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Diet change or nutritional supplements? Towards a rational approach in mental health- Pt. 1

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Disclosures:

Past/current consulting to:

Johnson and Johnson

Novo Nordisc





Objectives

Summarize the following:

How is diet associated with mental health?

Is there evidence that diet change improves mental health?

What about nutritional supplements?

Clinical strategies





Nutrition 201

Terms to know

“Nutrition Transition”

Dietary Patterns

Whole foods

Food security and insecurity

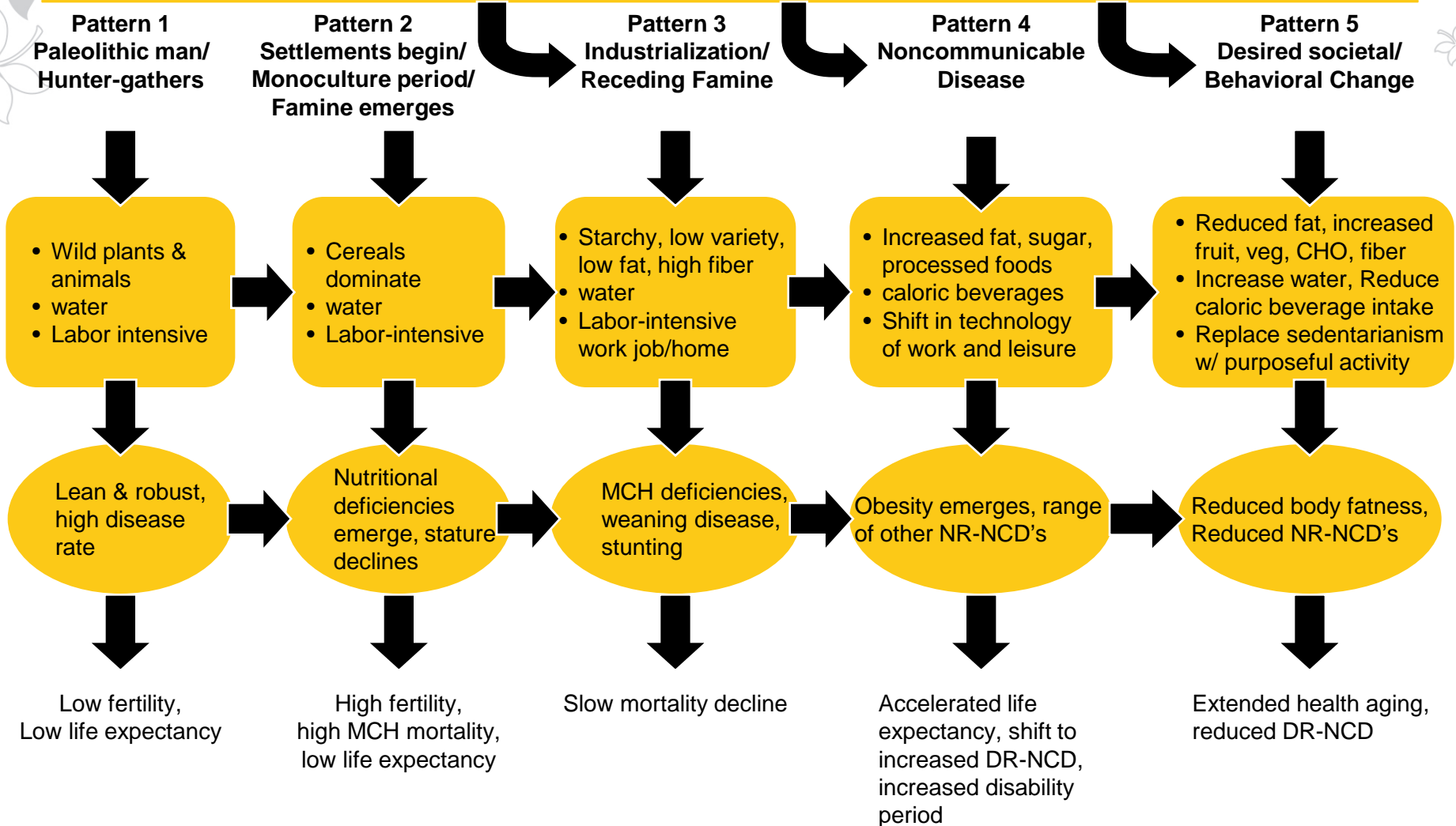


The nutritional transition is cultural, technological and evolutionary



Stages of the Nutrition Transition

Urbanization, economic growth, technological changes for work, leisure, & food processing, mass media growth



Source: Popkin 2002 revised 2006.

Dietary Patterns

- **quantities, proportions, variety or combinations of different foods and beverages in diets**
 - Including the frequency at which they are habitually consumed

Can be measured by:

- 1) **an a priori index based on dietary recommendations for a healthy dietary pattern from scientific consensus, or an investigator proposal using an evidence-based approach**
 - 1) The Healthy Eating Index (HEI)
 - 2) DASH Score (Dietary Approaches to Stop Hypertension)
 - 3) Mediterranean Diet Score
- 2) **Cluster analysis (from Food Frequency surveys etc)**
- 3) **Individual report by foods included or eliminated**
 - 1) Ex. vegetarian, vegan

Mediterranean Dietary Pattern



The Standard American Diet: “SAD”



Most Americans are now overfed but undernourished

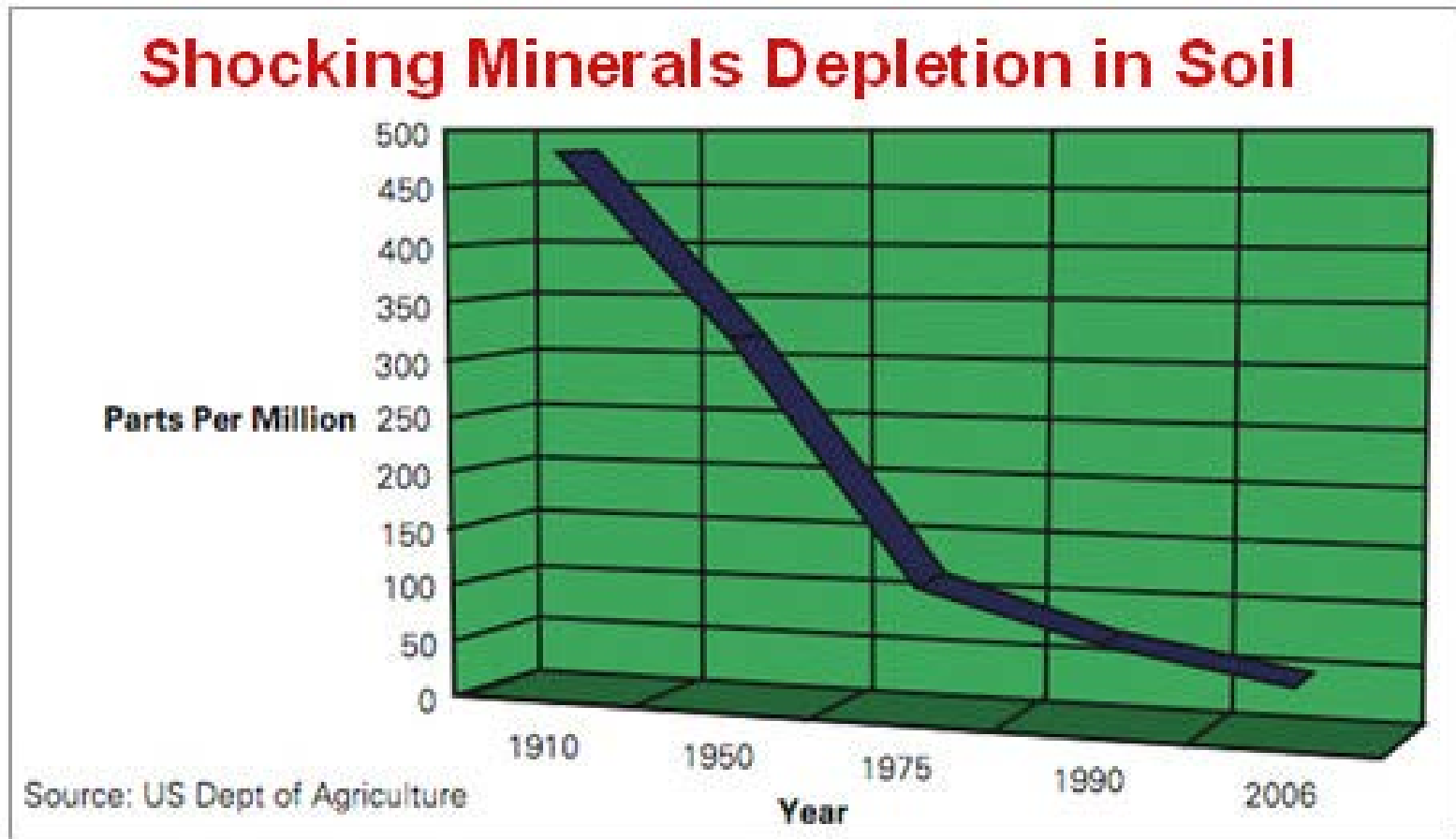
- **Calorie intakes are higher**
 - Average daily calorie intake increased by 24.5%, or 530 calories, from 1970 to 2000
- **Nutrient intakes are lower**

per IOM average dietary requirements

- 92% do not get enough potassium
- 86% not enough vitamin E
- 69% not enough calcium
- 57% not enough Mg⁺⁺



