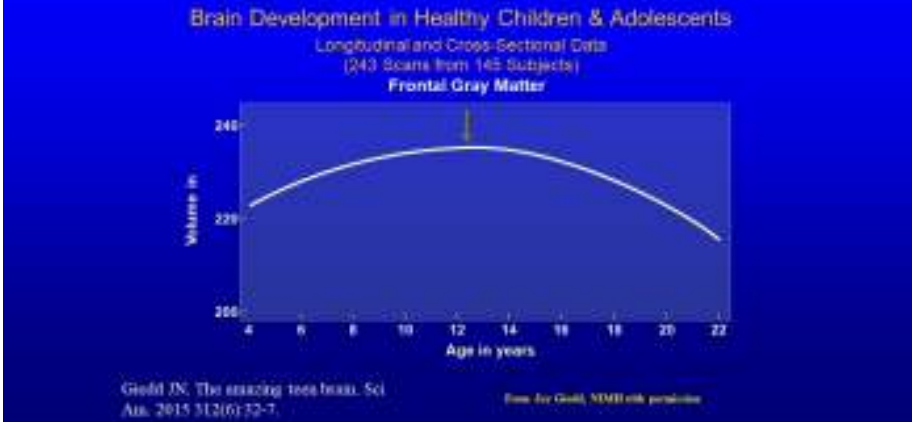
- The brain is developing until age 22-23y.

Giedd JN. The amazing teen brain. Sci Am. 2015 312(6):32-7.

- SLE "meets" a different brain in every time point of development

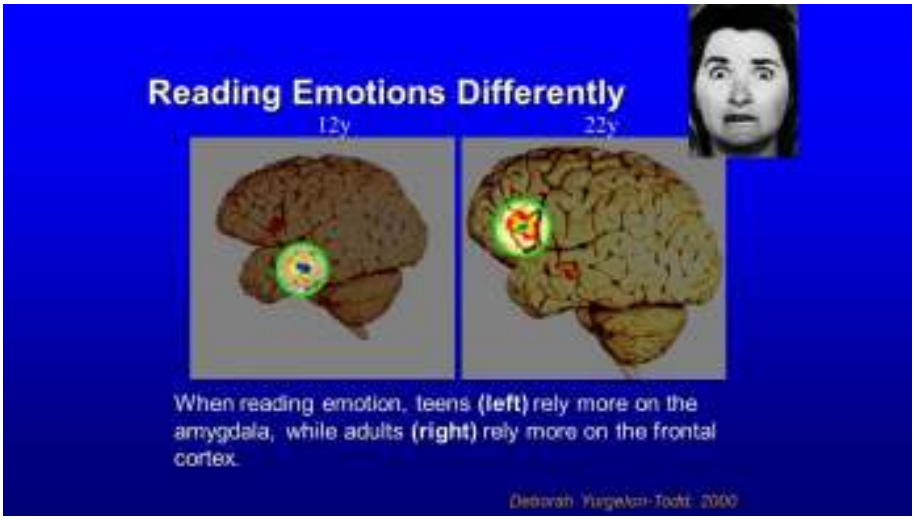
Are brains of children and adolescents different?

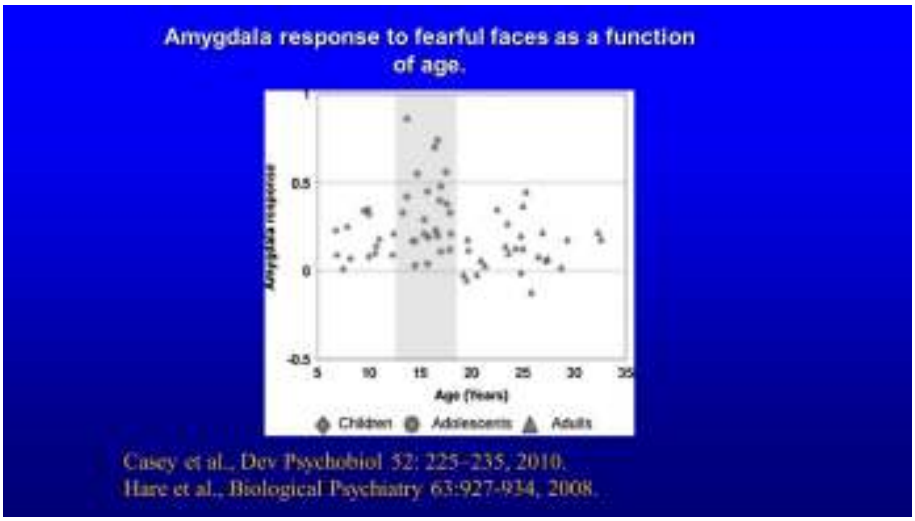
Gray Matter



Giedd JN. The amazing teen brain. Sci Am. 2015 312(6):32-7.


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


Reading Emotions Differently
12y
22y
When reading emotion, teens (left) rely more on the amygdala, while adults (right) rely more on the frontal cortex.
Deborah Yurgelun-Todd, 2000


Amygdala response to fearful faces as a function of age.
Amygdala response
0.5
0
-0.5
5
10
15
20
25
30
Age (Years)
Children
Adolescents
Adults
Casey et al., Dev Psychobiol 52: 225–235, 2010.
Hare et al., Biological Psychiatry 63:927-934, 2008.

WKY Rat
Animal model for depression, despair and anhedonia

GxExT

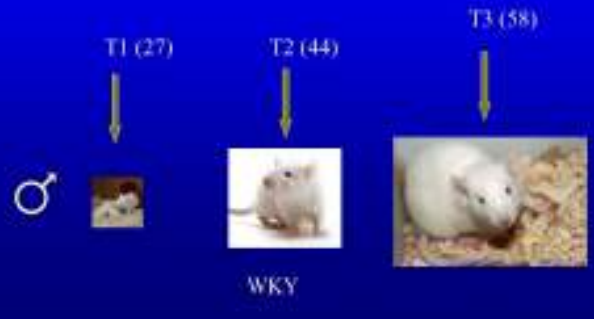
ELSEVIER

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

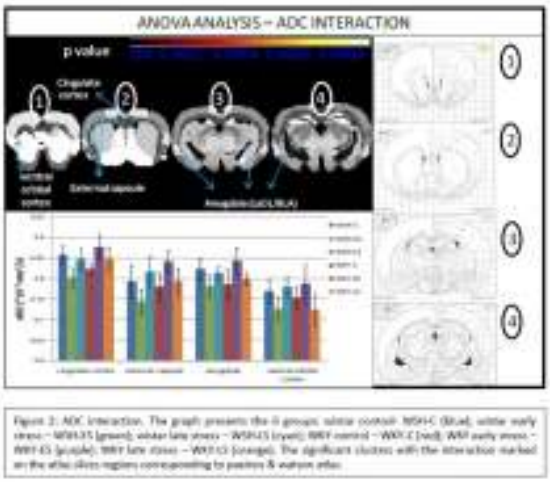
Gil Zahman[1,2,*], Anthay Gutman[1,2], Liat Shbiro[3], Ruth Rosenan[3], J. John Mann[1], Aron Weller[3]

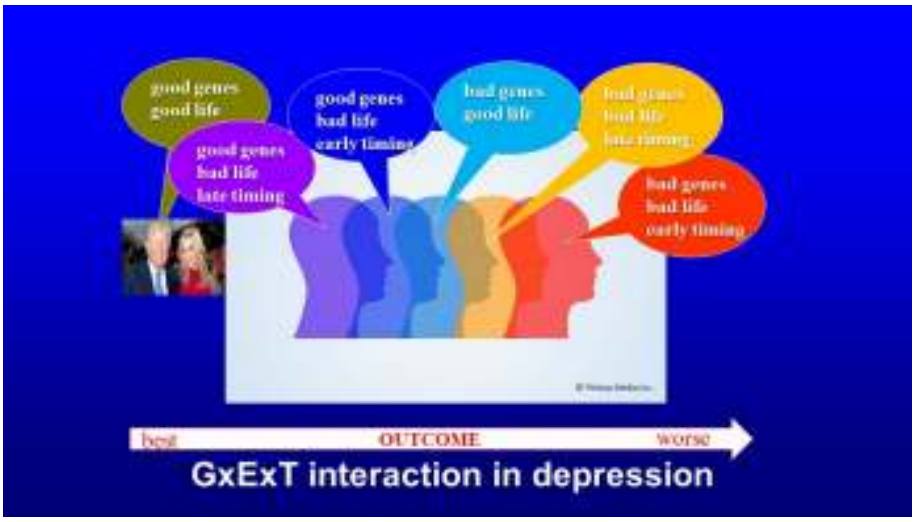
(Exposure to stress) at different developmental windows

G x E x Gender x T




Rats MRI
Tel Aviv University MRI


ANOVA ANALYSIS – ADC INTERACTION
p value

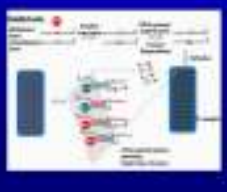

good genes
good life
good genes
bad life
early timing
good genes
bad life
late timing
bad genes
good life
bad genes
bad life
late timing
bad genes
bad life
early timing
best
OUTCOME
worse
GxExT interaction in depression

Epigenetics may be the link between G and E

Epigenetics

- Changes in DNA that change gene expression. These changes can be permanent (cell type) or temporary (developmental window , environmental ques)
- Types:

1. Methylation
2. Histones modification
3. Non coding RNAs=MiRNA



From: Yaron Goren with permission

Geha

Future Direction: Micro RNA as a biomarker

Short RNA fragment that prevents the production of a particular protein by binding to and destroying the messenger RNA that would have produced the protein.

