Nutritional Psychiatry

Ernährung und psychische Gesundheit
APS-Kongress 2022

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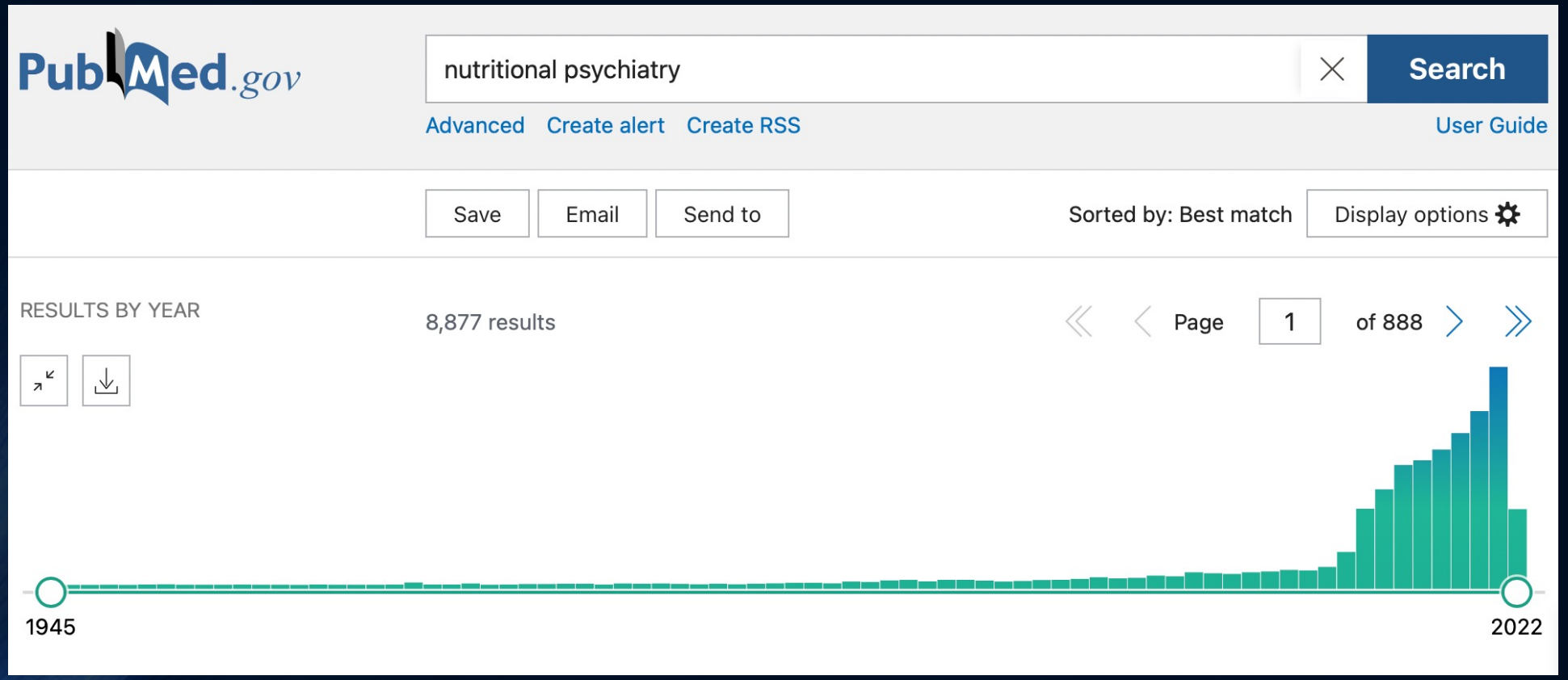
Überblick

- Das Mikrobiom und die Gut-Brain-Axis
- Probiotika
- Ernährung
- Nahrungsergänzung
- «biologische» Therapieansätze

Und Gott sprach: Seht da, ich habe euch gegeben alle Pflanzen, die Samen bringen, auf der ganzen Erde, und alle Bäume mit Früchten, die Samen bringen zu eurer Speise.
1. Mose 1,29

Alles, was sich regt und lebt, das sei eure Speise; wie das grüne Kraut habe ich's euch alles gegeben.
1. Mose 9,3

Pubmed “Nutritional Psychiatry” (25.4.22)



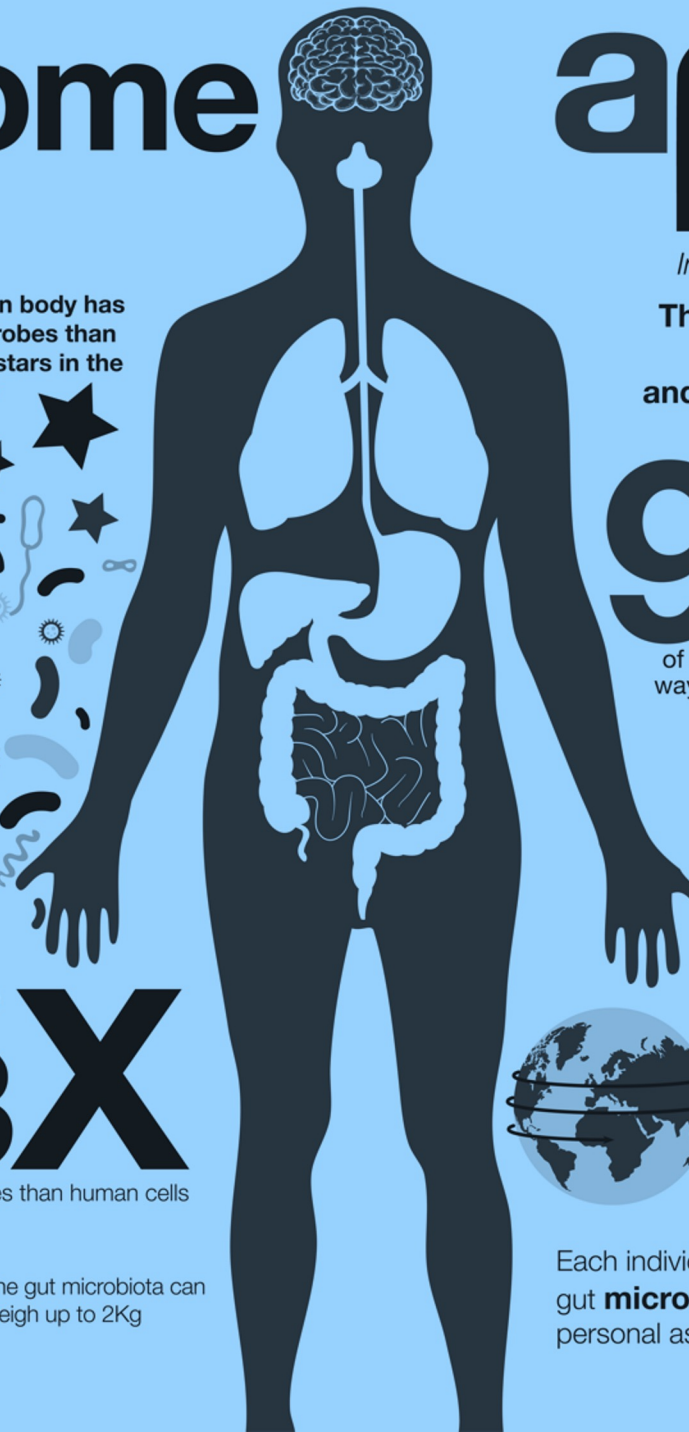
Das Mikrobiom

= Die Gesamtzahl aller Mikroorganismen (Viren, Bakterien, Pilze, Protozoen, …), die ein Lebewesen besiedeln/ deren Genome

- symbiotisch, kommensal, pathogen
- Vor der Geburt ist der Mensch (mehr oder weniger…) keimfrei
- Sehr oft symbiotische Beziehung…! 95% der Bakterien helfen uns gegen Stress, Allergien, Krebs, …

Microbiome

IN NUMBERS



Microbiome Ireland

Interfacing Food & Medicine

100 Trillion

symbiotic microbes live in and on every person and make up the human microbiota

The human body has more microbes than there are stars in the milky way

95%

of our microbiota is located in the GI tract

150:1

The genes in your microbiome outnumber the genes in our genome by about 150 to one

The surface area of the **GI tract** is the same size as 2 tennis courts

You have 1.3X

more microbes than human cells

>10,000

Number of different microbial species that researchers have identified living in and on the human body

2kg

The gut microbiota can weigh up to 2Kg

The microbiome is more medically accessible and manipulable than the human genome

It is thought that **90%** of disease can be linked in some way back to the gut and health of the microbiome

5:1

Viruses:Bacteria in the gut microbiota

2.5 The number of times your body's microbes would circle the earth if positioned end to end

Each individual has a unique gut **microbiota**, as personal as a fingerprint

Quelle: https://worldmicrobiomeday.com/resources/

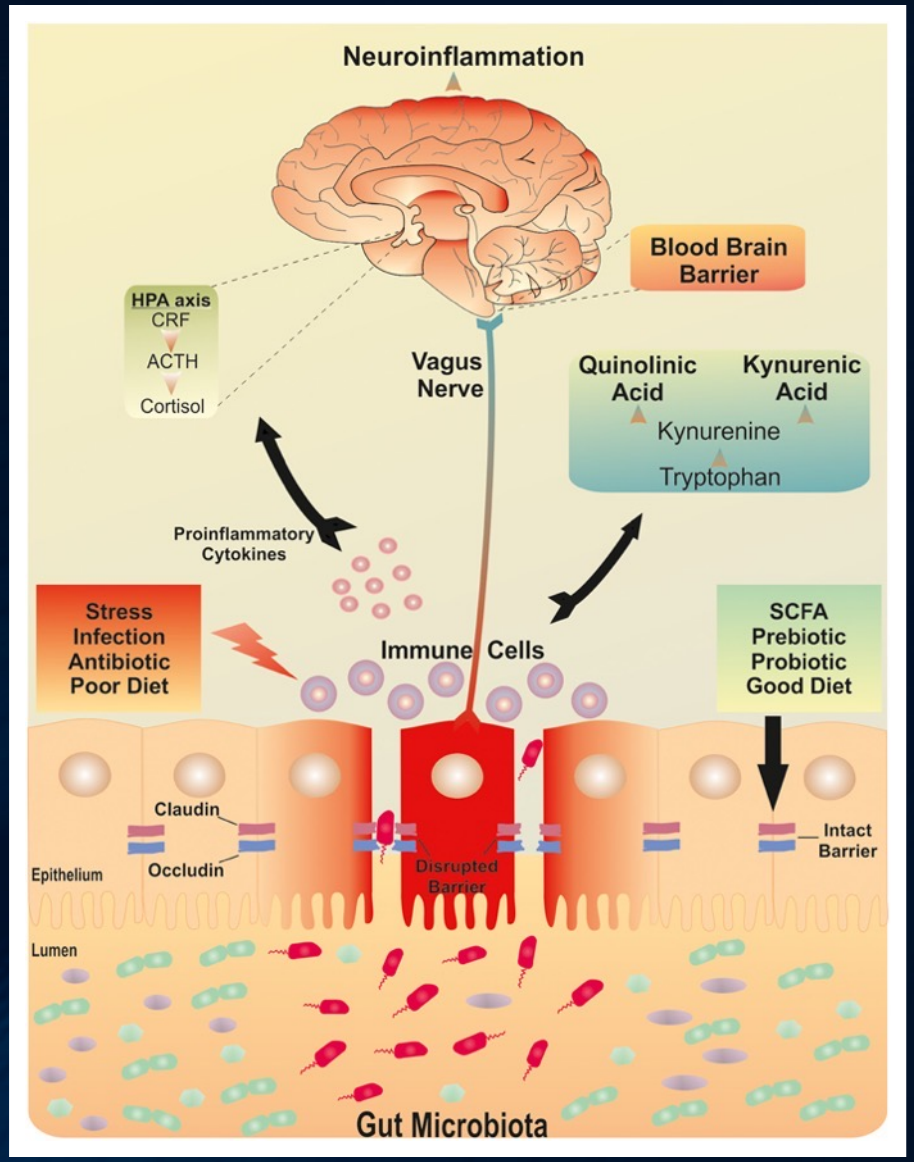
Aufgaben des Darmmikrobioms
(=90-95% des Mikrobioms)

- Hilft die Nahrung zu verdauen
- Synthese von Vitaminen, Hormonen und kurzkettigen Fettsäuren
- Stimulation des Immunsystems
- Verhindert Ausbreitung von pathogenen Bakterien

«Die Pharmaindustrie hat in der Vergangenheit nur über Medikamente nachgedacht, die Bakterien töten. Ich vermute, dass in den kommenden Jahren ein Umdenken stattfinden wird.«
Michael Fischbach, Mikrobiologe

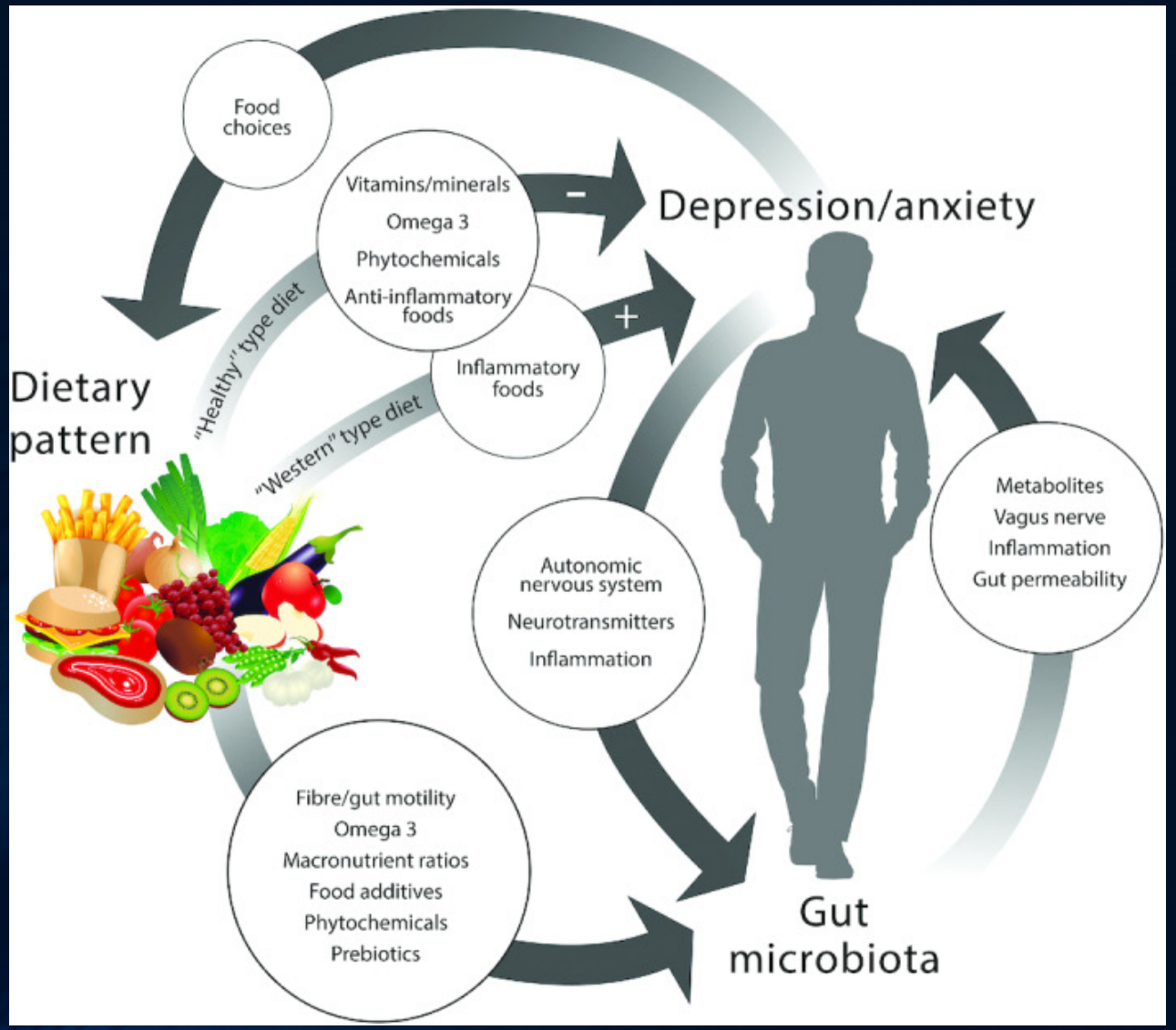
Darm-Gehirn-Kommunikation:

- Neuronal,
- immunmediiert,
- (neuro-)endokrin



Ernährung, Mikrobiom und Angst/Depression

Bear TLK, Dalziel JE, Coad J, Roy NC, Butts CA, Gopal PK. The Role of the Gut Microbiota in Dietary Interventions for Depression and Anxiety. *Adv Nutr*. 2020;11(4):890-907. doi:10.1093/advances/nmaa016 (Link)

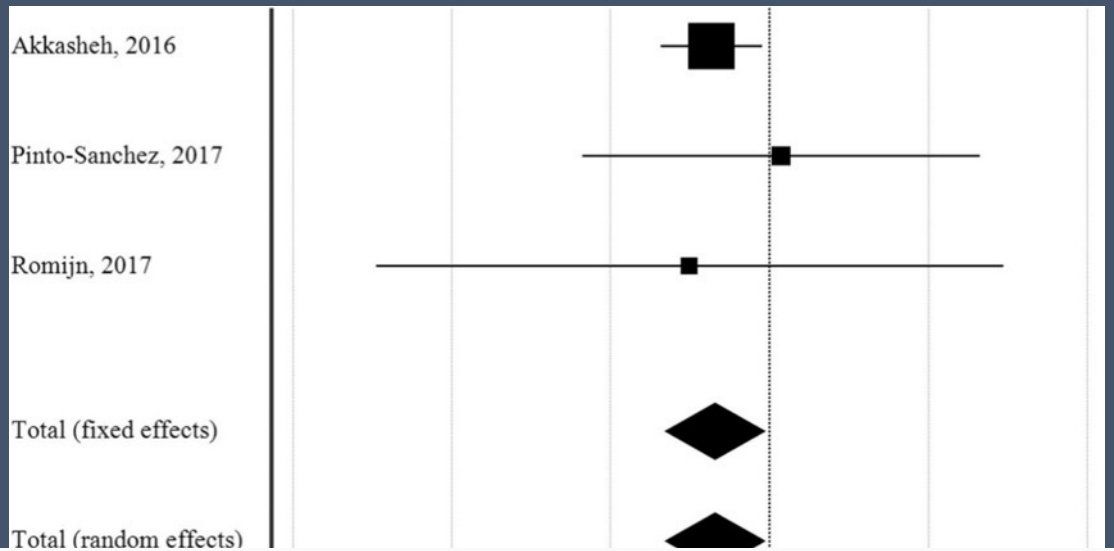


Probiotika und psychische Gesundheit

A meta-analysis of the use of probiotics to alleviate depressive symptoms

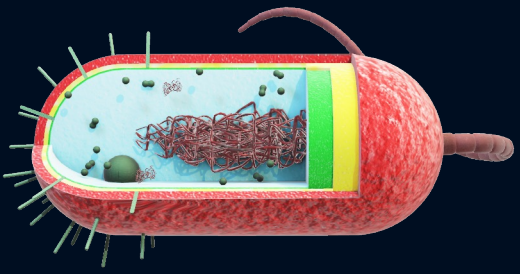
Qin Xiang Ng, Christina Peters, Collin Yih Xian Ho, Donovan Yutong Lim, Wee-Song Yeo

Journal of Affective Disorders
Volume 228, Pages 13-19 (March 2018)



- Current evidence suggests that although the overall effect of probiotics is statistically insignificant for a combined data set of both depressed and healthy individuals (SMD −0.128, 95% CI −0.261 to 0.00463, P=0.059), a statistically significant benefit is seen in mild to moderately depressed patients (SMD −0.684, 95% CI −1.296 to −0.0712, P=0.029).
- Unlike SSRIs however, probiotics are well-tolerated with no adverse events reported by the 1349 patients collectively enrolled in the ten included studies.