Food Quality- changes due to agriculture practices



Dramatic depletion of many micronutrients in foods due to modern agricultural methods

- **Industrial food production has reduced the amount of micronutrients in crop foods from the 1930s to the 1980s**

- **Vegetables**

- Copper by 81%
- Na⁺ by 43%,
- Mg⁺⁺ by 34%

- **Fruits**

- Copper by 36%
- Iron by 32%
- K⁺ by 20%

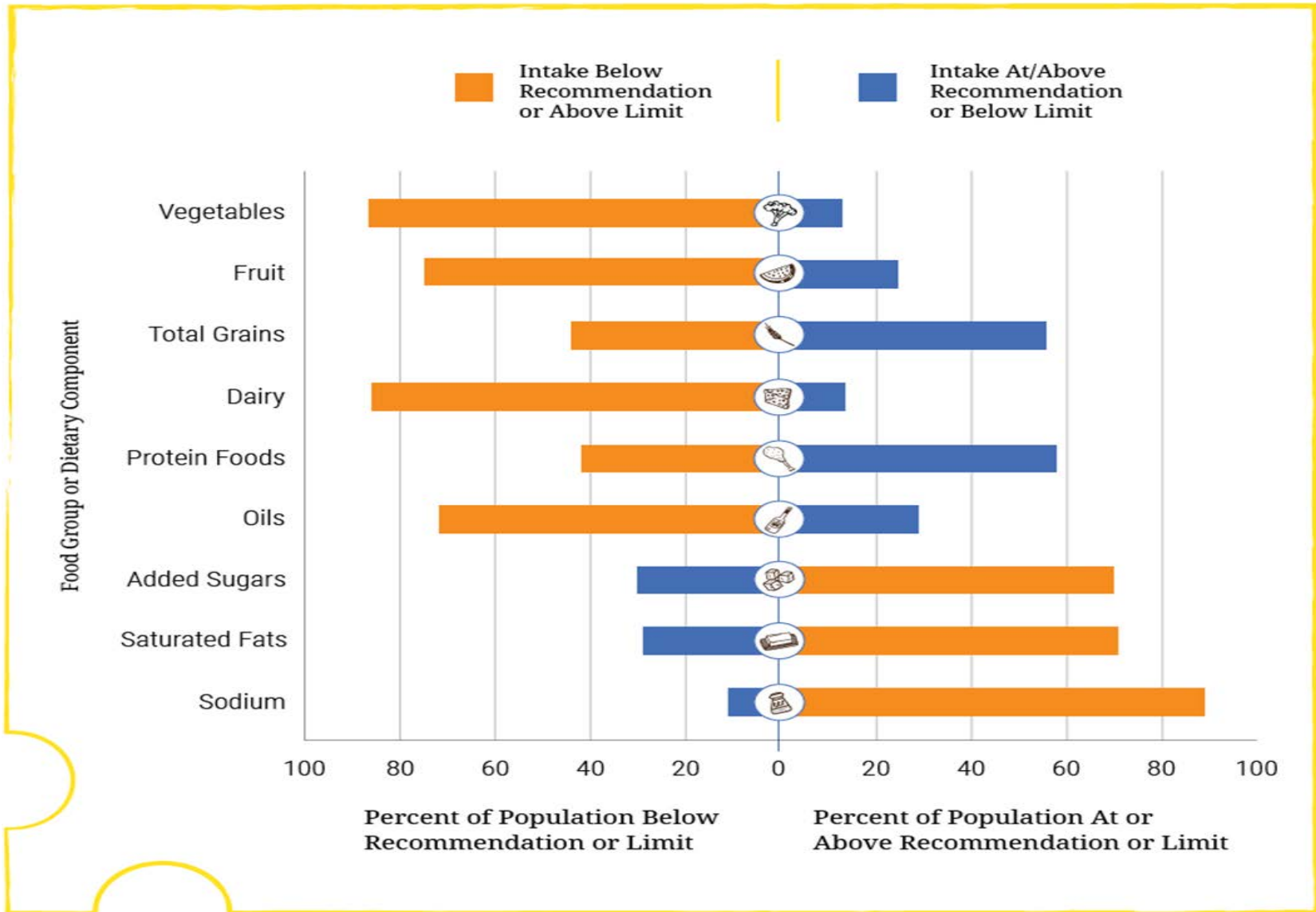


Food (1951 - 1999)	Nutrient & Amount of Change (Percentage)						
	Calcium	Iron	Vitamin A	Vitamin C	Thiamine	Riboflavin	Niacin
Apple	20.0	-55.3	-41.1	16.0	-75.0	-66.7	-30.0
Banana	-23.8	-41.7	-81.2	-13.0	0.0	-100.0	-1.4
Broccoli	-62.8	-33.9	-55.9	-10.1	-40.0	-42.9	-2.7
Onion	-37.5	-52.9	-100.0	-54.8	56.9	-41.2	135.3
Potato	-27.5	-58.6	-100.0	-57.4	-14.6	-50.0	44.9
Tomato	-55.7	-18.8	-43.4	-1.6	0.0	21.8	46.3

Review the chart and see for yourself where the nutrients are. You'll notice that there have been more losses than gains in nutrients across the chart. And only two areas showed no content change at all, and that's for Thiamine.

Meyer et al.1997

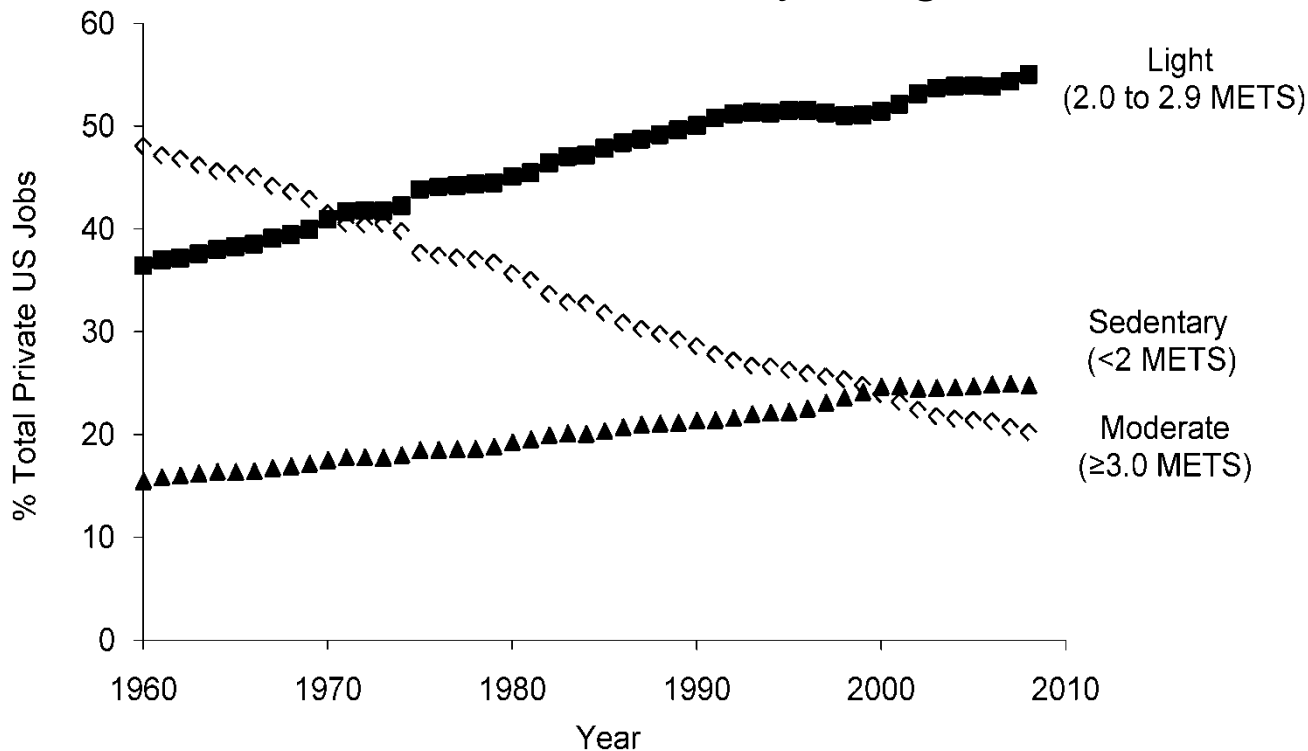
% of US population below, at, or above RDIs