A genetic Isolate- the Bedouin Tribes in Israel

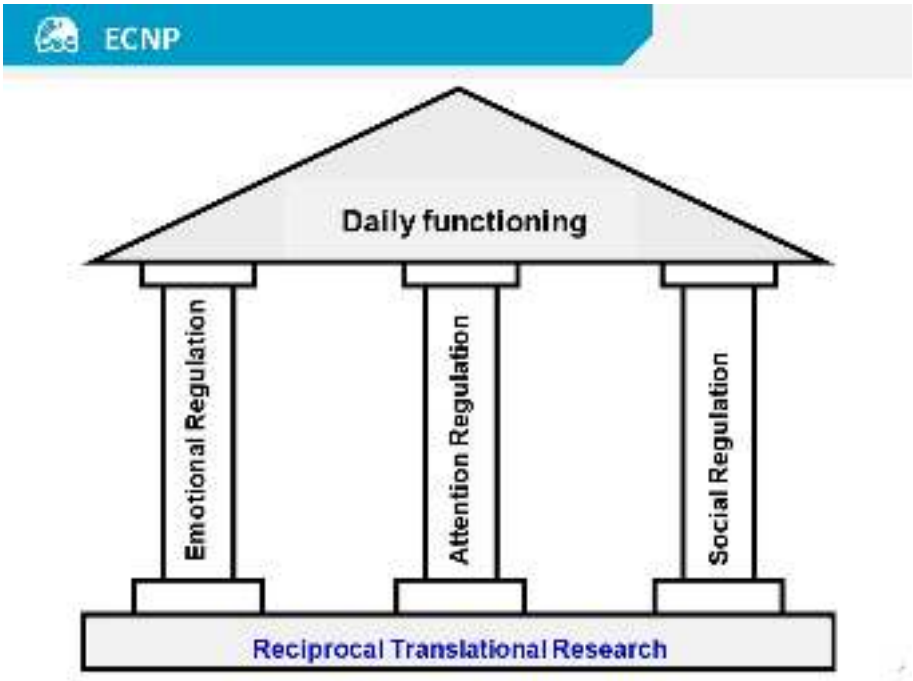
- Stratification bias in genetic studies
- Bedouin a are still a genetic isolate
- Intra-familial marriage
- High rates of medical inherited diseases
- High rates of depression and suicide
- Micro RNAs as a marker to SSRI response and subtyping of depression-suicide phenotypes
- Blood from suicidal- depressed patients and healthy family members

A birth of an hypothesis

- Depression runs in families
- GxE interaction seems logical but failed replication
- New data on brain development appeared
- A new hypothesis needed a proof
- Animal model proved GxExT interaction

Thank you

AVI AVITAL: "HOW TO PHRASE A RESEARCH QUESTION: ATTENTION, METHYLPHENIDATE AND PTSD, BASIC STATISTICS REMINDER AND DESIGN"



Outline

ECNP

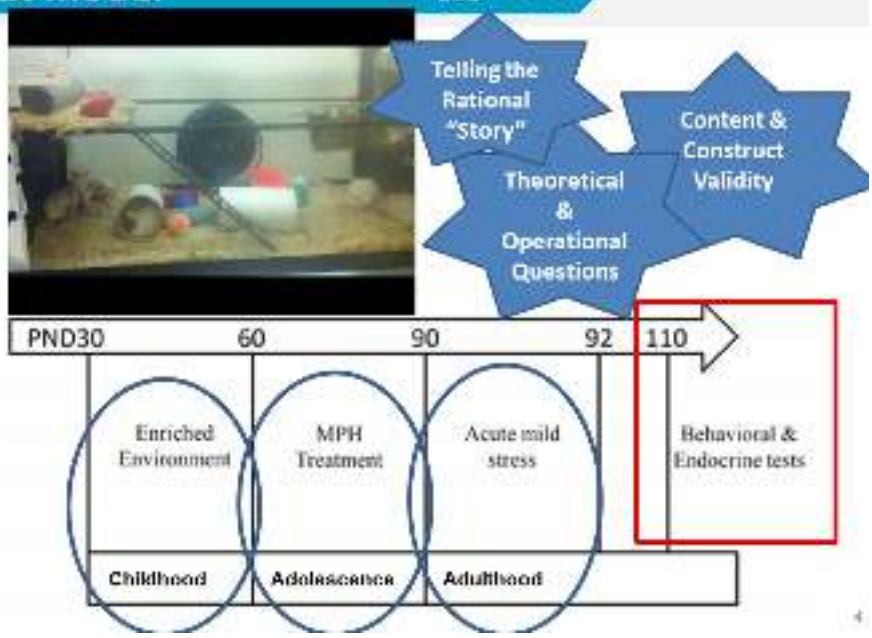
MPH abuse.

Implication of stress-sensitive period in an animal model for PTSD and examining possible treatment.

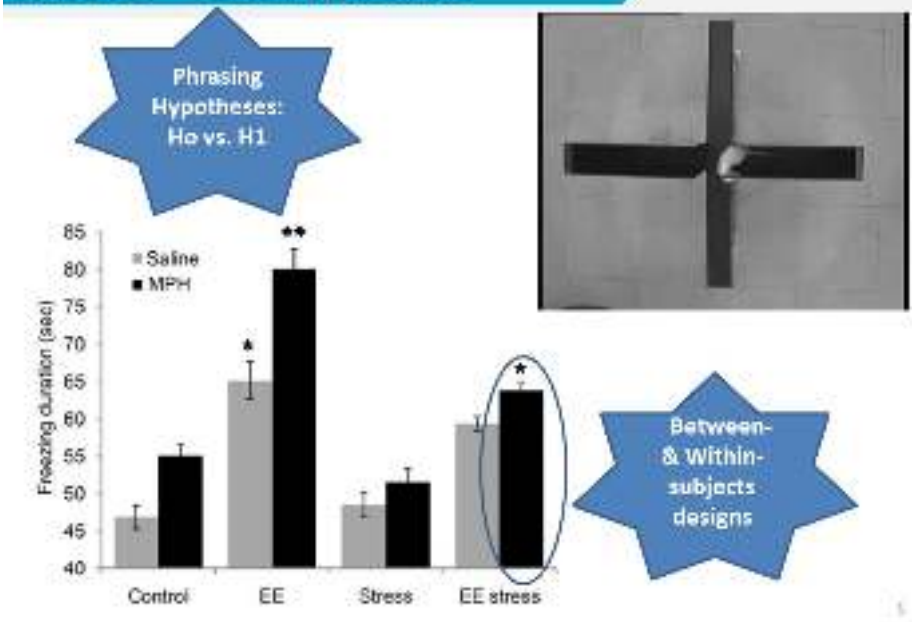
Behavioral and physiological effects of 'Dog-therapy' on adolescents suffering from PTSD.

