UNIVERSITÄTS KLINIKUM jena

Department of Child and Adolescent Psychiatry,
Psychosomatics and Psychotherapy

Mental Health and Nutrition:

A Blind Spot in Clinical Service Delivery?

Perth, February 11th 2021

Prof. Dr. med. Florian Zepf

Disclosure &
Conflict of interest statement

Funding received:

- European Union (EU)
- Telethon New Children's Hospital Research Fund (TPCHRF)
- German Federal Ministry for Economics & Technology (BMWi)
- Dr. August-Scheidel Foundation
- Paul & Ursula Klein Foundation
- American Psychiatric Association (APA)
- American Psychiatric Institute for Research and Education (APIRE) & Astra Zeneca
- German Society for Social Pediatrics & Adolescent Medicine (DGSPJ)
- GlaxoSmithKline Foundation (Travel Grant)
- Research Funding UKA
- DFG via RWTH Aachen
- Princess Margaret Hospital Foundation
- Telethon Kids RFA Working Group Grant
- Raine Medical Research Foundation
- Unrestricted Educational Grant & speaker honoraria & consultancy, Shire / Takeda

What this presentation will not do

- Explain all nutritional components relevant for your patients
- Tell you how to put a meal together for your patients
- Tell you how to run your service regarding diet composition for patients
- Explain all psychopathology by nutritional changes only
- Provide a full causality model for mental health problems

But I will try…

-To introduce you to the concepts of nutrition in mental health and nutritional psychiatry

-To show you some brief examples of research findings

-To demonstrate how simple nutritional modifications can have a significant impact on behaviour and brain function

-To articulate and summarize implications for service development

Overall goal for today:

To demonstrate how exciting and yet difficult research in this area is (role of confounders…)

Overview of presentation

1. Concept of nutritional psychiatry

First field data

2. Impact of nutrition on psychiatric symptoms – research findings on the role of amino acids

Study approaches & methodology
Cognitive processes
Mood
Aggression and impulsivity

3. Implications for service development & delivery

Overview of presentation

1. Concept of nutritional psychiatry

First field data

2. Impact of nutrition on psychiatric symptoms – research findings on the role of amino acids

Study approaches & methodology
Cognitive processes
Mood
Aggression and impulsivity

3. Implications for service development & delivery

Why look at nutrition in mental health?

Role of nutrition

- Nutrition is part of everyday life

- In comparison to the frequency with which people consume foods rather little is known about the impact of nutrition on mental health

Examples

In clinical files the medication chart is critically reviewed by treating team

Apart from patients with eating disorders dietary aspects are often neglected or not always monitored in sufficient detail

Why look at nutrition in mental health?

Questions to think about

Do you know your patients' nutritional intake?

If so, to what degree / in what detail? Quantity? Quality? How regularly?

What are potential clinical implications?

Concept of nutritional psychiatry (NP)

- The field of ‘nutritional psychiatry’ has evolved with rapidity over the past several years

- Increasing amount of dietary or nutrient-based (nutraceutical) intervention studies being initiated

- More preclinical and epidemiological data becoming available

Sarris, 2019

Nutritional psychiatry – Selected findings

- Data suggest that severe maternal macronutrient deficiencies during critical developmental periods of pregnancy may be implicated in the pathogenesis of

> Depressive disorders

> psychotic disorders

in the offspring!

Brown et al., 1995; Sarris, 2019; Steenweg-de Graaff et al., 2014

Nutritional psychiatry – Selected findings

- Epidemiological studies, including longitudinal studies (in maternal cohorts and their offspring, children, adolescents, and adults) demonstrated

→ significant associations between healthy dietary patterns and a reduced risk and prevalence of symptoms (in particular depression)

Lassale et al., 2018; O' Neil et al., 2014*; Sarris, 2019;*

Nutritional psychiatry – Selected findings

•Systematic reviews have tentatively found a relationship between

→ **‘unhealthy’ dietary patterns** and **poorer mental health** in children, adolescents, and adults

Lassale et al., 2018; O’ Neil et al., 2014*; Sarris, 2019;*

Nutritional psychiatry – Selected findings

- **Examples:**

  European PREDIMED study demonstrated a reduced risk for incident depression in people with type 2 diabetes who were randomised to a **Mediterranean diet with nuts**, compared with a low-fat diet control group

Paans et al., 2018; Sanchez-Villegas et al., 2013; *Sarris, 2019;*

Nutritional psychiatry – Selected findings

- **Examples:**

  MoodFOOD prevention study shows that in a sample of participants (*N* = 990)

→ Subjects with subsyndromal depressive symptoms and a history of depression have higher levels of emotional and uncontrolled eating

→ These subjects also have lower levels of cognitive restrained eating compared with those without a former depression diagnosis

Paans et al., 2018; Sanchez-Villegas et al., 2013; *Sarris, 2019;*

Concept of nutritional psychiatry (NP)

- NP involves the clinical consideration (where appropriate) of prescriptive dietary modification or intervention
- NP covers improvement, and/or the select use of nutrient-based supplementation to prevent or manage psychiatric disorders
- So far the role of nutrition in the diagnostic process has been rather poorly considered (with the exemption for eating disorders)

Sarris, 2019

Concept of nutritional psychiatry (NP)

- In the last several years, significant links have increasingly been established between dietary quality and mental health
- However, not all data are supportive
- Maternal and early-life nutrition may also affect the mental health outcomes in offspring

Sarris, 2019

Concept of nutritional psychiatry (NP)

- In nutraceutical research, like with many recent conventional drug studies, results are fairly mixed
- In many cases there is not clear evidence to support the use of nutraceuticals in patients with various psychiatric disorders
- Such findings may in part be due to a preponderance of recent studies within the field revealing marked placebo effects
- Because current indicators pointing towards mental disorders having an increasing burden of disease, new and innovative approaches on a societal level are now required

Sarris, 2019

Concept of nutritional psychiatry (NP)

- There is a common use of nutrient supplements by people with and without mental disorders
- Critical that scientifically rigorous methodologies are used to assess the efficacy of such supplements
- Important to determine if, or what dose of, a nutrient supplement is required, for whom, and when, and under what circumstances
- Simplified studies of additional isolated nutrients are not of great benefit to the field (unless studied in for example supra-dosage in an individualised, biomarker-guided manner)

Sarris, 2019

Overview of presentation

1. Concept of nutritional psychiatry

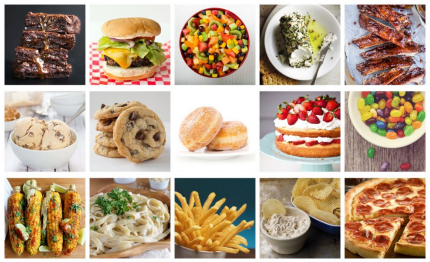
First field data

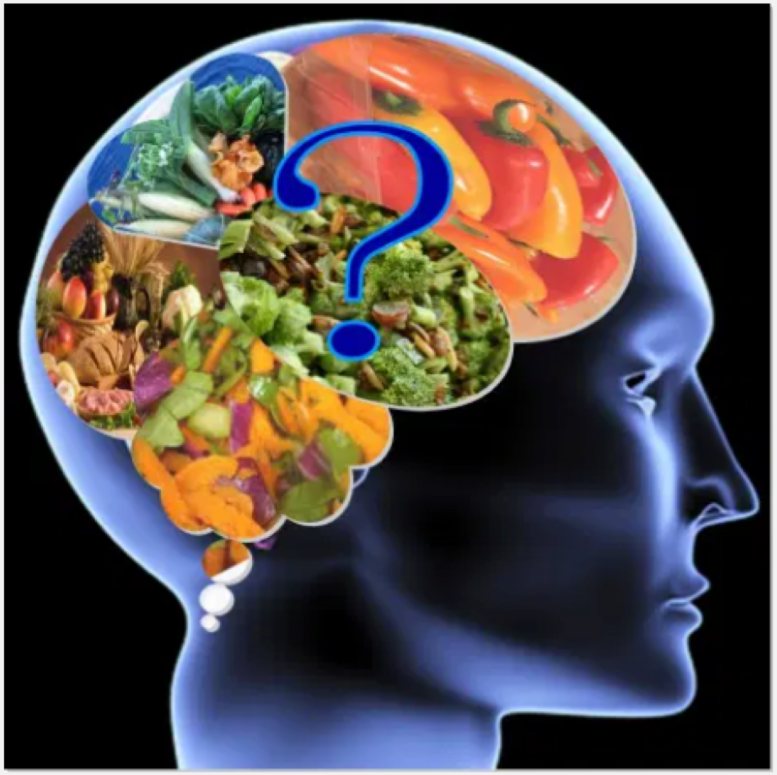
2. Impact of nutrition on psychiatric symptoms – research findings on the role of amino acids

Study approaches & methodology
Cognitive processes
Mood
Aggression and impulsivity

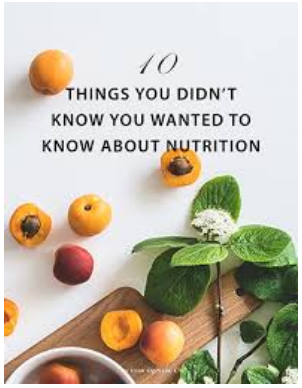
3. Implications for service development & delivery

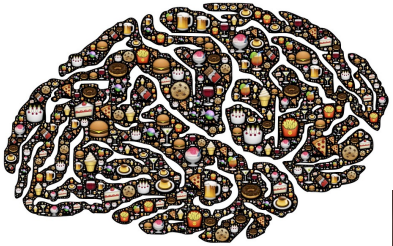
Diet, food & neuroscience – The beginning of a journey

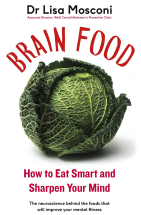


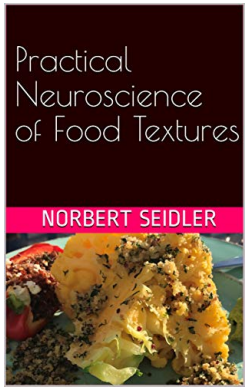


http://bit.ly/1CqaPuw

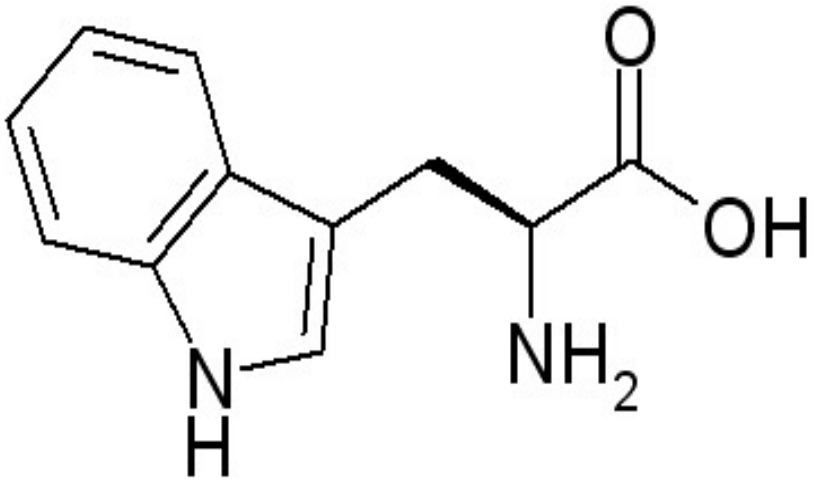






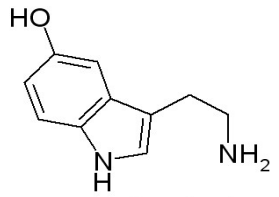


Tryptophan = Precursor of serotonin



Relevance of serotonin (5-HT)

- Mood: Affective disorders
- Cognition: Attention processes
- Appetite regulation: Eating disorders
- Behavioural inhibition: Aggressive behaviour

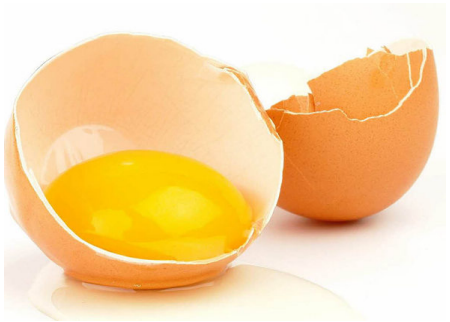


Serotonin (5-Hydroxy-tryptamine, 5-HT)

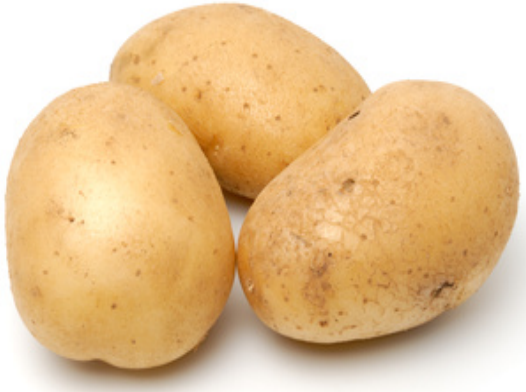
→ Serotonin is a neurotransmitter who's availability is regulated by the diet

Breakfast


müller
Reine
Butter
Milch
müller
Reine
Butter
Milch
EINFACH SCHÖN TRINKEN



Lunch



Dessert

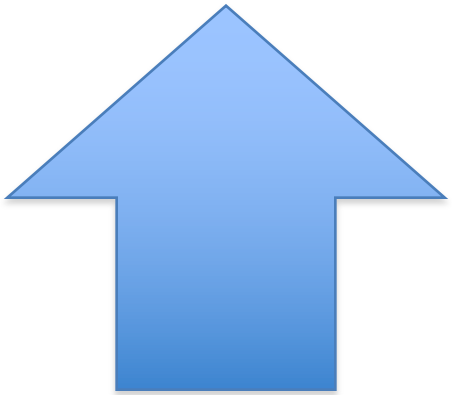
How can you study the effects of tryptophan & serotonin in people?