<https://health.gov/dietaryguidelines/2015>

And less calories are expended...

- Over the last 50 years, U.S. daily occupation-related energy expenditure has decreased by > 100 calories
- This reduction accounts for a significant portion of the increase in mean U.S. body weights for women and men.



Food Security

Per the United Nations' Committee on World Food Security:

- the condition in which all people, at all times, have physical, social and economic access to sufficient safe and nutritious food that meets their dietary needs and food preferences for an active and healthy life.



Food Security in Florida by county

2014	Food Insecure Households	Food Insecure Persons
Alachua County	20.4%	51,240
Miami Dade	11.3%	293,070
Gadsden	24.4%	11,440

<http://www.feedingamerica.org/hunger-in-america/our-research/map-the-meal-gap/data-by-county-in-each-state.html>

defined by the United Nations' Committee on World Food Security, the condition in which all people, at all times, have physical, social and economic access to sufficient safe and nutritious food that meets their dietary needs and food preferences for an active and healthy life.



Food Quality- “Ultraprocessed Foods”

- **Ingredient formulations (besides salt, sugar, oils, and fats) including substances not used in culinary preparation**
 - In particular, flavors, colors, sweeteners, emulsifiers and other *additives used to imitate sensorial qualities of unprocessed or minimally processed foods/their preparations*, or to disguise undesirable qualities of the final product.
- **Using cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) 2009–2010, ultra-processed foods:**
 - comprised 57.9% of energy intake
 - contributed 89.7% of the energy intake from added sugars
- **Added sugar content in ultra-processed foods (21.1% of calories) was 8x higher than in processed foods (2.4%) and 5x higher than in unprocessed/minimally processed foods**

How is diet associated with mental health?