Journal of Affective Disorders 2018 228, 13-19DOI: (10.1016/j.jad.2017.11.063)



Einige Studien im Überblick

- Schwangerschaft: Lactobacillus rhamnosus führte zu signifikant geringeren Depressions- (p=0.037) und Angstraten (p=0.014),
  (n=423 Frauen, 212 in Probiotikum-Arm, 211 Placebo)
  (Slykerman et al., 2017)
- Manie: 24 Wochen Einnahme von Probiotika (Lactobacillus rhamnosus und Bifidobacterium animalis subsp. lactis) führte bei Patienten mit Manie (n=66) zu signifikant (p=0.009) weniger Rehospitalisationen (24/33 bei Placebo, 8/33 bei Probiotika), zudem zu weniger Hospitalisationstagen (8.3 vs. 2.8 Tage, P=0,017)
  (Dickerson et. al., 2018)
- Depressionsrisiko: Probiotika wichtig um Depressionsrisiko bei Gesunden zu reduzieren (p=0.005) (Huang et al., 2016, Metaanalyse)
- Depressionsbehandlung: Probiotika über 8 Wochen bei depressiven Personen führten zu einer signifikanten Verbesserung der Depressionssymptome (BDI-Wert), p=0.04 (Kazemi et al, 2018)

Kim, N., Yun, M., Oh, Y. J., & Choi, H. J. (2018). Mind-altering with the gut: Modulation of the gut-brain axis with probiotics. *Journal of Microbiology*, *56*(3), 172-182.

Table 2. **Links between altered gut microbiota composition and a variety of neurological and psychiatric disorders**

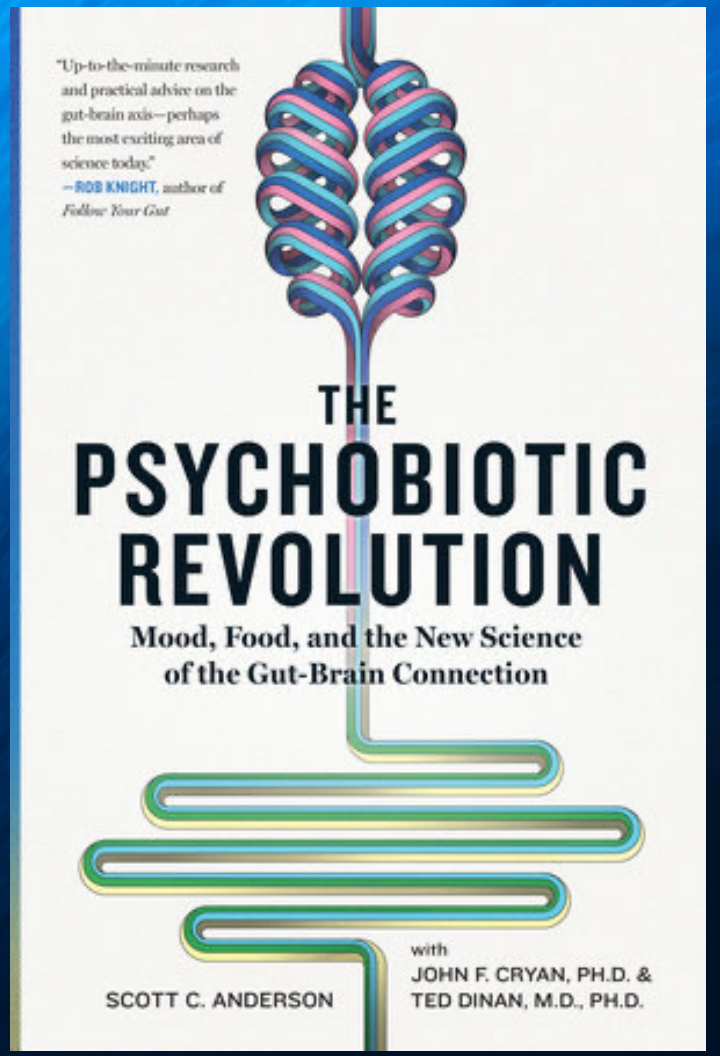
Disease	Altered gut microbiota	References
Stress	Porphyromonadaceae ↓	Bailey *et al.* (2010)
	Clostridium ↑, *Bacteroides* ↓	Bailey *et al.* (2011)
	Oscillibacter ↑, *Anaerotruncus* ↑, *Peptococcus* ↑, *Lactobacillus* ↓	Golubeva *et al.* (2015)
Depression	*Bifidobacterium* ↓, *Lactobacillus* ↓	Aizawa *et al.* (2016)
	Bacteroidetes ↑, Proteobacteria ↑, Actinobacteria ↑, Firmicutes ↓	Jiang *et al.* (2015)
Autism	*Clostridium* ↑	Song *et al.* (2004), Parracho *et al.* (2005)
	Sutterella spp. ↑, *Ruminococcus torques* ↑, *Akkermansia muciniphila* ↓	Wang *et al.* (2011, 2013)
	Clostridium ↑, Sutterellaceae ↑, Enterobacteriaceae ↑, *Bifidobacterium* ↓	De Angelis *et al.* (2013)
	Collinsella ↑, *Corynebacterium* ↑, *Dorea* ↑, *Lactobacillus* ↑, *Alistipes* ↓, *Bilophila* ↓, *Dialister* ↓, *Parabacteroides* ↓, *Veillonella* ↓	Strati *et al.* (2017)
	Desulfovibrio ↑, *Bacteroides vulgatus* ↑, *Ruminococcus* ↑, *Bifidobacterium* ↓	Finegold *et al.* (2010)
Alzheimer's disease	Association with bacterial and viral infection	Bu *et al.* (2015)
	Bacteroidetes ↑, Tenericutes ↑, Firmicutes ↓, Verrucomicrobia ↓, Proteobacteria ↓ Actinobacteria ↓, *Allobaculum* ↓, *Akkermansia* ↓	Harach *et al.* (2017)
	Bacteroidetes ↑, Firmicutes ↓, *Bifidobacterium* ↓	Vogt *et al.* (2017)
Parkinson's disease	*Ralstonia* ↑, *Blautia* ↓, *Coprococcus* ↓, *Roseburia* ↓, *Faecalibacterium* ↓	Keshavarzian *et al.* (2015)
	Enterobacteriaceae ↑, Prevotellaceae ↓	Scheperjans *et al.* (2015)

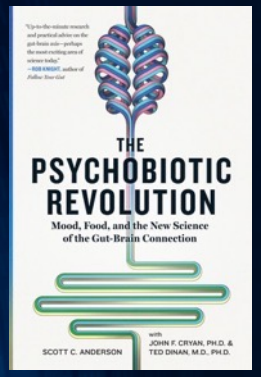
Table 3. Effects of probiotics on brain function and behavior

Probiotic strain	Model	Duration	Effects	References
Bifidobacterium infantis	Rodent (maternal separation model of depression)	45 days	Normalized the immune response, reduced behavioral deficits	Desbonnet *et al.* (2008, 2010)
Bacteroides fragilis	Rodent (maternal immune activation)	6 days	Reversed ASD-related behavior, improved gut barrier integrity	Hsiao *et al.* (2013)
A mixture of *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175	Rodent (healthy)	2 weeks	Reduced anxiety-like behavior	Messaoudi *et al.* (2011a)
Bifidobacterium longum 1714, *Bifidobacterium breve* 1205	Rodent (innately anxious BALB/c)	6 weeks	Reduced anxiety-like behavior	Savignac *et al.* (2014)
A mixture of *Bifidobacterium animalis* subsp. *lactis*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp. *lactis*	Human (healthy)	4 weeks	Influenced brain activity in emotional centers	Tillisch *et al.* (2013)
Lactobacillus helveticus R0052 and *Bifidobacterium longum* R0175	Human (healthy)	30 days	Less psychological distress	Messaoudi *et al.* (2011a, 2011b)
Lactobacillus casei Shirota	Human (healthy, exposed to academic stress)	11 weeks	Reduced stress–related gastrointestinal symptoms	Kato-Kataoka *et al.* (2016)
Lactobacillus casei Shirota	Human (healthy)	3 weeks	Improved mood	Benton *et al.* (2007)
A mixture of *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, and *Lactococcus lactis* (W19 and W58)	Human (healthy)	4 weeks	Reduced rumination and aggressive cognition	Steenbergen *et al.* (2015)
Lactobacillus acidophilus	Human (autistic children)	2 months	Reduced D-arabinitol level in urine, improvement in ability of concentration and carrying out orders	Kaluzna-Czaplinska and Blaszczyk (2012)
VSL#3 (VSL Pharmaceuticals Inc.), a multi-strain mixture of ten probiotics	Human (ASD child, case report)	4 weeks	Improved autistic core symptoms, relieved gastrointestinal symptoms	Grossi *et al.* (2016)
Lactobacillus casei Shirota	Human (PD)	5 weeks	Reduced constipation	Cassani *et al.* (2011)
Lactobacillus acidophilus, *Lactobacillus casei*, *Bifidobacterium bifidum*, and *Lactobacillus fermentum*	Human (AD)	12 weeks	Improved cognition	Akbari *et al.* (2016)

The Psychobiotic Revolution

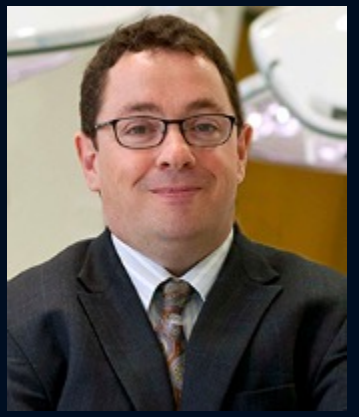
MOOD, FOOD, AND THE NEW SCIENCE OF THE GUT-BRAIN CONNECTION



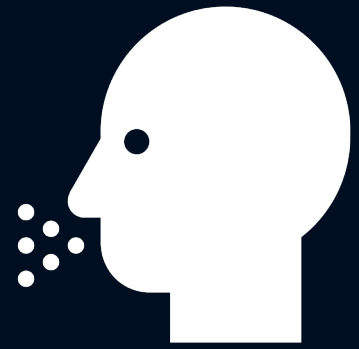


Autoren

- Scott C. Anderson is a veteran science journalist with specialization in medical topics and computer programming.
- John F. Cryan is professor and chair of the Department of Anatomy and Neuroscience, University College Cork, Ireland, and a principal investigator in the APC Microbiome Institute, a leading-edge institute researching the role of the microbiome in health and disease.
- Ted Dinan is professor of psychiatry and a principal investigator in the APC Microbiome Institute at University College Cork, Ireland. He was previously chair of Clinical Neurosciences and professor of psychological medicine at St. Bartholomew's Hospital, London.



Depression – Endured Sickness behavior?



Ist Depression ansteckend?

- In our lab, we were able to show that we could transfer "the blues" with gut microbes.
- We transferred fecal matter from human patients with major depression into rats and noted that they, unlike the controls, became depressed, too.
- Mood was not only transferable by fecal microbes but also from humans to rats, demonstrating that psychobiotic effects are, to some extent, independent of species.

John R. Kelly, Yuliya Borre, Ciaran O'Brien, Elaine Patterson, Sahar El Aidy, Jennifer Deane, Paul J. Kennedy, et al., "Transferring the Blues: Depression-Associated Gut Microbiota Induces Neurobehavioural Changes in the Rat," Journal of Psychiatric Research 82 (November 2016): 109–18, doi:10.1016/j.jpsychires.2016.07.019.

Gesunde Männer werden stressresistenter, wenn sie Bakterien essen…! Und klüger…

- We gave healthy male subjects some psychobiotic bacteria, and they became less anxious. The effect was large enough for them to perceive less stress.
- These healthy men also underwent an intelligence test. We found a statistically significant improvement in cognitive function, particularly memory. This was a study in which we managed to find in humans exactly what we have found in animals.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Körper und Psyche übers Essen beeinflussen

- It turns out that you can take back control of your body with a simple, all-natural diet and specific microbial foods and supplements. Amazingly, for many people these changes can be as powerful as any medication.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Wer steuert mein Essverhalten?

- Each type of bacteria has its own food preferences.
- Bacteroidetes have a thing for fat,
- Prevotella enjoy carbs, and
- Bifido are fiber lovers.
- They each have their own way of asking for an appropriate meal, and they also have ways of thanking you.
- …when you think of your cravings as microbial longings, it may be easier for you to take back control.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Böse Bakterien führen uns ins Elend…

- Our evolutionary history, which included very few pastries rolling across the savanna, didn't prime us for glazed doughnuts.
- We are inadequately prepared for this temptation, and that is a problem, because the bacteria that crave sugar are not the ones that support a good mood.
- Short-term bliss, yes, but in the long term a sugar-centered microbiota can potentially make you anxious and depressed.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Bakterien als Neurotransmitter-Produzenten

- The nature and condition of neurotransmitters affect your mood, and most pharmacological drugs address depression and anxiety by treating your neurotransmitters.
- The fact is: Your bacteria naturally produce neurotransmitters in a volume that rivals that provided by prescription drugs. Although it's still not clear how these neuroactive molecules get to your brain, if we can control the type and amount of them secreted by your bacteria, we might have a more natural treatment for mood disorders.
- Neurotransmitters, and the bacteria that produce them, play a key role in psychobiotic therapy.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Serotonin-Produktion durch Streptokokken und Escherichia – Konkurrenz für SSRIs?

- In the colon, Streptococcus and Escherichia species produce serotonin—the "happiness" neurotransmitter that is an important player in mood and provides the guiding rationale for selective serotonin reuptake inhibitors (SSRIs).
- We could soon see pharmaceutical SSRIs augmented or replaced by psychobiotics. It's not an unreasonable expectation, because some 90 percent of the body's serotonin is found in the gut.
- That's because your gut—the second brain—uses the same neuroactive chemicals to compute and process information as the first brain does. Serotonin plays a major role in digestion, because it's the main neurotransmitter behind peristalsis. In fact, a quarter of people who take SSRIs end up with changes in gut motility. In low doses, Prozac can be used to treat the gut, helping ease constipation by encouraging peristaltic motion.
- It isn't too much of a stretch to posit that some of the success of SSRIs has to do with their effect on the gut.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Entzündung, Dysbiose und psychische Erkrankungen

- Chronic inflammation produces stress hormones indefinitely, leading to a surprising number of mental issues, including bipolar disorder, post-traumatic stress disorder, attention deficit disorder, depression, and anxiety.
- A simple contagion can lead to long-term dysbiosis and consequent mental distress. Antidepressants are often prescribed for these maladies, but if your own psychobiotic microbes can reduce the inflammation, your HPA axis can return to homeostatic normalcy and you may be able to treat some of these conditions without drugs.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Probiotika bei Angst und Depression

- Angststörungen
  Probio'Stick, L. helveticus, L. plantarum, B. breve, B. longum
- Depression
  B. bifidum, B. breve, B. longum + L. helveticus, L. acidophilus, L. brevis, L. casei, L. delbrueckii, L. plantarum, L. rhamnosus, L. salivarius, L. lactis, S. thermophilus

L=Lactobacillus
B=Bifidobacterium
S=Streptococcus

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

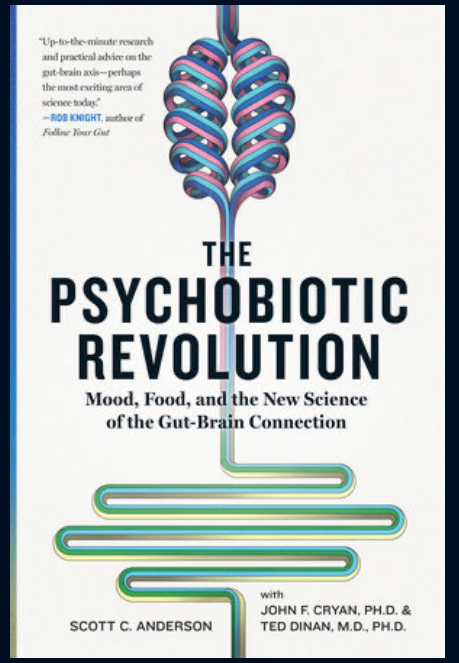
Stuhltransplantation bei Depression...??!?

One patient tossed off his depression in just a few hours after a fecal transplant.

Anderson, Scott C., John F. Cryan, and Ted Dinan. *The psychobiotic revolution: mood, food, and the new science of the gut-brain connection*. National Geographic Books, 2017.

Menu der Wahl…

- Just to get you off on the right footing, a healthy diet consists of vegetables, fruit, fish, high-fiber grains, nuts, eggs, and quality vegetable oil. These are elements of both the Nordic and Mediterranean diets, known to add healthy years to your life.



Ernährung und psychische Gesundheit

Ernährung als weltweites Problem

- Global Burden of Disease Study (April 2019)

Inside Out *by David Dodwell*

Poor diets, both among the overindulged and malnourished, kill more people every year than smoking, Lancet study finds

- A study last week by The Lancet found that poor diets - both by the overindulged and the malnourished - cause one in five deaths worldwide every year, more than smoking

Health effects of dietary risks in 195 countries - GBDS (The Lancet, April 2019)

- We found that improvement of diet could potentially prevent one in every five deaths globally.
- Our findings show that, unlike many other risk factors, dietary risks affected people regardless of age, sex, and sociodemographic development of their place of residence.
- Our findings show that suboptimal diet is responsible for more deaths than any other risks globally, including tobacco smoking (!!!), highlighting the urgent need for improving human diet across nations.