Ways of studying a specific neurotransmitter

Ways of studying a specific neurotransmitter

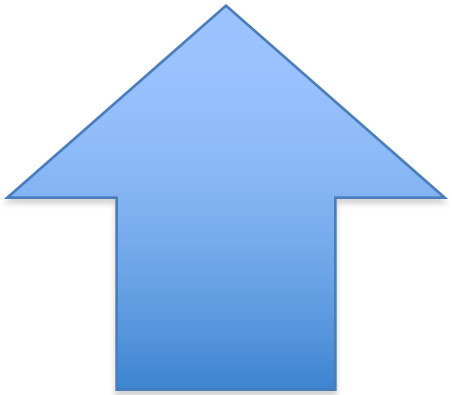
Serotonin

Ways of studying a specific neurotransmitter



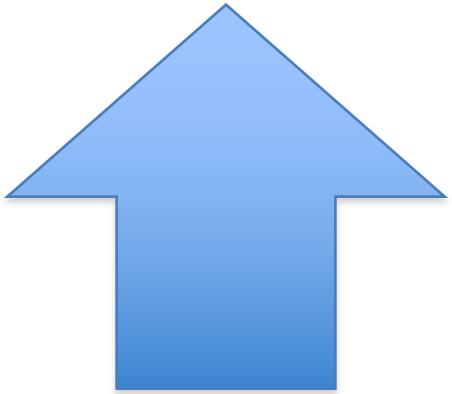
Serotonin

Ways of studying a specific neurotransmitter

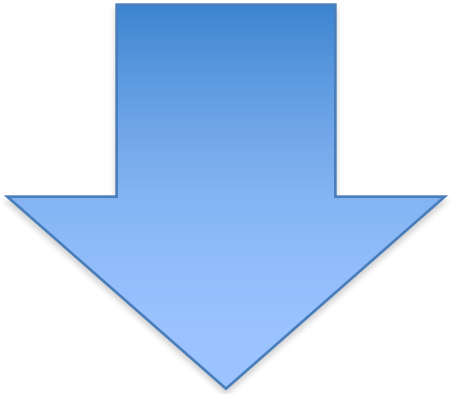


Serotonin

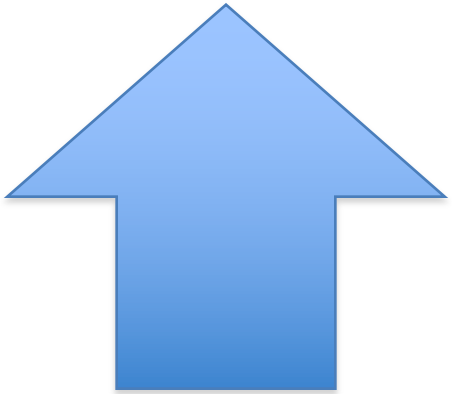
Ways of studying a specific neurotransmitter



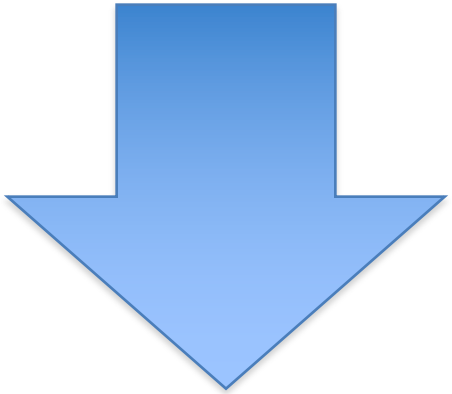
Serotonin



Ways of studying a specific neurotransmitter



Serotonin



Tryptophan Depletion

How to study serotonin in humans

- Assessment of serotonergic metabolites (5-HIAA)
- Update of 5-HT in platelets
- Prolactin-Fenfluramine-Challenge
- SSRIs
- Tryptophan Depletion-Test

Zepf, F.D., et al., The Lancet Psychiatry Vol. 2: e19, 2015

Dingerkus, V.L.S., ..., Zepf, F.D. Journal of Neural Transmission 119(9): 1037-45, 2012

Zepf, F.D. In: Amino Acids in Human Nutrition and Health. D'Mello J.P.F. (Ed). CABI Publishing, Oxfordshire, 418-426, 2012

How to study serotonin in humans

- Assessment of serotonergic metabolites (5-HIAA)
- Update of 5-HT in platelets
- Prolactin-Fenfluramine-Challenge
- SSRIs
- Tryptophan Depletion-Test

Zepf, F.D., et al., The Lancet Psychiatry Vol. 2: e19, 2015

Dingerkus, V.L.S., ..., Zepf, F.D. Journal of Neural Transmission 119(9): 1037-45, 2012

Zepf, F.D. In: Amino Acids in Human Nutrition and Health. D'Mello J.P.F. (Ed). CABI Publishing, Oxfordshire, 418-426, 2012

How to study serotonin in humans

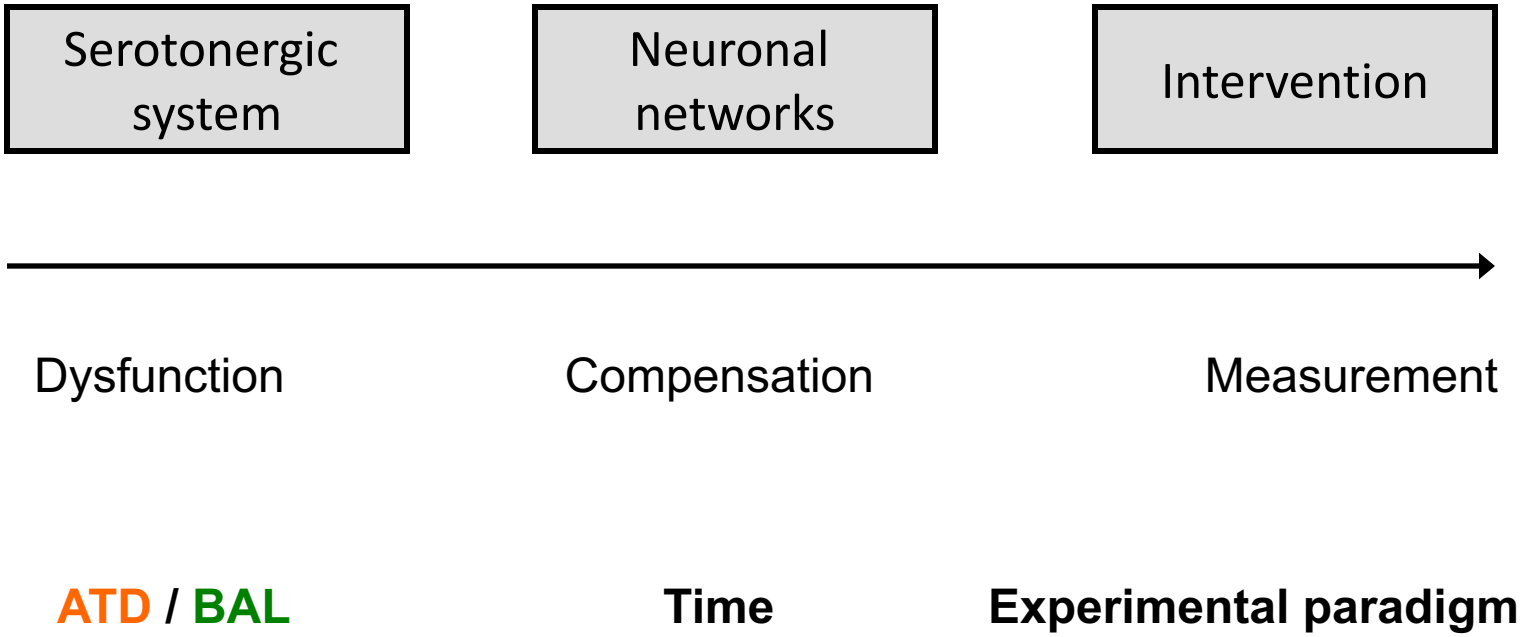
- Assessment of serotonergic metabolites (5-HIAA)
- Update of 5-HT in platelets
- Prolactin-Fenfluramine-Challenge
- SSRIs
- Tryptophan Depletion-Test → **Acute Tryptophan Depletion (ATD)**

Zepf, F.D., et al., The Lancet Psychiatry Vol. 2: e19, 2015

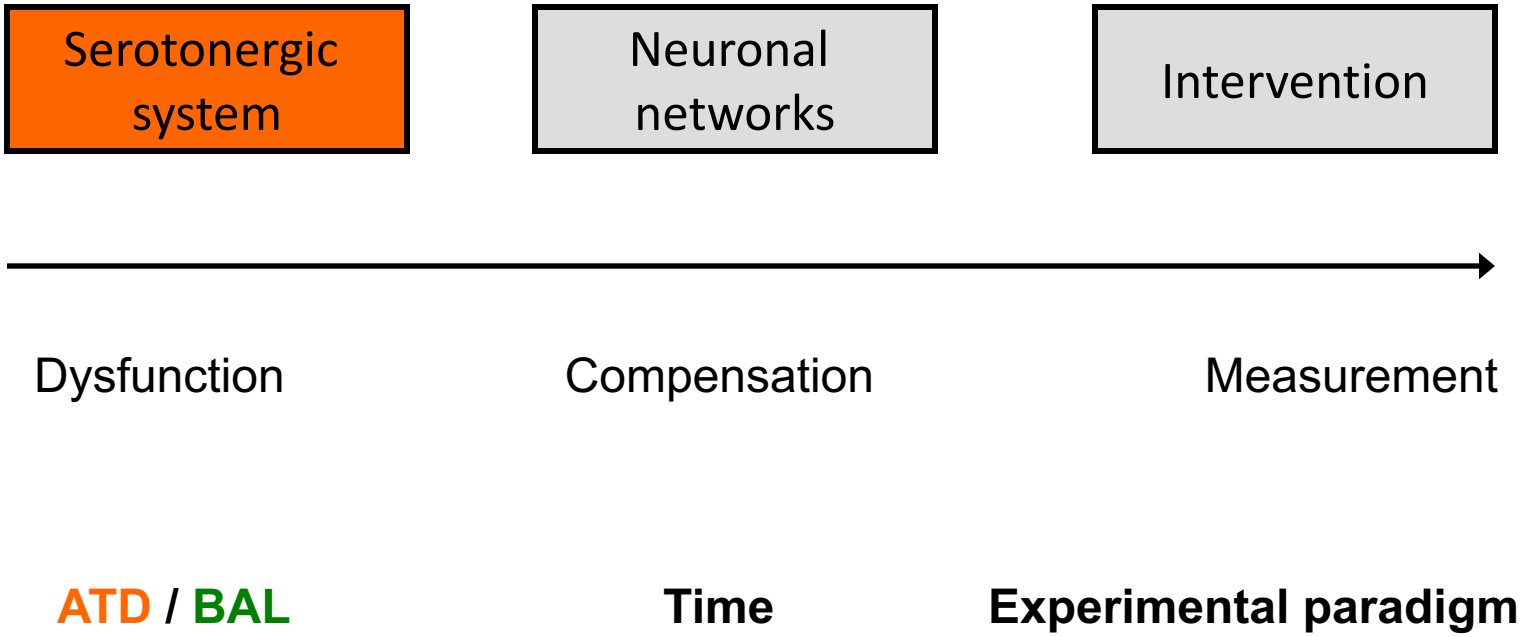
Dingerkus, V.L.S., ..., Zepf, F.D. Journal of Neural Transmission 119(9): 1037-45, 2012

Zepf, F.D. In: Amino Acids in Human Nutrition and Health. D'Mello J.P.F. (Ed). CABI Publishing, Oxfordshire, 418-426, 2012

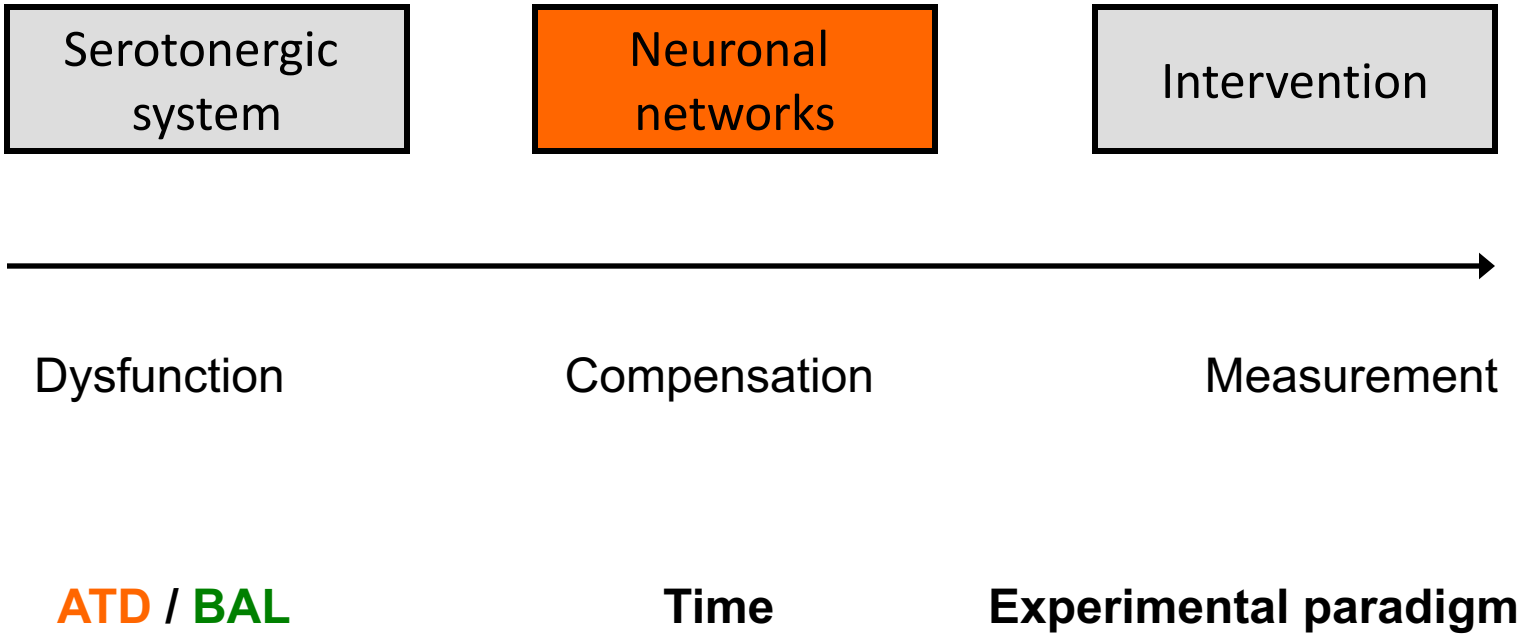
Principle of depletion studies



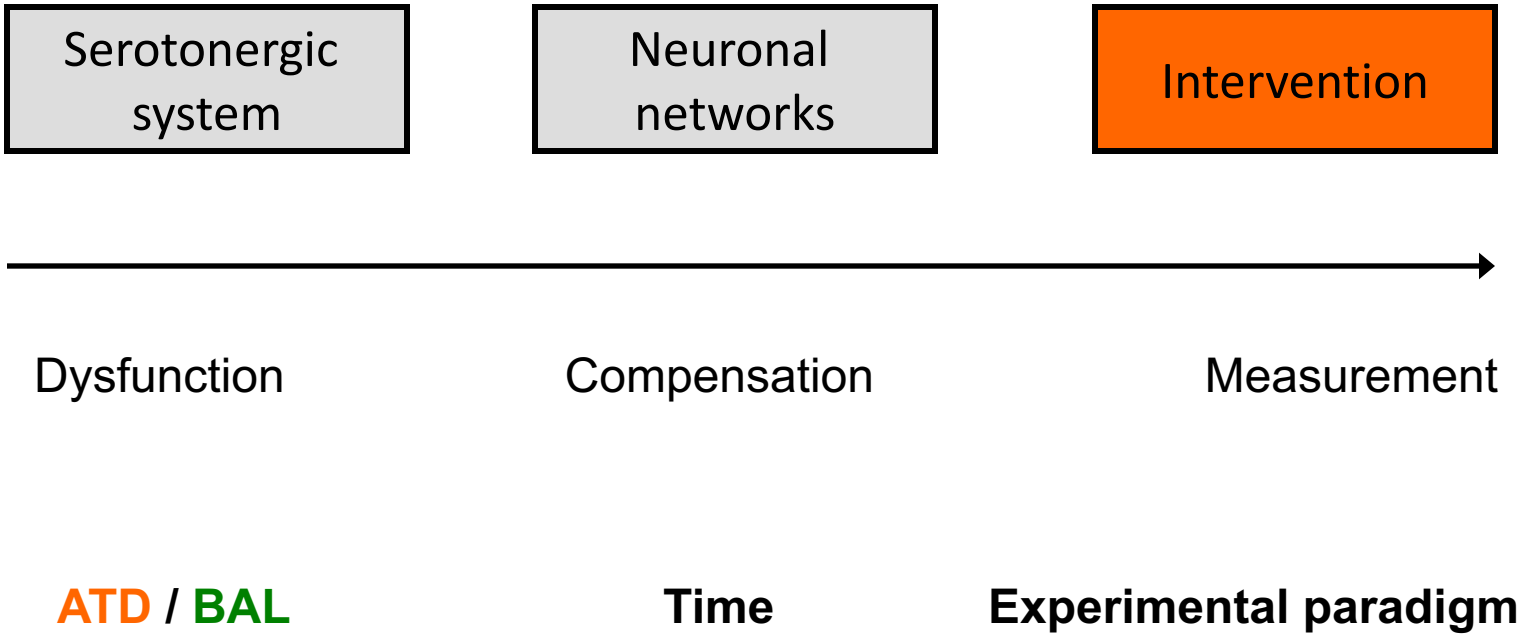
Principle of depletion studies



Principle of depletion studies



Principle of depletion studies



ATD challenge

ATD = Acute Tryptophan Depletion

= Mixture of essential amino acids (LNAAs)