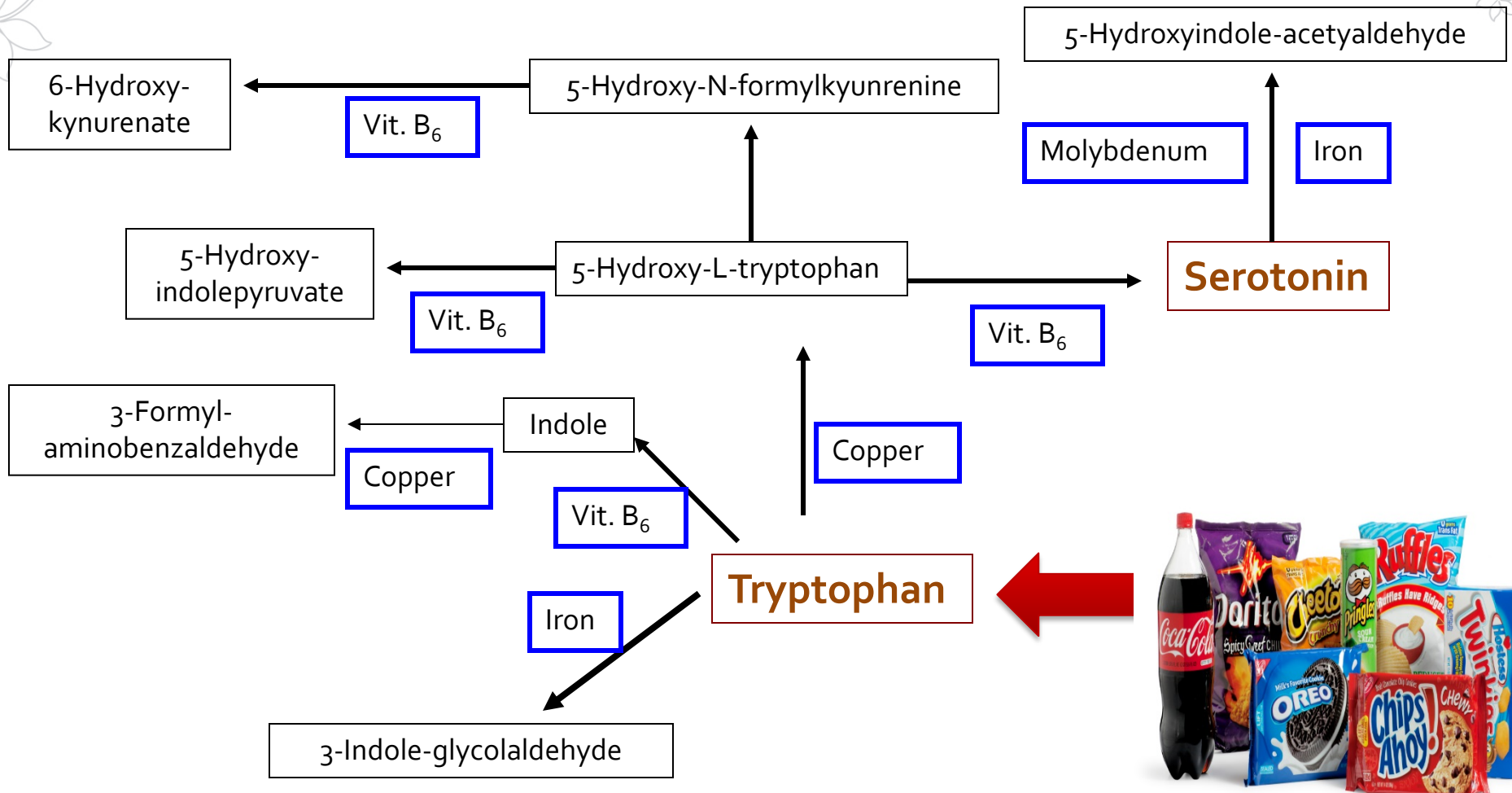
Mechanisms and Descriptive Studies



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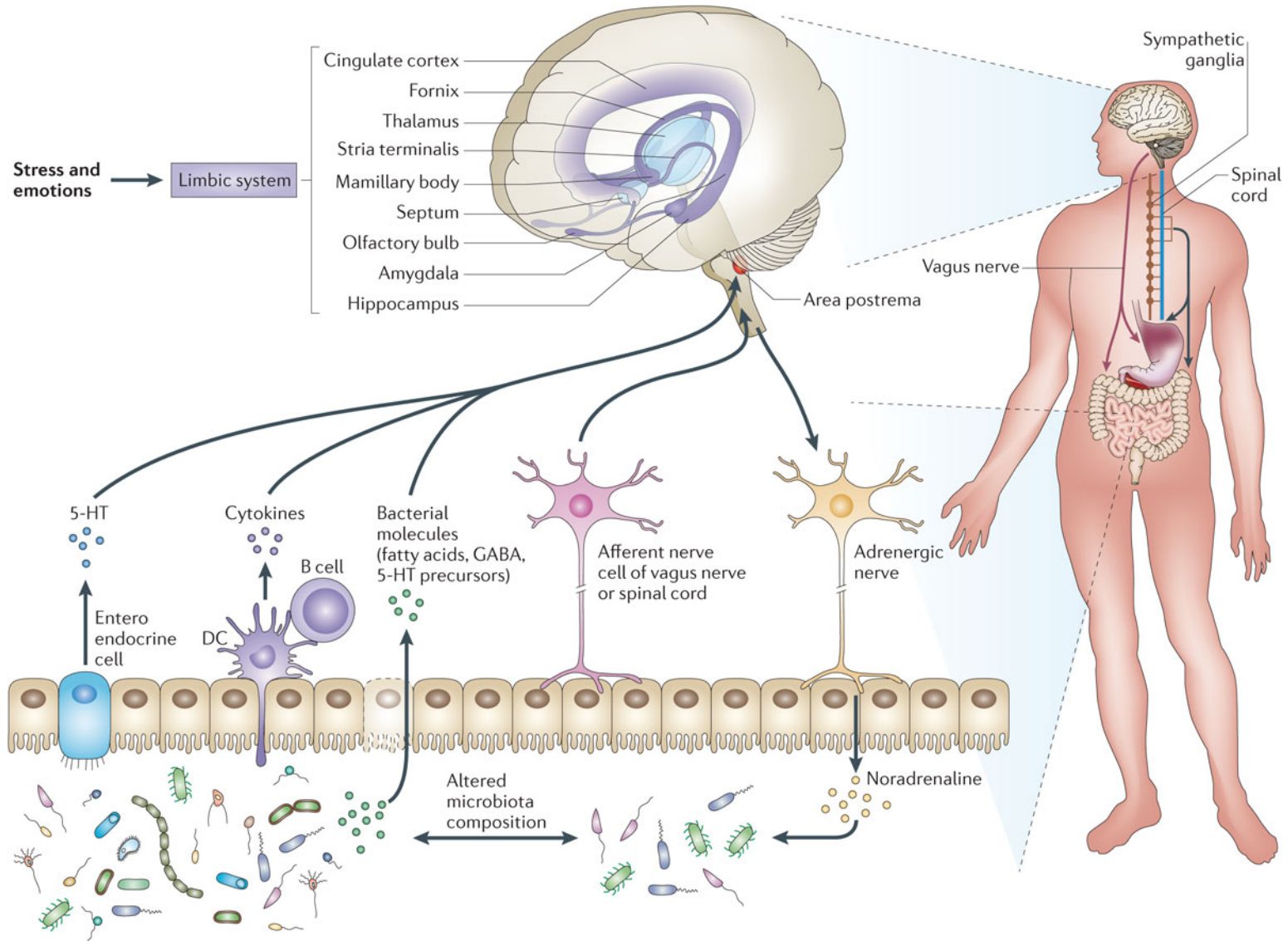
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One small portion of serotonin pathway

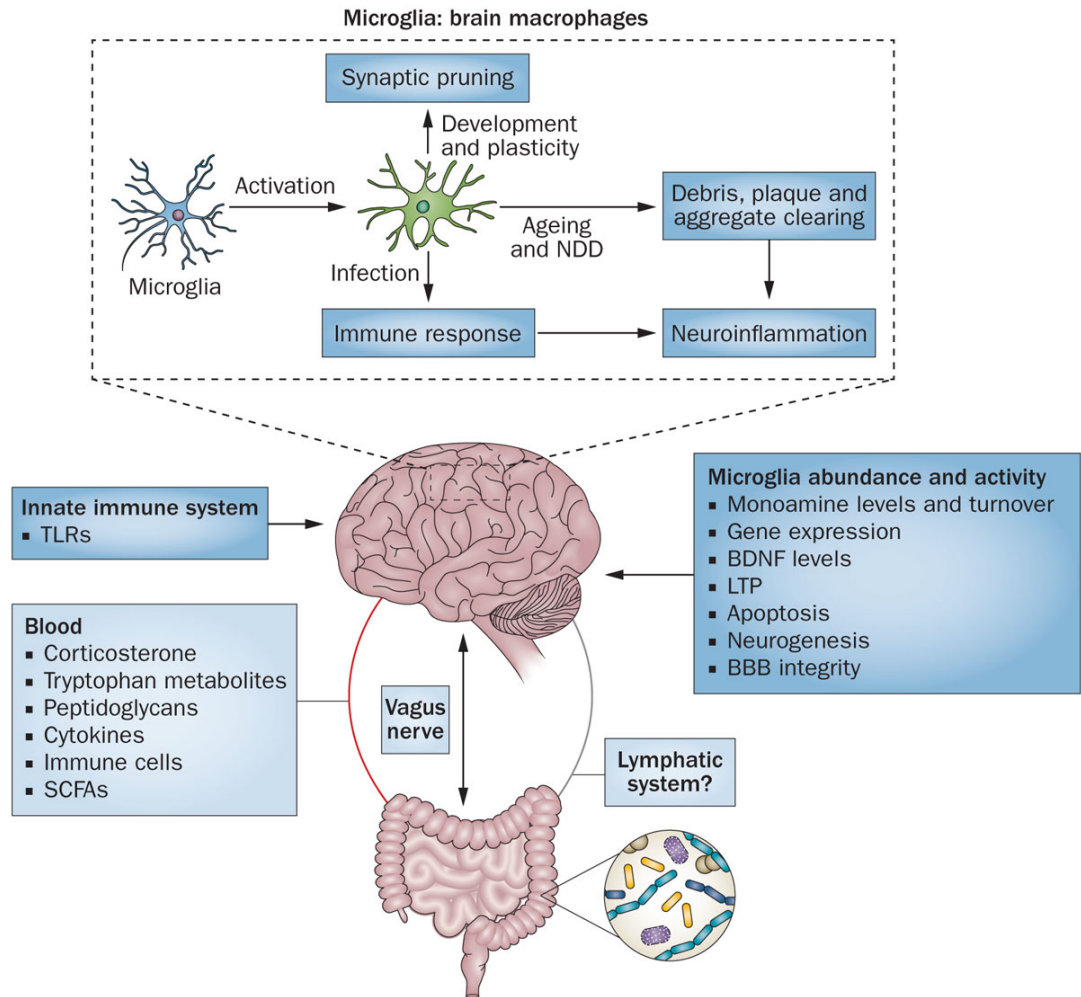


The bidirectional microbiota–gut–brain axis.

From: The interplay between the intestinal microbiota and the brain



Mechanisms for microbiota regulation of neuroimmune signalling



Nature Reviews | **Gastroenterology & Hepatology**

Figure developed by Dr R. Stilling, APC Microbiome Institute, University College Cork

Selected diet studies in mental health

- Cross-sectional
 - Longitudinal
 - Prospective cohorts
 - Meta-analyses
 - RCTs
- Major centers: Australia, Spain, the Netherlands, Canada, and the UK



Longitudinal diet studies in youth

- Perth Longitudinal Cohort Study
 - 14 y/o youth with Western diet patterns had more internalizing (withdrawn/depressed) and externalizing (delinquent/aggressive) behaviors
 - Especially for sweets, take-out food, and red meat
 - Related to more TV time, parental smoking, lower incomes
 - The 11% of youth who ate 3 food groups at breakfast had more favorable CBCL scores
 - Youth with better diets were more likely to be female, have greater maternal education, lower television exposure, better family functioning, and a two-parent household

Oddy et al 2009; Ambrosini et al 2009; O'Sullivan et al 2009; Larsen et al 2007



Fruits and vegetables lower risk for mood and anxiety disorders in adults and teens

- Canadian cohort including adolescents
 - across all 5 waves, ~ 2 years apart, greater fruit and vegetable intake associated with lower odds of MDE in the previous 12 months (OR 0.72; 95% CI 0.71-0.75);
 - previous mood or anxiety disorder diagnosis also related to lower fruit and vegetable intake ($p < 0.05$)
- Perth cohort
 - Youth with more green leafy vegetable and fresh fruit intakes had better behavioral scores
 - Family meals during adolescence predicted higher quality diet at young adulthood
 - greater intake of fruit, vegetables, especially dark-green and orange vegetables, and lower intakes of soft drinks

McMartin et al 2013; Larson et al 2007



NCH D-asthma study in youth: does vitamin D or their diet affect mood and anxiety symptoms?

- Objective: Characterize dietary patterns and their correlations with MH symptoms in youth with inhaled steroid-dependent asthma.
- 122 youth aged 8-17 were recruited from asthma and allergy specialty clinics at Nationwide Children's Hospital, Columbus, OH
- Inclusions: PFT-confirmed asthma, using a daily steroid inhaler, and BMI < 99th percentile.
- 42 youth/parents completed the Block Kids 2004 Food Frequency Questionnaire (FFQ; NutritionQuest, Berkeley, CA) to assess nutritional intake patterns.
- Parents/guardians completed a Child Behavior Checklist (CBCL; ASEBA, Burlington, VT) to rate emotional and behavioral concerns.