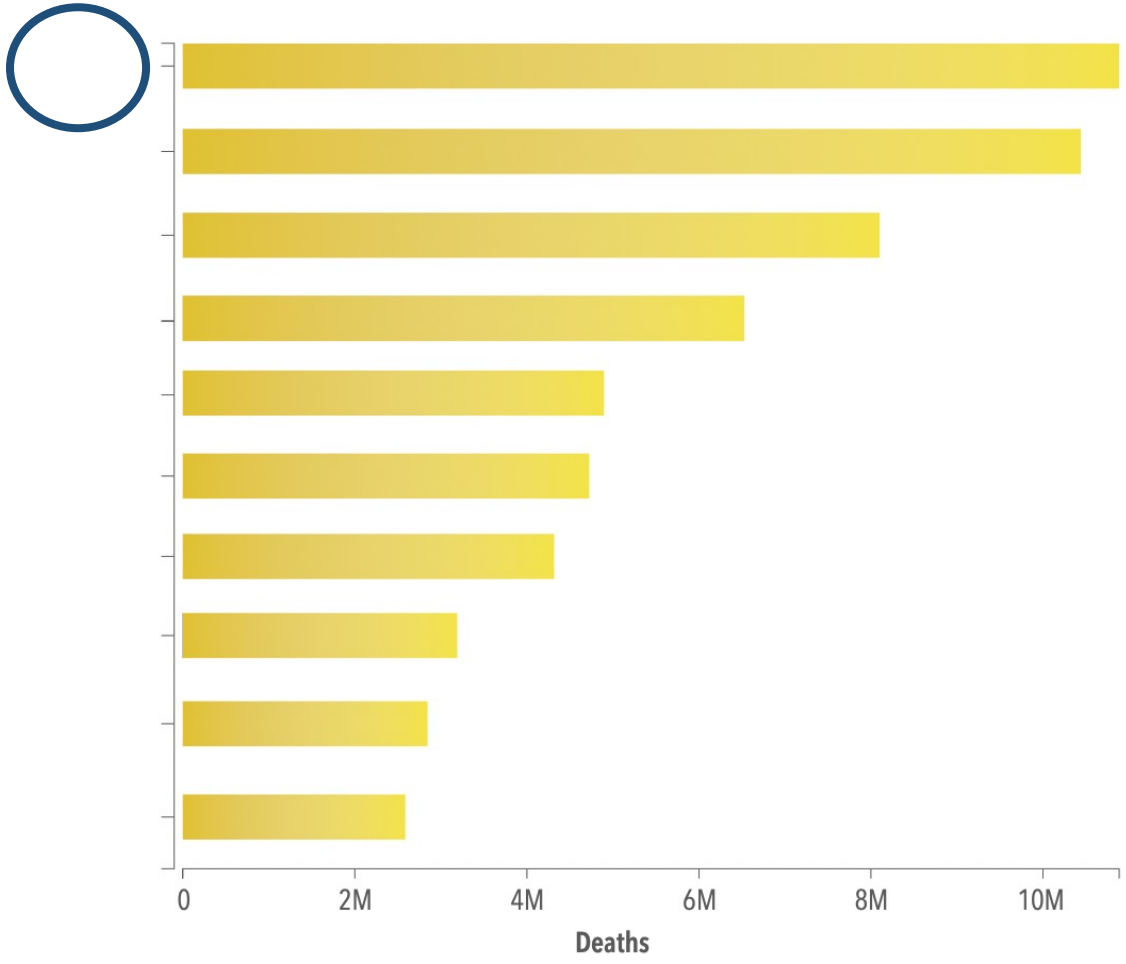
the leading dietary risk factors for mortality are diets
- high in sodium
- low in whole grains
- low in fruit
- low in nuts and seeds
- low in vegetables, and
- low in omega-3 fatty acids

each accounting for more than 2% of global deaths.

Afshin, Ashkan, et al. "Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017." *The Lancet* (2019). (Link)

Poor diet causes more deaths than any other risk factor.

TOP 10 RISK FACTORS FOR DEATH, GLOBALLY, IN 2017



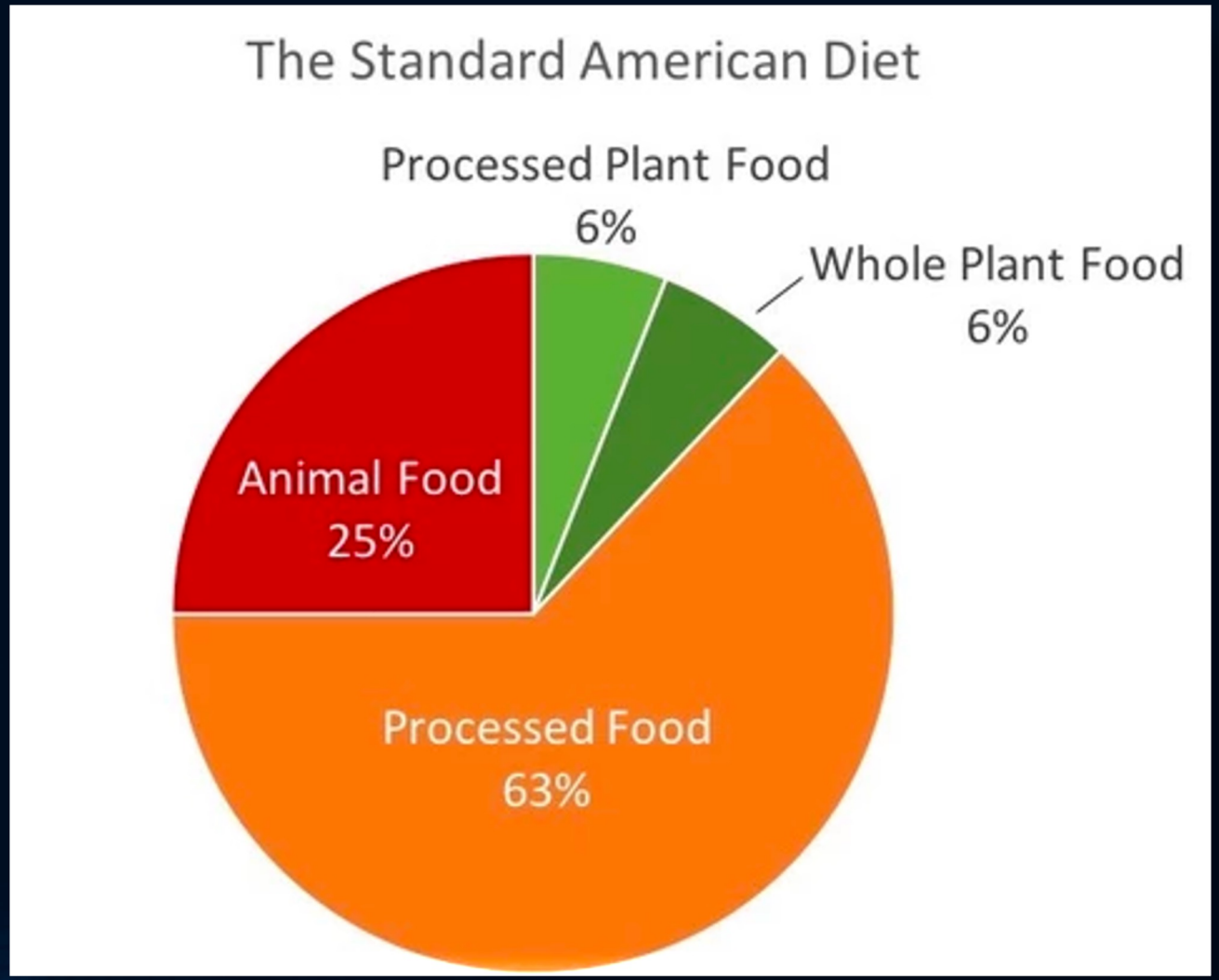
Worldwide in 2017, poor diet was linked to 11 million deaths.

Among those deaths were:

- **9.5 million deaths from cardiovascular disease**
- **913,090 deaths from cancer**
- **338,714 deaths from diabetes**

Gesundes Essen?

"STANDARD AMERICAN DIET" (SAD)



«Antidepressive» Nahrungsmittel?

- Hülsenfrüchte
- Früchte
- Gemüse

- Süssigkeiten und raffinierter Zucker?

Grases, G., et al. "Possible relation between consumption of different food groups and depression." BMC psychology 7.1 (2019): 14.

Die Qual der Wahl…?

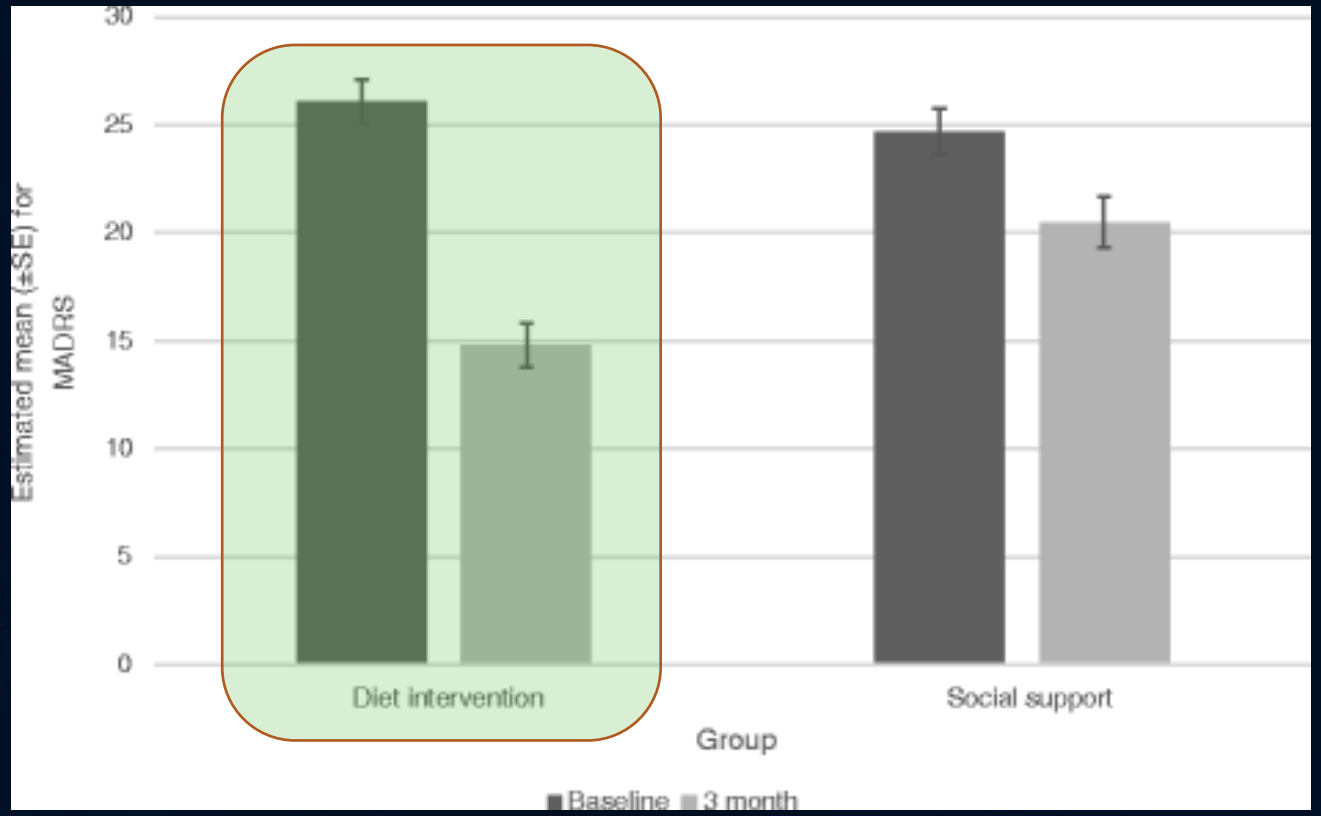
- Ketogene Ernährung
- Low carb, z. B. LOGI-Diät
- Pflanzenbasierte Ernährung / vegan
- Paleo
- Mediterrane Kost

The SMILES-Trial – 1. RCT zu Diät und Depression

- SMILES: 'Supporting the Modification of lifestyle In Lowered Emotional States'
- In the SMILES study we aimed to investigate the efficacy of an adjunctive dietary improvement program for the treatment of major depressive episodes using a 12-week, parallel group, single blind randomised controlled trial design.
- The intervention comprised the 'Mod*i*MedDiet'
- Participants, most of whom were already receiving psychotropic medications and/or psychotherapy, received seven individual dietary coaching sessions of approximately 60 min each, delivered by an accredited dietitian, and the control group received manualised social support ('Befriending') to the same schedule and intensity.
- The results were notable, with the intervention group demonstrating significantly greater improvement between baseline and 12 weeks than the control group with a very large effect size (Cohen's d – 1.16: 95% CI: – 1.73, – 0.59) and a number needed to treat (NNT) of 4.1.
- Moreover, 32.3% of individuals in the dietary group achieved remission (MADRS score < 10)

Jacka, Felice N., et al. "A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES'trial)." *BMC medicine* 15.1 (2017): 23. (Link)

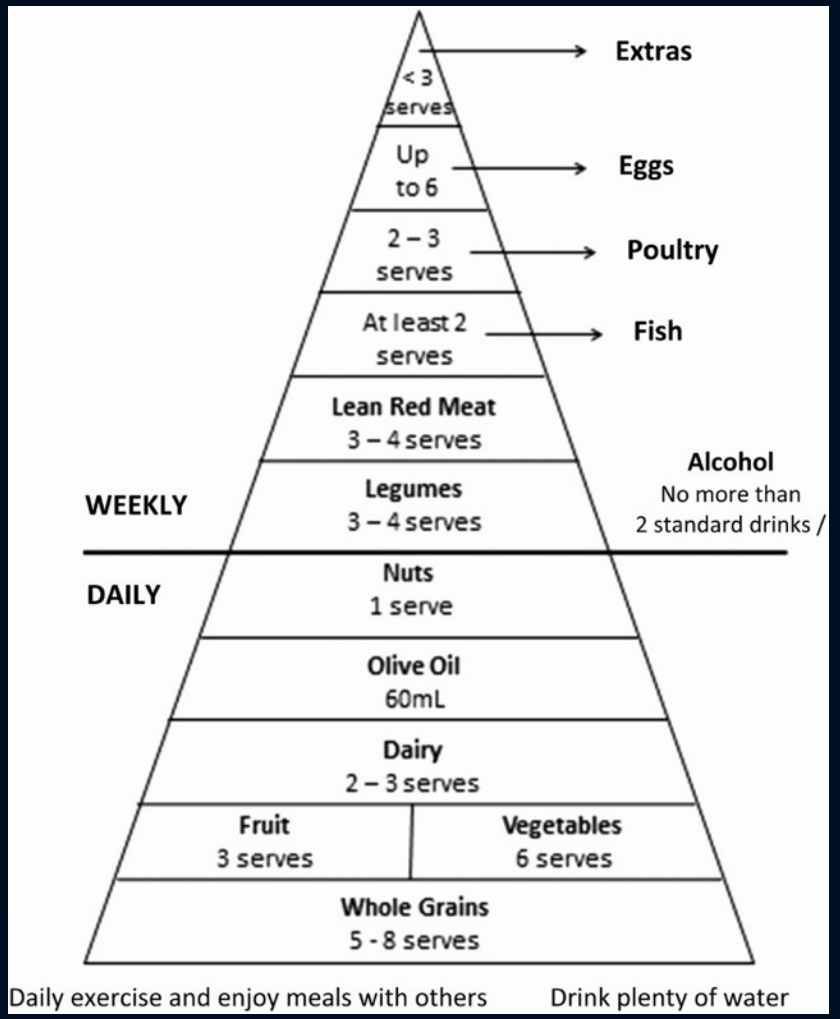
The SMILES-Trial – 1. RCT zu Diät und Depression



Jacka, Felice N., et al. "A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES'trial)." *BMC medicine* 15.1 (2017): 23. (Link)

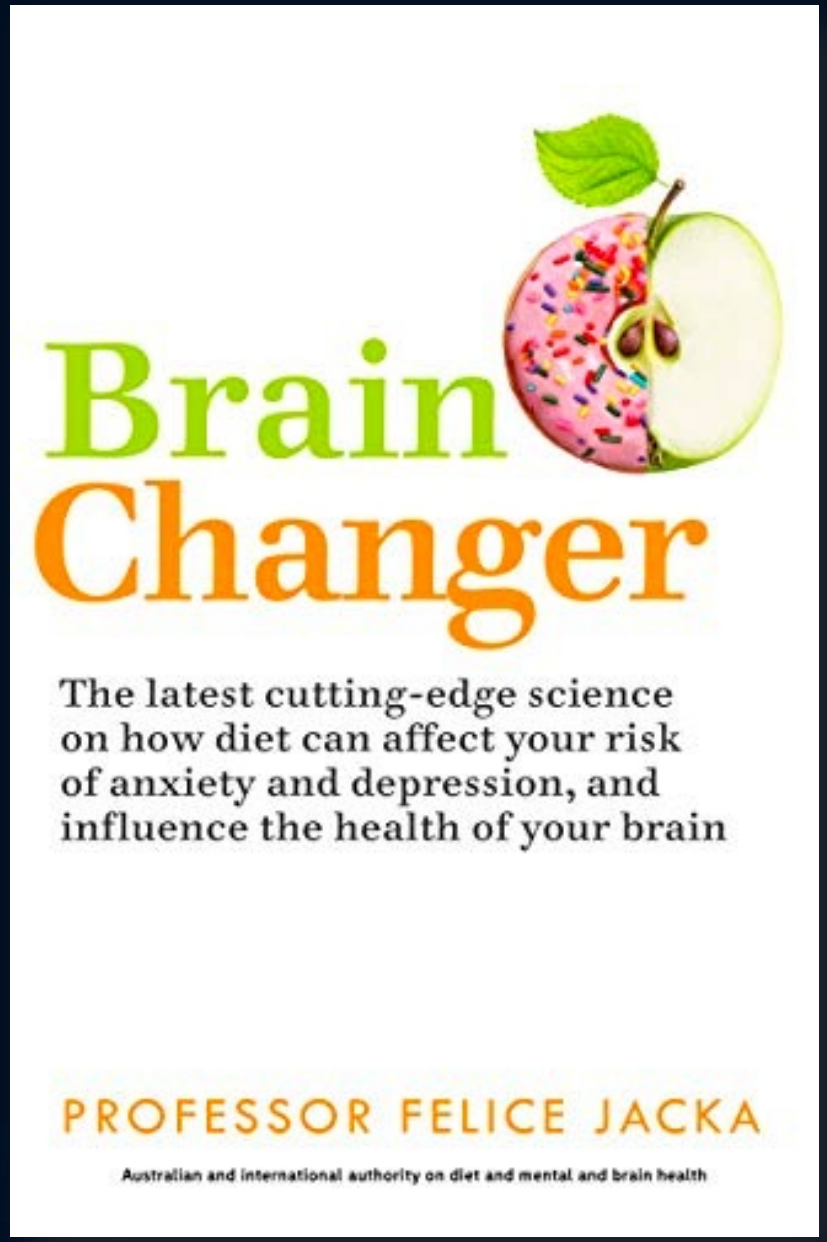
The ModiMedDiet (modified Mediterranean Diet in der SMILES-Studie)

- Like the traditional Mediterranean diet, the ModiMedDiet was designed to be rich in vegetables, fruits, and wholegrain cereals with an emphasis on increased consumption of oily fish, legumes, raw unsalted nuts and seeds, and extra virgin olive oil (as the main source of added fat).
- A moderate consumption of reduced fat natural dairy products was recommended to limit saturated fat intake in an effort to achieve the nutrient profile of a traditional Mediterranean diet.
- The diet was also modified to include a moderate consumption of lean red meat.
- Healthy diet can be affordable - Indeed, we estimated that participants spent an average of AU$138 per week on food and beverages for personal consumption at baseline, whilst the costs per person per week for the diet we recommended was AU$112 per week, with both estimations based on mid-range product costs