→ PHE, LEU, ILE, MET, VAL, TRE, LYS*

→ **Mechanism principle:** Tryptophan (TRP) is physiological precursor of 5-HT

→ **Goal:** Short-term reduction in brain 5-HT synthesis

**semi-essential*

Zepf et al., 2008a; Human Psychopharmacology: Clinical and Experimental

ATD challenge

ATD = Acute Tryptophan Depletion

= Mixture of essential amino acids (LNAAs)

→ PHE, LEU, ILE, MET, VAL, TRE, LYS*

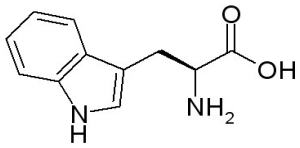
→ **Mechanism principle:** Tryptophan (TRP) is physiological precursor of 5-HT

→ **Goal:** Short-term reduction in brain 5-HT synthesis

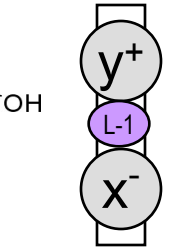
**semi-essential*

Zepf et al., 2008a; Human Psychopharmacology: Clinical and Experimental

ATD challenge

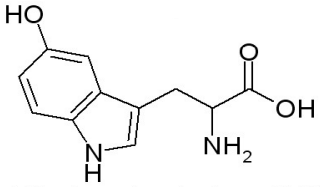


L-Tryptophan

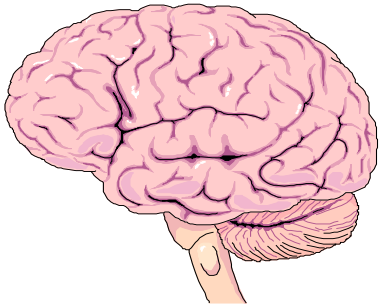


Blood brain barrier

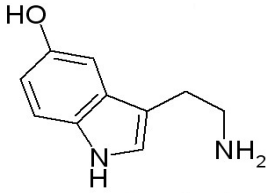
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

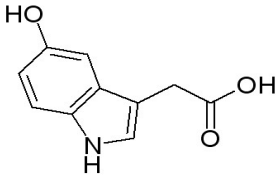


5-Hydroxy-tryptophan-decarboxylase



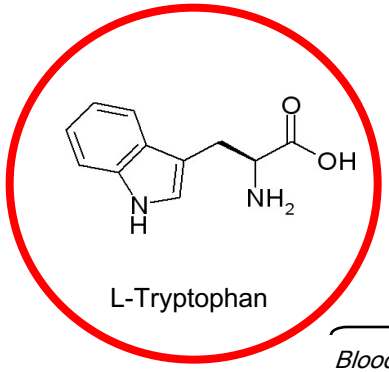
Serotonin (5-Hydroxy-tryptamin, 5-HT)

MAO

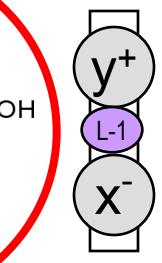


5-hydroxyindoleacetic acid (5-HIAA)

ATD challenge

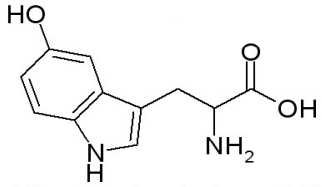


L-Tryptophan

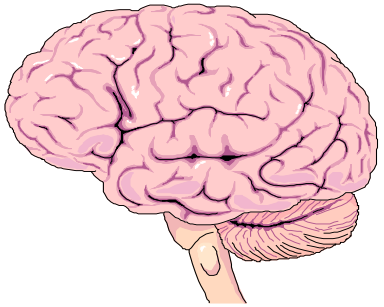


Blood brain barrier

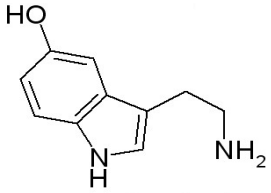
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

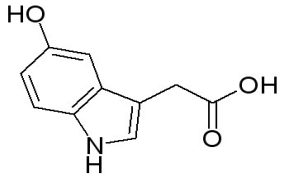


5-Hydroxy-tryptophan-decarboxylase



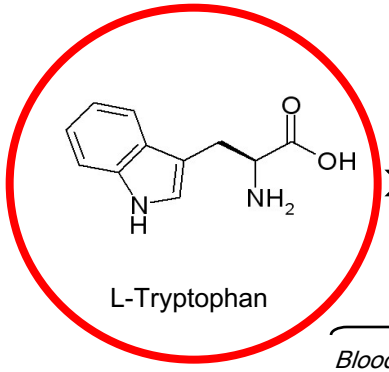
Serotonin (5-Hydroxy-tryptamin, 5-HT)

MAO

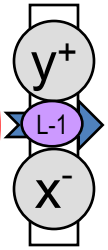


5-hydroxyindoleacetic acid (5-HIAA)

ATD challenge

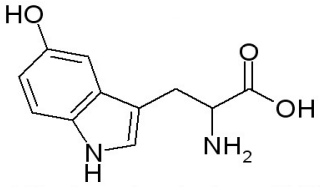


L-Tryptophan

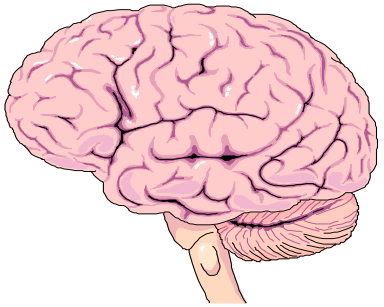


Blood brain barrier

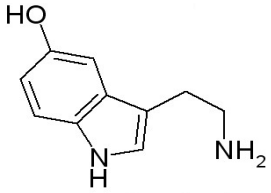
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

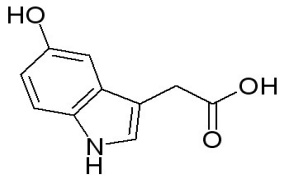


5-Hydroxy-tryptophan-decarboxylase



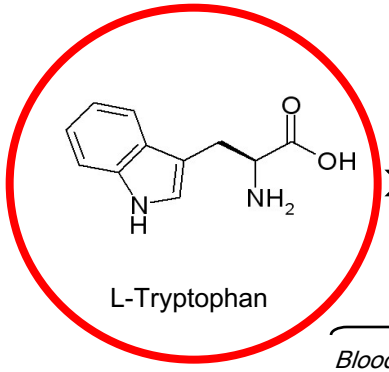
Serotonin (5-Hydroxy-tryptamin, 5-HT)

MAO

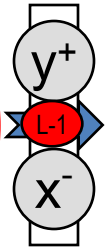


5-hydroxyindoleacetic acid (5-HIAA)

ATD challenge

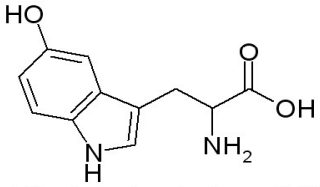


L-Tryptophan

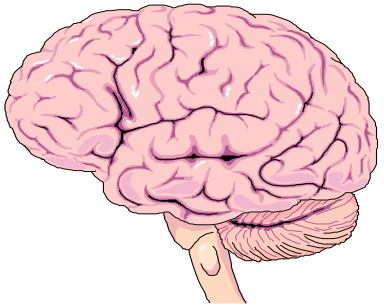


Blood brain barrier

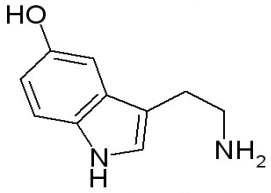
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

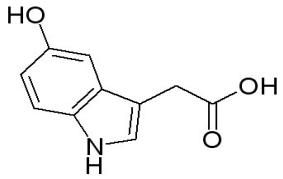


5-Hydroxy-tryptophan-decarboxylase



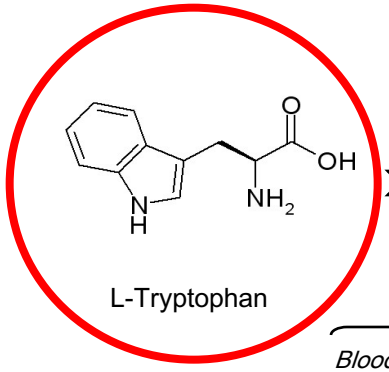
Serotonin (5-Hydroxy-tryptamin, 5-HT)

MAO

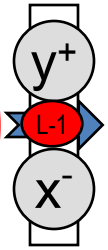


5-hydroxyindoleacetic acid (5-HIAA)

ATD challenge

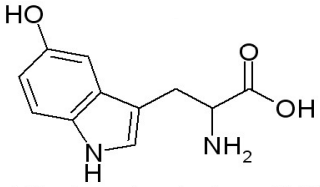


L-Tryptophan

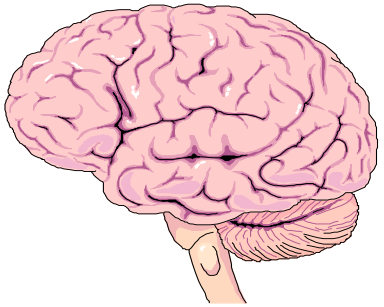


Blood brain barrier

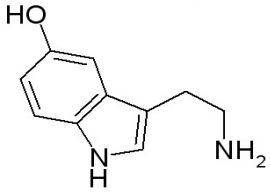
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

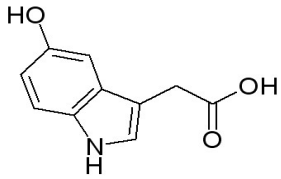


5-Hydroxy-tryptophan-decarboxylase



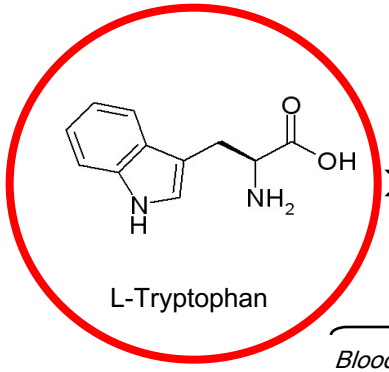
Serotonin (5-Hydroxy-tryptamin, 5-HT)

MAO

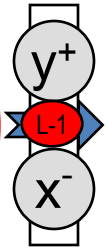


5-hydroxyindoleacetic acid (5-HIAA)

ATD challenge

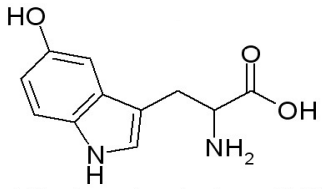


L-Tryptophan

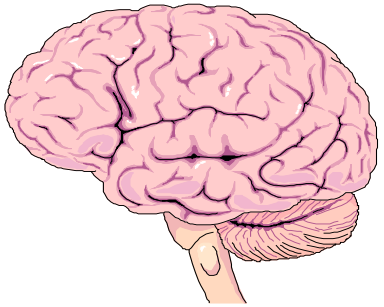


Blood brain barrier

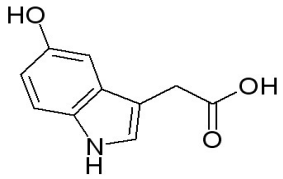
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

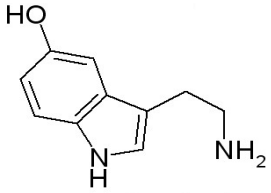


5-Hydroxy-tryptophan-decarboxylase



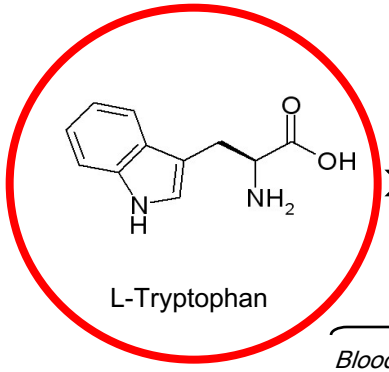
5-hydroxyindoleacetic acid (5-HIAA)

MAO

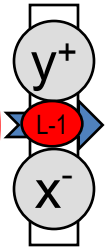


Serotonin (5-Hydroxy-tryptamin, 5-HT)

ATD challenge

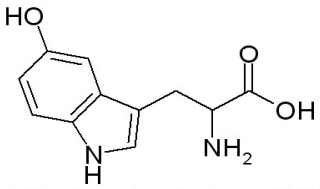


L-Tryptophan

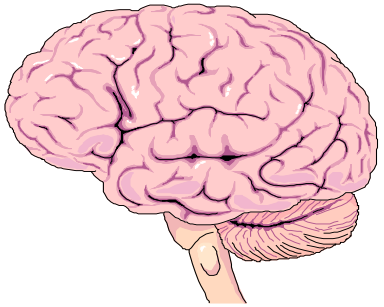


Blood brain barrier

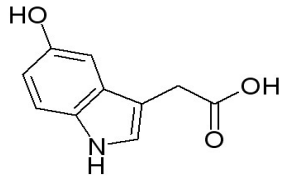
Tryptophanhydroxylase 2 (TPH-2)



5-Hydroxy-tryptophan

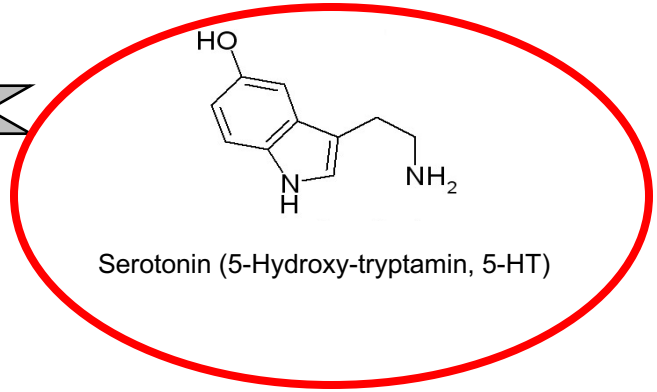


5-Hydroxy-tryptophan-decarboxylase

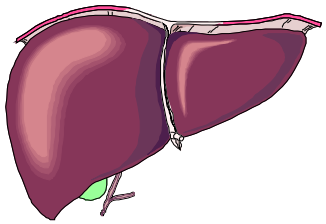


5-hydroxyindoleacetic acid (5-HIAA)

MAO



Serotonin (5-Hydroxy-tryptamin, 5-HT)