Results: Distribution of significant Nutritional Intake differences between Clusters

		Cluster 1 (FAT diet type)	Cluster 2 (SWEET diet type)
	p-value	Median (IQR)	Median (IQR)
*Food energy (kcal)	0.01	1814.34 (663.04)	1514.11(705.39)
*Protein (gms)	0.00	65.02(12.51)	49.81(18.87)
*Fat (gms)	0.00	69.93(14.26)	48.58(16.44)
*Saturated Fat (gms)	0.00	25.12(7.57)	15.95(5.60)
*Monounsaturated fatty acids (gms)	0.00	27.87(5.05)	18.18(7.53)
*Polyunsaturated fatty acids (gms)	0.00	13.67(4.33)	9.59(3.40)
*Cholesterol (mg)	0.00	212.84(121.99)	151.05(86.40)
*Omega-3 fatty acids (gms)	0.00	1.20(0.43)	.89(0.41)
*Omega-6 fatty acids (gms)	0.00	12.21(3.63)	8.59(3.11)
*Trans fats, total (gms)	0.00	7.31(1.79)	4.11(1.94)
*Percent of kcal from fat	0.00	36.35(2.72)	29.98(5.00)
*Percent of kcal from carbohydrate	0.00	50.70(6.12)	58.45(6.73)
*Daily servings of meat, fish, poultry, beans, eggs	0.00	1.94(0.90)	1.19(0.90)



Results

- Asthma severity scores, BMI, vitamin D intake, and 25-OH vitamin D were not different between the 2 groups.
- Youth with a FAT diet type were:
 - more anxious and depressed ($p=0.034$),
 - had more somatic complaints ($p=0.050$),
 - had more social problems ($p=0.060$),
 - scored lower in social competence ($p=0.001$).
 - scored higher for internalized symptoms ($p=0.023$), affective problems ($p=0.043$), conduct problems ($p=0.083$), and were more aggressive ($p=0.093$).
- Mental health concerns may be mediated by diet in youth with asthma; further prospective study is needed

MH and diet patterns in women: The Geelong Osteoporosis Study

In over 1,000 women ages 20-93:

- A Western diet of processed or fried foods, refined grains, sugary products and beer
 - associated with a higher score on the 12-item General Health Questionnaire (GHQ-12)
- A traditional diet of vegetables, fruit, meat, fish, and whole grains
 - associated with lower odds for major depression, dysthymia, and anxiety disorders, via SCID (Structured Clinical Interview for DSM-IV-TR).

There were no confounds by age, SES, education, or other health behaviors on the GHQ-12 results.

Jacka et al 2010 Am J Psychiatry



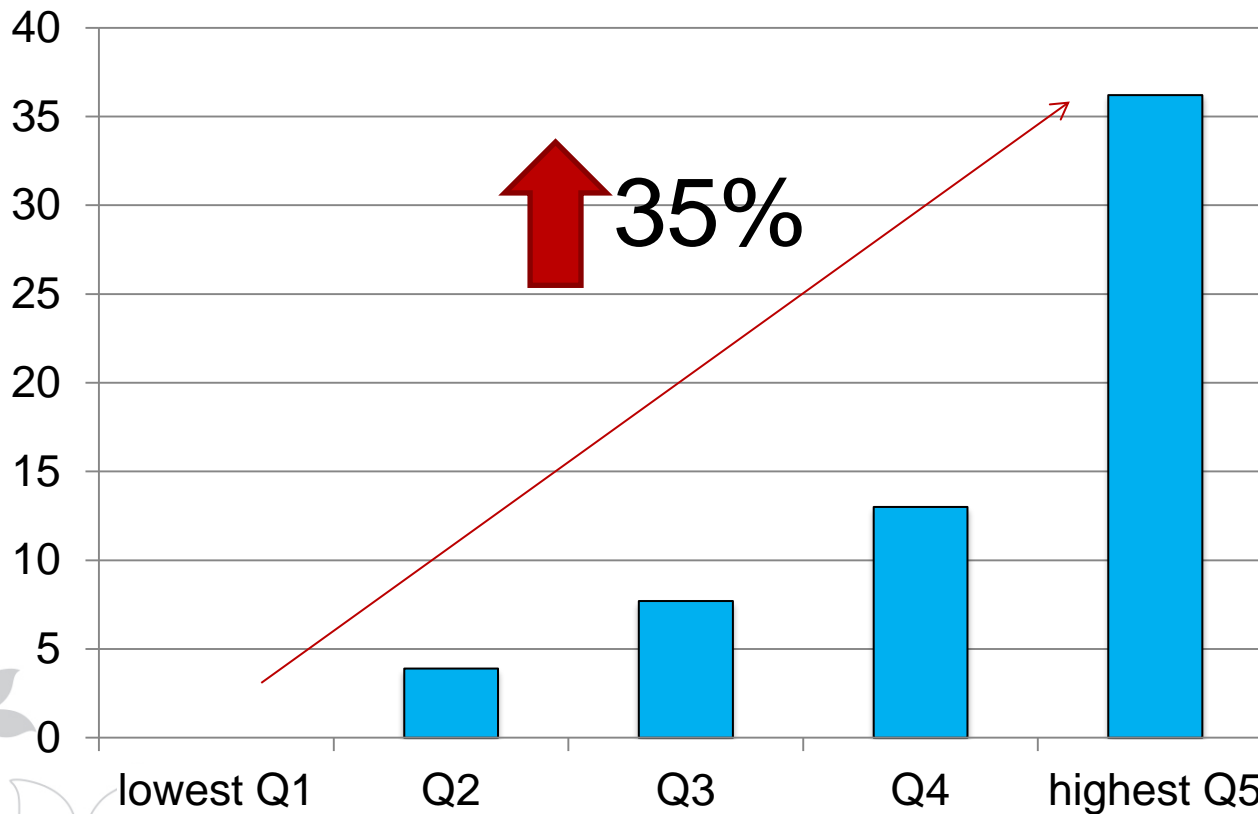
Diet patterns and women with bipolar disorder

- In population-based adult women (also the Geelong study, using the Cancer Council Victoria FFQ and the SCID-I/NP):
 - women with BP disorder had higher scores for a Western diet ($p < 0.03$) vs. those without psychopathology
 - trended toward higher glycemic loads;
 - Adjusted odds (for energy intake) for BP disorder increased for each standard deviation increase in:
 - **unfavorable ‘western’ diet- OR 1.88** (95% CI 1.33-2.65)
 - **‘modern’ diet- OR 1.72**, (95% CI 1.14-2.39)
 - **glycemic load- OR 1.56**, (95% CI 1.13-2.14)
 - Jacka et al 2011, J Affect Disord



Risk of depression within 6.2 years in ~9,000 people

Based on processed pastries (muffins, doughnuts)