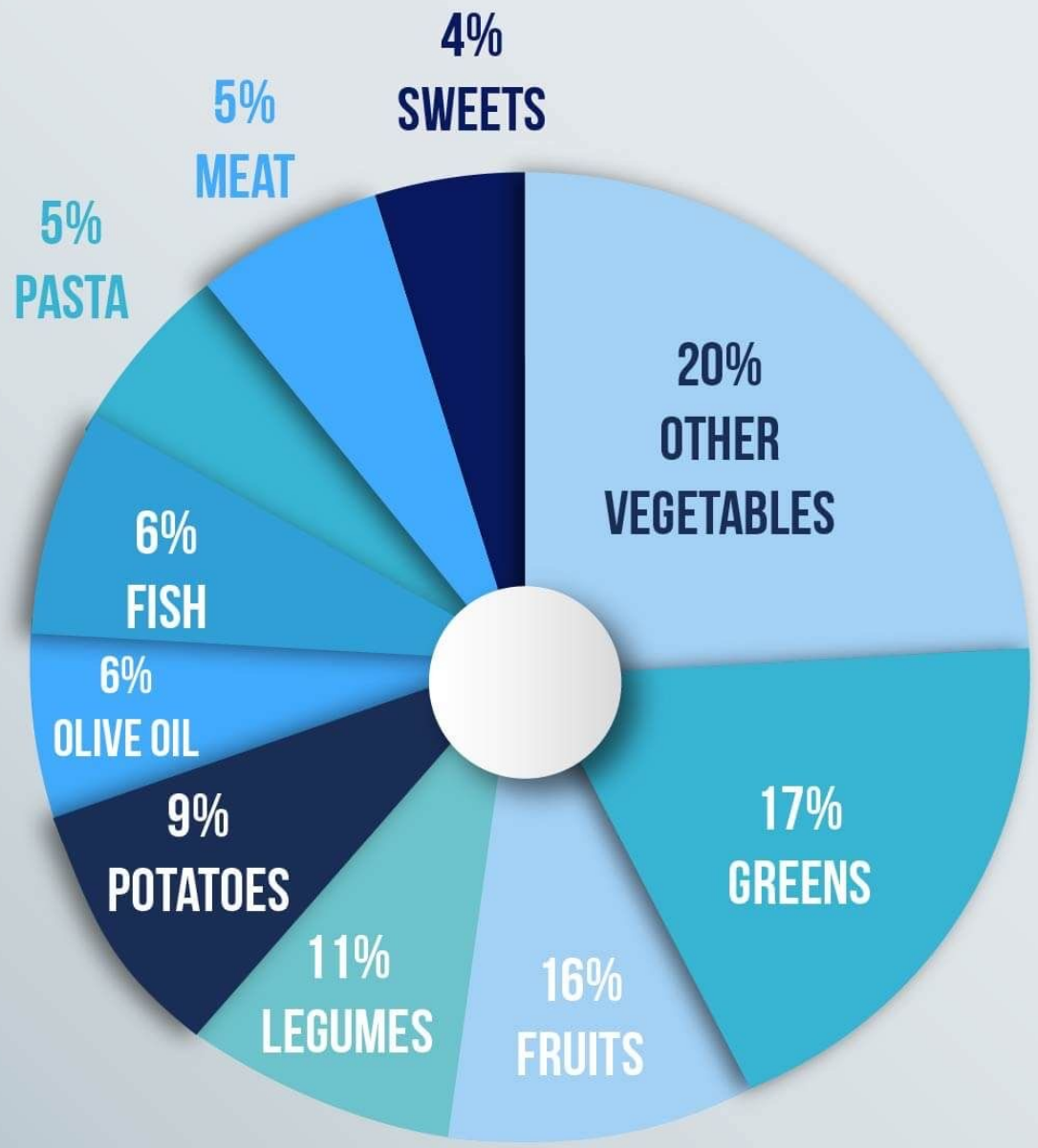
Opie, Rachelle S., et al. "A modified Mediterranean dietary intervention for adults with major depression: Dietary protocol and feasibility data from the SMILES trial." *Nutritional neuroscience* 21.7 (2018): 487-501.Link

Mediterrane Diät



IKARIA, GREECE

HOW IKARIAN CENTENARIANS ATE FOR MOST OF THEIR LIVES



BLUE ZONES™

A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED)

Natalie Parletta, Dorota Zarnowiecki, Jihyun Cho, Amy Wilson, Svetlana Bogomolova, Anthony Villani, ...

Published online: 07 Dec 2017

- Replikation der SMILES-Studie: HELFIMED-Studie
- Fulltext-Link

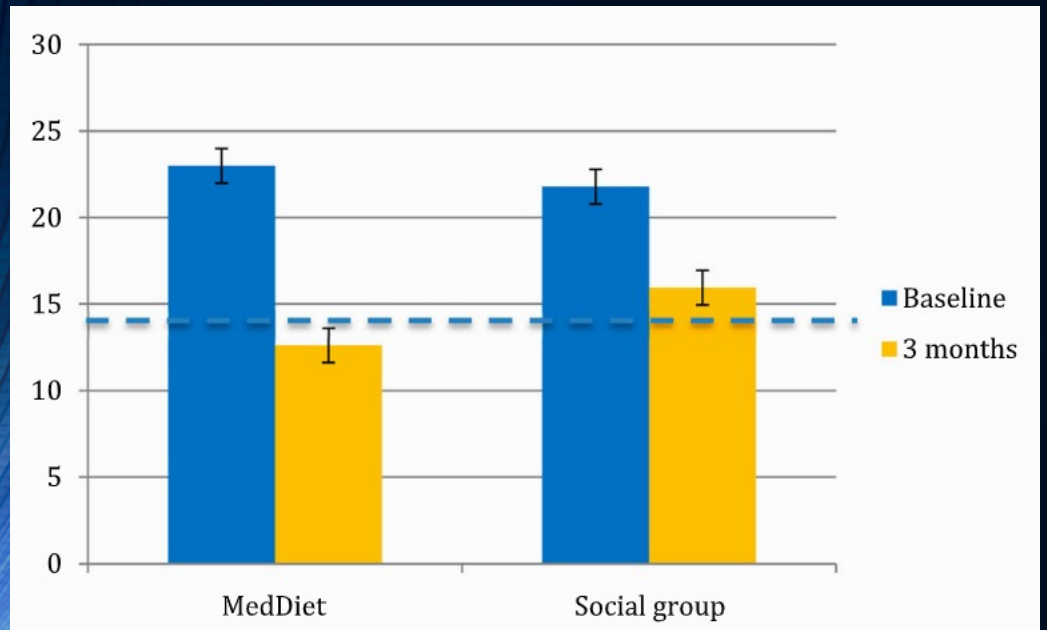


Figure 3 DASS depression scores in each group at baseline and 3 months ($P = 0.027$). Bars represent standard error of the mean. Dotted line represents cut-off for 'extremely severe depression'.

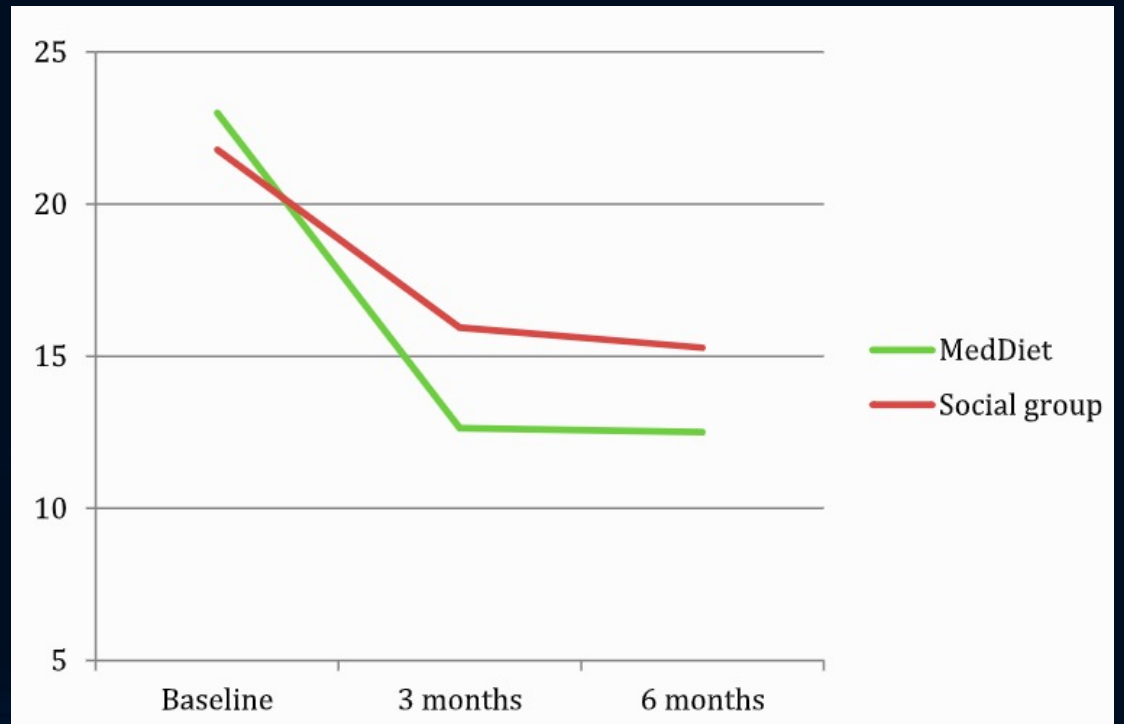


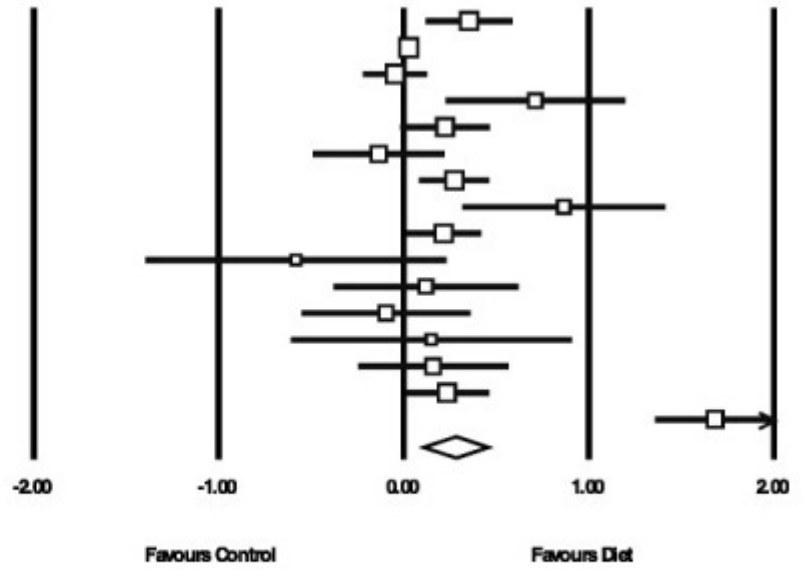
Figure 4 DASS depression scores at baseline, 3 and 6 months.

Mediterrane Diät bei rezidivierender Depression – PREDI_MED-Studie

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6371613/

Ernährungsinterventionen sind wirksam – Metaanalyse von 16 Studien (RCTs) mit insgesamt 45’826 Teilnehmern (2019)

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Agarwal et al. 2015	0.353	0.120	0.014	0.118	0.589	2.941	0.003
Assaf et al. 2015	0.027	0.010	0.000	0.008	0.046	2.744	0.006
Eirvik et al. 2010	-0.048	0.089	0.008	-0.222	0.127	-0.534	0.593
Endevelt et al. 2010	0.711	0.248	0.061	0.226	1.196	2.873	0.004
Forster et al 2012	0.223	0.124	0.015	-0.020	0.466	1.798	0.072
Hyyppa et al. 2003	-0.136	0.182	0.033	-0.492	0.220	-0.749	0.454
Imayama et al. 2011	0.273	0.096	0.009	0.085	0.461	2.844	0.004
Jacka et al. 2017	0.865	0.279	0.078	0.319	1.412	3.102	0.002
Jenkinson et al. 2009	0.216	0.103	0.011	0.013	0.418	2.088	0.037
Kaseckow et al. 2014a	-0.583	0.414	0.172	-1.395	0.230	-1.406	0.160
Kaseckow et al. 2014b	0.120	0.255	0.065	-0.381	0.620	0.469	0.639
Kiernan et al. 2001	-0.095	0.233	0.054	-0.552	0.362	-0.408	0.683
McMillan et al. 2011	0.149	0.388	0.150	-0.611	0.908	0.383	0.702
Nieman et al. 2000	0.159	0.207	0.043	-0.247	0.565	0.768	0.442
Scheier et al. 2005	0.234	0.115	0.013	0.009	0.459	2.035	0.042
Wardle et al. 2000	1.683	0.166	0.028	1.358	2.008	10.139	0.000
	0.275	0.099	0.008	0.100	0.450	3.074	0.002

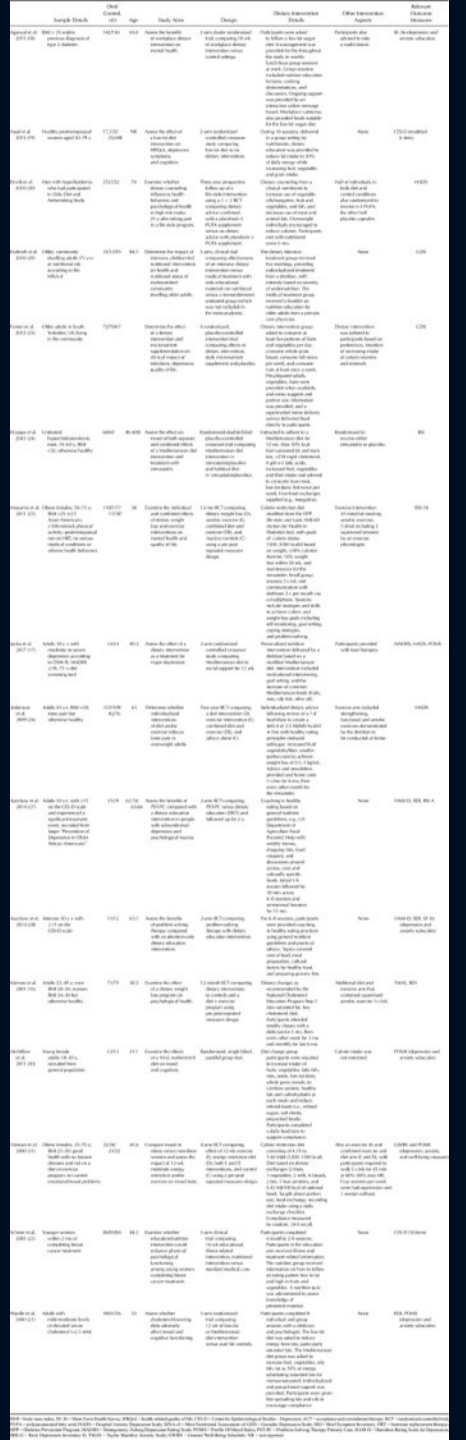


Meta-analysis of the effects of dietary interventions on depressive symptoms. Box size represents study weighting. Diamond represents overall effect size and 95% CIs.

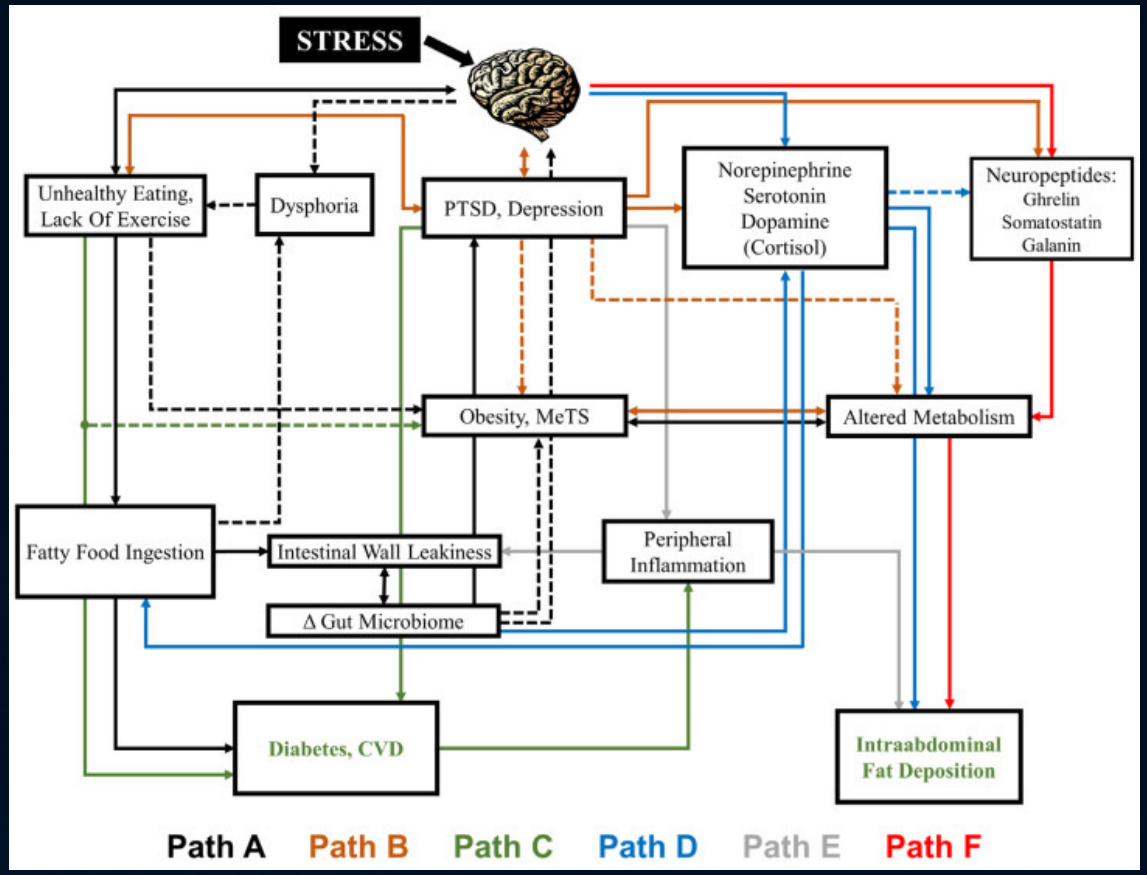
J. Firth, W. Marx, S. Dash, R. Carney, S.B. Teasdale, M. Solmi, B. Stubbs, F.B. Schuch, A.F. Carvalho, F. Jacka, J. Sarris **The effects of dietary improvement on symptoms of depression and anxiety: a meta-analysis of randomized controlled trials,** Psychosom. Med., 81 (2019), pp. 265-280

Hauptsache weg von Junk-Food?

- …all dietary intervention generally hold some common features, such as
  - aiming to reduce the intake of "junk" foods (e.g., high-fat, high-sugar discretionary foods and takeaways),
  - while replacing these with high-fiber, nutrient-dense alternatives, such as vegetables.