Rat model

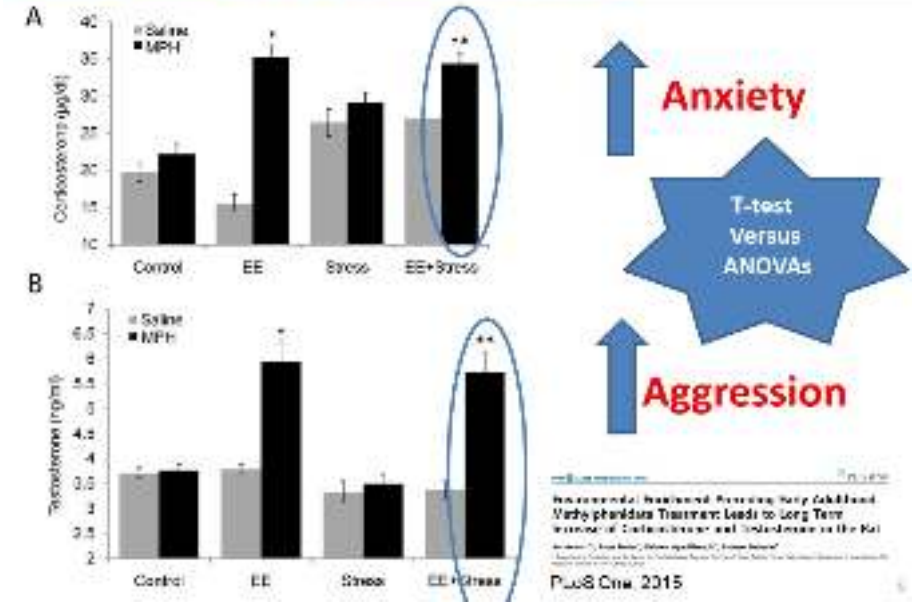
ECNP



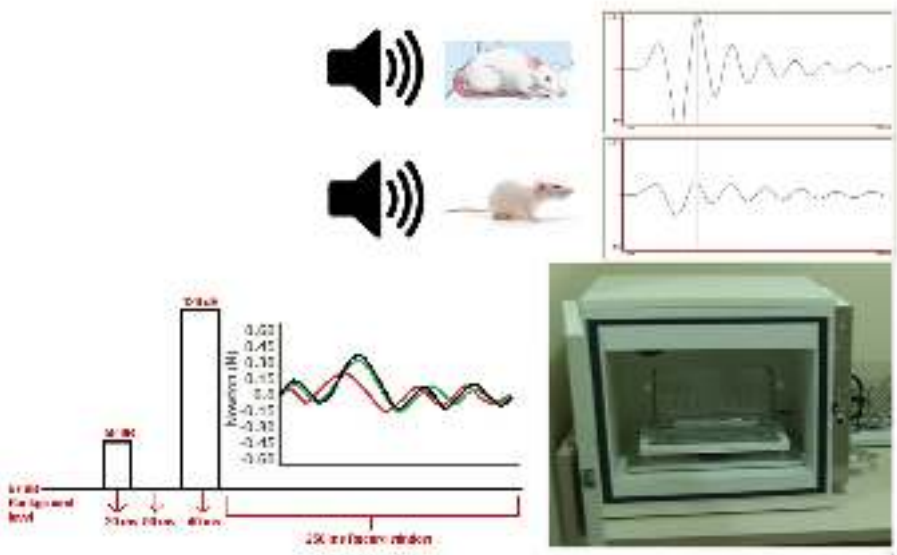
Results – Anxiety/stress



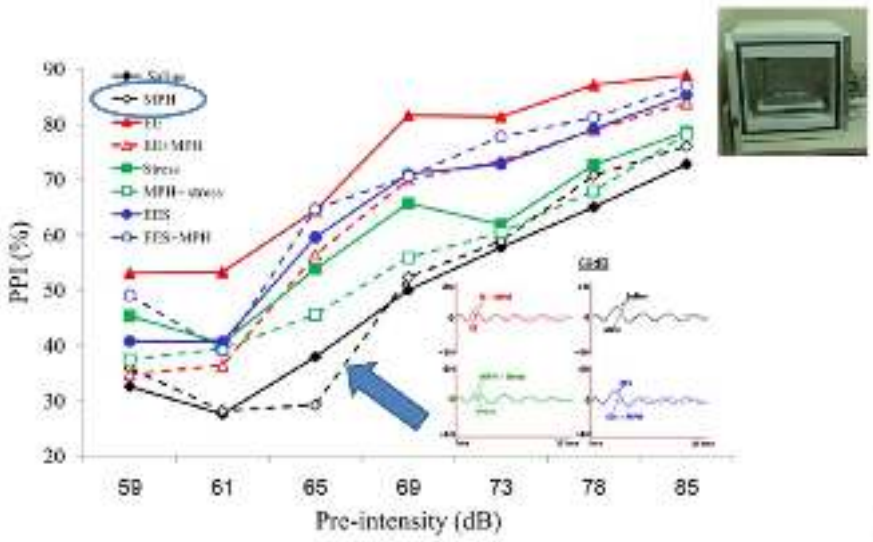
Results – Endocrine modulation



Methods – ASAT by PPI



Results – ASAT by PPI



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Methods

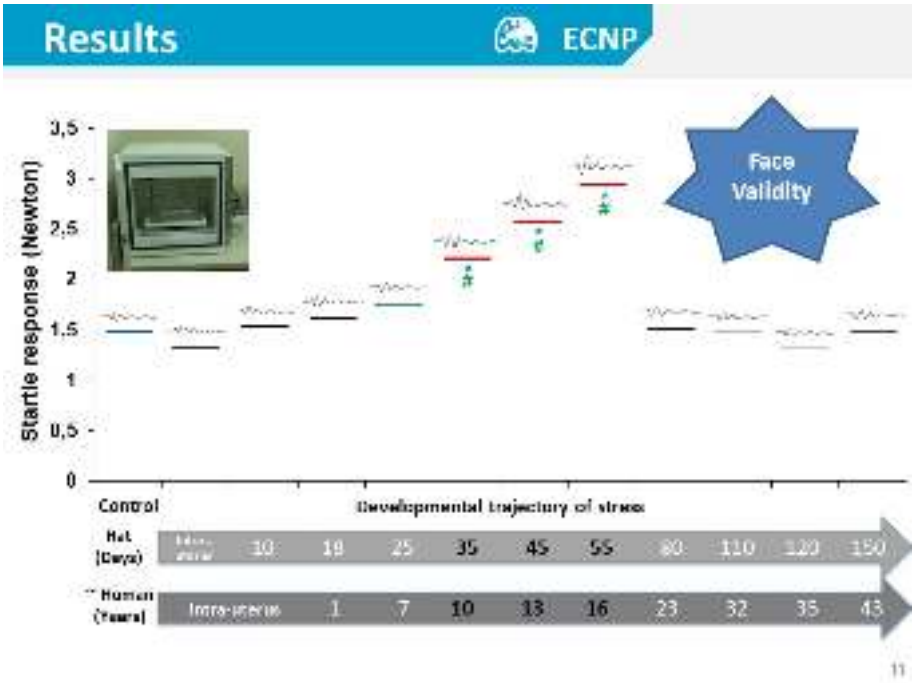
ECNP

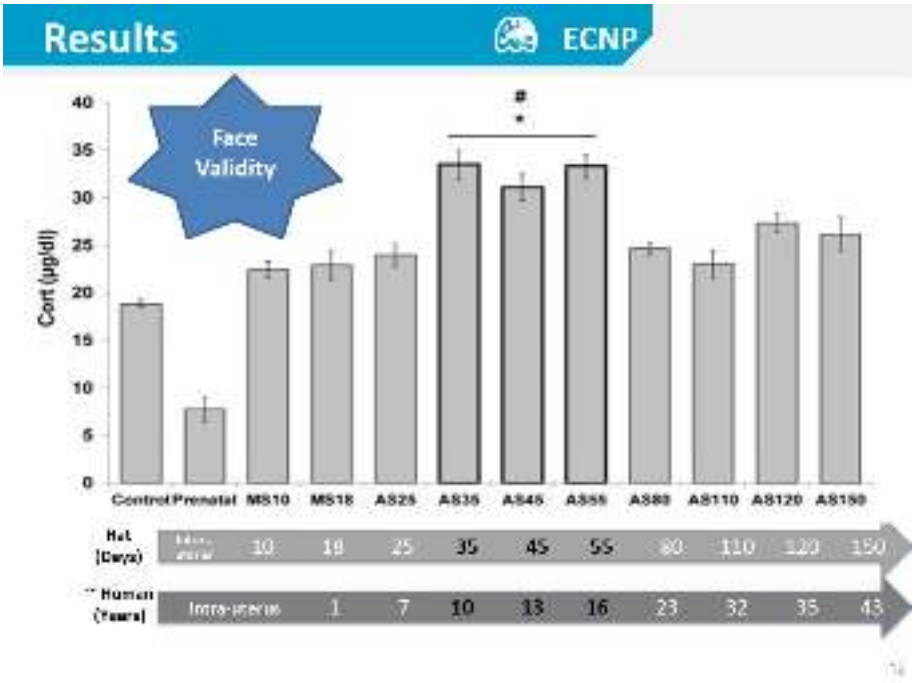
Stress protocol consisted of 3 different stressors applied during 3 consecutive days

(Room light set at 1000±25lux):

Face Validity

Psychoneuroendocrinology 2015 a b 2019


Results
ECNP
Face Validity
Startle response (Newton)
3,5
3
2,5
2
1,5
1
0,5
0
Control
Developmental trajectory of stress
Rat (Days)
Human (Years)
Intra-uterine
10
19
25
35
45
55
80
110
120
150
1
7
10
13
16
23
32
35
43


Results
ECNP
Face Validity
Cort (µg/dl)
40
35
30
25
20
15
10
5
0
Control
Prenatal
MS10
MS18
AS25
AS35
AS45
AS55
AS80
AS110
AS120
AS150
Rat (Days)
Human (Years)
Intra-uterine
10
19
25
35
45
55
80
110
120
150
1
7
10
13
16
23
32
35
43

Introduction

ECNP

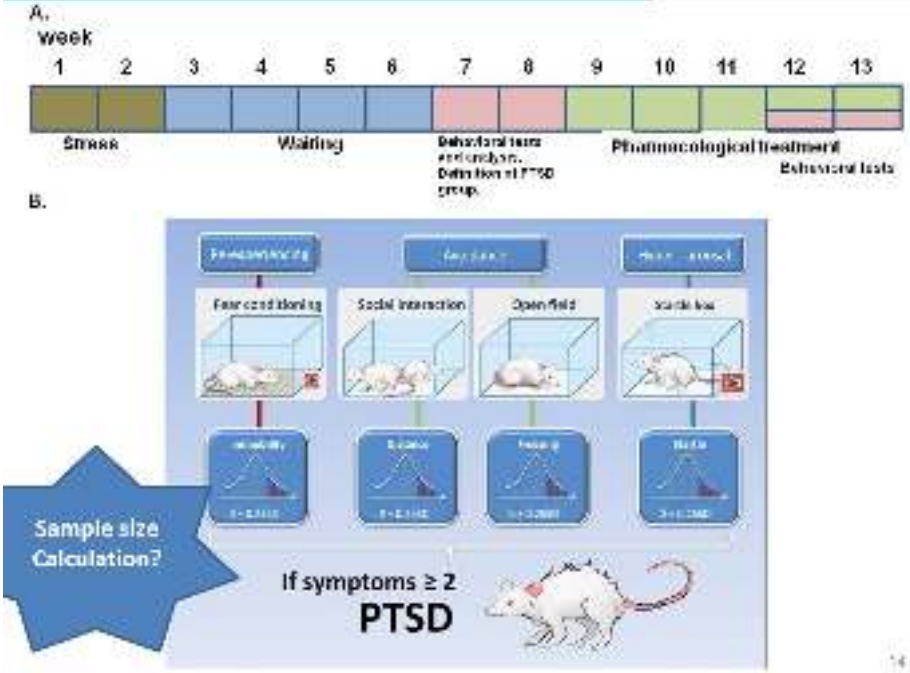
The characteristic symptoms of post-traumatic stress disorder (PTSD) include: re-experiencing, avoidance and hyper-arousal.

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.