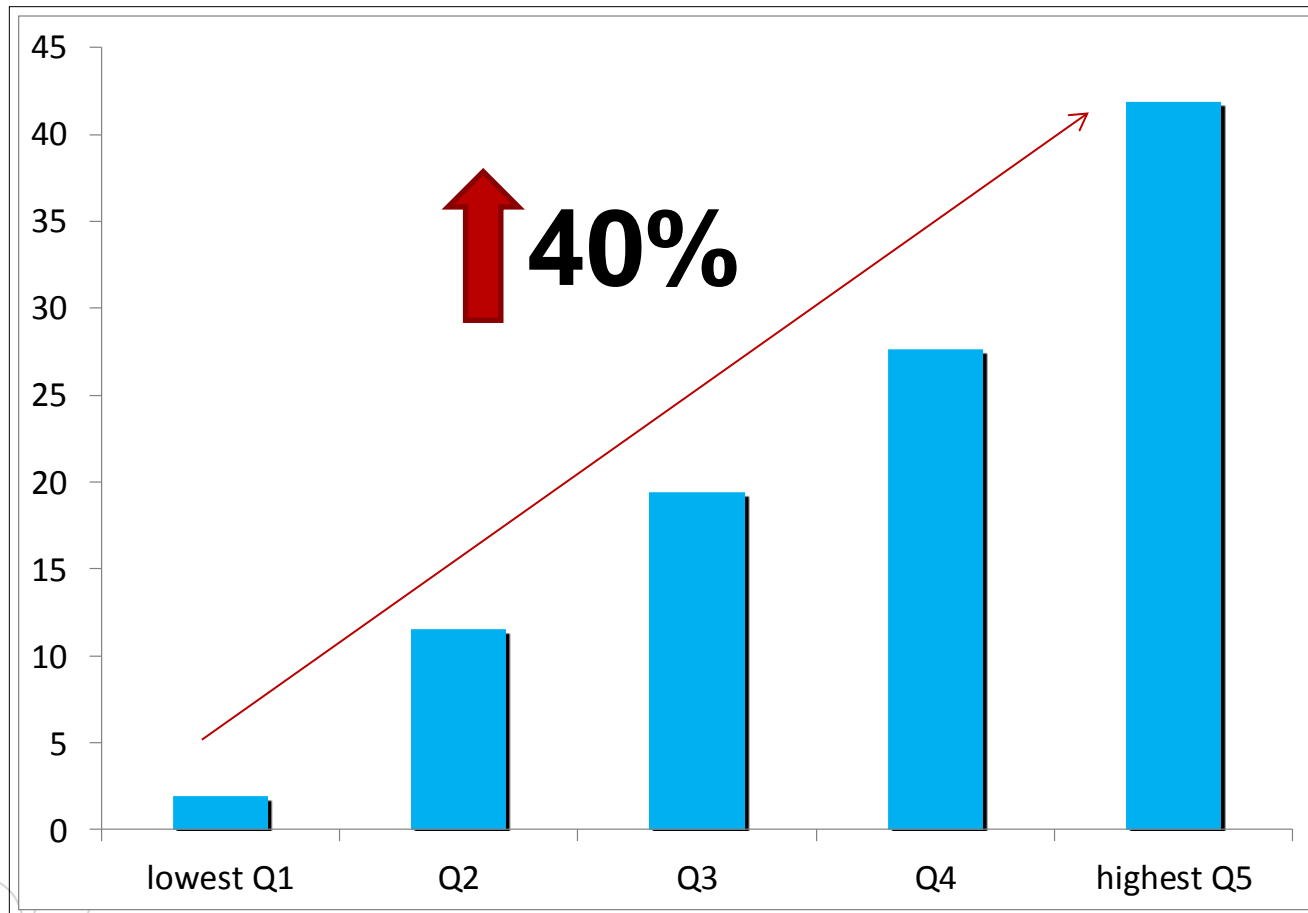


Sanchez-Villegas et al., *Public Health and Nutrition*, 2012



Risk of depression within 6.2 years in ~9000 people

Based on fast food (hamburgers, pizza)



Meta-analyses: Mediterranean Diet and CNS health

- Lai et al. Am J Clin Nutrition; 2014
 - 13 observational studies pooled for meta-analysis
 - The healthy diet pattern was associated with reduced odds of depression (OR: 0.84; 95% CI: 0.76, 0.92; $P < 0.001$).
 - high intakes of fruit, vegetables, fish, and whole grains may be associated with reduced risk for depression
- Psaltopoulou et al. Ann Neurol. 2013:580-91.
 - 22 studies pooled for meta-analysis (11 stroke, 9 depression, and 8 cognitive impairment)
 - High adherence to Mediterranean diet reduced risk for:
 - stroke (RR = 0.71, 95% [CI] = 0.57-0.89)
 - depression (RR = 0.68, 95% CI = 0.54-0.86)
 - cognitive impairment (RR = 0.60, 95% CI = 0.43-0.83)

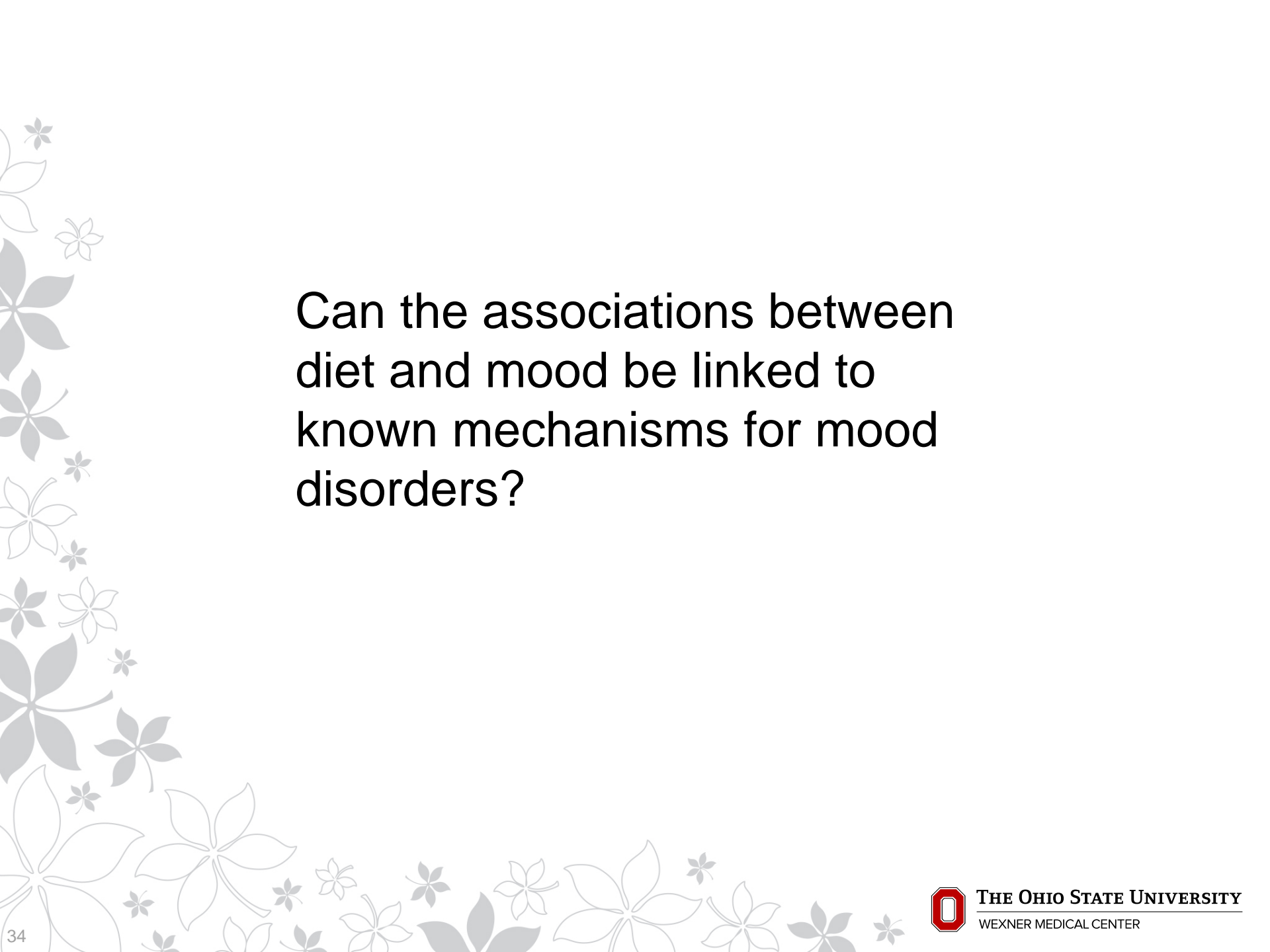


Population Health Studies:

>15 nutritional epidemiology studies from Australia, Spain, UK/EU, Japan, Canada

Conclusions:

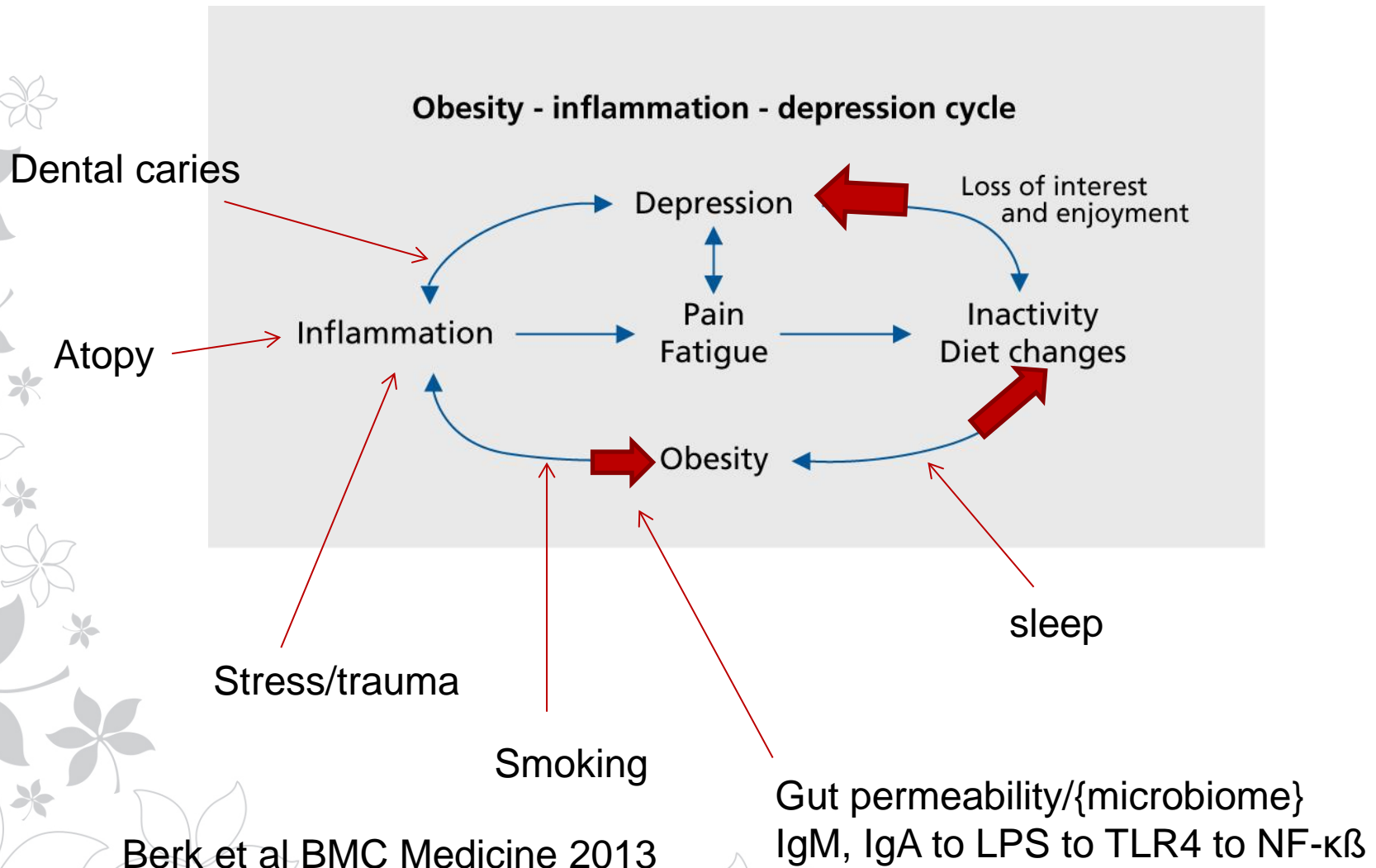
- People who eat ‘traditional’ ‘unprocessed’ ‘Mediterranean’ ‘prudent’ diets have ***lower rate of mood and anxiety symptoms***
- People who eat ‘Western’ ‘processed’ diets have ***higher rate of mood and anxiety symptoms***



Can the associations between diet and mood be linked to known mechanisms for mood disorders?



Depression is an inflammatory disease, but where does the inflammation come from?



Berk et al BMC Medicine 2013



Major diet patterns are linked to inflammation and endothelial dysfunction

In a cross-sectional study of 732 women from the Nurses' Health Study I cohort:

using FFQs and factor analysis, and adjusting for age, BMI, physical activity, smoking status, and alcohol consumption,

- A “prudent pattern” inversely associated with
 - CRP (P = 0.02),
 - E-selectin (P < 0.001),
 - sICAM-1 (P = 0.002) and sVCAM-1 (P = 0.02)

A “Western pattern” positively associated with

- CRP (P = 0.02),
- E-selectin (P < 0.001),
- sICAM-1 (P = 0.002) and sVCAM-1 (P = 0.02)

Lopez-Garcia et al. Am J Clin Nutr. 2004



Development of the Inflammatory Dietary Pattern

Dietary Inflammatory Index Development Study, Cancer Prevention and Control Program, U South Carolina

- defined a dietary pattern related to ↑ inflammation markers CRP, IL-6, TNF α -r2
- prospective analysis of this pattern with depression risk
 - Validated using the Nurses' Health Study:
 - 43,685 women aged 50-77 without depression at baseline (1996), followed until 2008, FFQs q2years.
 - After adjusting (BMI etc), RRs for extreme quintiles of the IDP were 1.41 (95% [CI], 1.22-1.63; P-trend<.001) for depression

“Chronic inflammation may underlie the association between diet and depression”

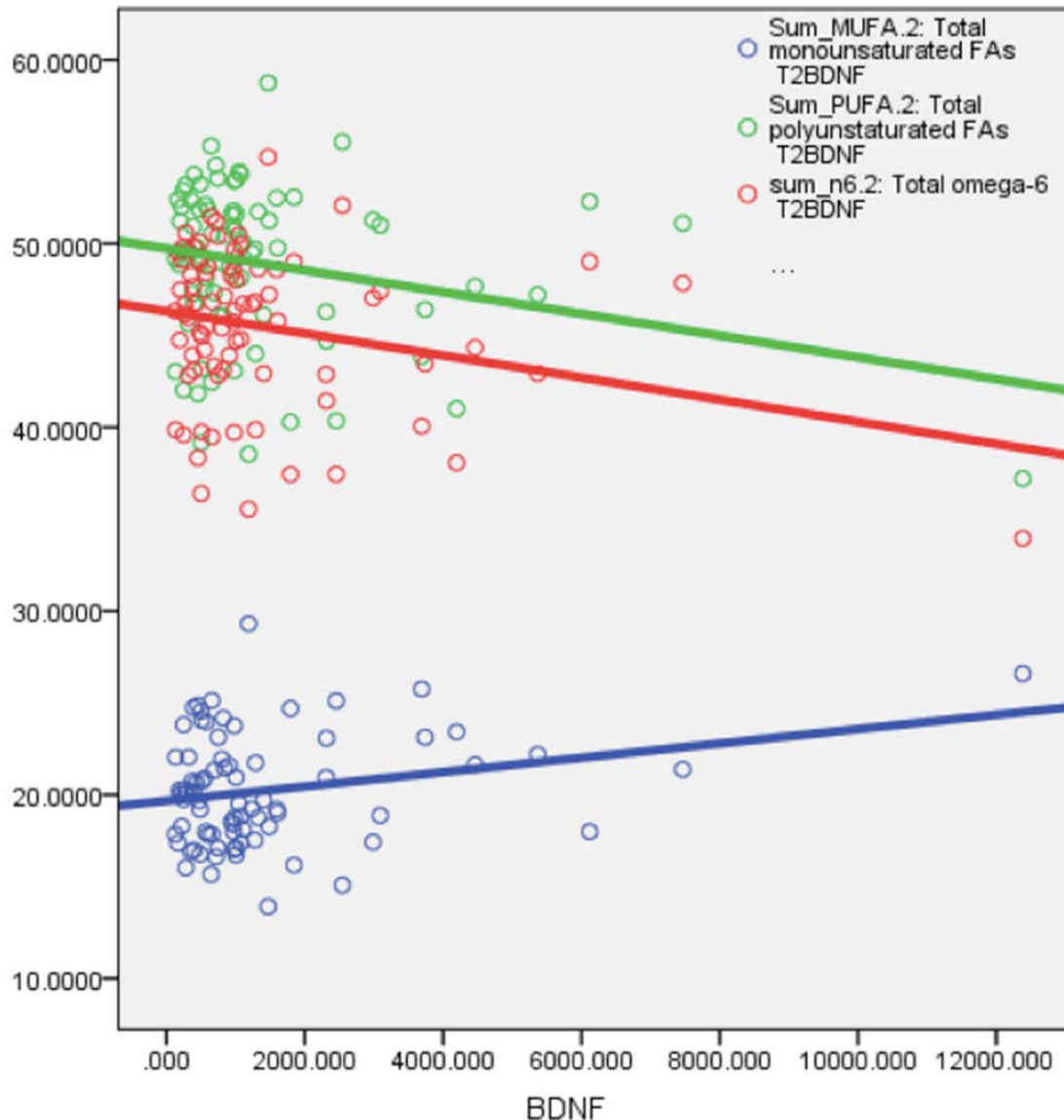
Shivappa N et al., Public Health Nutr. 2014 Aug;17(8):1689-96.