Beziehung zwischen Ernährung und Verhalten



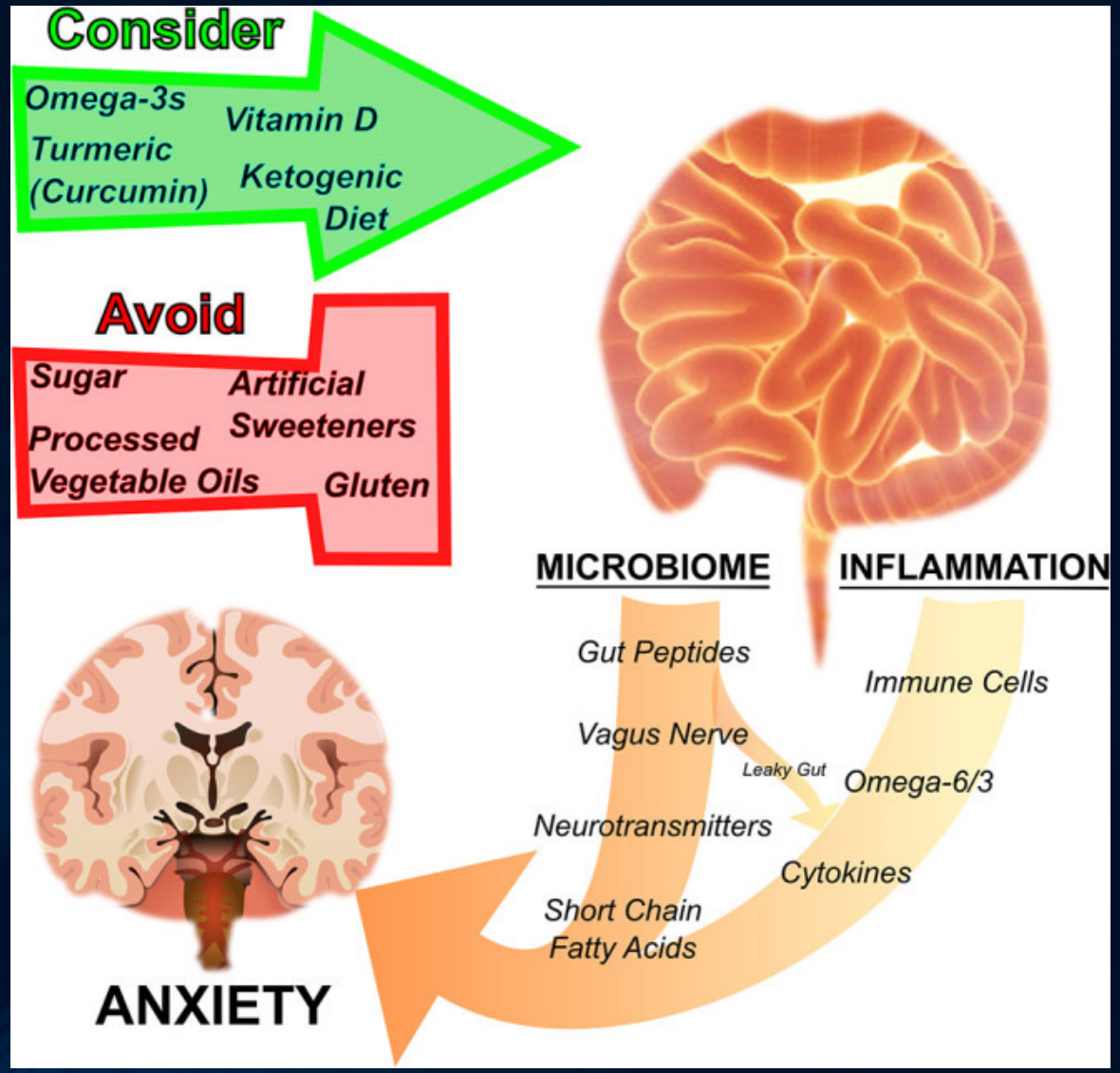
Bremner JD, Moazzami K, Wittbrodt MT, et al. Diet, Stress and Mental Health. *Nutrients*. 2020;12(8):2428. Published 2020 Aug 13. doi:10.3390/nu12082428 (Link)

Daniel – gesund “trotz“ pflanzlicher Diät?

Ernährung bei Angststörungen

Norwitz NG, Naidoo U. Nutrition as Metabolic Treatment for Anxiety. *Front Psychiatry*. 2021;12:598119. Published 2021 Feb 12. doi:10.3389/fpsyt.2021.598119

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7907178/



Ernährung und Schizophrenie? Pilotstudie (2019)

- Approximately one-third of people with schizophrenia have elevated levels of anti-gliadin antibodies of the immunoglobulin G type (AGA IgG) — a higher rate than seen in healthy controls. We performed the first double-blind clinical trial of gluten-free versus gluten-containing diets in a subset of patients with schizophrenia who were positive for AGA IgG.
- 16 participants with schizophrenia or schizoaffective disorder who had elevated AGA IgG (≥ 20 U) but were negative for celiac disease were admitted to an inpatient unit for a 5-week trial. All participants received standardized gluten-free meals and were randomized in a double-blind fashion to receive a shake containing 10 g of gluten flour or 10 g of rice flour each day. Participants were rated for psychiatric, cognitive and gastrointestinal symptoms at baseline and endpoint.
- Of the 16 participants, 14 completed the 5-week trial (2 discontinued early for administrative reasons). Compared with participants on the gluten-containing diet, participants on the gluten-free diet showed improvement on the Clinical Global Impressions scale (Cohen d = –0.75) and in negative symptoms (Cohen d = –0.53).

Kelly, D. L., et al. "Randomized controlled trial of a gluten-free diet in patients with schizophrenia positive for antigliadin antibodies (AGA IgG): a pilot feasibility study." *Journal of psychiatry & neuroscience: JPN* 44.3 (2019): 1-9. (Link)

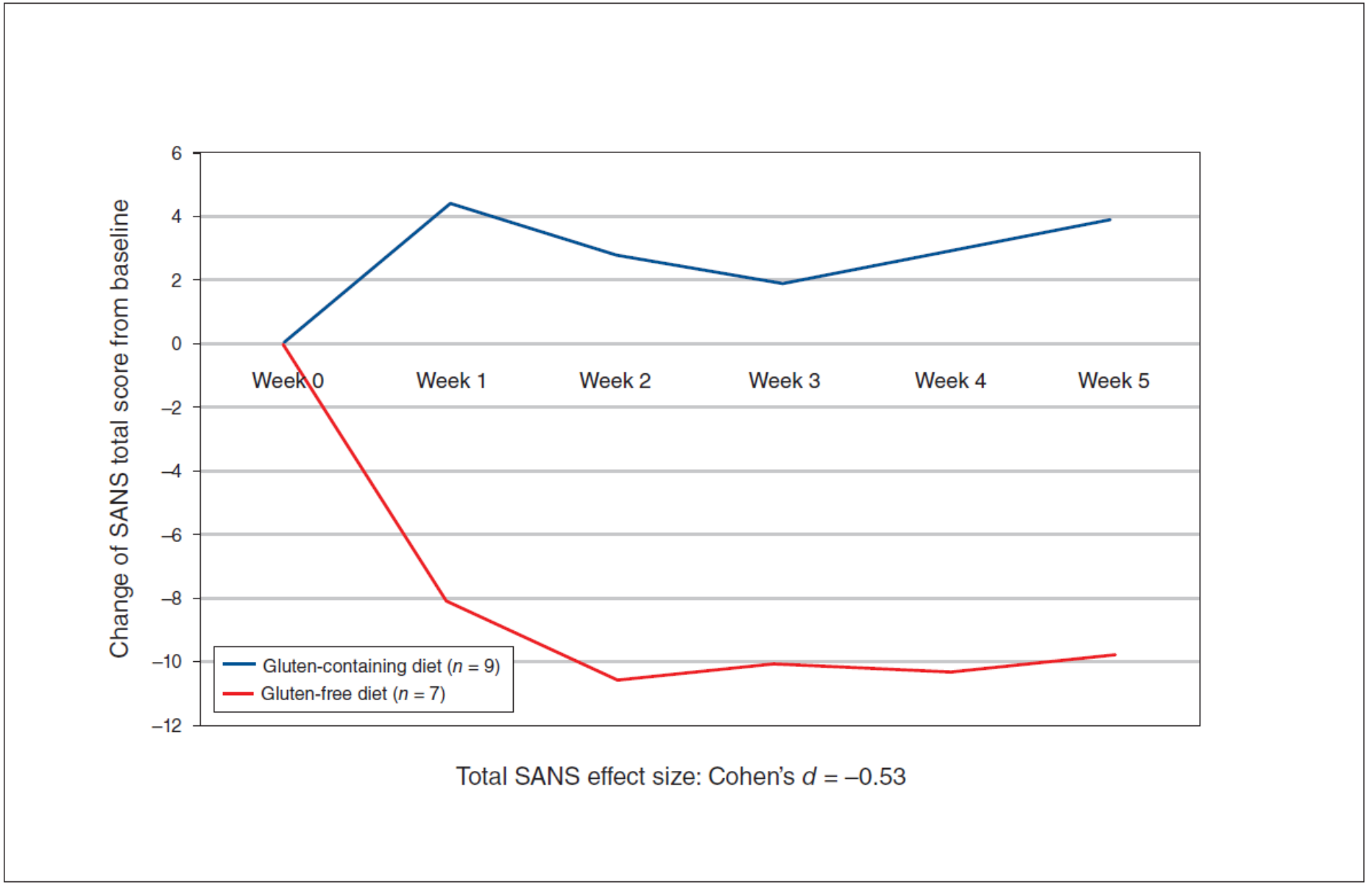
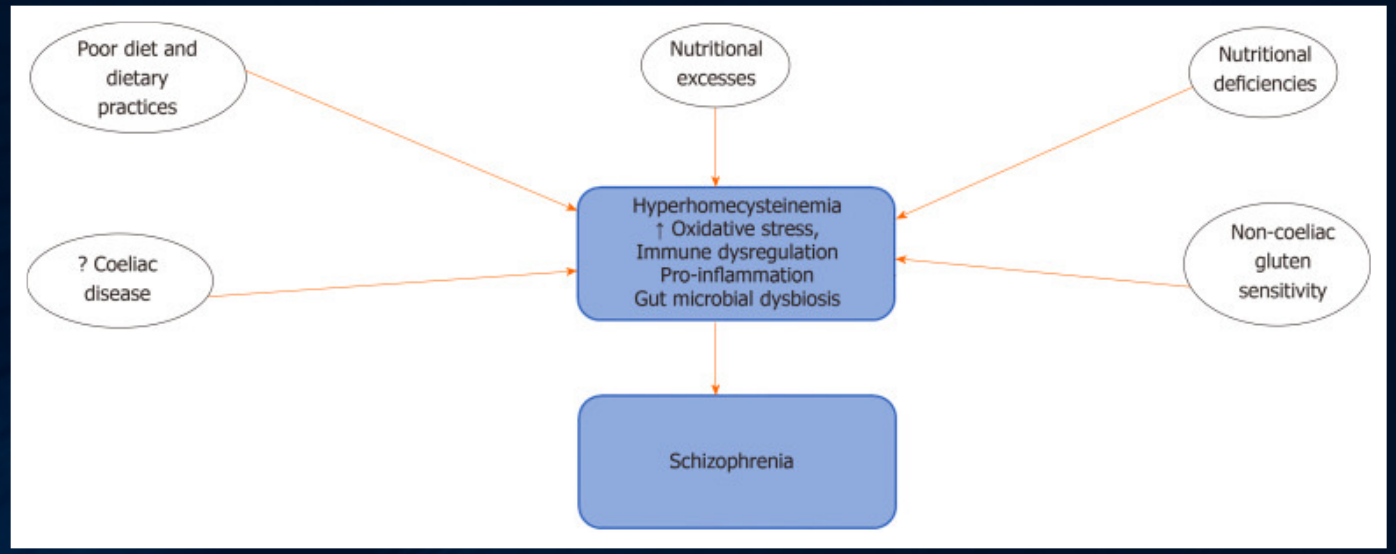


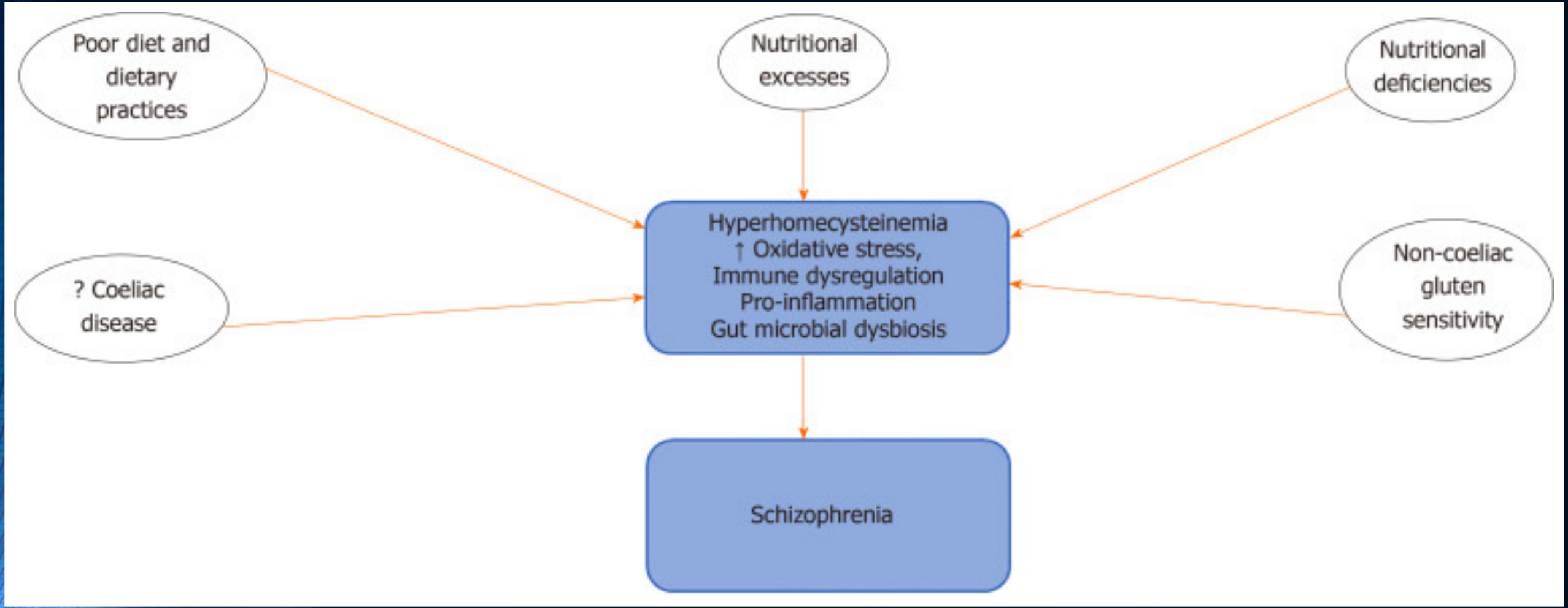
Fig. 2: Change in SANS score by group (least squares mean). SANS = Scale for the Assessment of Negative Symptoms.

Kelly, D. L., et al. "Randomized controlled trial of a gluten-free diet in patients with schizophrenia positive for antigliadin antibodies (AGA IgG): a pilot feasibility study." *Journal of psychiatry & neuroscience: JPN* 44.3 (2019): 1-9.

Ernährung und Schizophrenie (Review)



Onaolapo OJ, Onaolapo AY. Nutrition, nutritional deficiencies, and schizophrenia: An association worthy of constant reassessment. *World J Clin Cases*. 2021;9(28):8295-8311. doi:10.12998/wjcc.v9.i28.8295 (Link)

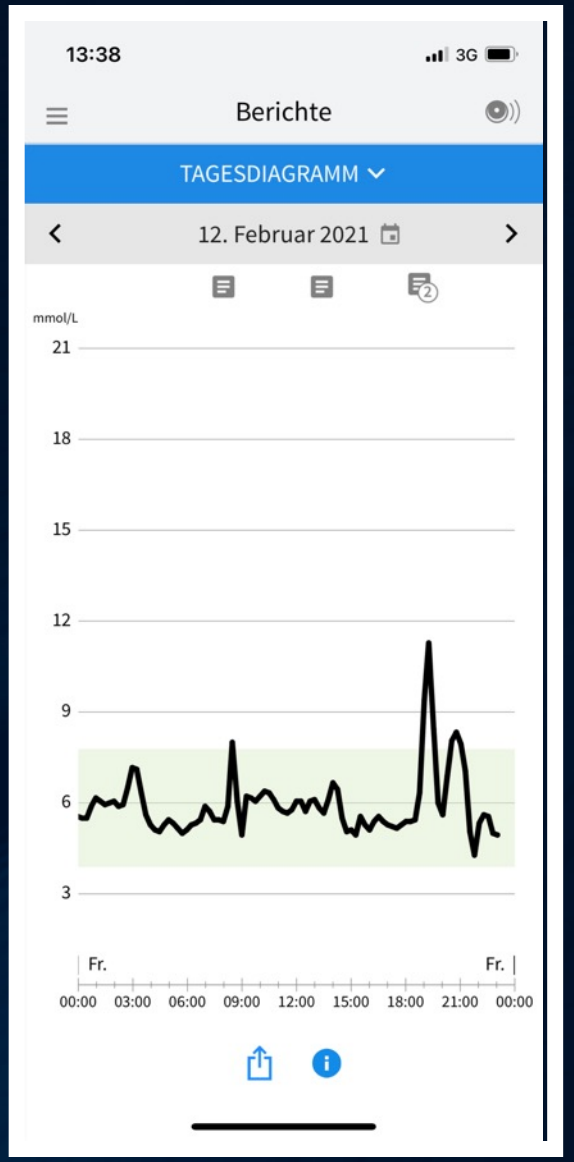


Onaolapo OJ, Onaolapo AY. Nutrition, nutritional deficiencies, and schizophrenia: An association worthy of constant reassessment. *World J Clin Cases*. 2021;9(28):8295-8311. doi:10.12998/wjcc.v9.i28.8295 (Link)

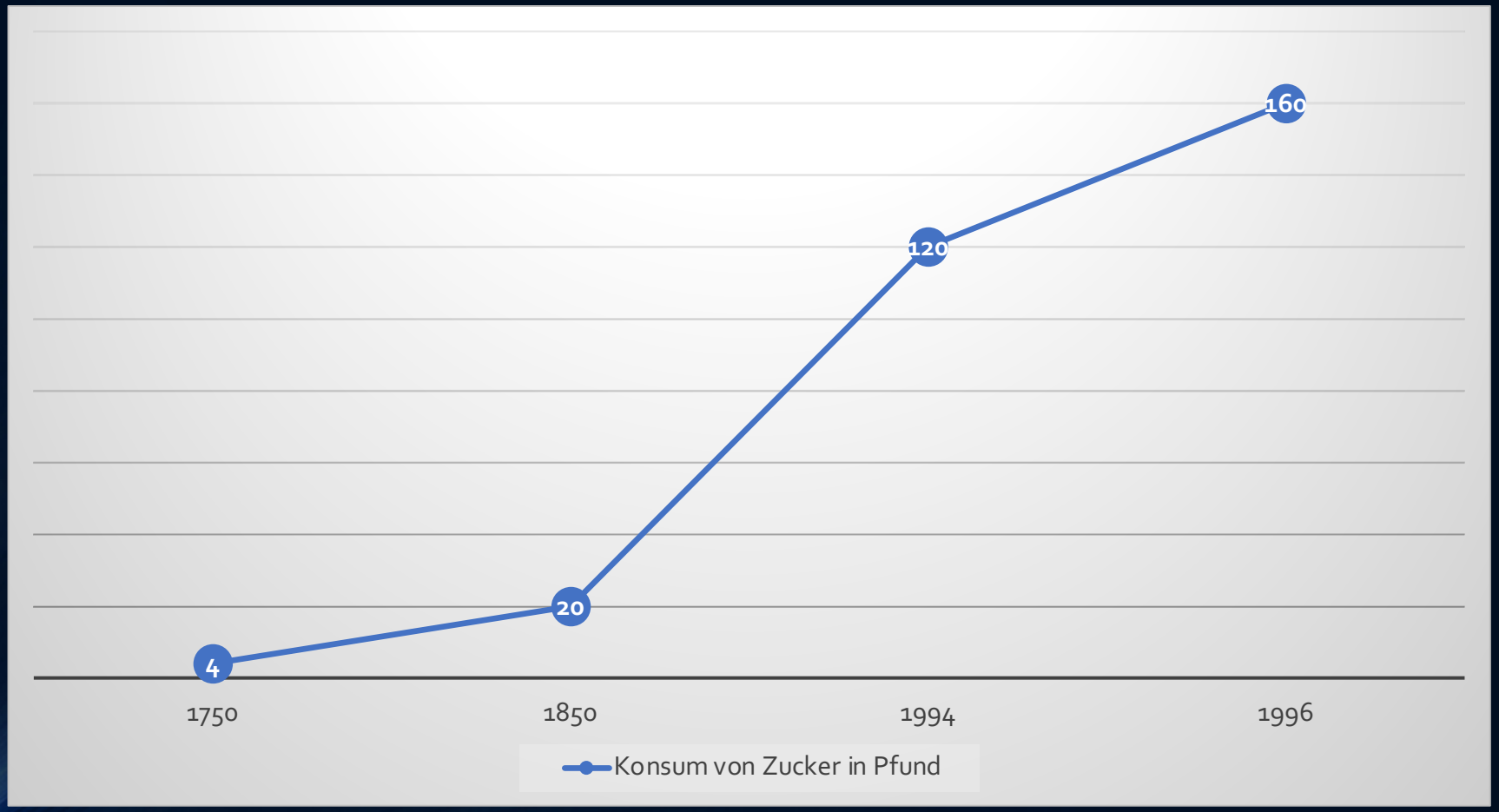
Ernährungswissenschaften auf den Kopf gestellt? „Die letzte Diät“

- Prof. Eran Segal und
  Prof. Eran Elinov,
  Weizmann Institute of Science, Israel
- Von
  „Was ist gesunde Ernährung?“ zu
  “Was ist gesunde Ernährung FÜR DICH?“
- Personalisierte Ernährung…?