ATD Moja-De

Dosage per 10 kg body weight

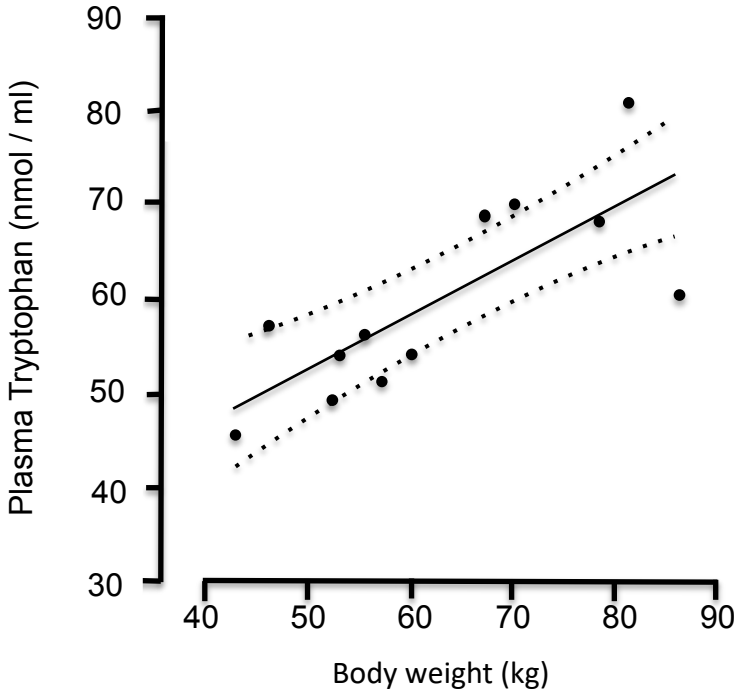
→ PHE: 1.32g
→ LEU: 1.32g
→ ILE: 0.84g
→ MET: 0.5g
→ VAL: 0.96g
→ TRE: 0.6g
→ LYS: 0.96g

→ Without TRP = ATD

→ With TRP = Control condition / balanced amino acid load (BAL)

Zepf et al., 2008a; Human Psychopharmacology: Clinical and Experimental

TRP & body weight



Correlation (Pearson, 95% error interval) between body weight (kg) & plasma TRP (nmol/ml) (r_{xy} = 0.8 ; p = 0.001) under baseline conditions

Kewitz 2002;
Demisch et al., Eur Arch Psych Clin Neurosci, 2002

ATD Moja-De vs. other ATD protocols

- Methionine ↓
- Phenylalanine ↑
- Lower total amino acids ↓
- Body weight adapted dosing regime

→ fewer side effects (nausea, vomiting, etc.)

Zepf et al., 2008a; Human Psychopharmacology: Clinical and Experimental

Animal research

Advantage:

→ Invasive methods can be used

→ Post-mortem data

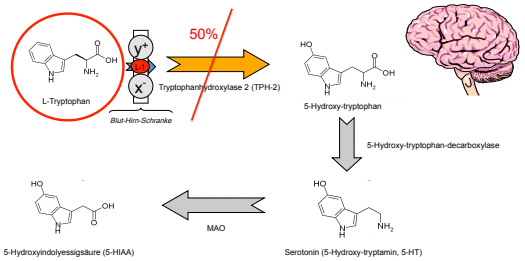
→ Combination of knock-out mice or hypomorph rodents (z.B. Balb c/J mice) with neurochemical challenge techniques

Animal research

C57 mice (controls)

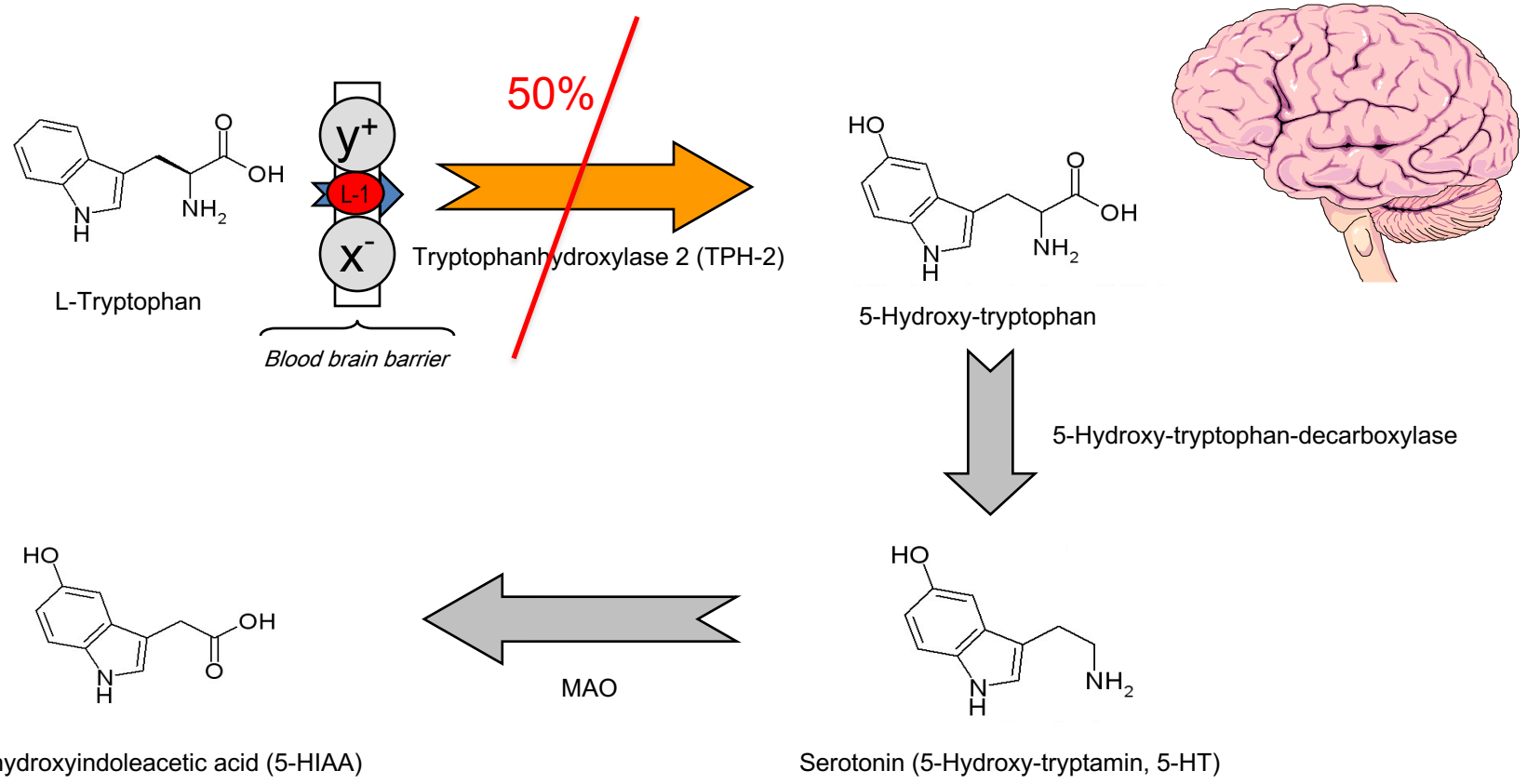
- Standard mouse model
- Often used as baseline in strain comparison

Balb c/J mice (TPH-2 hypomorph mice)



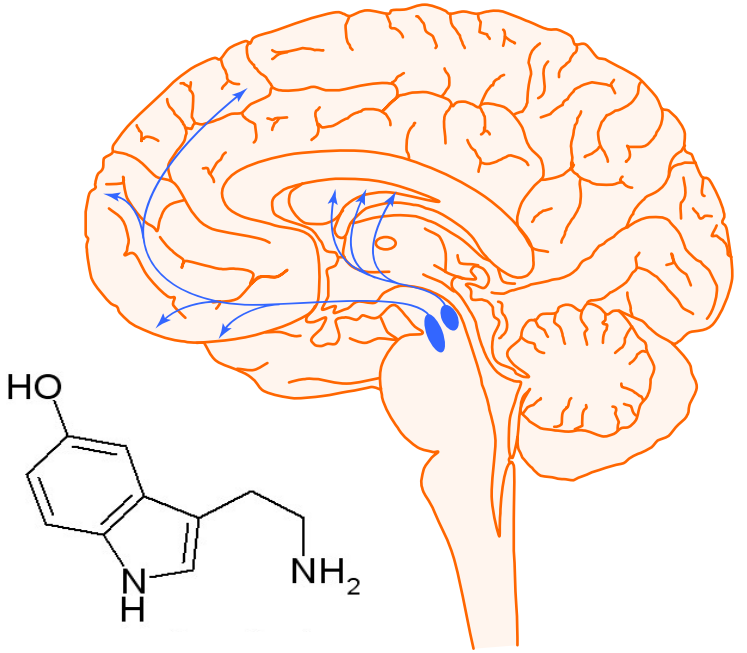
- TPH-2-Mutation, reduced brain serotonin synthesis
- Often used as a model for depression or social anxiety