Hypothesis

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

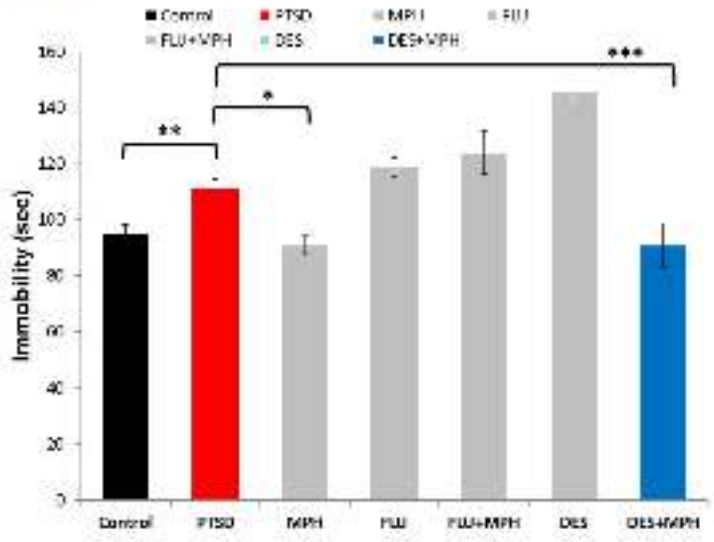
Translational Psychiatry, 2014

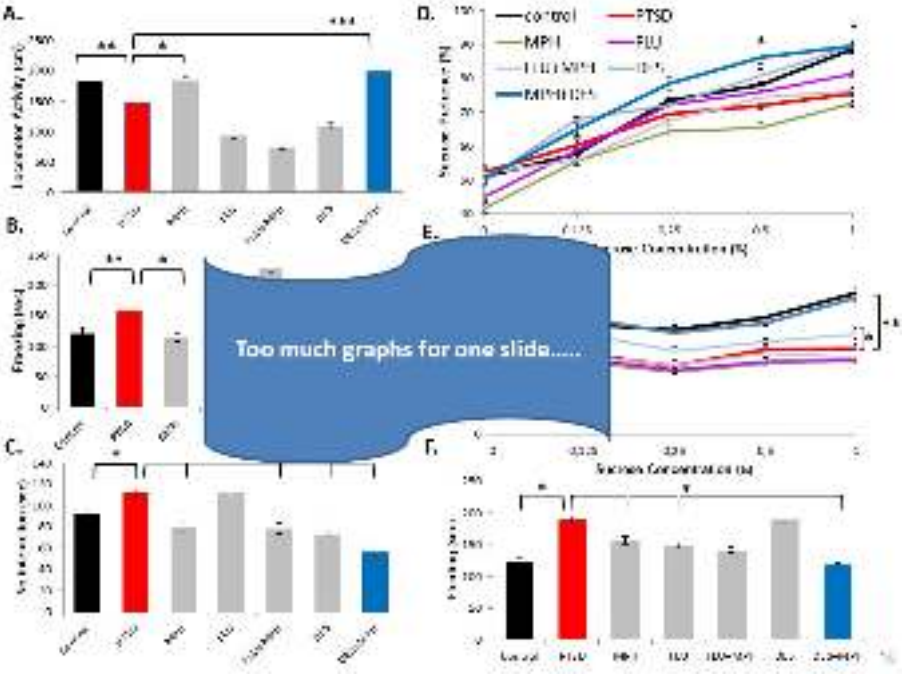


Results

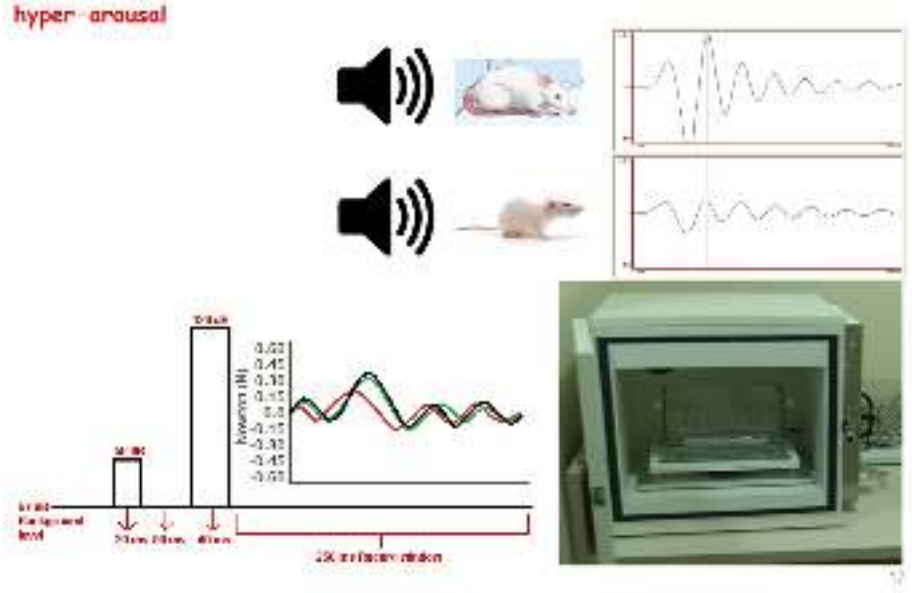
ECNP

Re-experiencing

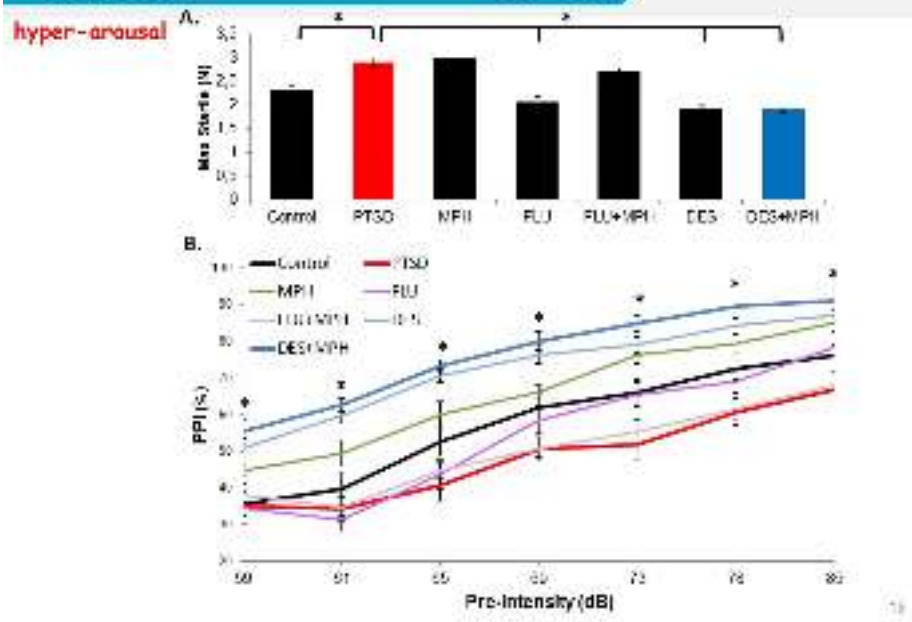




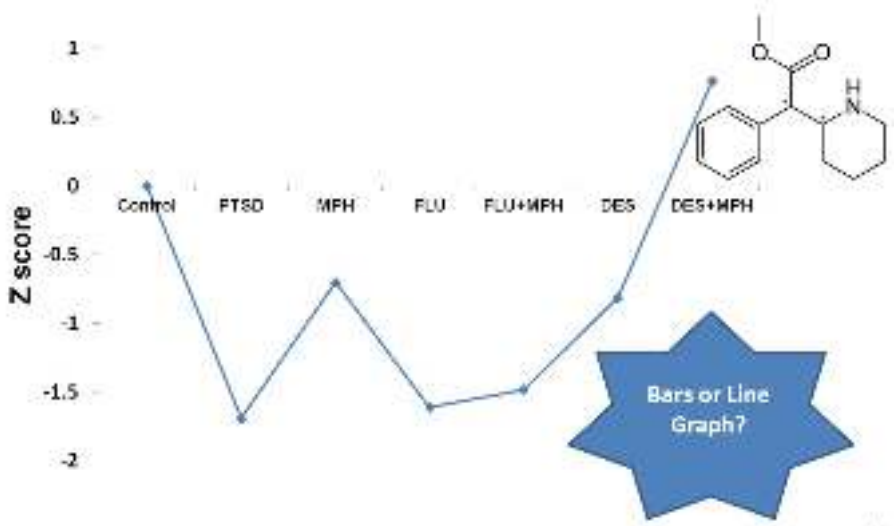
Methods



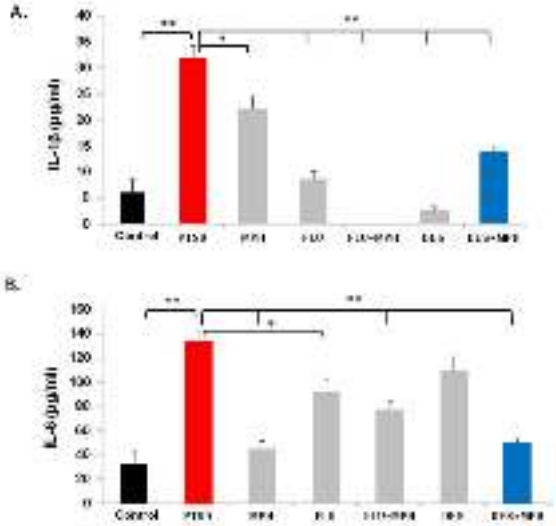
Results



Summary



Results - possible mechanism



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.

Outline

ECNP

MPH abuse.

Implication of stress-sensitive period in an animal model for PTSD and examining possible treatment.

Behavioral and physiological effects of 'Dog-therapy' on adolescents suffering from PTSD.

Introduction

ECNP

In recent years, non-pharmacological approaches and specifically animal-therapy were suggested to remedy different disorders such as ADHD and PTSD. However, the literature is sparse and provide no mechanistic evidence for the possible beneficial effects on daily living and functioning.

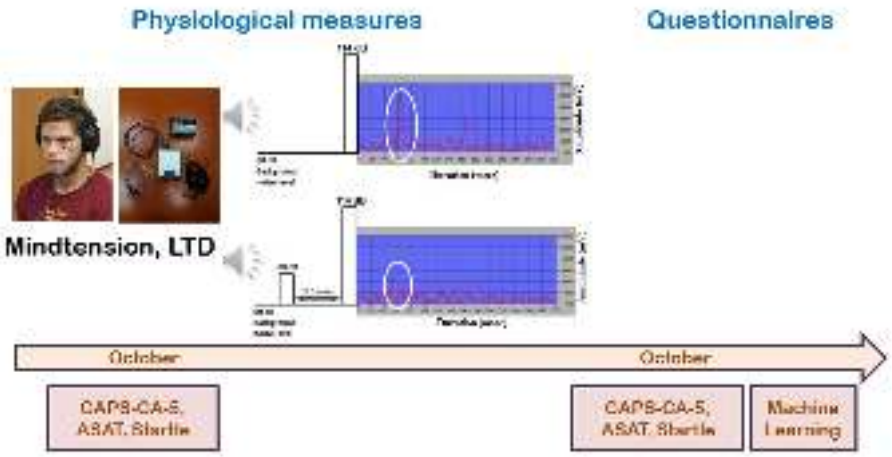
Objectives

ECNP

- We aim to methodologically and physiologically examine the influences of 'Dog-therapy' on PTSD symptoms in adolescents, and specifically on emotional and attentional dysregulations.

- To examine the dog subject interaction effects on the dogs' attention and emotional reactivity.

Procedure and Methods

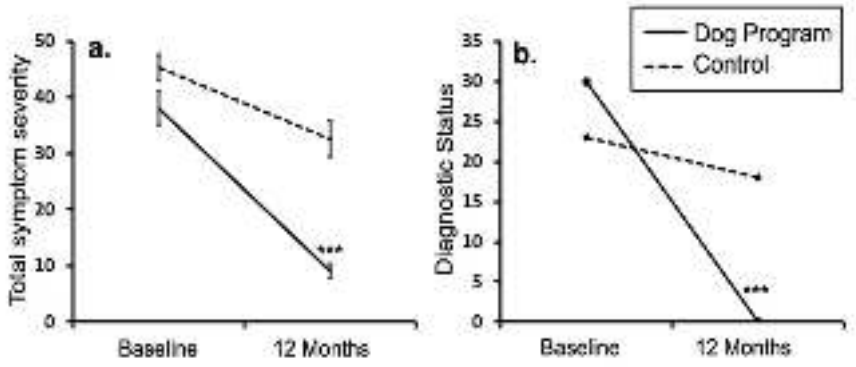


Procedure and Methods

1. CAPS CA 5: a questioner developed by the NMIH for diagnosing PTSD symptoms in adolescents.
2. ASAT: a physiological measurement for sustained attention (attention dysregulation).
3. Startle response: a physiological measurement of anxiety/emotional dysregulation.

Sample size Calculation?

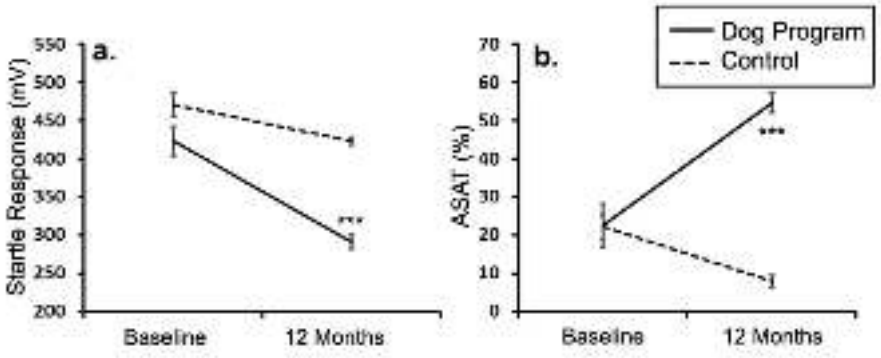
Results: Caps-CA-5 (2)



(a) Total severity score of the CAPS criteria at baseline vs. post 12-months.
(b) Number of positive PTSD diagnostic status at baseline vs. post 12-months.

(***P<0.0001).