Lucas et al Brain Immun Behav 2014.



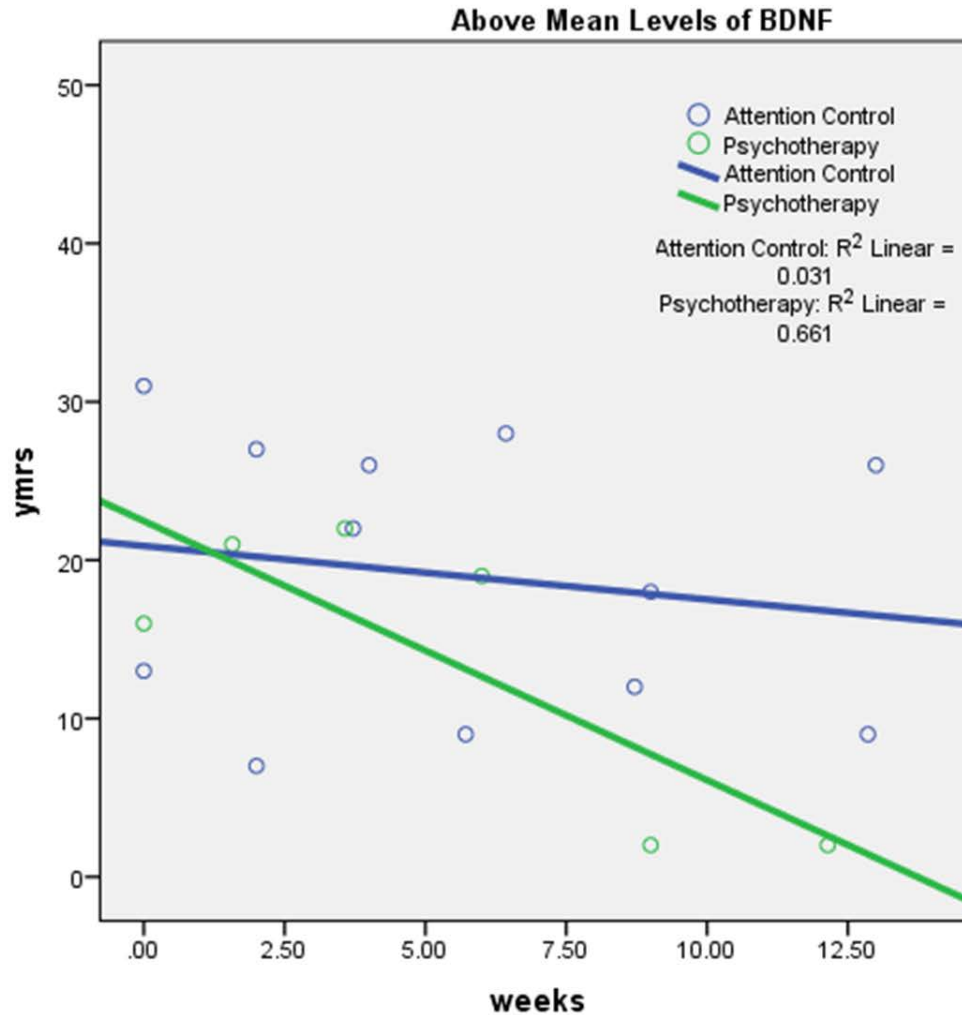
BDNF and dietary fats in the OATS studies- 2x2 RCTs for youth with mood disorders

BDNF & Fatty Acids



Serum BDNF correlates with serum monounsaturated fatty acids ($r=.240^*$), polyunsaturated fatty acids ($r= -.253^*$) and serum n6 ($r= -.264^*$)
* $p<.05$

Higher baseline BDNF predicts response to psychotherapy for improved manic symptoms



Is there any level “A” evidence documenting positive effects of diet change on mood symptoms?



Fruit and vegetable intervention for inflammation: proof of concept

Do different vegetable and fruit intakes modulate immunologic markers?

• In an RCT of nonsmoking men:

- consumed x 4 wks ≤ 2 servings veggies and fruit/day
- randomly assigned to 1 of 3 groups, 2 vs. 5 or 8 servings /day x 4 weeks, of carotenoid-rich vegetables and fruit
- plasma vitamins C and E and carotenoids, N and activity of natural killer cells, cytokines, lymphocyte proliferation, and plasma CRP concentrations measured

• CRP was lower at wk 8 in those eating 8 servings/day of vegetables and fruit vs. those eating 2 servings/day.



Watzl et al.
Am J Clin Nutr 2005

The SMILES TRIAL= 1st RCT of diet as adjunct tx

- Inclusion criteria:
 - Adults with MADRAS score > 18
 - Poor diet quality
 - Antidepressant dose stable x 2 weeks
- Randomized to social vs. dietary support
 - 7-60 minute sessions across 12 weeks
 - Focus on “Modern Mediterranean Diet”
- Results: 67 randomized; 56 completed
 - Outcome: MADRAS <10: 32% for diet vs. 8% controls
 - NNT 4.4; top 25% adherence associated w/ improvement
 - Legumes, fish, vegetable soup cost-effective
 - Gut health, BDNF, inflammatory biomarkers pending
- Jacka F, oral presentation July 2016, ISNPR; under review



Currently underway:

- The MoodFOOD prevention trial
 - 1000 adults 18 to 75 years at risk for MDD due to overweight/class I obesity and depressive symptoms
 - 2x2 factorial design, 4 European sites, randomized to:
 - Daily multi-nutrient supplements (O3FA, calcium, selenium, B11(folic acid) and D3) vs. placebo;
 - Food-related Behavioral Activation vs. control
 - 12-month intervention with outcome measures quarterly
 - Mediterranean diet-based
 - €11.4 million cost

<http://www.exeter.ac.uk/mooddisorders/research/currentprojects/moodfood/>

Roca et al. BMC Psychiatry 2016;16:192



Next frontiers for diet intervention studies in MH

- “Dysbiotic forces” and the evolutionary mismatch:
 - A call to return to our evolutionary lifestyle, including diet!!



Nutritional psychiatry research intersects with...

- Global urbanization
 - Decreased physical activity, ‘food deserts’, food waste
 - Screen-based media consumption
 - Compromised sleep
 - Excessive exposure to blue light, suppressing melatonin
 - Unhealthy diet changes
 - Food is now produced, transported, marketed and priced
 - Energy-dense sugar-fat-salt marketed in lower SES areas, already less walkable
 - Western diets dampening the stress response
 - Less steaming/boiling, more oxidative stress from AGEs, advanced glycation end-products
 - Acid-heavy diets may induce anxiety, risk for CVD/T2DM
 - Bicarbonate may help!
- Environmental - biodiversity loss raises chronic stress



So what to recommend, part 1 for diet:

- Minimize added sugar- beverages to start!
- A whole foods largely plant-based diet
- Eat the “colors of the rainbow”
- Eat with others, 3x/day
- Take a brief diet/lifestyle history-
 - Does the youth eat/drink dairy?
 - Do they get enough protein early in the day?
 - Any foods or food groups they refuse to eat?
 - Are they physically active regularly?
 - How much/what time screen time/day?
- Check for nutrient deficiencies (iron studies, B12, 25-OHD; consider Zn, Mg)
- Consider screening with hsCRP, LFTs, homocysteine



Tad and Nancy Jeffrey



At the end of the 19th century, a Columbus man capitalized on a natural resource and created a company that forever changed how coal was retrieved from the Earth.



Joseph A. Jeffrey was a deliberate and disciplined opportunist who was so enthralled with a mining machine in a city storefront in 1877 that he invested in the idea and established a legacy that continues today.

The Jeffrey Manufacturing Co. was a massive complex off North Fourth Street that sprawled over multiple acres and in its heyday employed between 4,000 and 5,000 people. The Jeffrey family retained control of the company for 97 years until 1974.

URMC Psychiatry & Clinical Translational Science Center

The KL2 Mentored Career Development program provides 2 years of support for new investigators interested in a career in clinical or translational research. The program is designed to support the career development of those who wish to pursue research careers in multidisciplinary clinical and translational science.



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