ATD challenge



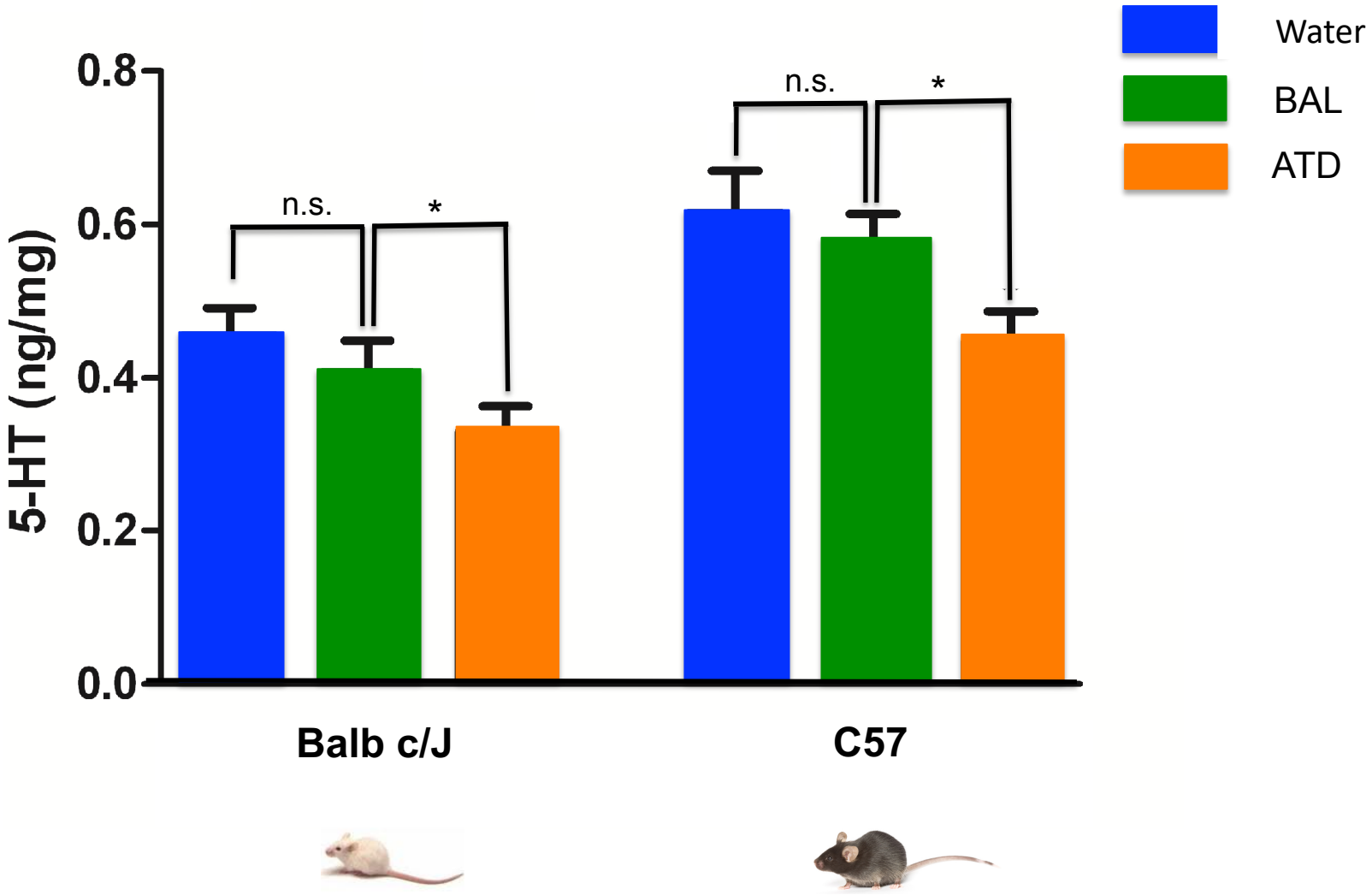
Brain regions

- Hippocampus
- Prefrontal cortex
- Frontal cortex

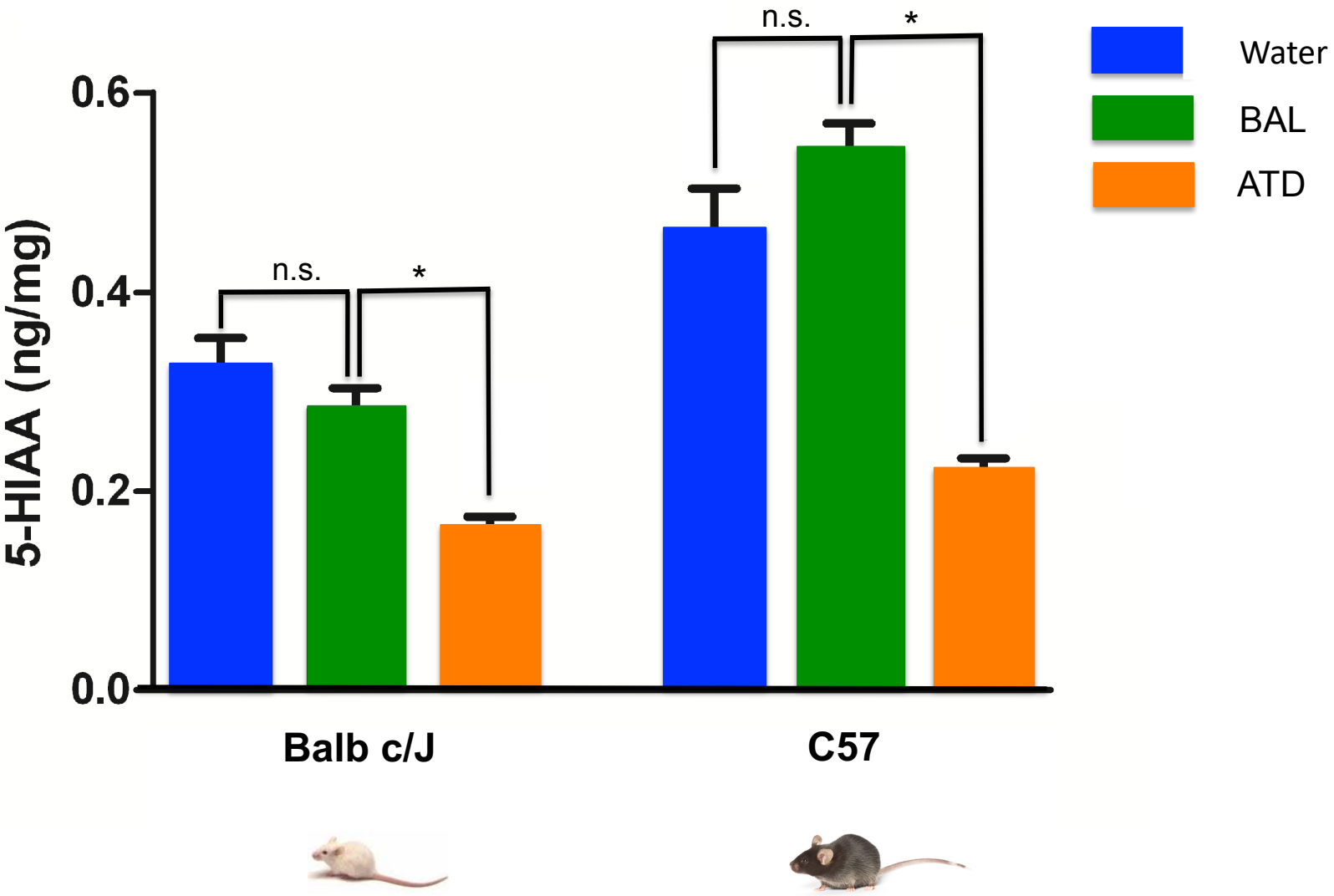


Biskup, C.S., ..., Zepf, F.D. PLoS One 7(5): e35916, 2012

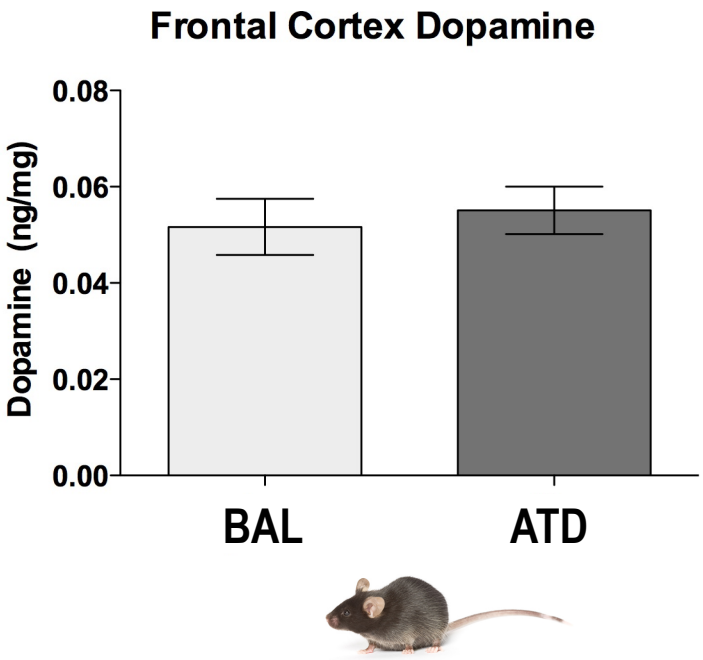
5-HT (Hippocampus)



5-HIAA (Hippocampus)



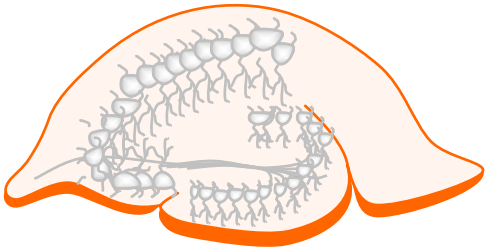
C57 mice



Biskup et al., 2012, PLoS One

Animal data - Summary

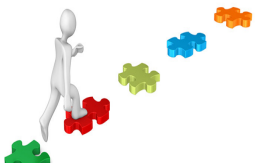
- BAL mixture is a valid control condition
- ATD was effective in both strains of mice
- No effects on dopamine



Data on TRP & serotonin in humans - Adults

ATD - methodological aspects

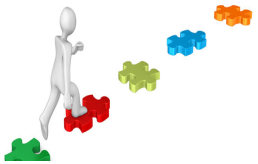
Exclusion criteria:



- Somatic disorders
- Psychotic disorders
- Abnormal BMI
- Substance abuse
- Severe developmental disorders

ATD - methodological aspects

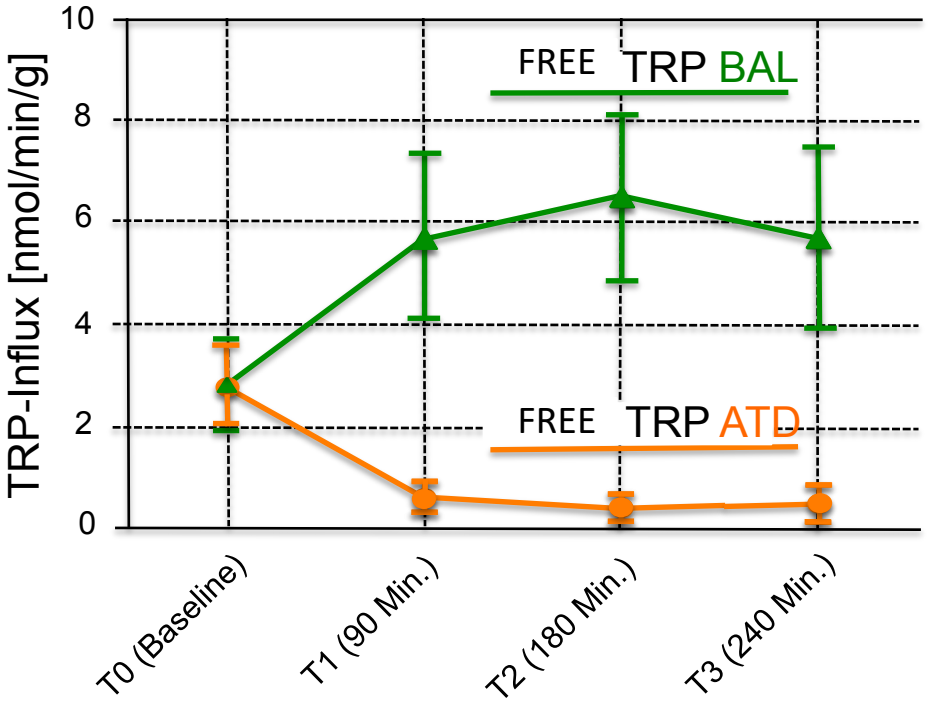
Diet:



- Overnight protein fast
- Standardised breakfast (no TRP)
- Vitamin/Niacin supplementation

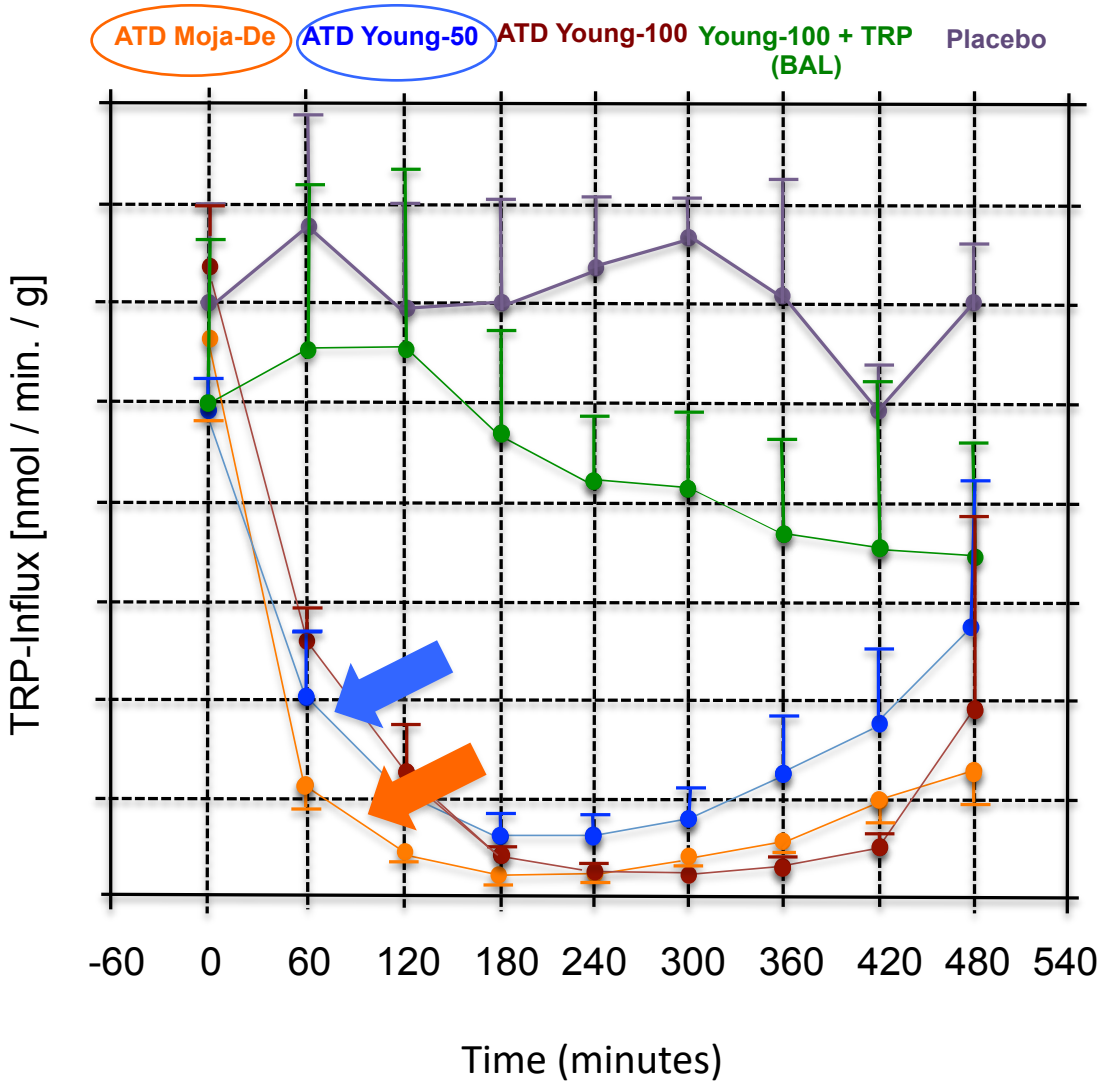
→ Co-enzymes NAD^+, NADH, $NADP^+$, NADPH

Tryptophan influx into the brain



Dingerkus, V.L.S., ..., Zepf, F.D.
Journal of Neural Transmission 119(9): 1037-45, 2012

Comparison of ATD challenge protocols



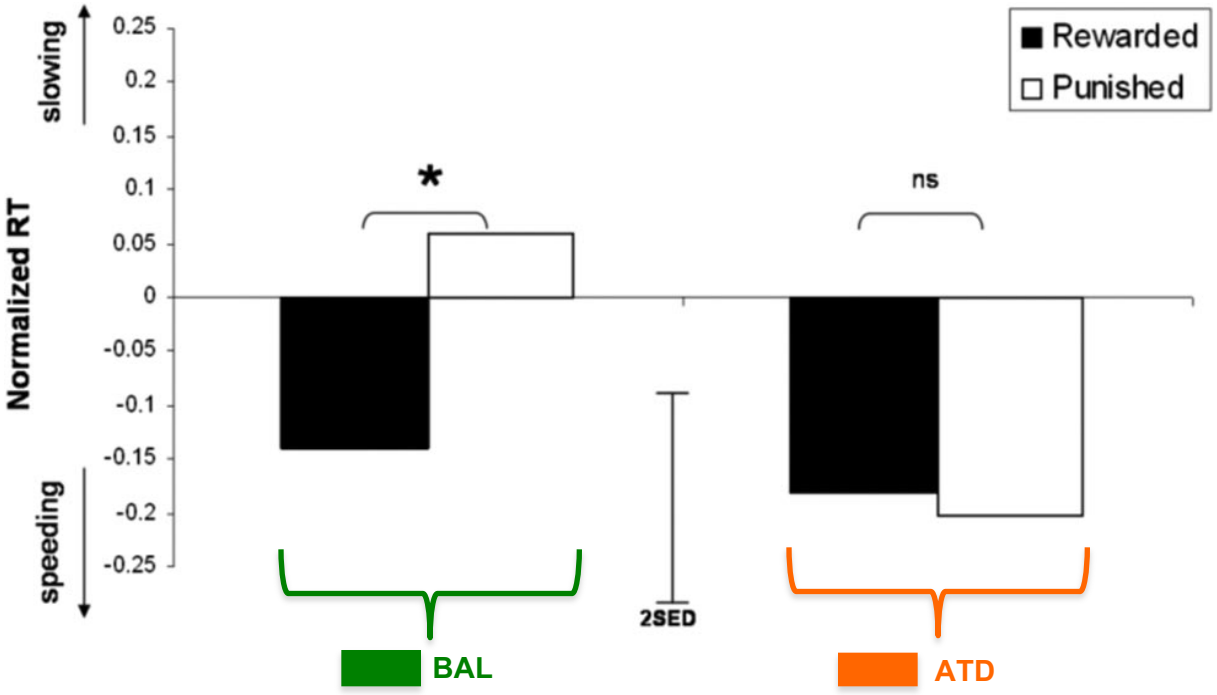
Demisch et al., Arch Psych Clin Neurosci, 2002

Serotonin, tryptophan & behaviour

How do changes in diet affect our behaviour via tryptophan supply and serotonin?

Behavioural inhibition / disinhibition

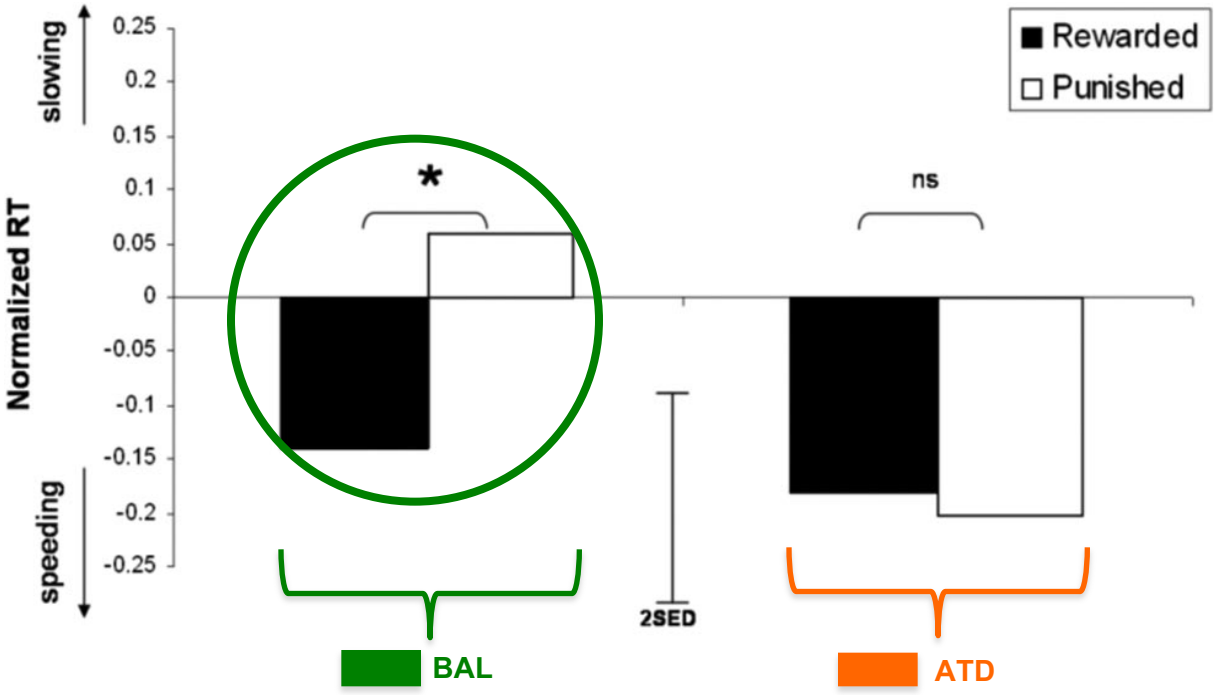
Diminished brain serotonin synthesis led to lower punishment-induced behavioural inhibition