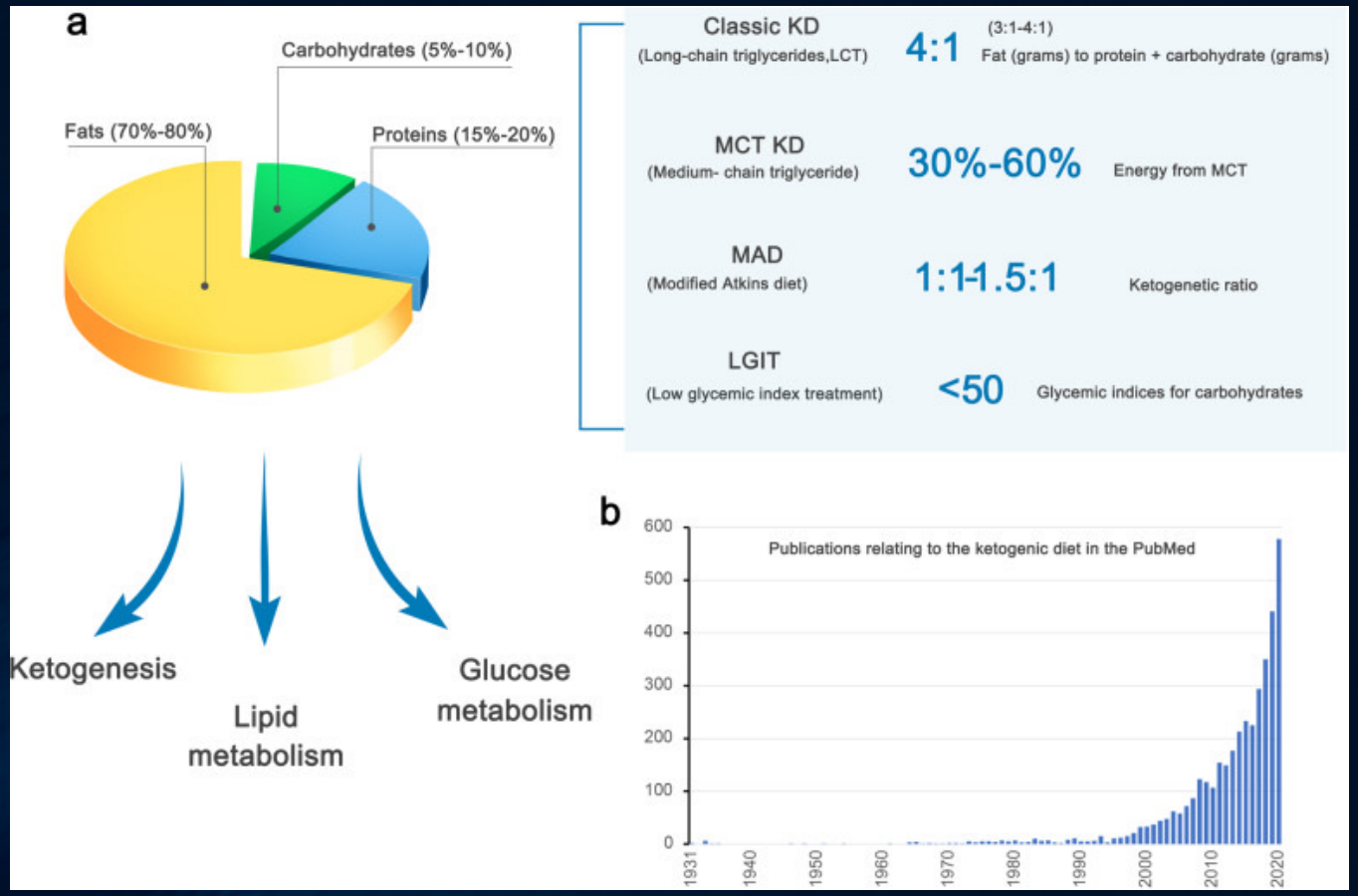
Eigene Erfahrung mit Blutzucker...



Jährlicher Zucker-Konsum in den USA



Ketogene Ernährung



Zhu H, Bi D, Zhang Y, et al. Ketogenic diet for human diseases: the underlying mechanisms and potential for clinical implementations. *Signal Transduct Target Ther*. 2022;7(1):11. Published 2022 Jan 17. doi:10.1038/s41392-021-00831-w (Link)

Biologische Mechanismen und ketogene Diät

BIOLOGISCHE MECHANISMEN BEI PSYCHISCHEN STÖRUNGEN

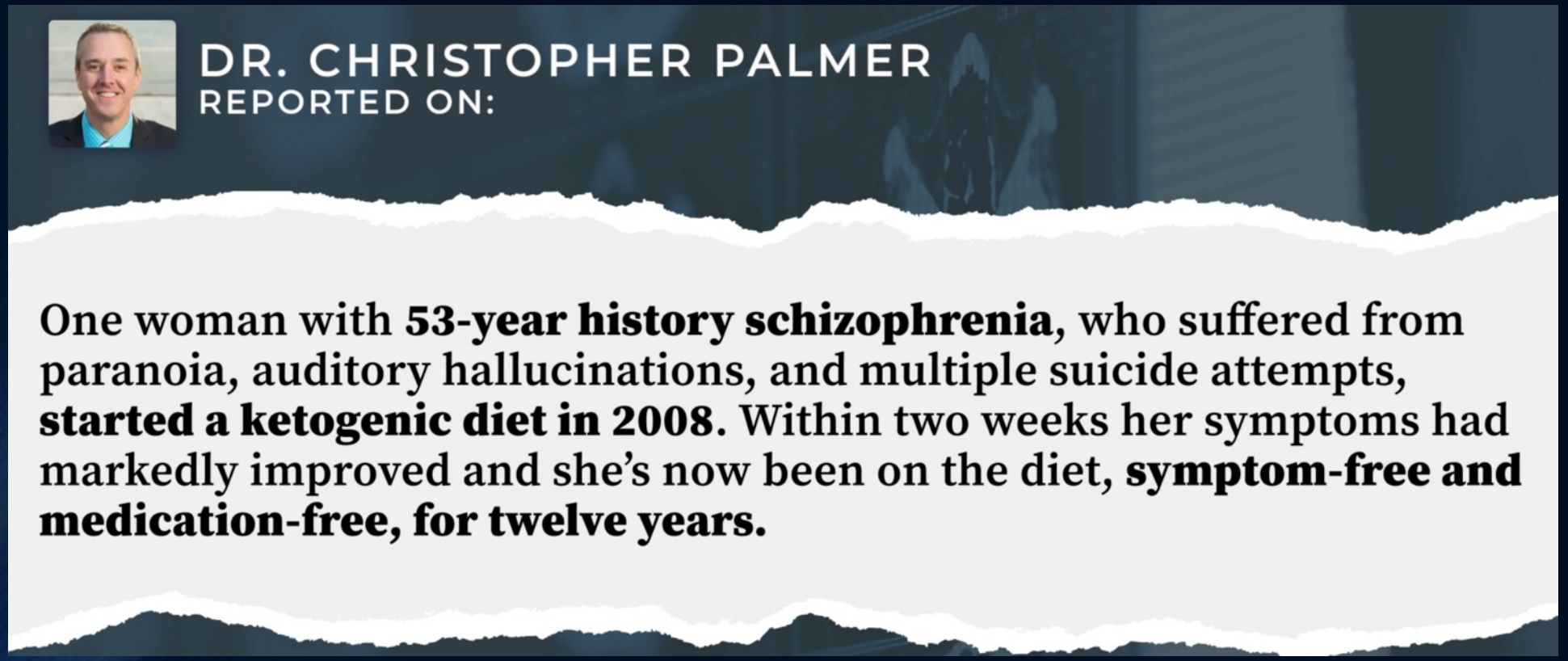
- Glucose hypometabolismus
- Neurotransmitter-Imbalances
- Oxidative Stress
- Inflammation

EFFEKTE VON KETOGENER DIÄT

- Circumvents glucose hypometabolism
- Rebalances neurotransmitters
- Reduces oxidative stress and
- Reduces inflammation

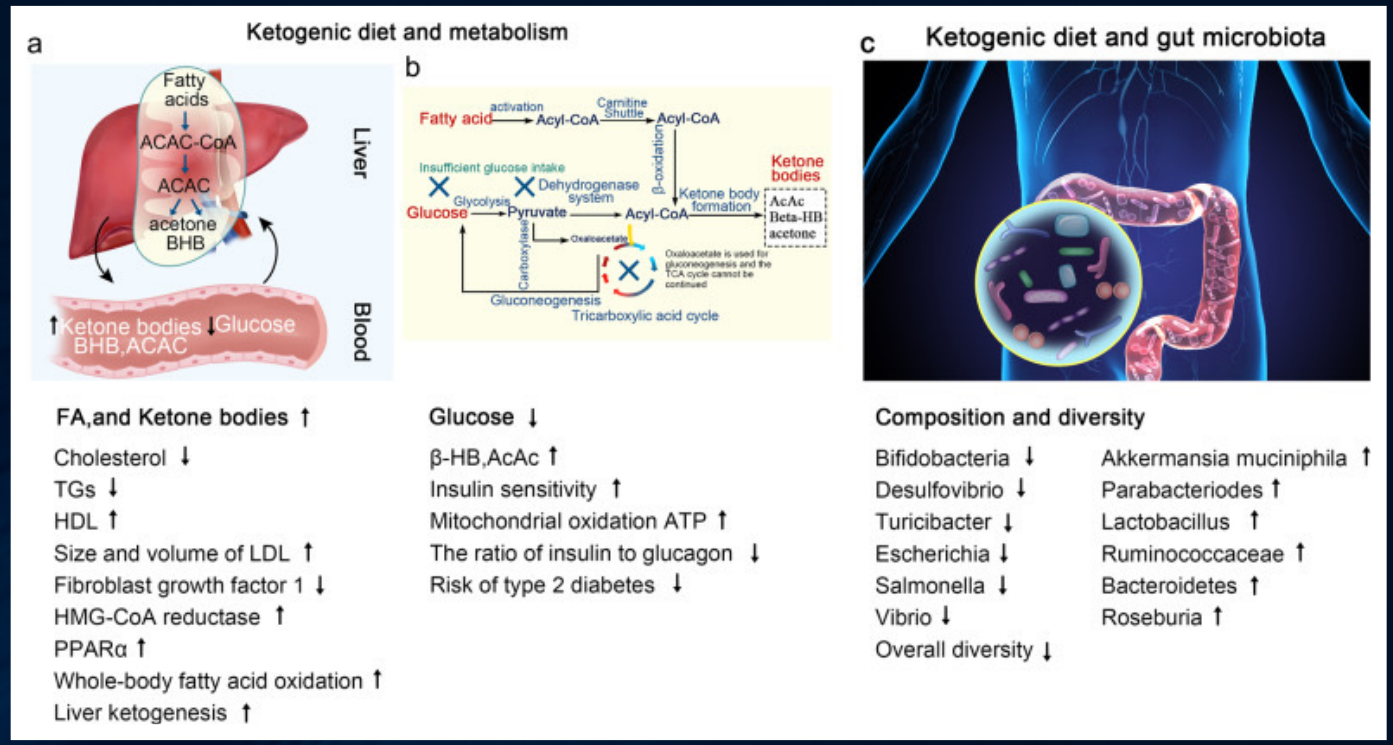
Norwitz NG, Dalai SS, Palmer CM. Ketogenic diet as a metabolic treatment for mental illness. Curr Opin Endocrinol Diabetes Obes. 2020 Oct;27(5):269-274. doi: 10.1097/MED.0000000000000564. PMID: 32773571. (Link)

Fallbericht Schizophrenie und ketogene Ernährung



Aus: Video-Zusammenfassung von „Ketogenic Diet as a Metabolic Treatment for Mental Illness“:
https://cdn-links.lww.com/permalink/coe/a/coe_2020_07_08_palmer_med270505_sdc1.mp4

Ketogene Ernährung – Effekte auf Metabolismus und Mikrobiom



Zhu H, Bi D, Zhang Y, et al. Ketogenic diet for human diseases: the underlying mechanisms and potential for clinical implementations. *Signal Transduct Target Ther*. 2022;7(1):11. Published 2022 Jan 17. doi:10.1038/s41392-021-00831-w (Link)

Ketogene Ernährung – positive Effekte bei

- Diabetes mellitus Typ 2
- Übergewicht
- Nicht alkoholische Fettleber
- PCO-Syndrom
- Morbus Alzheimer
- Morbus Parkinson
- Amyotrophe Lateralsklerose
- Epilepsie (seit 1921!)
- Depression
- Angststörungen
- Krebserkrankungen

Zhu H, Bi D, Zhang Y, et al. Ketogenic diet for human diseases: the underlying mechanisms and potential for clinical implementations. *Signal Transduct Target Ther*. 2022;7(1):11. Published 2022 Jan 17. doi:10.1038/s41392-021-00831-w (Link)

Ketogene Ernährung – Studien zu

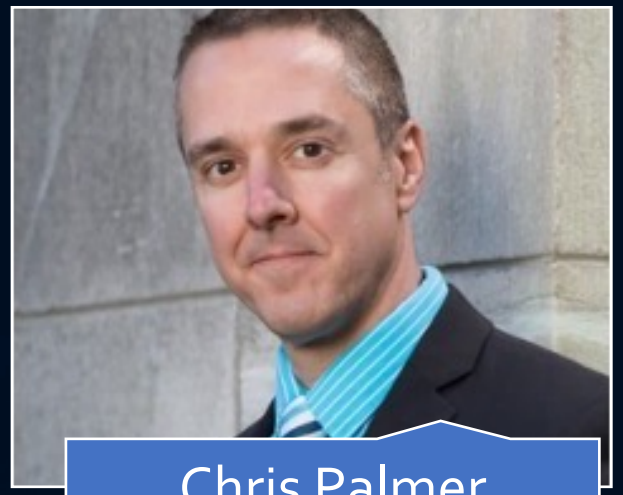
- Alzheimer
- Anorexia nervosa (!)
- Autismus Spektrum Störung
- Bipolare Störung
- Depression
- Narkolepsie
- Schizophrenie

„Metabolic Psychiatry"

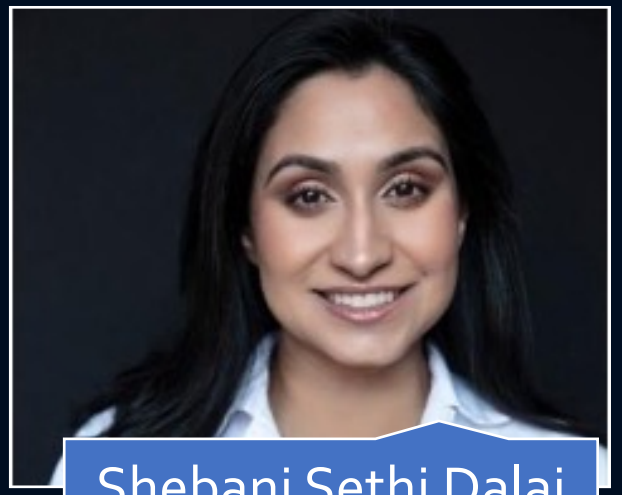
Tillery EE, Ellis KD, Threatt TB, Reyes HA, Plummer CS, Barney LR. The use of the ketogenic diet in the treatment of psychiatric disorders. *Ment Health Clin*. 2021;11(3):211-219. Published 2021 May 12. doi:10.9740/mhc.2021.05.211 (Link)

Ketogene Ernährung wird aktuell beforscht

Georgia Ede
(Harvard)



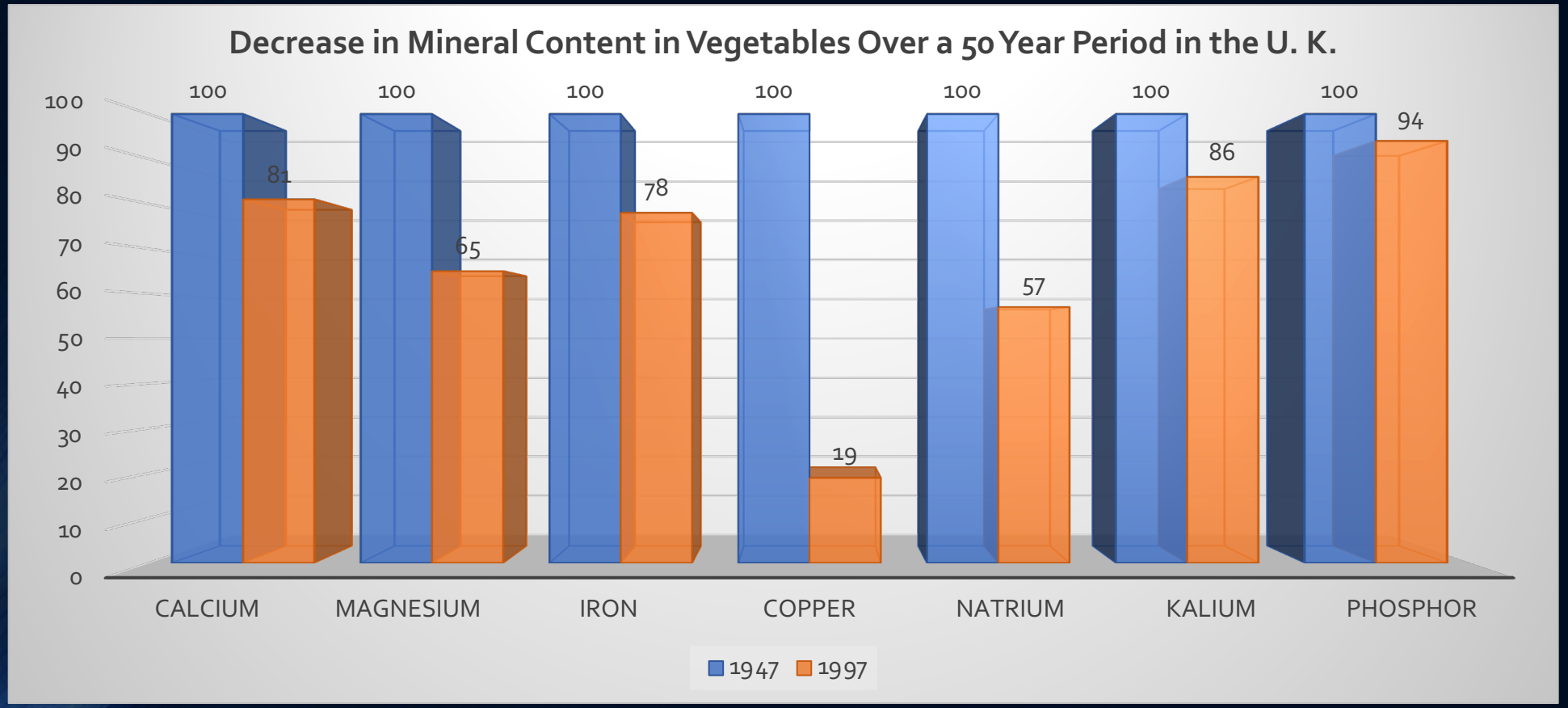
Chris Palmer
(Harvard)



Shebani Sethi Dalai
(Stanford)

Nahrungsergänzung

Mineralstoffgehalt von Gemüse 1947 - 1997



Mayer, Anne-Marie. "Historical changes in the mineral content of fruits and vegetables." *British Food Journal* 99.6 (1997): 207-211.