Results: Emotional & Attention dysregulations

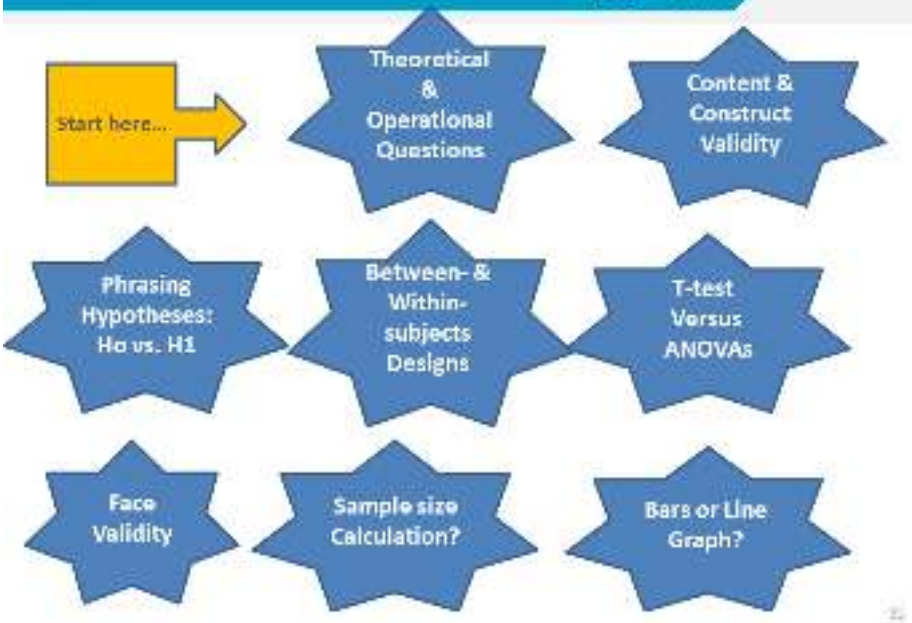


(***P<0.0001).

Conclusions

- Examining an alternative non-pharmacological treatment for PTSD, we found physiological evidence for the beneficial effects of 'Dog-therapy' on PTSD symptoms.
- Our findings support our hypothesis that the ASAT may provide attention and emotional dysregulation indications for PTSD and for the efficacy of its treatment strategies.
- Further research is needed to determine the endurance of these effects, and generalization to adult patients suffering from complex PTSD.

What have we learnt?



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MAFAT

MSc students

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Inon Mooz

Dr. Janne Lisse Hoogervorst

ISRAEL SCIENCE FOUNDATION

CARMEN MORENO: "SYMPTOMS AND TREATMENT OF SCHIZOPHRENIA: FROM CHILDHOOD TO ADULTHOOD"

Early-onset psychosis as an example for developing research in psychiatric disorders

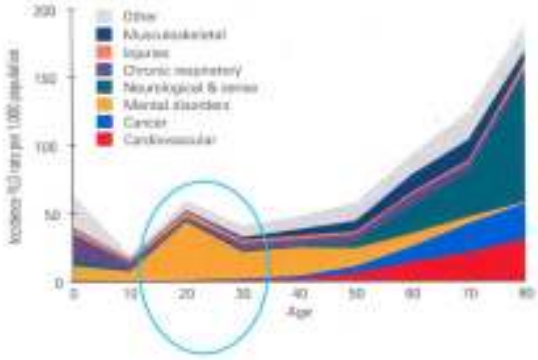
Carmen Moreno, MD, PhD

Institute of Psychiatry and Mental Health
Child and Adolescent Psychiatry Department
Hospital General Universitario Gregorio Marañón
CIBERSAM, IiSGM
School of Medicine, Universidad Complutense
Madrid, Spain

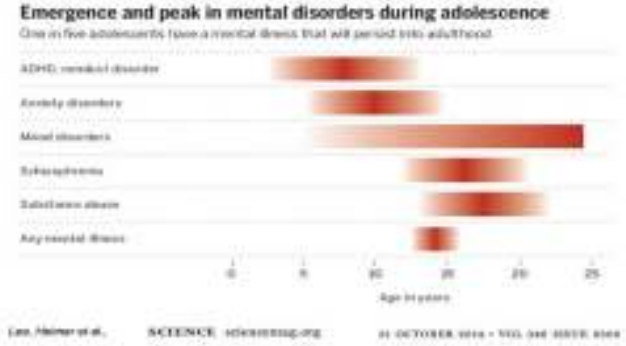
Research questions

- Is early-onset psychosis a neurodevelopmental illness?
- Is prognosis different depending on time from illness onset to treatment implementation?

Disease Incidence over Age



Psychiatric (and psychotic) disorders emerge during childhood and adolescence



- **Psychotic disorders account for 5% of mental disorders in adolescence and for 20% of the inpatients in adolescent psychiatric units.**
- **About 25% of the patients with schizophrenia had its onset before 18 years of age.**
- **Importance of early detection and early intervention for prognosis.**

Loranger, 1989; Remschmidt et al., 1994; Beiden et al., 2001; Arango et al., 2005

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

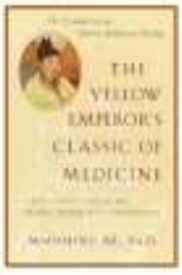
The hypothesis

- The brain undergoes a change in its development (mainly in the second trimester in utero) leading to symptoms that only manifest or are seen when the dysfunctional areas are used (in adolescence)

1987

"People are born to have the illness of craziness, how does it come about?...It is an illness started in the womb, resulting from a bad scar of the mother when she was pregnant"

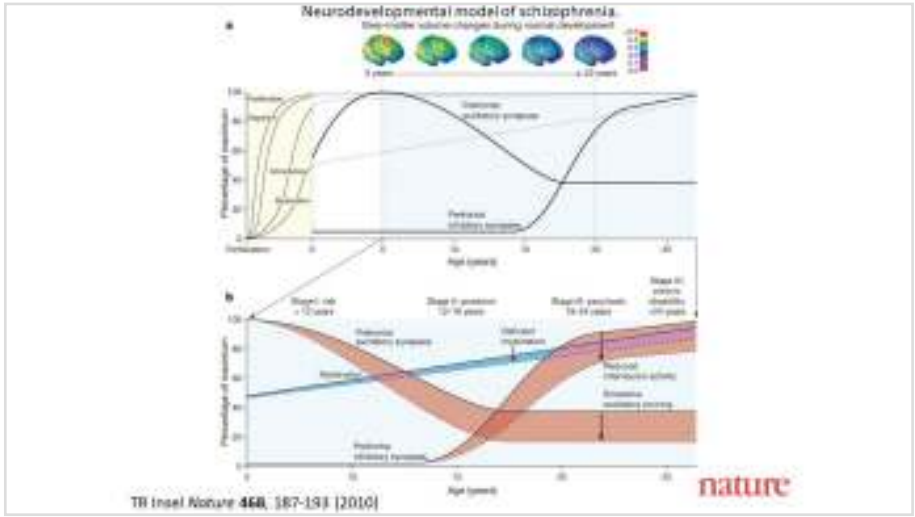
Yellow Emperor's Classic of Internal Medicine (Chinese medical text written roughly 2,000 years ago, translated in Lam CW and Berrios GE, 1992)



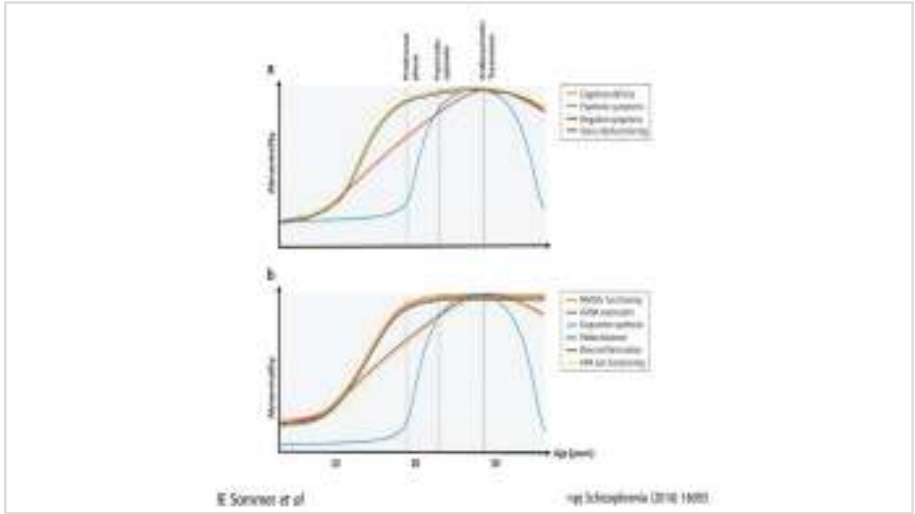
"Diseases affecting the juvenile brain have more powerful effects because they destroy maturing tissues"

"Various developmental stages of a mental disorder correspond to the gradual extension of a morbid process thoughout more and more areas of the brain"

Emil Kraepelin,
The manifestations of insanity, 1920



TR Insel Nature 468, 187-193 (2010)



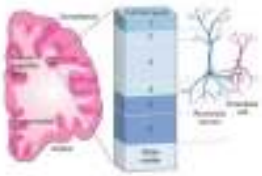
E Sommer et al

Increased incidence of mental disorders in offspring of mothers exposed during pregnancy to:

- Natural disasters
- Psychological stress
- Famine
- Viral infections
- Wars

Evidence from postmortem studies

Alteration in early laminar organization and neuronal orientation



Pyramidal cells from layer III of DLPFC have lower spine density disminuida la densidad de espinas (lower excitatory input): disruption of talamo-cortical and y cortico-cortical circuits

Patenc, Sch Bull 2009

In the investigation of markers of deviant development in the history of psychotic patients, the study of **first-episode early onset cases** with a **very recent onset** becomes especially informative

- **Methodological advantages:**
  - less confounding variables (*adverse life events, exposure to drugs or medications, effect of progression of illness*)
  - more homogeneous sociodemographic factors (*most attend compulsory school*)
  - higher genetic loading
- Study of EOP may clarify etiology and prognosis of the different psychotic disorders

METHODS

- Patients were consecutively recruited from 6 Spanish hospitals as a part of a multicenter, longitudinal, follow-up study (CAFEPS).
- Study designed to evaluate clinical, neuropsychological, neuroimaging, biochemical, immunological, and genetic variables in EOP first episode patients in Spain
- GOAL: to assess clinical characteristics, prognostic factors, diagnostic specificities of findings, and pathophysiological, changes in the brain during the first 2 years after the first psychotic episode through an integrative and translational approach

Castro-Fornieles et al., 2007

METHODS

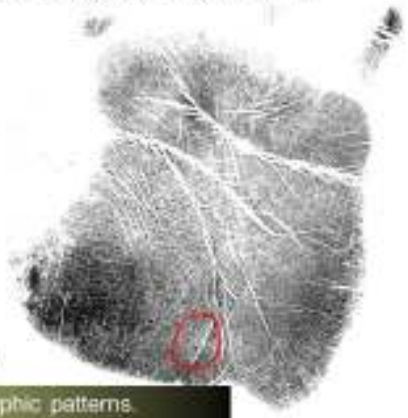
Sample

INCLUSION CRITERIA	EXCLUSION CRITERIA
PATIENTS	PATIENTS AND CONTROLS
✓ Aged 7–17 years	✓ Concomitant Axis I disorder
✓ Positive psychotic symptom less than 6 month duration	✓ Medical or neurological illness
✓ Spanish as first language	✓ Pervasive developmental disorder or mental retardation
✓ Informed consent / assent	✓ Traumatic brain injury or loss of consciousness
CONTROLS	✓ Pregnant or breast feeding
✓ Same geographical areas	