Crockett, M.J.et al.
J Neurosci. 23;29(38):11993-9, 2009

Behavioural inhibition / disinhibition

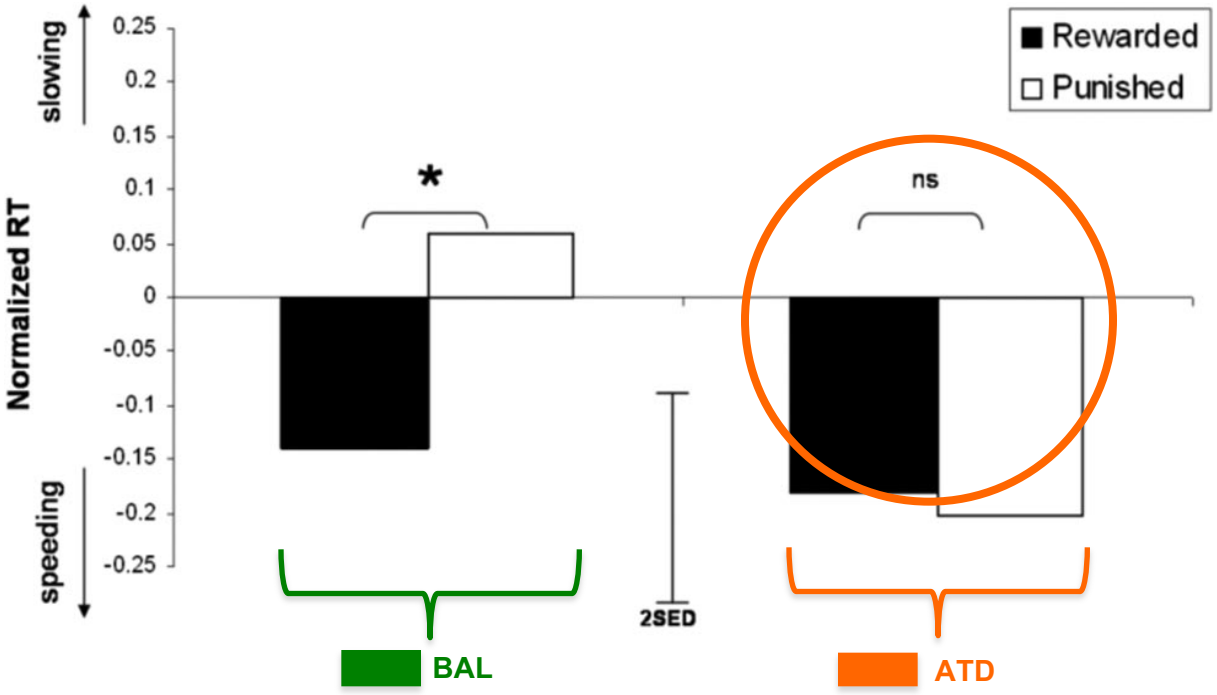
Diminished brain serotonin synthesis led to lower punishment-induced behavioural inhibition



Crockett, M.J.et al.
J Neurosci. 23;29(38):11993-9, 2009

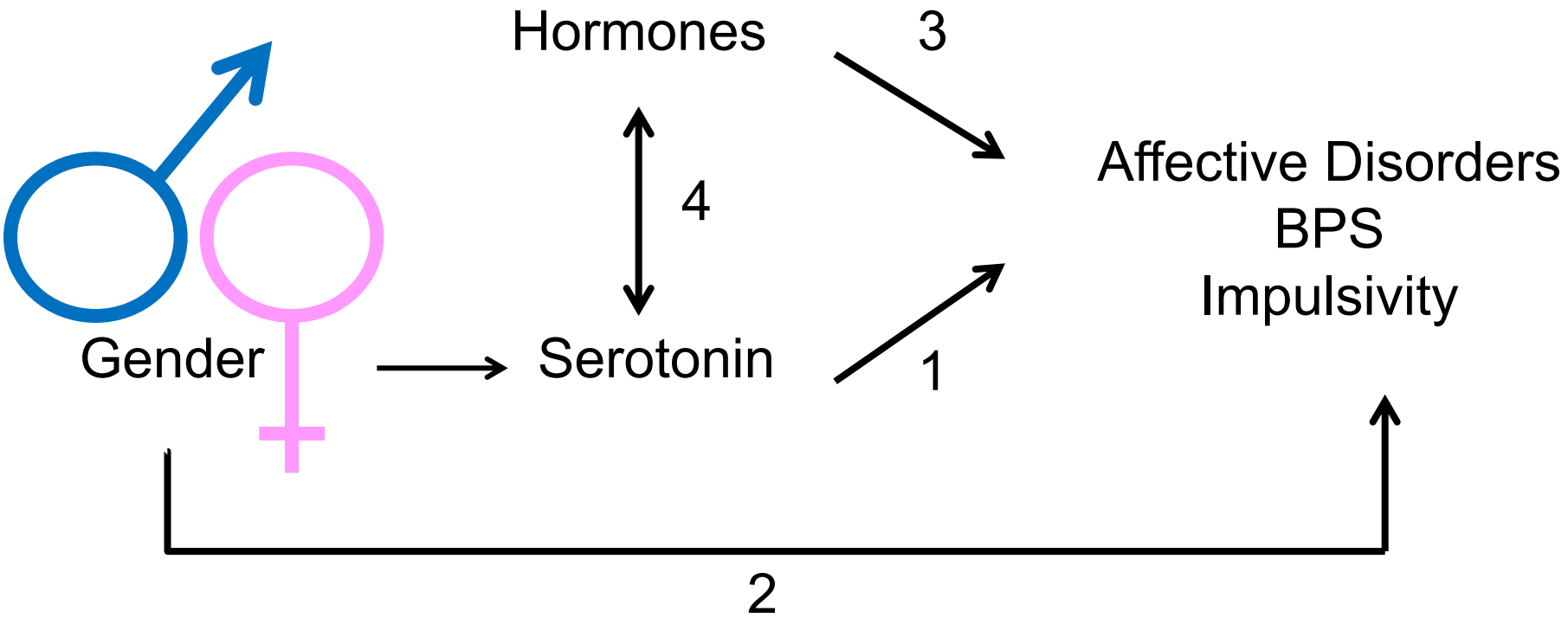
Behavioural inhibition / disinhibition

Diminished brain serotonin synthesis led to lower punishment-induced behavioural inhibition



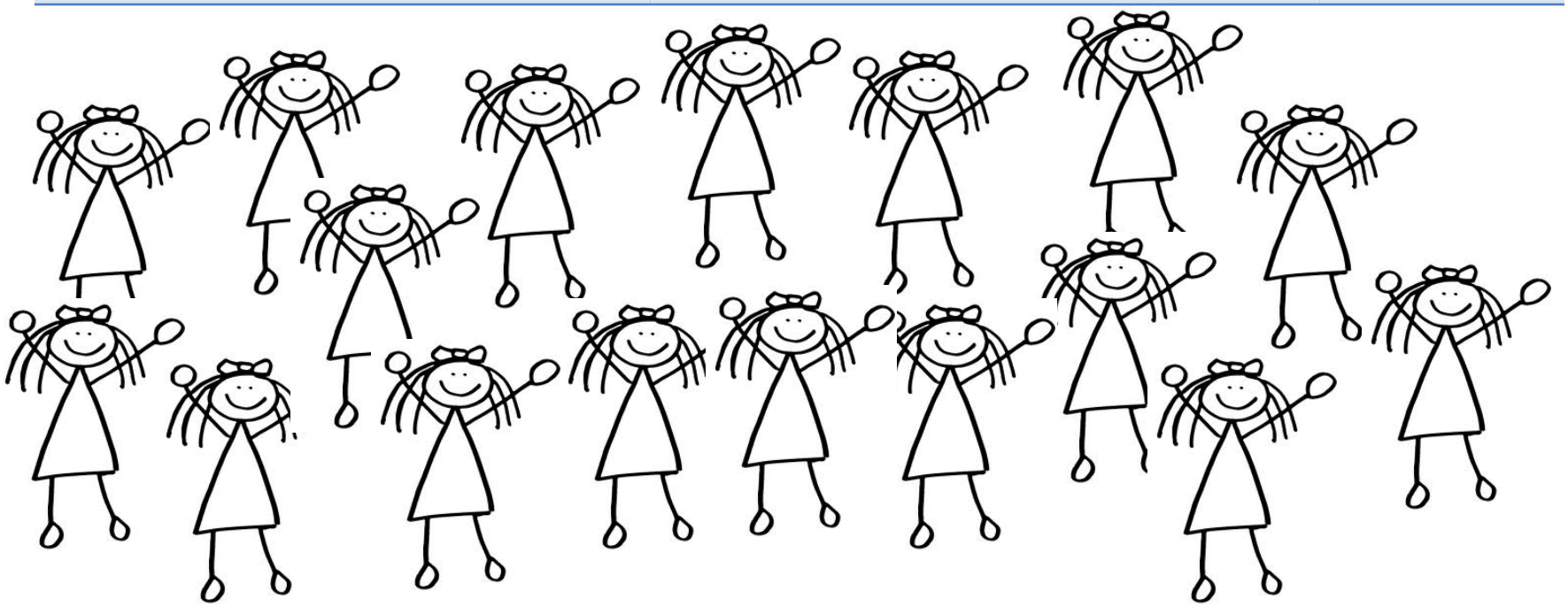
Crockett, M.J.et al.
J Neurosci. 23;29(38):11993-9, 2009

Punishment & inhibition - Role of serotonin



Methods – Study sample

N	Study days	Gender	Age	BMI	IQ	I7-Eysenck (impulsivity at baseline)
18	2	Female	M = 24.22 SD = 2.9	M = 23.58 SD = 3.7	M = 110.28 SD =10.5	M = 42.93 SD = 8.6



Helmbold, K., ... Zepf, F.D. Effects of serotonin depletion on punishment processing in the orbitofrontal and anterior cingulate cortices of healthy women. Eur Neuropsychopharmacol. 2015 Jun;25(6):846-56.

Punishment & inhibition - Role of serotonin

Goal: Investigating the neuronal correlates of punishment-induced behavioural inhibition and their serotonergic modulation

Important: Controlling for the individual menstrual cycle

Menstrual phase	BAL	ATD
Early follicular phase (34/36) or last days of luteal phase (2/36)	Mean= 2.72 SD=2.37	Mean= 3.89 SD=1.74

	Estradiol [pmol/l]	FSH [U/l]	LH [U/l]	Day of menstrual cycle
BAL	155.22±100.25	4.83±2.11	5.74±2.83	2.7±2.4
ATD	148±61.11	5.65±1.21	7.79±4.17	3.9±1.74
z- or t- value	z = - 544	$t_{(17)}$ = -1.74	z = -1.26	$t_{(17)}$ = -1.69
p-value	.586	.099	.206	.110

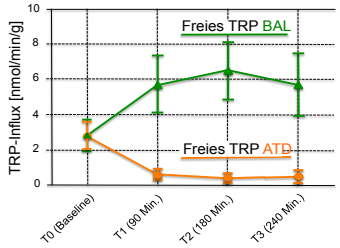
Helmbold, K., ... Zepf, F.D. Eur Neuropsychopharmacol. 25(6):846-56, 2015

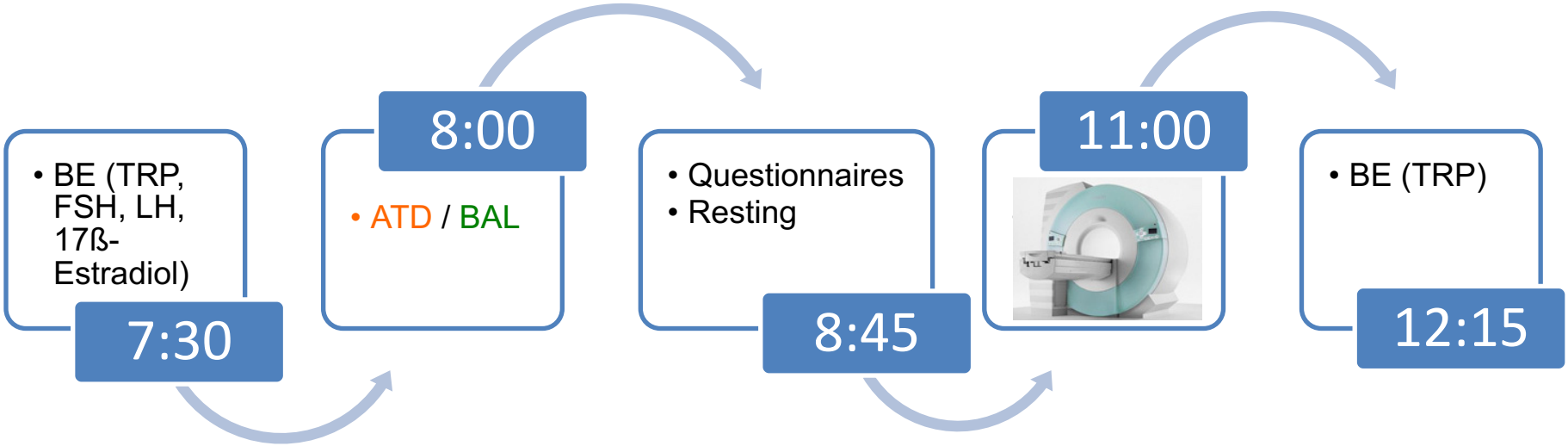
Study design

- Double-blind within subject cross-over design

- 2 study days (spaced at least 1 individual menstrual cycle apart)

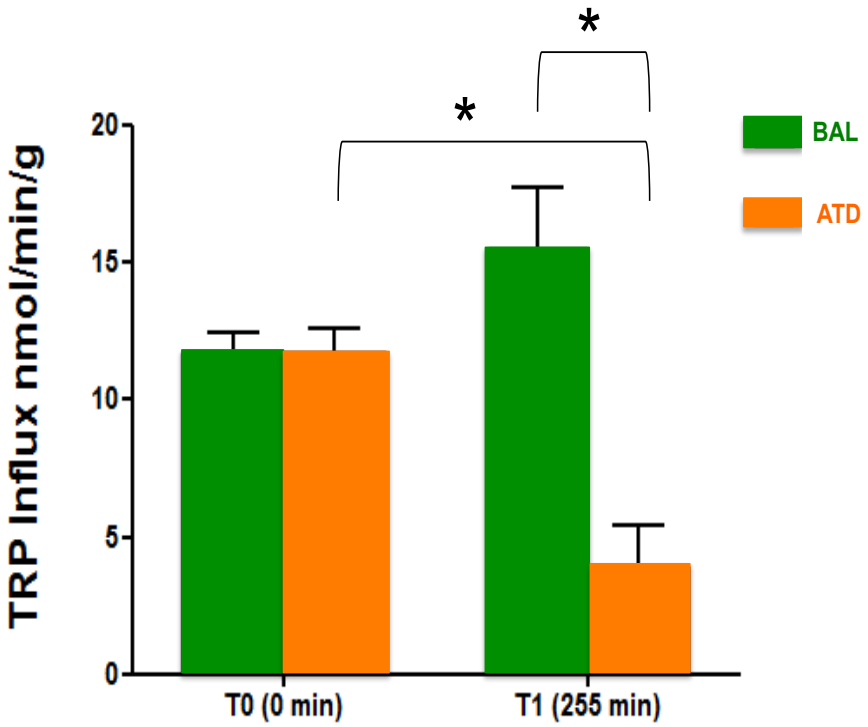
- “Overnight protein fast” before ATD / BAL