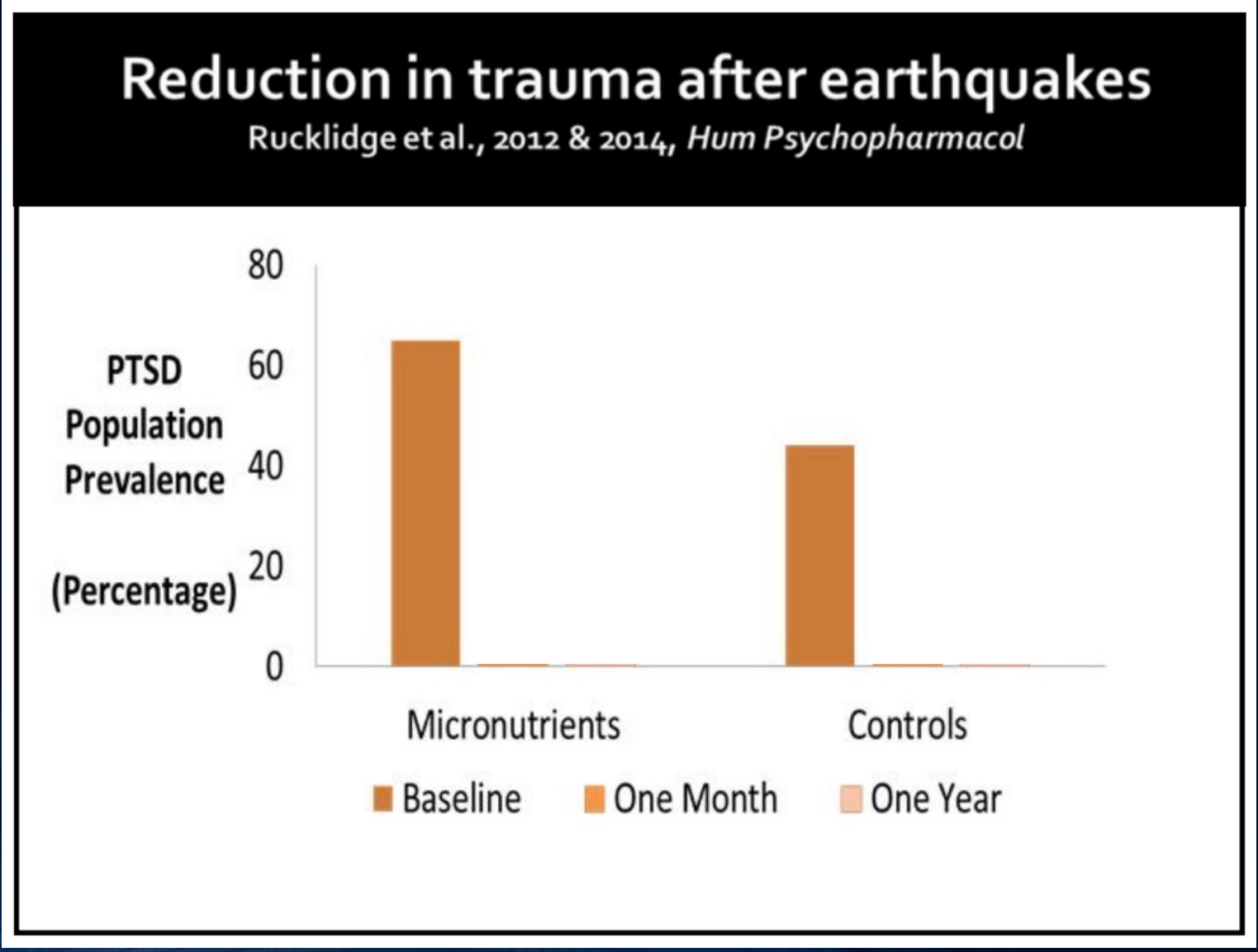
Überblick Studienlage mit Breitspektrum-Mikronährstoffen mit Benefit vs. Placebo (Stand März 2019, Prof. Julia Rucklidge)

- Aggression: 6 RCTs
- Autism: 3 RCTs
- Stress: 7 RCTs
- ADHD: 3 RCTs
- Mood: 14 RCTs

→Emotion regulation, lowering irritability, managing anger

→Some clinical, some nonclinical populations

Mikronährstoffe und PTSD?



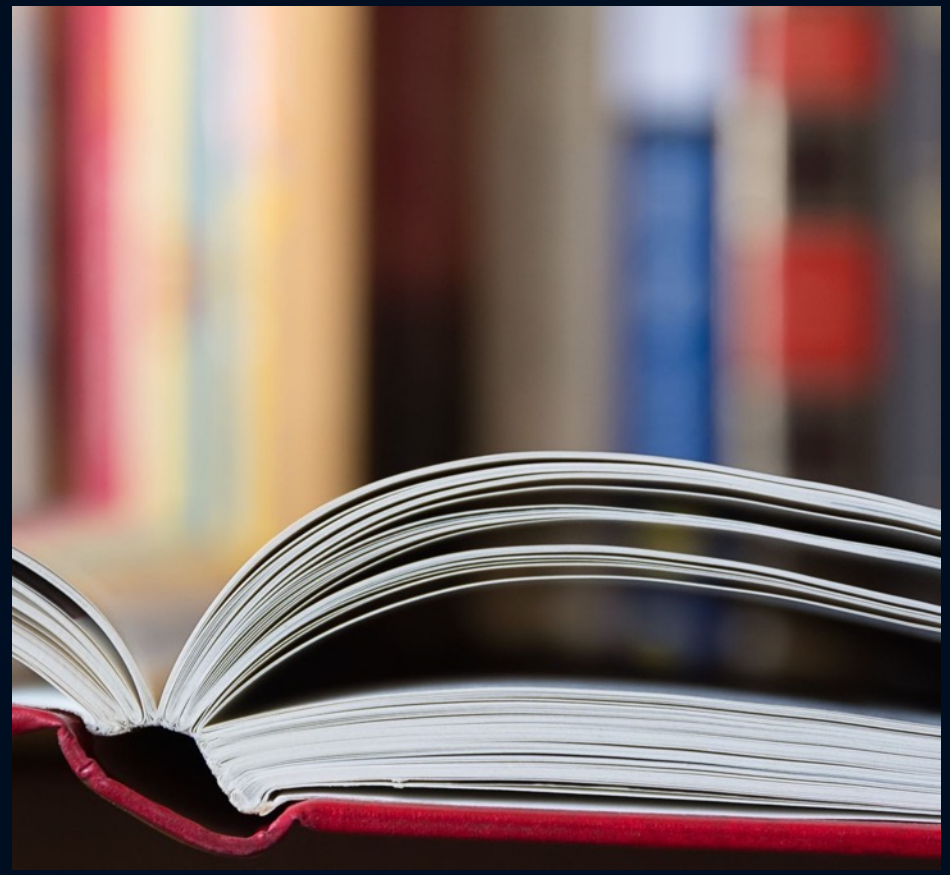
Nutritional Psychiatry: Where to Next?

- Verheissungsvolle «Nutraceuticals»: S-Adenosyl-Methionin (SAMe), Omega-3, Methylfolat und Vitamin D als wirksame Zusatztherapien bei Depression (Sarris et al., 2016)
- N-Acetylcystein (NAC) als Zusatztherapie bei Schizophrenie und Bipolarer Störung (Berk et al., 2008a, Berk et al., 2008b)
- Immer mehr Evidenz für den Einsatz von Probiotika (Allen et al., 2016, Tillisch et al., 2013, Akkasheh et al., 2016, Dinan et al., 2013), fermentiertes Essen kann hilfreich sein für psychische und Gehirn-Gesundheit (Kim et al., 2016)
- Schädliche Wirkung von "Junkfood", prozessiertem (weiterverarbeitetem) Essen, inkl. Emulgatoren (Chassaing et al., 2015), künstlichen Süssstoffen (Suez et al., 2014) and sehr fetthaltiger und zuckerhaltiger Ernährung (e.g. Molteni et al., 2002, Morrison et al., 2010, Zainuddin and Thuret, 2012) auf Darm und Gehirn

Jacka, Felice N. "Nutritional psychiatry: where to next?." *EBioMedicine* 17 (2017): 24-29. (Link)

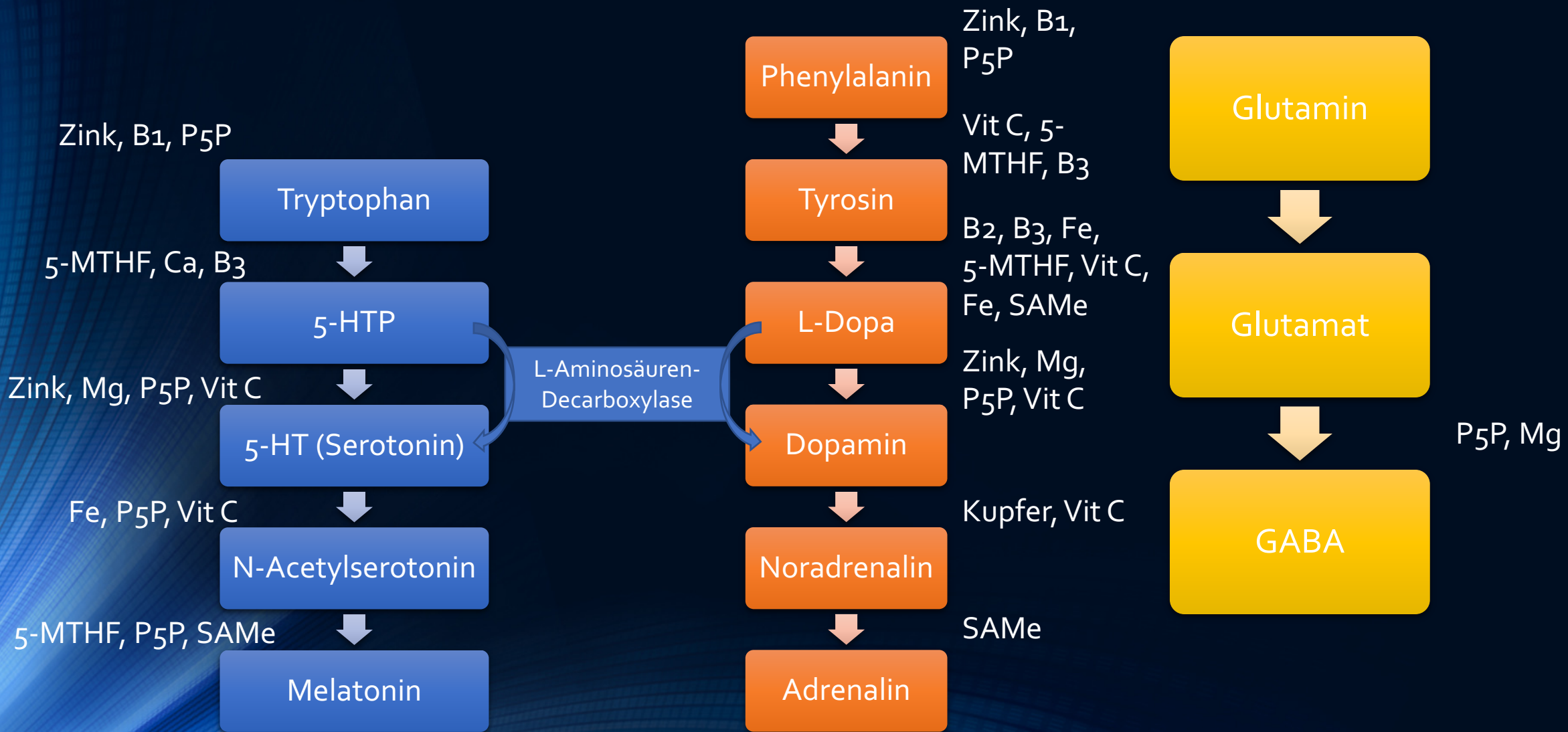
Psychische Gesundheit und Nahrungsergänzung – weitere „biologische“ Therapieansätze

- Aminosäuren
- Hormone, z. B. Nebennierenschwäche
- Mitochondrien-Dysfunktion
- Gen-Varianten/SNPs (MTHFR Mutation, …)
- Low-dose Lithium (Lithiumorotat 5-20(-45?) mg/d)



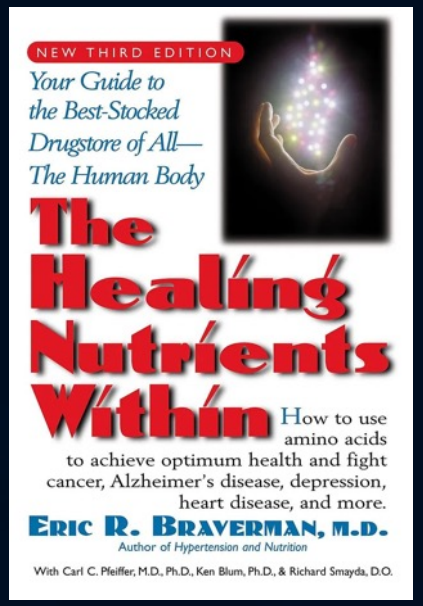
Neurotransmitter-Synthese

Proteine aus der Nahrung
(mithilfe von Mikroorganismen, v. a. E. coli, in Aminosäuren aufgeteilt)

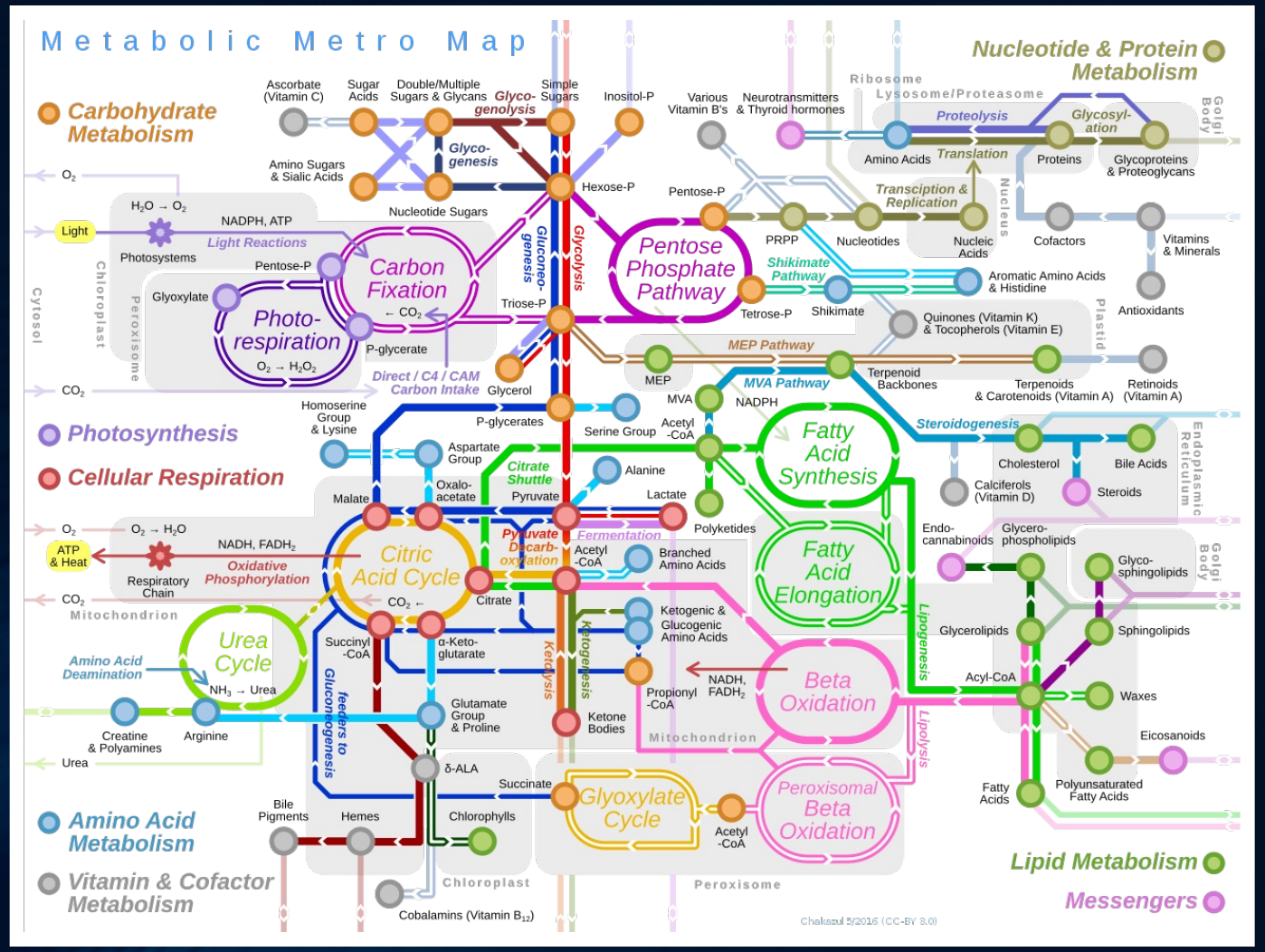


Aminosäuren bei psychischen Störungen

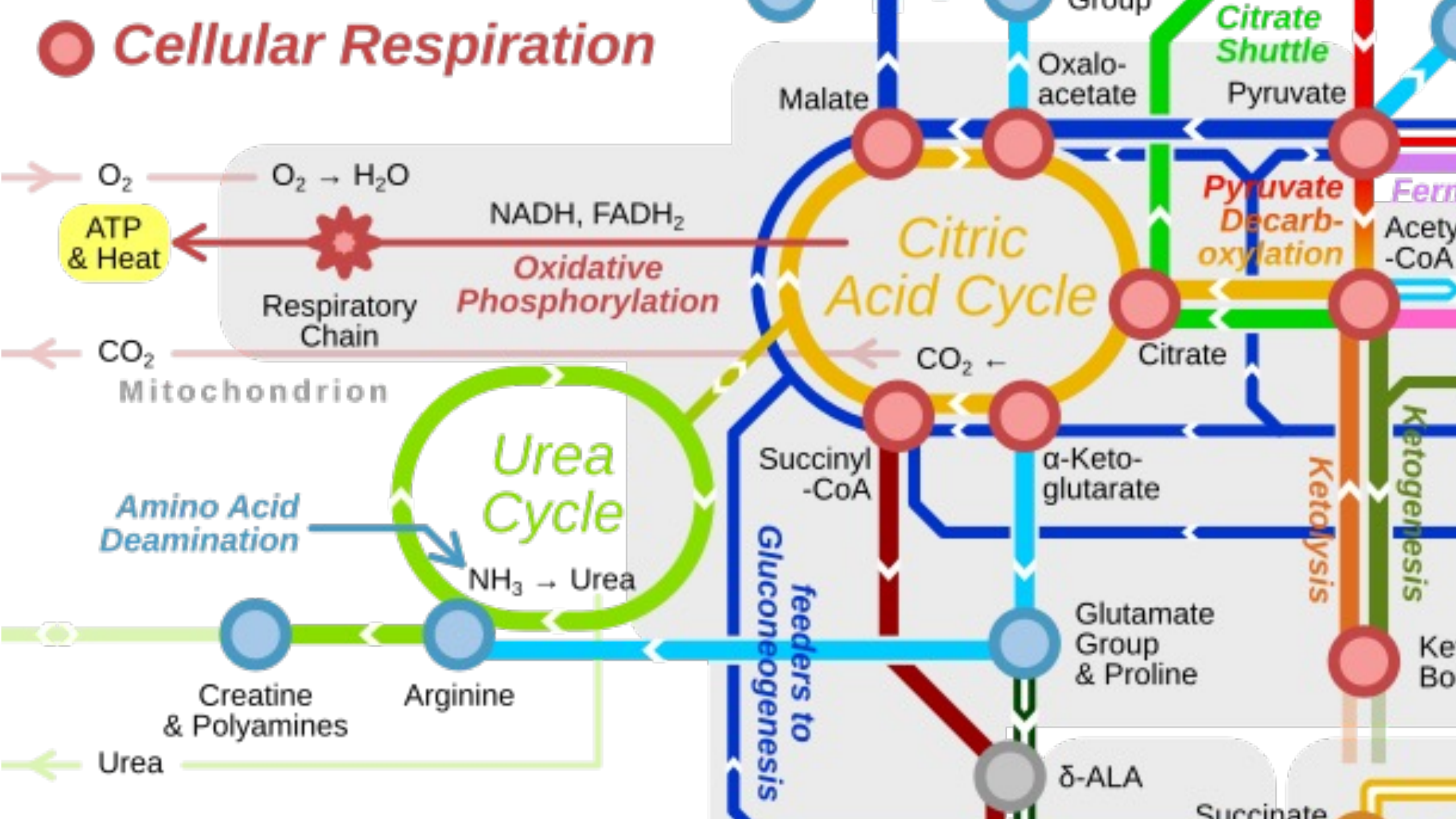
- Serotonin (und Melatonin)
- Katecholamine: Dopamin, Adrenalin, Noradrenalin
- GABA
- Endorphine
- Glutamin