METHODS

Assessments	Baseline	6 months	12 months	24 months
DIAGNOSTIC EVALUATION				
K SADS-PL	X			X
DSM-IV	X	X		X
Escala de complicaciones obstetricas (OCS)	X			
[illegible]	X	X	X	X
Family Environment Scale (FES)	X	X	X	X
Strauss-Carpenter				
NEUROPSYCHOLOGY				
Neuropsychological battery	X			X
WCS	X			X
PSYCHIATRIC EVALUATION				
PANSS, YMRS, CDI, CDRS, MASC	X	X	X	X
CGI	X	X	X	X
SOQ	X			X
WHODAS	X	X	X	X
GAF	X	X	X	X
SUMD	X	X	X	X
NEUROIMAGING				
MRI	X			X
Spectroscopy	X			X
IMMUNOLOGY				
Immunology	X	X		
BIOCHEMISTRY				
Biochemistry	X	X	X	X
GENETICS				
Genetics	X			

Dermatoglyphic patterns



*OR=4.32, p=0.04, schizophrenia vs control

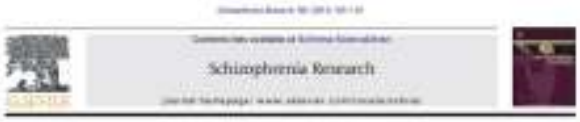
Abnormal dermatoglyphic patterns. Dissociations.-

Parellada 2006

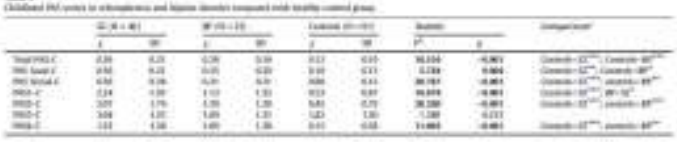
Obstetric complications and psychosis

Obstetric complications as a risk factor for first psychotic episodes in childhood and adolescence

Premorbid adjustment difficulties in EOP


Schizophrenia Research

Premorbid impairments in early-onset psychosis: Differences between patients with schizophrenia and bipolar disorder



Neurocognitive outcomes in EOP and controls

	BASELINE ASSESSMENT			2-YEAR ASSESSMENT		
	EOP (N=24)	Controls (N=29)	Analysis	EOP (N=22	Controls (N=29)	Analysis
Attention	-0.72±0.92	0.01±0.74	p= 0.002	-0.30±0.75	0.30±0.55	p= 0.002
Working memory	-1.33±0.98	0.03±0.85	p≤ 0.001	-1.10±0.82	0.28±0.99	p≤ 0.001
Executive function	-0.88±0.73	0±0.66	p≤ 0.001	-0.53±0.61	0.25±0.56	p≤ 0.001
Learning & memory	-1.80±1.47	0.01±0.79	p≤ 0.001	-1.03±1.39	0.16±0.91	p≤ 0.001
Global	-1.17±0.74	0.01±0.53	p≤ 0.001	-0.71±0.75	0.24±0.91	p≤ 0.001

-EOP showed lower scores than controls in overall cognitive functioning and in all specific cognitive domains assessed both at Baseline and at 2-year FU

-Significant differences between EOP subtypes only for Learning and memory (p=0.04), but significance disappeared after covarying with PANSS scores at 2-yr (p=0.35)

Mayoral et al. Eur Psychiatry 2008; 23(5):375-83

Neurological Soft Signs in first-episode EOP and controls

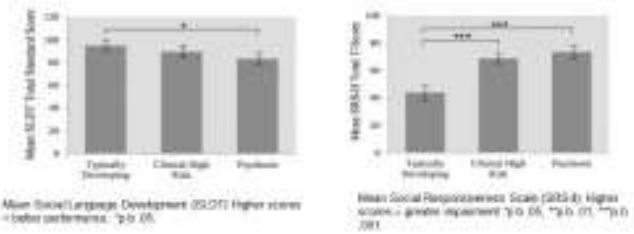
NES (neurological evaluation scale)	BASELINE			2-YEAR		
	EOP (N=24)	Controls (N=30)	Analysis	EOP (N=22)	Controls (N=29)	Analysis
Sensory integration	4.9±3.34	2.10±2.08	P=0.001	3.23±2.31	1.0±1.86	P=0.002
Motor coordination	3.20±2.24	1.13±1.28	P=0.000	2.81±2.55	1.48±1.15	P=0.006
Sequencing of complex motor acts	3.79±3.10	1.70±2.14	P=0.004	3.22±2.56	1.10±1.83	P=0.003
Other	11.25±4.3	5.08±3.18	P=0.000	9.45±4.77	3.10±3.10	P=0.001
Total number of signs	11.70±3.3	7.20±3.43	P=0.000	9.59±3.89	5.03±2.25	P=0.001
Total score	23.2±9.86	12.16±6.72	P=0.000	19.22±9.87	9.65±5.11	P=0.000

-EOP showed more NSS than controls at Baseline and FU

-IQ lower in EOP than in controls at B (P≤0.005) and 2-yr FU (P≤0.005). However, differences between EOP and controls remained significant when controlling for IQ on the soft sign total score at Baseline (P=0.003) and FU (P=0.008)

Mayoral et al. Psychiatry Research 2009

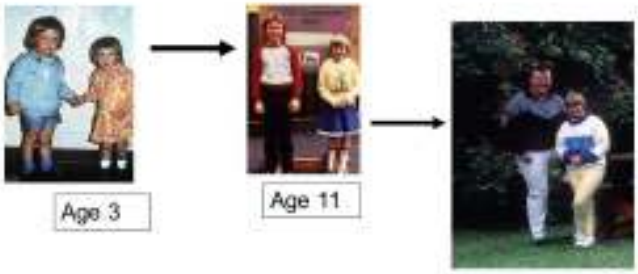
Social impairment and social language deficits in children and adolescents with and at risk for psychosis



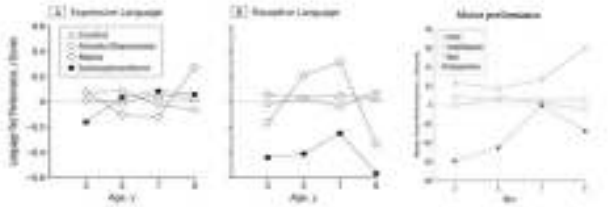
D'Angelo et al., 2018

The longitudinal dimension

Dunedin Multidisciplinary Health and Development Study
Total birth cohort born 1972/73 in Dunedin (N=1037)

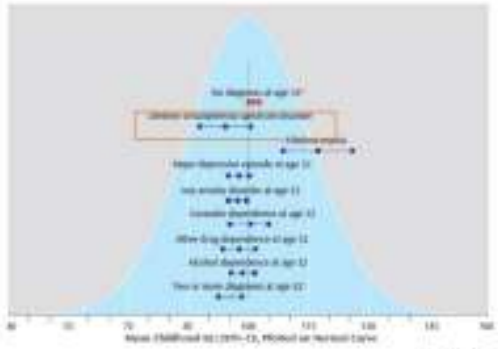


Abnormalities in language and motor development in psychosis



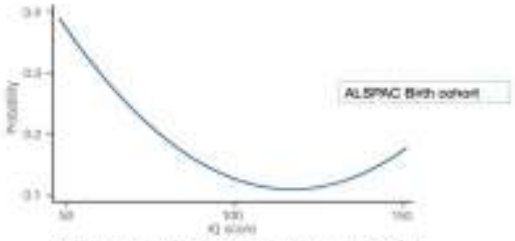
Dunedin Multidisciplinary Health and Development Study Total birth cohort born 1972/73 in Dunedin (N=1037), age 26

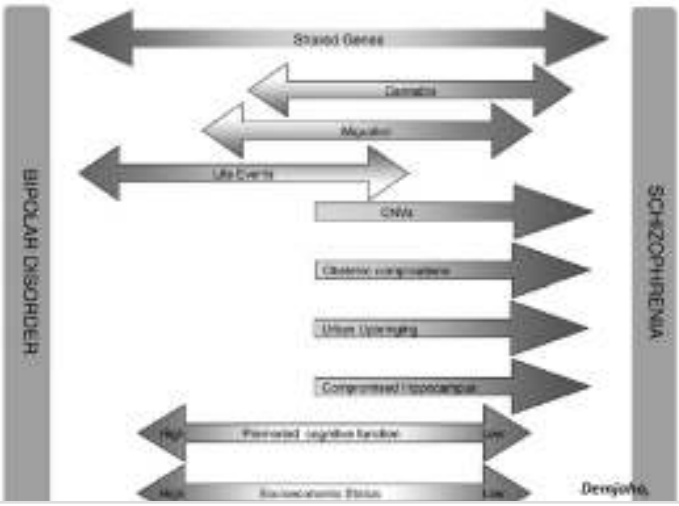
Childhood IQ for individuals with adult mental disorders



Koenen et al., 2009

Childhood IQ as a risk factor for psychosis



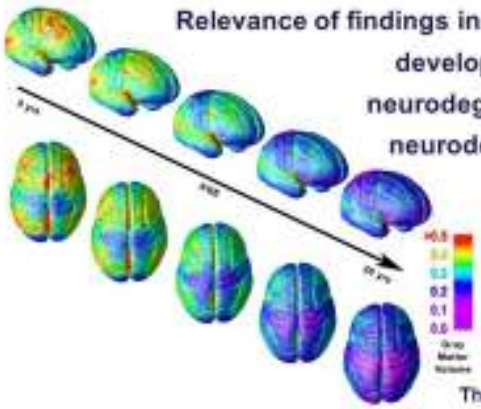


Schizophrenia Bulletin Advance Access published December 26, 2013

Differential Neurodevelopmental Trajectories in Patients With Early-onset Bipolar and Schizophrenia Disorders

Celso Arango*,[1,2], David Fraguas[1], and Mara Parellada[1]

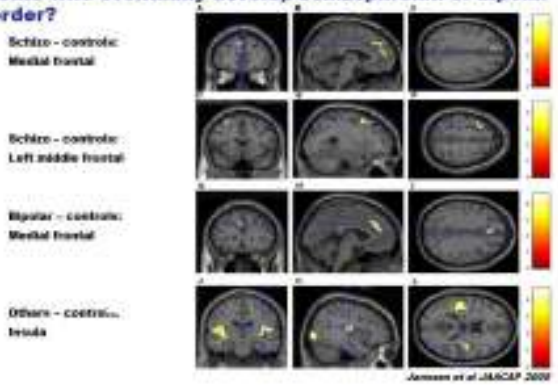
Schizophrenia and bipolar disorders share not only clinical features but also some risk factors such as genetic markers and childhood adversity, while other risk factors such as urbanicity and obstetric complications seem to be specific to schizophrenia. An intriguing question is whether the well-established abnormal neurodevelopment present in many children and adolescents who eventually develop schizophrenia is also present in bipolar patients. The literature on adult bipolar patients is controversial. We report data on a subgroup of patients with pediatric-onset psychotic bipolar disorder who seem to share some developmental trajectories with patients with early-onset schizophrenia. These early-onset psychotic bipolar patients have low intelligence quotient, more neurological signs, reduced frontal gray matter at the time of their first psychotic episode, and greater brain changes than healthy controls in a pattern similar to early-onset schizophrenia cases. However, patients with early-onset schizophrenia seem to have more social impairment, developmental abnormalities (eg, language problems), and lower academic achievement in childhood than early-onset bipolar patients. We suggest that some of these abnormal developmental trajectories are more related to the pharmacological interventions and lack of treatment of these 2 syndromes than to categorically defined Diagnostic and Statistical Manual of Mental Disorders disorders.