Helmbold, K., ... Zepf, F.D.
Eur Neuropsychopharmacol.
25(6):846-56, 2015

Findings – Tryptophan influx into the brain



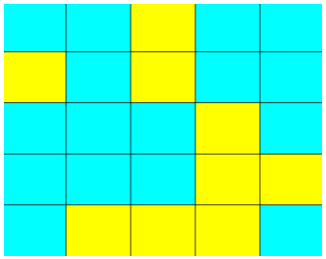
Typtophan depletion:

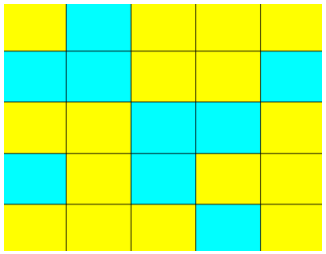
T0 vs. T1: 67,27 % reduction
$t_{(17)}=17.5$, $p < 0.001$

T1 ATD vs. BAL
$t_{(17)}=17.3$, $p < 0.001$

Helmbold, K., ... Zepf, F.D.
Eur Neuropsychopharmacol.
25(6):846-56, 2015

Methods - Crockett-Paradigm





Stimulus Go	Stimulus NoGo	
correct	incorrect	missing impulse control comission error
correct	incorrect	
correct	incorrect	
incorrect	correct	omission error

Crockett, M.J.et al.
J Neurosci. 23;29(38):11993-9, 2009

Methods - Crockett-Paradigm

Condition	Blocks	Feedback correct answer	Feedback wrong answer
Reward	Go Reward	Only positive, winning points	0 points
	NoGo Reward		
Punishment	Punish Go	0 points	Only negative, loss of points
	NoGo Punish		

Punishment-induced behavioural inhibition = Ability to inhibit in aversive contexts

Critical condition:

NoGo-trials with punishment

(= wrongly pressed a button → punishment)

Data analysis

- ANCOVA: Contrast between BAL / ATD during NoGo-trials with punishment

- Whole brain correlation maps: Contrast BAL minus ATD (NoGo-punishment) with

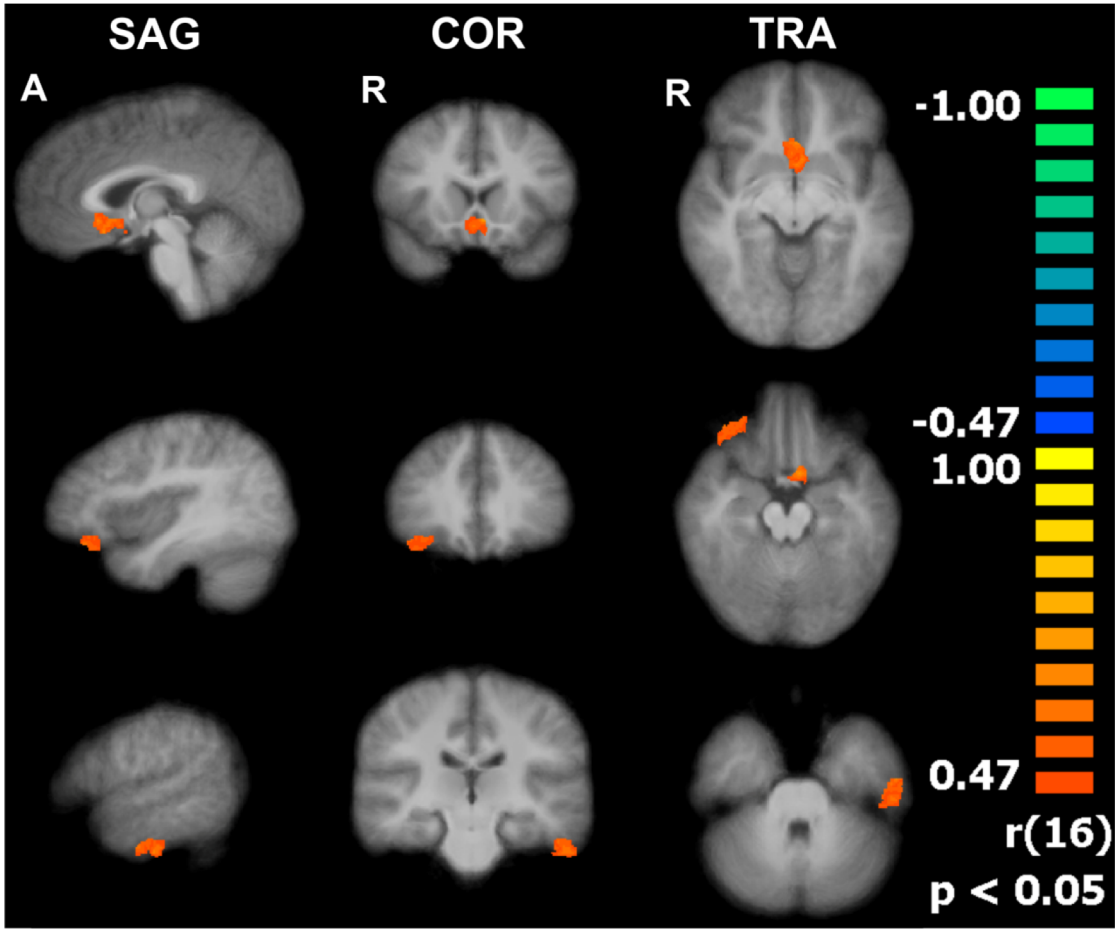
    1) Depletion magnitude (depletion magnitude)

    1) Trait-impulsivity (Eysenck I7)

Helmbold, K., ... Zepf, F.D. Effects of serotonin depletion on punishment processing in the orbitofrontal and anterior cingulate cortices of healthy women. Eur Neuropsychopharmacol. 2015 Jun;25(6):846-56.

Results:

Whole brain correlation - Contrast NoGo-trials "BAL punished" vs. "ATD punished" with "Depletion magnitude"



a) Left ventral and right subgenual ACC

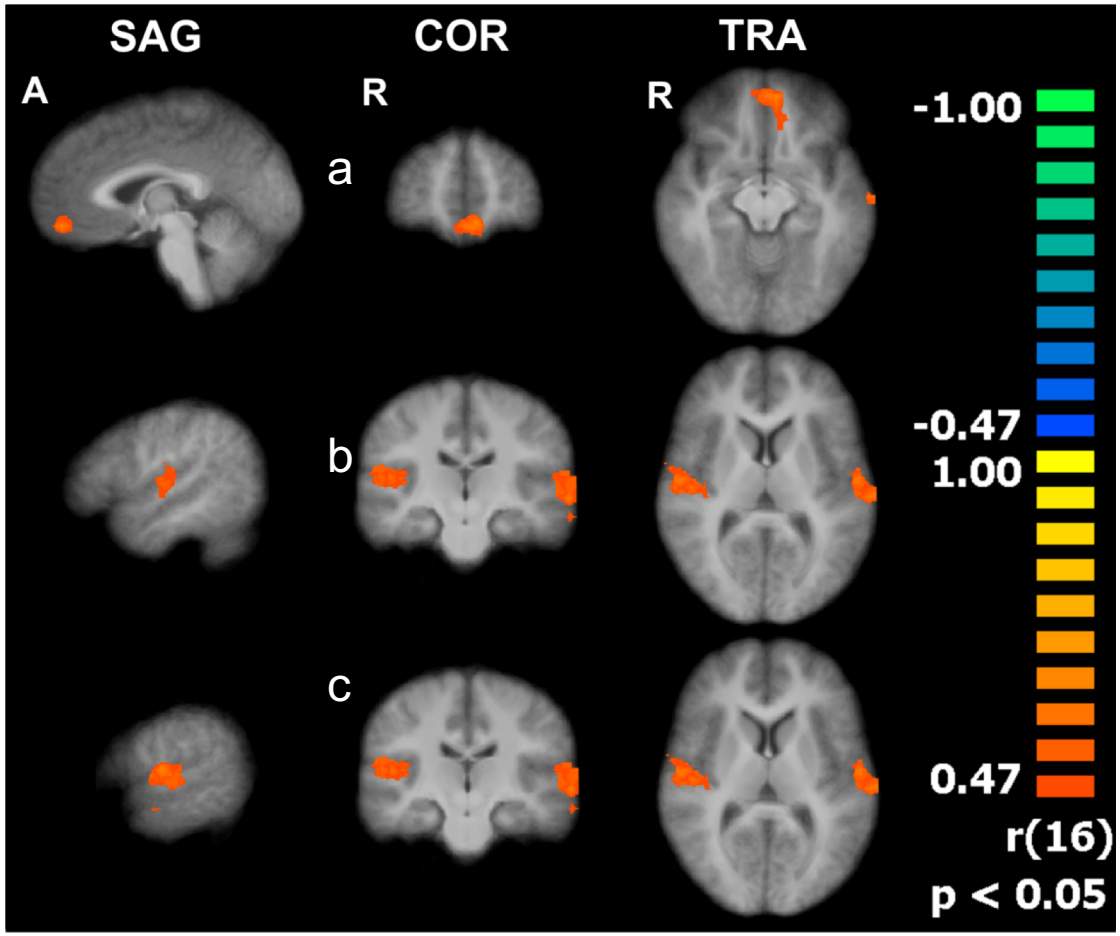
b) Right OFC

c) Left inferior temporal area

Helmbold, K., ... Zepf, F.D. Eur Neuropsychopharmacol. 25(6):846-56, 2015

Results:

Whole brain correlation - Contrast NoGo-trials "BAL punished" vs. "ATD punished" with trait-impulsivity



a) Right and left OFC and ACC

b) Right superior temporal area

c) Left superior temporal area

Helmbold, K., ... Zepf, F.D. Eur Neuropsychopharmacol. 25(6):846-56, 2015

Results - Summary

- Reduced dietary tryptophan availability in the brain impacted brain activation in the context of behavioural inhbition and punishment

Activation was modulated by

→ Tryptophan depletion magnitude

→ Trait-impulsivity (baseline impulsiveness)

Data on TRP & serotonin in humans – Children & adolescents

Serotonin & ADHD

- ADHD symptoms & comorbid symptoms impacted by serotonin

→ *Affective and emotional processes*

→ *Impulsive behaviour*

→ *Aggressive behaviour*

ADHD as a syndrome

Attention Deficit Hyperactivity Disorder (ADHD)

or also known as the

Kramer-Pollnow Syndrom

First publication in Germany in 1932 by Franz Kramer and Hans Pollnow, Charité Berlin

Characteristics

- Hyperactive behaviour
- Onset in childhood
- Attention problems
- Developmental problems
- Emotional problems / affective dysregulation
- Impulsivity / aggression

Characteristics

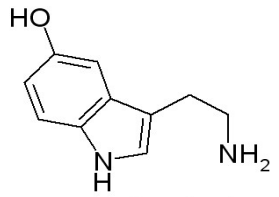
- Hyperactive behaviour
- Onset in childhood
- Attention problems
- Developmental problems
- Emotional problems / affective dysregulation
- Impulsivity / aggression

Characteristics

- Hyperactive behaviour
- Onset in childhood
- Attention problems
- Developmental problems
- Emotional problems / affective dysregulation
- Impulsivity / aggression

Relevance of serotonin (5-HT)

- Mood: Affective disorders
- Cognition: Attention processes
- Appetite regulation: Eating disorders
- Behavioural inhibition: Aggressive behaviour



Serotonin (5-Hydroxy-tryptamine, 5-HT)

→Aggressive responding

→ Physiological response

→ Mood

Effects of serotonin on impulsivity, aggression & mood

Animal research & adults

- Serotonin-hypothesis for aggressive behaviour

ADHD

- Because of impulsive and aggressive behaviour (comorbid conduct disorder) patients with ADHD are a population that allows studying the impact of 5-HT on these parameters

Serotonin & ADHD

- Symptoms of ADHD & comorbid symptoms suggested to be modulated by 5-HT (ATD / BAL)

→ *Aggressive / impulsive behaviour*

→ *Physiological parameters (heart rate)*

→ *Affective and emotional processes (mood)*

Study

- 22 patients with ADHD

- Double-blind within-subject crossover design (randomised)

- Point Subtraction Aggression Game (PSAG)

Questions:

- Impact of changed serotonergic neurotransmission (ATD / BAL) on

→*Anger / aggression*
→*Heart rate*
→*Mood related parameters?*

Study task

- PC-based provocation of anger / aggression

- Fictive opponent

- Winning & loosing trials were pre-arranged

Study task

Pressing a button when a stimulus (soccer ball) appeared

Provocation

High provocation (HP) – Opponent subtracts 80-100 points

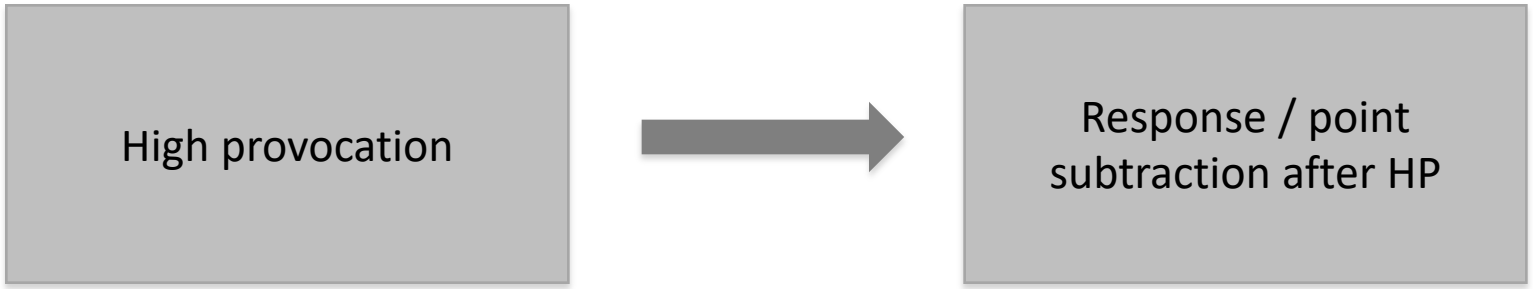
Low provocation (LP) – Opponent subtracts 20-40 points

Response of participants

High provocation (HP) – Opponent subtracts 80-100 points
Low provocation (LP) – Opponent subtracts 20-40 points