Zell-Metabolismus

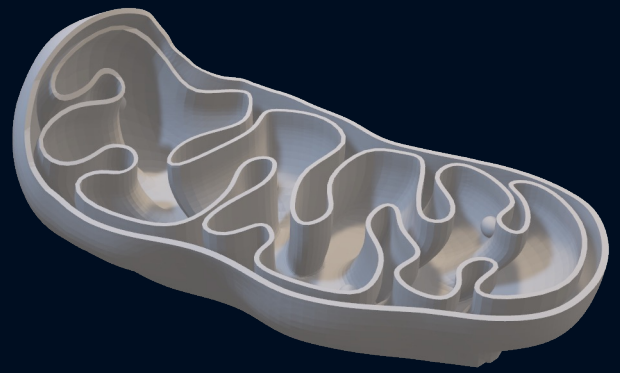


Chakazul (https://commons.wikimedia.org/wiki/File:Metabolic_Metro_Map.svg), https://creativecommons.org/licenses/by-sa/4.0/legalcode


Cellular Respiration
Malate
Oxalo-
acetate
Citrate
Shuttle
Pyruvate
O_2
$O_2 \rightarrow H_2O$
ATP
& Heat
NADH, $FADH_2$
Respiratory
Chain
Oxidative
Phosphorylation
Citric
Acid Cycle
Pyruvate
Decarb-
oxylation
Acety
-CoA
CO_2
CO_2 ←
Citrate
Mitochondrion
Urea
Cycle
Amino Acid
Deamination
$NH_3 \rightarrow$ Urea
Succinyl
-CoA
α-Keto-
glutarate
Ketolysis
Ketogenesis
feeders to
Gluconeogenesis
Glutamate
Group
& Proline
Creatine
& Polyamines
Arginine
Urea
δ-ALA

Kraftwerke der Zellen: Die Mitochondrien

- Energiegewinnung: abgefederte Knallgasreaktion – ATP als Energielieferant
- Pro Tag produzieren wir etwa so viel ATP wie wir wiegen (!)
- Kofaktoren Zitratzyklus: Eisen, Mangan, Magnesium, die Vitamine B1 – B3, B5, α-Liponsäure und Biotin
- Kofaktoren Atmungskette: Omega-3-FS, Eisen, Coenzym Q10, Vitamin B2 und B3, Kupfer, Häm, Selen und Zink
- Interessantes aktuelles Forschungsgebiet: Anti-Aging, chronische Erkrankungen, Krebs…



MTHFR-Mutation

- Häufigste genetische Störung im Folsäurestoffwechsel, single nucleotid polymorphism
- L-Methylfolat moduliert die Synthese von Monoaminen (Serotonin, Noradrenalin, Dopamin)
- Mutationen (T/T genotyp) in 10% der Kaukasier und bis 22% der Menschen aus Spanien oder dem Mittelmeerraum
- Oft bei therapieresistenten schweren Depressionen (Häufigkeit einer MTHFR-Mutation bis 70% der Major Depression-Fälle)
- Hyperhomocysteinämie, Methylierungsstörung
- Folsäure (synthetisch) kann nicht verstoffwechselt werden → Folat oder L-Methylfolat (15mg)
- Als Add-on und auch ohne zusätzliche Medikation bei Depression und Schizophrenie als wirksam erwiesen (15-25mg, ev. niedrigdosiert starten)
- Vorsicht bei bipolarer Störung

Jain, R., Manning, S., & Cutler, A. (2020). Good, better, best: Clinical scenarios for the use of L-methylfolate in patients with MDD. *CNS Spectrums*, *25*(6), 750-764. doi:10.1017/S1092852919001469 (Link)

Mögliche „biologische“ Therapie-Ebenen

Ernährung

- Mediterran
- BZ-adaptiert/ low carb/LOGI
- Keto?

Aminosäuren

- 5HTP/Tryptophan
- L-Tyrosin
- GABA
- DL-Phenylalanin
- Glutamin

Hormone

- Nebenniere
- Schilddrüse

Mitochondrien

- Diagnostik und spezifische Supplementation?

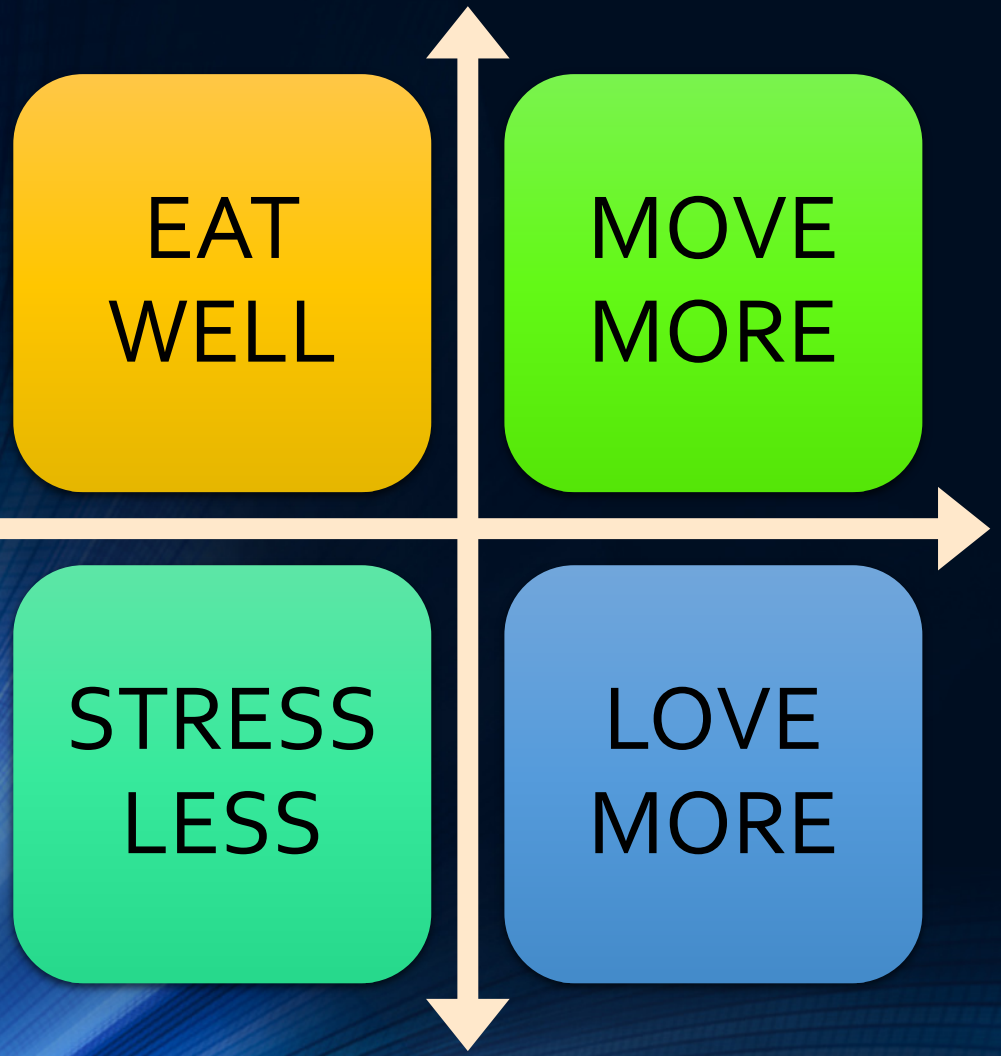
Genetische Testungen?

- MTHFR
- COMT

Was würde ich selber einnehmen?
Was würde ich einem lieben Verwandten raten?
Was empfehlen wir unseren Patienten?

- Gesunde Ernährung?
- Probiotika?
- 5-HTP, Tryptophan, Tyrosin, D-/L-Phenylalanin & Co?
- SAMe
- Kurkuma?
- Magnesium?
- Low-dose Lithium?
- Safran?
- Cannabidiol??
- Omega-3, EPA?
- Vitamin D?
- B-Vitamine? Zink, Mangan?
- Rosenwurz?
- Johanniskraut?
- Antidepressiva?
  Neuroleptika?
  Sedativa/Hypnotika?
  Antiepileptika?
  Hochdosiertes Lithium?
  Stimulanzien? …

Interessante Übereinstimmung…



THE DANIEL PLAN
GOD'S PRESCRIPTION FOR YOUR HEALTH
Faith Food Fitness Focus Friends

Glaube	Genuss	Gesundheit
Gelassenheit	Gemeinschaft	

Aus: Der Daniel-Plan: In 40 Tagen zu einem ganzheitlichen Leben, Rick Warren, 2015, Gerth Medien

Aus: Undo It!: How Simple Lifestyle Changes Can Reverse Most Chronic Diseases, Dean and Anne Ornish, 2019, Ballantine Books

Empfehlungen

Eat the rainbow!

Eat real food.
Not too much.
Mostly plants.
Michael Pollan

Iss nur Dinge, die Deine (Ur-) Grossmutter als Essen erkennen würde!

Iss kein Essen, für welches Werbung gemacht wird!

Iss eine "nutritarian diet"!
Iss keine "leeren Kalorien"!

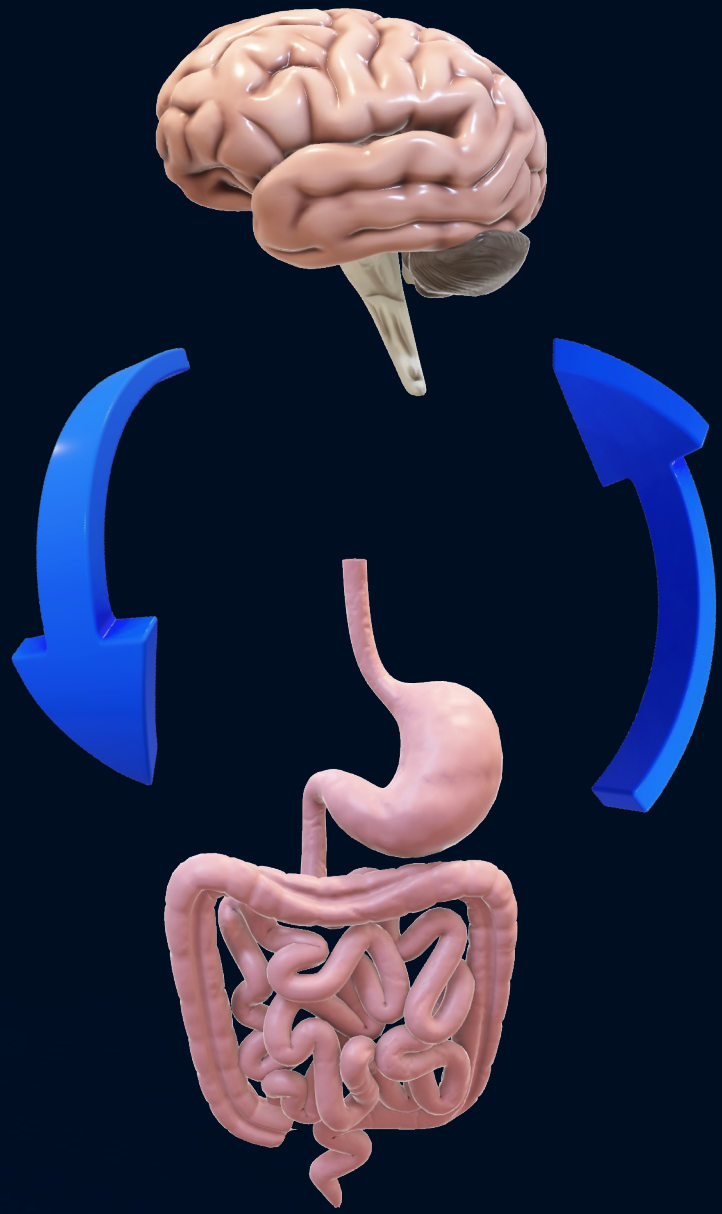
Wer isst, der verachte den nicht, der nicht isst; und wer nicht isst, der richte den nicht, der isst; denn Gott hat ihn angenommen.
Röm 14,3

Alles ist erlaubt, aber nicht alles dient zum Guten. Alles ist erlaubt, aber nicht alles baut auf.
1. Kor 10,23

Er aber antwortete und sprach: Es steht geschrieben: «Der Mensch lebt nicht vom Brot allein, sondern von einem jeden Wort, das aus dem Mund Gottes geht.»
Matt 4,4

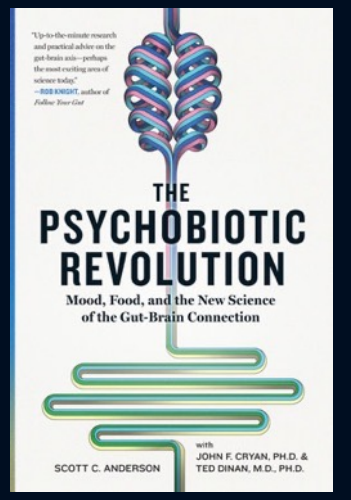
Zusammenfassend

- Darm-Hirn-Achse als interessanter Angriffspunkt für die (Erklärung?,) Behandlung und Prävention von psychischen Erkrankungen
- Evidenz für Mediterrane Diät, Omega-3, einzelne Supplemente (SAMe, L-Methylfolat, N-Acetyl-Cystein, B-Vitamine, Vitamin D) und Breitspektrum-Mikronährstoffe, zunehmende Berichte über ketogene Ernährung und (teilweise radikale) Verbesserung der psychischen Gesundheit
- Zudem vielversprechend: Mikrobiom über Probiotika/ Psychobiotika beeinflussen (und natürlich über die Ernährung…)

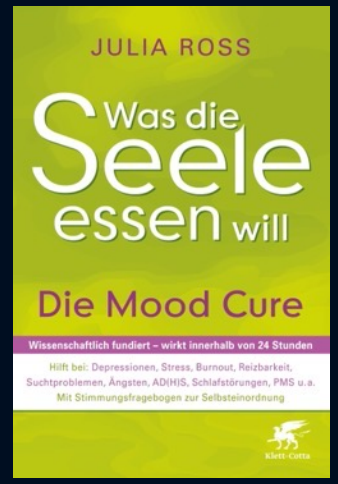


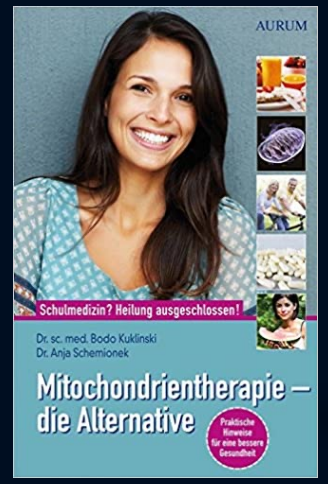
Ressourcen

- International Society for Nutrional Psychiatry Research: http://www.isnpr.org/
- Food and Mood Centre: http://foodandmoodcentre.com.au/
- MoodFood: https://moodfood-vu.eu/, https://moodfood-vu.eu/wp-content/uploads/2019/03/eatingformentalhealth-16ppA5_v5-1.pdf
- https://www.gutmicrobiotaforhealth.com/en/the-gut-microbiota-news-watch-2019-top-10/
- https://worldmicrobiomeday.com/resources/
- Happify – Übersicht: https://news.happifyhealth.com/infographic-what-to-eat-for-optimal-mental-health-69cod20aeb7
- TED-Talk Prof. Julia Rucklidge: https://www.youtube.com/watch?v=3dqXHHCc5lA
- Vortrag Prof. Julia Rucklidge, Feeding the Brain (Link Youtube)
- Vortrag Prof. Felice Jacka – Diet and Depression: https://www.youtube.com/watch?v=Zsyq_job1dk
- Aktuell: Omega-3-Studien (Depression bei Kindern und Psychoseprävention bei Adoleszenten) https://www.omega3.uzh.ch/de.html
- https://www.metabolicpsychiatry.com



Weitere Quellen





- Julia Ross, Aminosäuren
- Mitochondrien
- http://biochemical-pathways.com/#/map/1
- Blutzucker und Ernährung – die letzte Diät
- Integrative Psychiatry Institute https://psychiatryinstitute.com/
- Ketogene Ernährung:

Ketogene Ernährung

- Morris, Gerwyn, et al. "Induced ketosis as a treatment for neuroprogressive disorders: food for thought?." *International Journal of Neuropsychopharmacology* 23.6 (2020): 366-384. (Link)
- Sarnyai, Zoltán, and Christopher M. Palmer. "Ketogenic Therapy in Serious Mental Illness: Emerging Evidence." *International Journal of Neuropsychopharmacology* 23.7 (2020): 434-439. (Link)
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8120987/ (2021)
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8761750/ (2022)
- Video-Zusammenfassung von „Ketogenic Diet as a Metabolic Treatment for Mental Illness“: https://cdn-links.lww.com/permalink/coe/a/coe_2020_07_08_palmer_med270505_sdc1.mp4
- **Ketogenic diet as a metabolic therapy for bipolar disorder: Clinical developments**Yu, B., Oz, R., Sethi Dalai , S., et alResearch Square Preprint .2021 (Link)

Danke für Eure Aufmerksamkeit!

- Fragen, Ergänzungen…?
- Guten Appetit! ☺