- Progressive loss of cortical gray matter volume and increase in ventricular volume have been reported during adolescence in patients with childhood-onset schizophrenia (COS).
- Progressive changes are also present in non-schizophrenia early-onset psychosis.
- Previous studies were conducted in patients with early-onset schizophrenia/other psychosis with a mean duration of the illness of 26 months (range 16 months to 4 years).

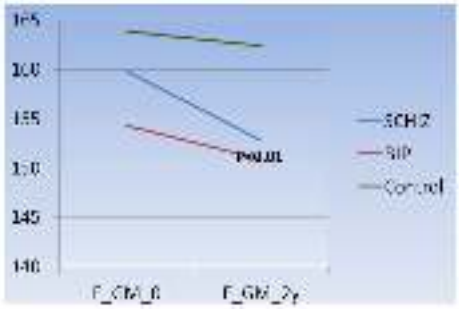
Neuroimage

Are local gray matter volumes different between patients who eventually develop schizophrenia or bipolar disorder?



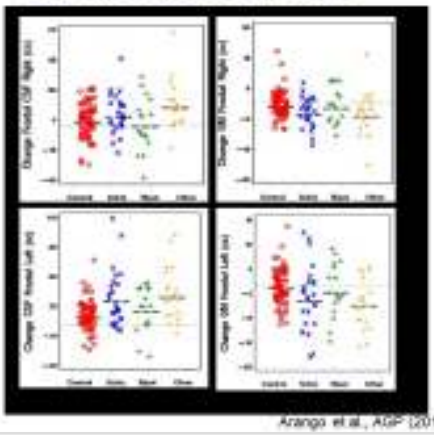
Jamesson et al. JAACAP, 2009

Progressive brain changes in children and adolescents with first-episode psychosis: 2-year follow-up



Arango et al. AGP 2012

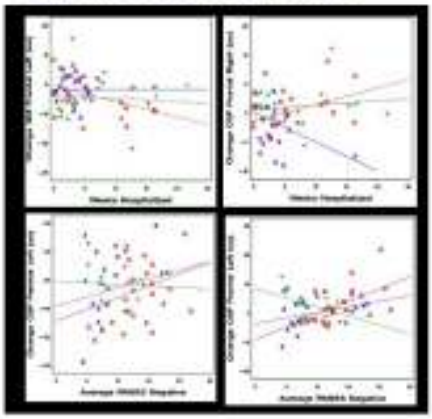
Progression of brain volume changes in first-episode EOP and controls over 2-years



- Schizophrenia patients showed greater Frontal GM volume loss: left -3.3cc vs. -0.6cc; p=0.004; right -3.7cc vs. -0.8cc; p=0.005) and left frontal CSF volume increase (left 6.7cc vs. 2.4cc p=0.006).
- Changes for total GM (-37.1cc vs. -14.5cc; p=0.001), and left parietal GM (-4.3cc vs. -2.2cc; p=0.04) were significantly different in schizophrenia patients.
- No significant differences emerged for bipolar patients.

Arango et al., AGP (2012)

Progression of brain volume changes in first-episode EOP and controls over 2-years



- Greater **left frontal GM volume loss** was related to **more weeks of hospitalization**
- **Severity of negative symptoms** correlated with **CSF increase** in patients with schizophrenia.

Arango et al., AGP (2012)

REVIEW ARTICLE OPEN

Predictors of outcome in early-onset psychosis: a systematic review

The most replicated predictors of worse clinical, functional, cognitive, and/or biological outcomes in EOP

- Premorbid difficulties (developmental delays and poor premorbid adjustment)
- Symptom severity (especially of negative symptoms) at baseline
- Longer duration of untreated psychosis (DUP)

Díaz-Caneja et al., 2015

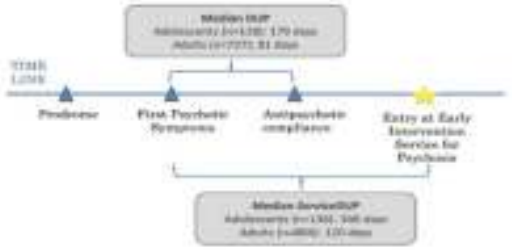
Functional deterioration from the premorbid period to 2 years after the first episode of psychosis in early-onset psychosis

DUP and CGI
73.7 % variance explained

SS and affective psychoses had comparable deterioration

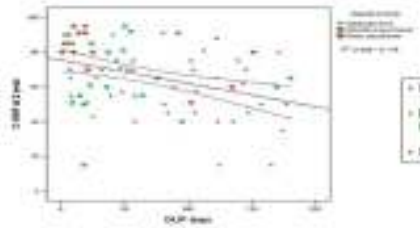
Del Rey-Mejías et al., 2015

DUP for adolescent- vs adult-onset psychosis



Dominguez et al., 2013

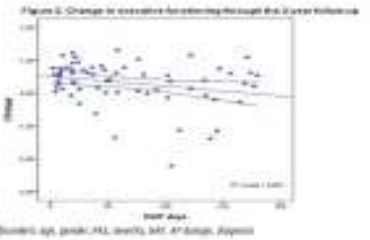
Duration of untreated psychosis predicts functional and clinical outcome in children and adolescents with first-episode psychosis: A 2-year longitudinal study



DUP <6 months

- DUP predicted 2-year functioning
- DUP and PAS predicted C-GAS improvement from baseline
- DUP effect only in schizophrenia patients

A longitudinal study on the relationship between duration of untreated psychosis and executive function in early-onset first-episode psychosis



- Greater severity of negative symptoms predicted lower EF at 2-year follow-up
- Negative symptoms and DUP predicted change in EF through the 2-year follow-up

Schizophrenia Research, 2014

-Start by studying and posing a research question
-Find your study population

-Research is a collaborative effort

-Value of building a database that can be explored further and by different people

-A research question needs an appropriate study population to be tested

Thank you

LIST OF PARTICIPANTS

Last name	First name	City	Country
Agović Pervinšek	Amila	Borovnica	Slovenia
Bokalič	Melita	Ljubljana	Slovenia
Dšuban	Maja	Ljubljana	Slovenia
Gerčer	Katja	Celje	Slovenia
Grobelšek	Gašper	Maribor	Slovenia
Horvat	Urban	Vrhnika	Slovenia
Kirič	Barbara	Ljubljana	Slovenia
Klasinc	Matija	Ljubljana	Slovenia
Koroša	Aleksander	Murska Sobota	Slovenia
Kruljac	Ivona	Ljubljana	Slovenia
Lušicky	Petra	Kranj	Slovenia
Maček	Jerneja	Ljubljana	Slovenia
Micev	Borče	Ljubljana	Slovenia
Mirković	Ana	Ljubljana	Slovenia
Mitrović	Marija	Ljubljana	Slovenia
Šenica	Nina	Maribor	Slovenia
Sobočan Kaučič	Ira	Ljubljana	Slovenia
Tomašević Kramer	Anja	Izola	Slovenia
Turin	Anja	Preserje	Slovenia
Ülen	Ina	Slovenska Bistrica	Slovenia
Zupanič	Sanja	Ljubljana	Slovenia

ABSTRACTS OF PARTICIPANTS

Agović Pervinšek Amila

A young male was hospitalized for the first time in psychiatric hospital in 2016 when he was 20 years old. He was admitted because of heteroagression and disorganized speech and behavior.
In the next year and a half, he was hospitalized four more times and was diagnosed with paranoid schizophrenia. He was treated with risperidone (caused EPS), olanzapine (lack of clinical effect) and aripiprazole. In his last hospitalization in fall of 2017, he started taking clozapine (400 mg) which led to complete remission that lasts to these days. He now works as a welder, takes medication regularly and is asymptomatic.

Bokalič Melita

9-year-old boy with autism and moderate intellectual disability was hospitalized because of self-mutilation and aggression towards things and family members.
He was born after normal pregnancy and birth. His motor development was normal. There was obvious speech regression in his development, he got aggressive at age 3. He started seeing a child psychiatrist at the age 6. Since then, he had a lot of different medications:
Haloperidol, aripiprazole, risperidone, sertraline, quetiapine, diazepam 2 mg, melatonin.
We found pathologic liver enzymes. We tried to give him methylphenidate, but it did not show improvement. When discharged he got aripiprazole 2.5 and quetiapine.

Dšuban Maja

A 17-year-old girl comes, accompanied by her mother, on a first pedopsychiatric ambulant check-up. The mom said, that her daughter problems started 1 year ago, as she became insomniac, she had difficulties with concentration at school, was listless and tired with low energy. She also started to avoid social contacts. Before that she had no similar problems, she was brilliant at school and a perfectionist with high self-expectations. They already went to a psychologist, but no psychological testing was made yet.
The girl said, that she has low energy and has no more interest in connecting with friends, also that her main problem is insomnia because of anxiety. She loves school but has difficulties in concentration what worsens her anxiety. Also, she had suicidal thoughts without a suicidal plan.
The psychiatrist assessed her as depressed. She was given antidepressant sertraline 50 mg at mornings to treat symptoms of depression and antipsychotic risperidone in low dose (0.5 mL at evenings) to treat insomnia. Also, she was sent to a clinical psychological testing.

Gerčer Katja

11-year-old girl was hospitalized in pediatric department because of unspecified event. The seizure started with vomiting, she had a feeling she could not speak, her lips were sweaty and she felt tingling around lips. She was nauseas and phonophobic, with a headache. She was partially amnestic for event, but she recalled weird feelings in right arm and left leg. Similar event happened two years ago.
Diagnostic: Blood test, ECG, ophthalmologic exam, MRI+MRA: no findings. EEG: nonspecific abnormalities. Differential diagnosis: epileptic seizure, migraine, conversion disorder?

Grobelšek Gašper

An 18 years old girl with trichotillomania and some symptoms of depressive-anxiety disorder, with self-observed attention deficits and impulsivity.

A 16 years old girl who is passive and anhedonic and without any will power to do something about it. Her parents are divorced. Her idea of spending a day is watching Netflix and YouTube videos.

An 18 years old boy who could be a bit on the autistic spectrum and feels anxious all the time. He has difficulty going to school (works from home with his mother help; separation difficulties) and is socially anxious.