Loosing trial

Winning trial

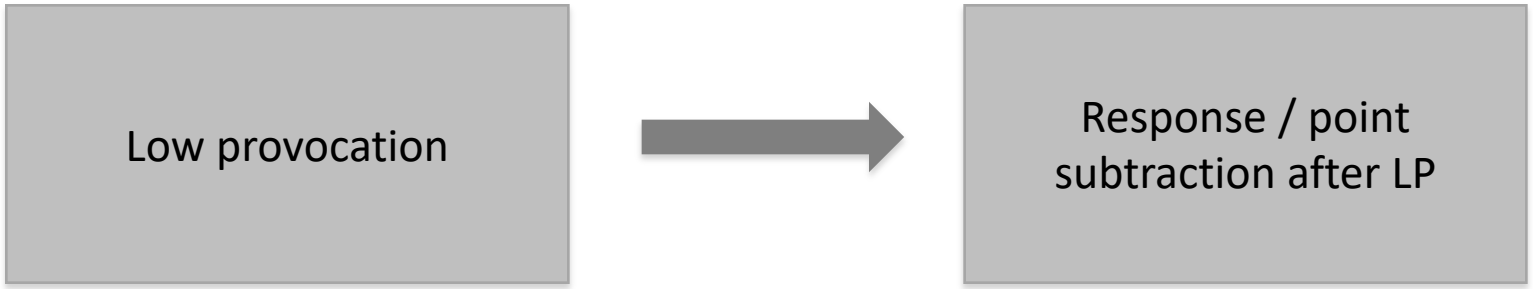


Response of participants

High provocation (HP) – Opponent subtracts 80-100 points
Low provocation (LP) – Opponent subtracts 20-40 points

Loosing trial

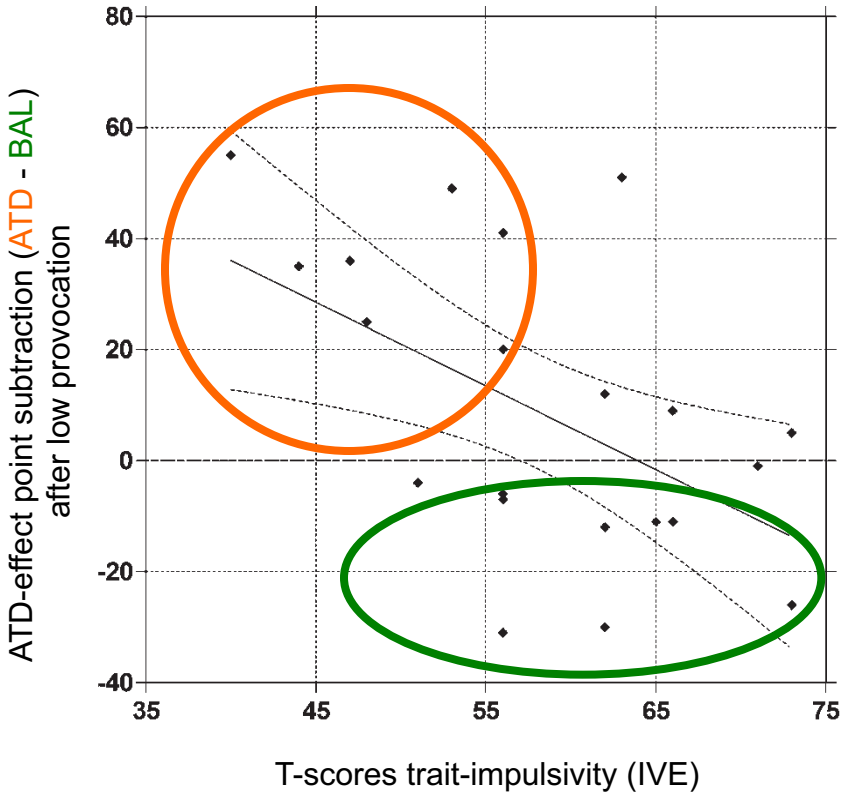
Winning trial



Dependent variables after ATD / BAL:

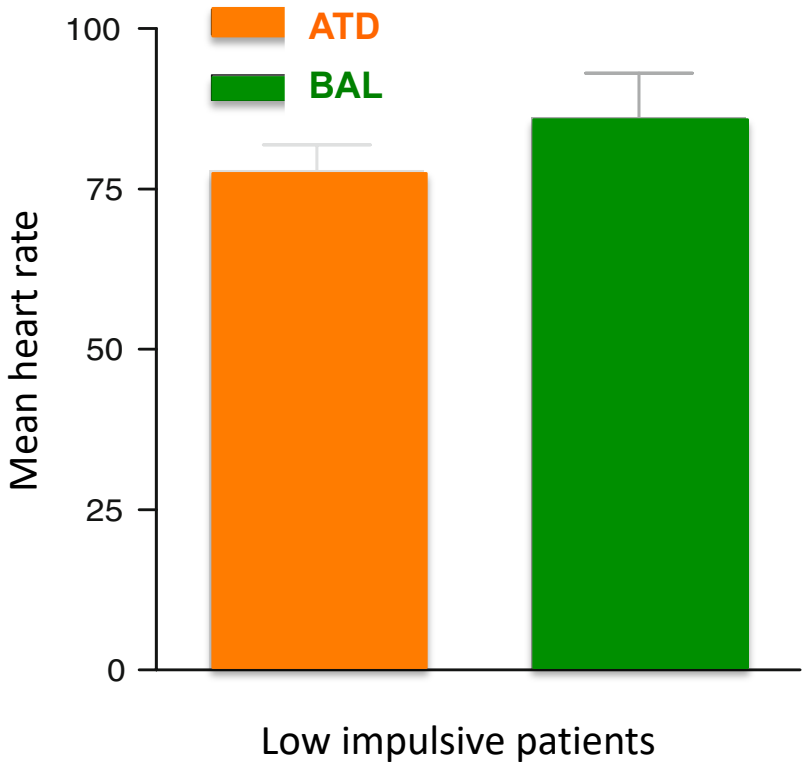
Point subtraction, heart rate, mood

Results – Point subtraction



Zepf et al., 2008a;
Human Psychopharmacology:
Clinical and Experimental

Results – Heart rate



Zepf et al., 2008b;
Journal of Neural Transmission

Results - Mood

- **ATD-Test:**

→ No ATD-effect on mood in children & adolescents with ADHD (Eigenschaftswörterliste [EWL-KJ, 20-item Version] nach Janke & Janke, 1998)

HUMAN PSYCHOPHARMACOLOGY
Hum. Psychopharmacol Clin Exp 2009; **24**: 87–94.
Published online in Wiley InterScience
(www.interscience.wiley.com) **DOI**: 10.1002/hup.1002

Diminished central nervous 5-HT neurotransmission and mood self-ratings in children and adolescents with ADHD: no clear effect of rapid tryptophan depletion

Florian Daniel Zepf[1]*, Martin Holtmann[1,2], Christina Stadler[1], Sophie Magnus[1], Lars Wöckel[1,3] and Fritz Poustka[1]

Zepf et al., Human Psychopharmacology: Clinical and Experimental, 2009

Overview of presentation

1. Concept of nutritional psychiatry

First field data

2. Impact of nutrition on psychiatric symptoms – research findings on the role of amino acids

Study approaches & methodology
Cognitive processes
Mood
Aggression and impulsivity

3. Implications for service development & delivery

Aspects of service delivery

Nutrition & mental health

- Nutrition can impact mental health symptoms

- Example: Amino acid metabolism → impact on disinhbition, aggressive behaviour, etc.

- **However:** Be careful with recommending specific (and sometimes possibly exotic) diets for your patients

Aspects of service delivery

Nutrition & mental health

→ There is still little evidence (if at all) for specific diets as regards symptom remission, in particular in children

→ There is a high risk that dietary advice may not be followed as exactly as prescribed, which leads to the risk of malnutrition

→ Very often there seems to be an impression by some clinicians and the lay public that “you cannot do wrong” because “it’s only the diet” → this is not the case

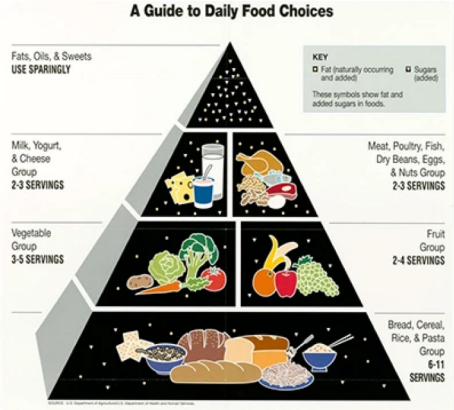
→ A balanced diet can help to mitigate against malnutrition

Aspects of service delivery

In a nutshell:

Balanced diet = *No evidence for "doing it wrong", but there could potentially be additional benefits once the impact of specific nutrients on symptoms of a specific disorders is further clarified*

Exotic diets: *No evidence for "doing it right"*



Aspects of service delivery

So, what can you do now?

→ Be aware of your patient's dietary intake (or non-intake) → Awareness about malnutrition

→ Be aware of your patient's eating habits: Scheduling of meals, fasting, etc.

→ Provide high quality foods: High nutritional value (quality)

→ Provide sufficient foods: Sufficient dietary intake (quantity)

→ Compliance: Make the food taste and look good → This is an important strategy for mitigating the risk of malnutrition

→ Be reflective: Ask your patients for their opinion about the food provided

Aspects of service delivery

So, what can you do now?

→ Improvement: Ask your patients about what they would like to see changed (consumer & carer engagement)

→ Assessment & monitoring: Have a dietician as part of your mental health team

→ Use of supplements: Know exactly what your patients are taking (who prescribed what, when, and with what rationale?)

Take home messages

Nutrition & mental health

- Nutrition in mental health: Still a blind spot in clinical service delivery, but there are strategies to make sure that diet is not a negative confounder in remission

- Specific nutrition as an accelerator for recovery in specific disorders: There's still a lot of research needed!

- Be careful about "nutrition Guru's": History shows that it is very (!) rare that only one person on the planet can do a particular thing

Take home messages

Nutrition & mental health

- The interplay between nutrition & MH is complex!
- Research in this area has a lot of confounders (gender, hormones, genetics, interactions, other nutrients, etc.)
- Nutritional psychiatry & mental health is an emerging field
- Impact of nutrition cannot be ignored (but it often is)

Take home messages

Nutrition & mental health

- **Tryptophan / serotonin pathway:** Example for complex interplay
- **Tryptophan / serotonin:** Impact on behavioural inhibition in adults
- **Children & adolescents**: Impact of tryptophan on aggression & heart rate
- **Reminder:** This is only 1 (!) nutritional component, there are many others!
- **Other influences:** Many other dietary components can impact behaviour, mood, sleep, and brain function

Research directions – Intervention & diagnostics

Neurophysiology

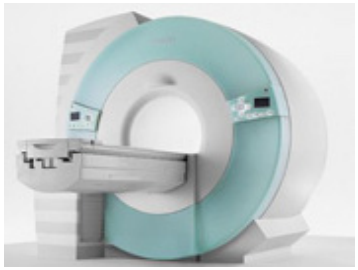
- *Psychopharmacology*
- *Immunology*
- *Animal models*
- *Genetics*

Molecular biology

Dietary neuroscience

Neuromodulation

Imaging / MRI



Developmental psychopathology

Nutritional psychiatry – An outlook

A next critical step for the field is

designing psychiatric interventional studies for both dietary modification and nutraceuticals, based on more of a personalised medicine approach, using biomarkers

> Nutrient deficiencies

> Inflammatory cytokine levels

> Genomic assessment

> Microbiome analysis

> A person's dietary patterns

> Individual macro/micronutrient requirements

Sarris, 2019

Nutritional psychiatry – An outlook

- Current indicators point towards mental disorders having an increased burden of disease that will continue to rise globally over the coming decades

- Psychiatry and mental health are at a critical juncture

- The current pharmacologically focused model has only achieved modest benefits in addressing the global burden of poor mental health

Whiteford et al., 2013; Sarris, 2019

Nutritional psychiatry – An outlook

- Early intervention research is also needed to study nutritional interventions at crucial developmental stages

- From this resultant research, the evidence needs to be communicated to clinicians and the wider public

- Implementation through educational institutions and the latter via public health campaigns

Sarris, 2019

Nutritional psychiatry – An outlook

- Formal education to clinicians from a broad range of fields should include training
- Training & education: The role of diet and nutrients on brain function and mental health
- Nutrition is increasingly being regarded as an important aspect of mental health
- Public policy will very likely reflect this evolving recognition in the future (if the appropriate and detailed research is done)

Sarris, 2019

Thank you

Jena:
C. Ligges, M. Ligges, C. Filz, M. Walter

Perth:
K. Runions, P. Rao, R.M. Stewart, S. Hood, Y. Martinez Ladino, J. Moore, W. Chen, A. John, H.A. Morandini, P. Drummond, A. Jaworska, A. Jablensky, A. Linh

Aachen / Jülich:
Prof. Dr. B. Herpertz-Dahlmann, Prof. Dr. F. Schneider, Prof. Dr. K. Konrad, Prof. Dr. U. Habel, Prof. Dr. K. Mathiak, Prof. Dr. G.R. Fink, Prof. Dr. P. Weiss-Blankenhorn, Prof. Dr. N. J. Shah, PD Dr. med. T. Vloet, PD Dr. med. L. Wöckel, Prof. K.-J. Langen, Dr. C. Filss, W. Königschulte, V. Dingerkus, W. Kötting, C.S. Biskup, M. Linden, A. Gallien, J. Albrecht, P. Hildebrand, J. Weaver, T. Schmitt, S. Dresbach, S. Sippas, J. Kempf, L. Swaid, L. Thelen

Frankfurt am Main:
L. Wöckel, M. Holtmann, C. Stadler, L. Demisch, D. Demisch, C.M. Freitag

Collaborators

Duke University: C.M. Kuhn, A. Arrant, A. Day van Swearingen, C.L. Sánchez López, Prof. J. S. March, R. Williams

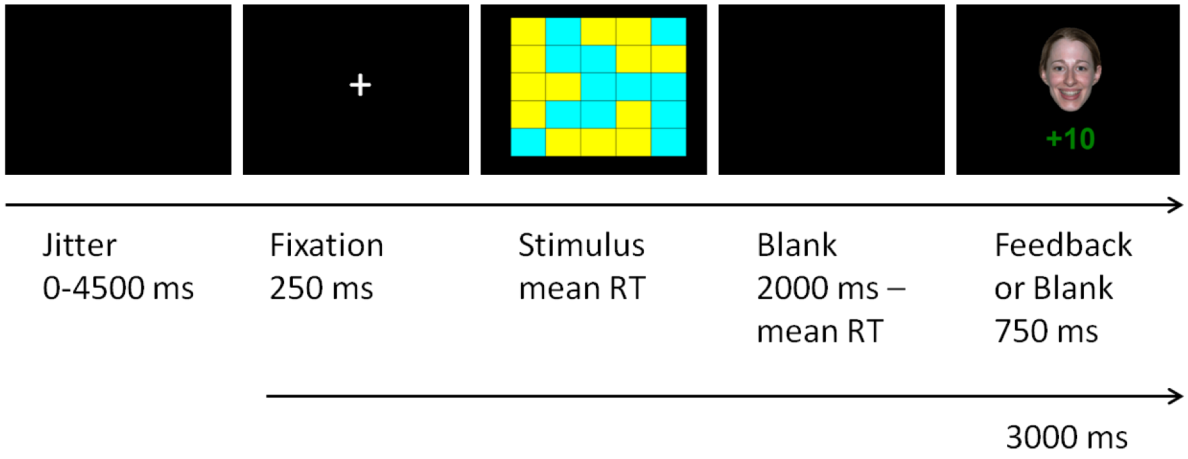
NIMH: D.S. Pine, E. Leibenluft

New York Child Study Center: F.X. Castellanos, M. Milham, C.-G. Yan

Oxford: M. Crockett, T.W. Robbins

Thank you for your attention!

Methods - Crockett-Paradigm



Crockett, M.J., Clark, L., Robbins, T.W. Reconciling the role of serotonin in behavioral inhibition and aversion: acute tryptophan depletion abolishes punishment-induced inhibition in humans. J Neurosci. 2009 Sep 23;29(38):11993-9.