Horvat Urban

A case report of a 15-year-old patient with a suspect neuroleptic malignant syndrome (NMS)
A nonverbal male patient with severe intellectual disability and autism spectrum disorder on multiple antipsychotics, benzodiazepines and valproate therapy was hospitalized in an intensive pedopsychiatric unit for the fourth time because of heteroaggression. During modification of therapy, he developed absent seizures and was evaluated at the paediatric clinic for EEG, receiving premedication with chlorpromazine. Upon return he was somnolent with subsequent development of hyperpyrexia, tachycardia and parkinsonian gait. He was transferred to the paediatric clinic for evaluation and treatment of suspect NMS.

Kirič Barbara

14-year-old girl with no previous psychiatric history presented with symptoms of depression (misery, tearfulness, anhedonia, deterioration in academic performance, changes in sleep) and panic attacks appearing soon after death of her favourite teacher five months ago. Her perception of reality seemed intact. Mother confirmed said history, but emphasised her curious made-up stories occurring in the last two years in which she generally presented herself as loved and admirable. While symptoms of depression improved (due to prescribed sertraline and risperidone), the fantasy world she created persisted and caused her even more distress and social impairment.

Klasinc Matija

17-year-old T.G. presented with acute onset of psychosis with delusions of religious content, grandeur, imprinted memories where he was convinced and auditory hallucinations. He was admitted to the Unit for intensive child and adolescent psychiatry. Medication with atypical antipsychotics (risperidone) was initiated. At the unit, we started with our “diagnostic protocol for first psychosis”. During diagnostics NMDA receptor antibodies where discovered. Additional diagnostics were done at the Neurology department and the patient started with IVIG treatment. Improvement was dramatic.

Koroša Aleksander

15,5-years-old female patient is in the treatment because of anxiety with occasional panic attacks, depressive symptoms, insomnia and unmourned death of the father. At first encounter she was taking sertraline 100 mg, quetiapine ER 100 mg in the morning and 200 mg in the evening. Information about her medicines were different between mother and the girl. She used to self-harm, but she has stopped. She was not suicidal. She has high BMI – 55,2 kg/m2.
How to manage pharmacological treatment in adolescent with obesity?

Kruljac Ivona

Case report of a 16-years old female with a history of psychotic symptoms, who has been hospitalized in departments for child and adolescent psychiatry three times since January 2020 (total time of hospitalization was six months with minor breaks).
At the time of the first hospitalization, she presented with auditory and cenesthetic hallucinations, accelerated and partially incoherent ductus, low mood, passive suicidal ideations and general decline in social functions. Her voice was gone because of repetitive episodes of screaming. After switching from therapeutic doses of risperidone and aripiprazole to therapeutic doses of quetiapine in combination with sertraline because of insufficient effectiveness, these two were also changed and olanzapine was started but still without attaining constant remission. Should we start clozapine if there is some strong evidence of psychodynamic factors that influence the intensity of the symptoms?

Lušicky Petra

A 12-year old girl has been experiencing audio and visual phenomena as well as mild paranoid delusions for past 6 months. Symptoms were gradually progressing and were especially grave at evening and night time. Sleep was often disturbed, school attendance was poor. During treatments she was often scanning the room, reported voices getting progressively louder, seeing shadows dancing and laughing. At first, risperidone in low dosage was prescribed, which further aggravated the symptoms. A trial with low dosage benzodiazepines was conducted with no effect. Sleep was improved with introduction of olanzapine.

Maček Jerneja

Peter is a 12 years old boy diagnosed with Asperger syndrome, ADHD, ODD, Tourette syndrome. He has increased sensitivity to sound, taste, touch and smell. He is afraid of ships, bicycles, plates, cups, forks, knives – he always uses the same cutlery. His fine and gross motor skills are impaired with poor motor coordination. He has awkward body language and gait. He shows a need for routines, rituals and consistency. He is interested in his peers, but approaches them in an inappropriate way, with lack of "common sense" and an inability to identify social cues. Hi is ignorant of the social situation when speaking, and sometimes seems to talk to themselves, commenting on his own actions and giving monologues without needing a listener. His unpredictable behaviour (aggressive outbursts) made him unpopular with the others
With school work he is too slow and too pedantic with major attention deficits, hyperactivity and impulsivity. He displays disciplinary problems, negativism and conduct difficulties, particularly at home with aggression (verbal and physical) towards mother, father, also to peers in different social situations. He has complex motor and vocal tics, is very anxious in social situations. He has sleeping problems (difficulties sleeping in).
At present most troublesome symptoms are: attention difficulties, impulsivity with verbal aggressive outbursts (less frequent), difficulties in peer relationship, rigidity.
He regularly attends psychiatric and psychological assessments.
Pharmacotherapy: aripiprazole (Abilify) 5 mg, atomoxetine (Strattera) 60 mg, fluoxetine (Prozac) 10 mg. History of methylphenidate (Ritalin), but omitted due to worsening tics.

Micev Borče

8 y. old boy with pharmacoresistant partial epilepsy with atrophic changes on right hemisphere is referred to the tertiary child psychiatry unit because of severe problems with attention and hyperactivity, developmental and behaviour problems that affect his everyday functioning and family wellbeing. His problems developed secondary, because of complications of ganglioneuroblastoma (severe hypertension) when he was 14 months old.
Therapy: valproic acid 750 mg, topiramate 2 x 75 mg, aripiprazole 5 mg.
Outpatient psychiatrist: risperidone 0.5 mg.- mild improvement for short period then switched for aripiprazole 5 mg then increased to 15 mg. daily-without improvement.
Our challenge: modification of pharmacotherapy.

Mirković Ana

17 – year old girl had a right side Scwannoma when she was 14 years old. The tumor was surgically removed and is currently in remission. She presented with anorexia nervosa, depression and anxiety symptoms at age 15 with emphasis on somatization and school absence. After that she was quickly involved in outpatient child psychiatry treatment. She is currently physically and emotionally stable enough to function but still shows signs of anxiety and school avoidance. Therapy: sertraline 50 mg.
Treatment question: what are treatment options in patients after head surgery that show psychiatric symptoms?

Mitrović Marija

16-years old patient was admitted to the Department of Adolescent Psychiatry after a suicide attempt and exacerbation of schizoaffective disorder.
During the hospitalization we decided to increase the dose of valproate and we started again with the lamotrigine. Instead of aripiprazole (she had akathisia) we gave her quetiapine sustained release. For depression symptoms we gave her bupropion had to discontinue it.
How we can use antidepressant therapy in adolescents with schizoaffective disorder who have a risk of a manic episode?

Šenica Nina

I am presenting 2 clinical cases, presenting with similar symptomatology, but during the treatment evolving to different diagnosis, response to treatment, and outcome in terms of everyday quality and functioning.

Both patients were 16-year-old females, presenting with symptoms of chronic, intermittent abdominal pain with bloating. There were no underlying somatic causes at hand in both patients.

In treating the first patient, the response to long lasting, intensive psychotherapeutic and other (pharmacotherapeutic, physiotherapeutic, family) interventions made an important improvement of body weight, but not to pain reduction. However, the similar therapeutic interventions in treatment of the second patient brought significant reduction of pain sensation.

Sobočan Kaučič Ira

18 years old patient first came in May 2020. She reported that she has had problems for two years now. Before, she was seeing an adult psychiatrist who prescribed sertraline for mixed depression and anxiety symptoms, which did not help.

She represented herself with depressed mood, lack of energy, hypobulia, lack of sleep, occasional suicidal ideations. In fall of 2019 she developed symptoms of OCD - hand washing, pillow folding, there was prominent fear of dead things touching her.
There was an impression of prominent family conflict and sister rivalry.
After starting treatment with fluoxetine, she told me about episodes (3 days) of having more energy than usual, followed by deeply depressed mood. These swings appeared for two to three months. (dd BMD?) Instead of risperidone, we tried with quetiapine, which showed to be effective in stabilising mood.

Tomašević Kramer Anja

16 yo patient was admitted to EIOAP (Intensive child and adolescent psychiatric unit) after a suicide attempt by ingesting analgesics. This was her fifth hospitalisation in the last year. She has regular outpatient visits with her pedopsychiatrist and was stable on a combination of slow release quetiapine with sertraline. Her farther committed suicide when she was 6 years old, he was terminally ill with a brain tumor. Her mother who is also treated for depression was diagnosed with breast cancer 2 months before the hospitalization. The patient was not capable of sharing her mom's illness with her therapist. She had a hard time talking about the subject with therapists, she kept diverting attention to being suicidal and feeling trapped in the intensive unit.

Turin Anja

Background/Objective: Type 1 diabetes (T1D) is among the most common chronic diseases in children/adolescents, the incidence continues to rise worldwide. Different environmental factors have been evaluated in the etiology. In the present study we investigated the role of attachment. We presumed insecure attachment to carers or carers' own attachment insecurity was related to a higher risk of T1D in children.

Methods: We included 101 children with T1D (mean age 11.8 years), 106 healthy controls (11.6 years) and one of their carers. We assessed children's attachment using the Child Attachment Interview and carers' attachment using the Relationship Structures Questionnaire. We constructed binary multinomial logistic regression models using attachment to mothers, carers' attachment representations, and stressful life-events as T1D predictors.
Results: Higher carer's attachment anxiety was associated with the child's T1D diagnose ($p < 0.05$; $R2 = 0.0613$) while security of attachment to mothers showed no significant association. After adjusting for education, both attachment anxiety in higher educated mothers and stressful life-events showed a significant association with the child's T1D ($p < 0.001$; $R2 = 0.293$).
Conclusions: Our findings suggest that higher attachment-related anxiety in carers with high education and stressful life-events are related to T1D in children.

Ülen Ina

Our double-blind pilot randomized placebo-controlled trial examined the possible effect of the probiotic strain Lactobacillus rhamnosus GG on symptoms of ADHD, health-related quality of life and serum levels of cytokines in children and adolescents with ADHD.
The trial evaluated 32 drug-naive youths aged between 4 and 17 years with a diagnosis of ADHD. Participants who received LGG supplementation reported better health-related QoL compared to their peers who received the placebo. This suggests that LGG supplementation could be beneficial. But results with psychometric tests conducted by parents and teachers as well as differences in the levels of inflammatory cytokines were ambiguous.

Zupanič Sanja

Detection of extrapyramidal side effects (EPS) with tensiomyography
Early extrapyramidal side effects (parkinsonism, dystonia, akathisia) are common side effects in young patients, treated with antipsychotics. One of the core symptoms of parkinsonism and dystonia is increased muscle tone. Tensiomyography is a non-invasive, evidence-based measurement method that precisely measures the contractile properties of a muscle. It is used in sports medicine, rehabilitation and research. In our study we will perform TMG measurements on young patients with acute EPS – before and after receival of biperiden – anticholinergic antiparkinsonian drug, which is used to relieve acute EPS, and observe the changes in TMG measurements.

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