Tuesday, 1:00 – 2:30, B6

Mood and Food

Olga Hadden

Sarah Raiyn
Sarah.raiyn@med.wmich.edu

Objectives:

Identify effective methods for the practical application of concepts related to improving the delivery of services for persons with developmental disabilities

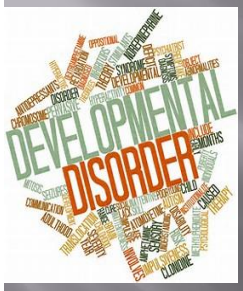
Notes:

MOOD AND FOOD

Olga Hadden, MD and Sarah Raiyn, MD

Outline

- Introduction
- Autism Spectrum Disorder
- ADHD
- Reward pathway and food
- Food addiction and mood
- Vitamin deficiencies



- **Developmental disorders (DD)** is a group of psychiatric conditions originating in childhood that involve serious impairment in different areas.
- Language disorders, learning disorders, motor disorders and ASD.
- ADHD is included as neurodevelopmental disorders.

Introduction

- Present from early life.
- Usually improve as the child grows older.
- However, entail impairments that continue through adult life.
- There is a strong genetic component.
- M>F.

Theories of DD

- 1. Genetic: Abnormalities pre-determined
  - about 1 : 300 children are born with spontaneous genetic mutations associated with rare developmental disorders.
- 2. Environment disrupts normal development (stress in early childhood)
  - DD caused by early childhood significant trauma. DD in traumatized children = PTSD in adults.
  - Even small stresses can accumulate to result in emotional, behavioral, or social disorders in children
- 3. combination of environmental and genetic factors.

Introduction: Why is this important?

- There is an epidemic of childhood obesity
- Prevalence of obesity in ages 2-19 years is 16.3%
- Prevalence of being overweight is 31.9%
- BMI for age or gender above the 95th percentile on CDC growth chart is considered obese
- BMI between the 85th and 94th percentile is considered overweight

- As this population ages, they have poor eating habits, limited food preparation skills, lack nutritional knowledge, and have low levels of physical activity
- More of those suffering from developmental disabilities have been transitioned from institutions to community-based living
  - Therefore, food skill programs must be developed and implemented for this population
- Teaching nutrition and food skills to this population, will allow them to be more independent as adults and provide them with knowledge, skills, and self confidence to make healthy meals

Individual level

- At the individual level, attitudes, knowledge, and skills can influence health behaviors
- It is important to address poor eating patterns, safety concerns, and low transferability of the skills
- It is found that those in this population often do not consume the recommended amount of fruit and vegetables and their nutrient intake tends to be high in saturated fat and simple carbohydrates
- Nutrition education and food skill programs must be developed
- Building self-efficacy is also very important

Interpersonal level

- Better training strategies for the support staff including general skill building and role playing, modeling, reinforcement, and corrective feedback being important
- Setting goals
- Social relationships are very important to establish

Organization level

- Addressing factors in the private, public, and non-profit sectors to which the individual belongs
- Staff training is very important
- There is found to be limited awareness of safe food handling practices and nutrition knowledge of the staff in the homes for this population
- Registered dieticians are strongly supported by literature

Community and public policy levels

- Personal support services
- Home-delivered meals
- Home health care
- Financial and legal assistance

How does this apply to those with Developmental Disabilities?

- There has been little research done in this field specifically geared toward children
- There is a disparity in health care between those suffering with developmental disability and the general population
- People with developmental disabilities appear to be equally and in some cases more affected by obesity

Why are individuals with DD mores susceptible to obesity?

- Highly sedentary
- Low levels of physical fitness
- Poor eating habits
- Fewer opportunities for teaching healthy habits and supporting them
- Family environment
- Media and marketing environment

Prevention and Treatment of Obesity in children with DD

- The following need to be addressed in order to help this epidemic:
  - The cognitive, behavioral, and physical factors that are linked with ID
  - The role of parents and other family members in teaching and reinforcing healthy habits
  - The environment we live in that makes it difficult to make healthy choices which creates challenges to independent living for young adults with ID

ASD: Definition

- ***DSM-5 definition of Autism Spectrum Disorder (ASD)-*** abnormalities in social communication and interaction, as well as the occurrence of repetitive, restricted patterns of behavior or activities.
- ASD represents a single continuum of impairments with a varying degree of severity.

ASD: Hypothesis

- Hypotheses:
  - genetic origin
    - mitochondrial dysfunction
    - parental age,
  - environmental agents (malleable, sometimes preventable):
    - exposure to environmental toxins in a fetal life and during the immediate neonatal period,
    - **nutritional deficiencies. Many of the ASD children are picky eaters, they exhibit sensitivities to foods, or have selective eating behaviors. Children with autism had more limited food repertoires, and this led to an inadequate intake of nutrients.**
    - MIA (Maternal Immune Activation theory)by infections during pregnancy,
    - Hormonal: fetal testosterone levels
  - interaction between genetic and environmental factors with oxidative stress as a potential mechanism linking the two
- Understanding these factors:
  - can address ASD prevalence
  - improve treatment opportunities

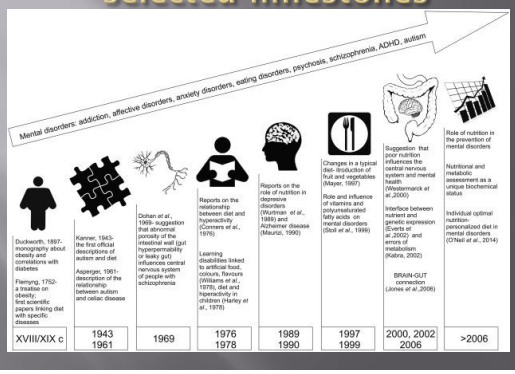
ASD: Nutrients on Mental DO

- Evidence demonstrates an interface between nutrients and:
- schizophrenia spectrum,
- depressive/anxiety disorders,
- eating disorders,
- neurocognitive disorders,
- neurodevelopmental disorders such as ASD and ADHD

ASD: History of impact of Nutrition

- The first strong evidence for the impact of nutrition on the occurrence and development of diseases was described at the turn of the 18th/19th centuries.
- It represents selected milestones in the field of knowledge connected with nutritional strategies and their influence on mental disorders.

selected milestones



ASD: NUTRITIONAL INTERVENTIONS

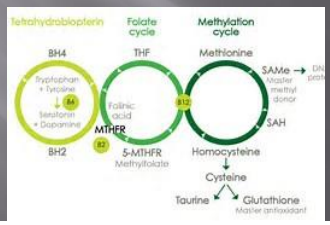
- can significantly help some ASD patients.
- probiotics,
- digestive enzymes,
- vitamins,
- minerals,
- amino acids,
- specialty supplements

ASD: VITAMINS

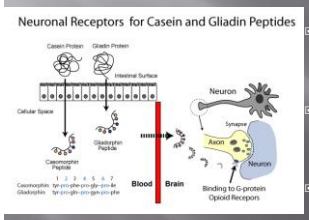
- The diet of autistic children is not balanced
- Nutritional deficits of ***folate, vitamin C, vitamins B1, B2, B6, and B12 and vitamin A.***
- Low in ***many minerals, essentials fatty acids, and amino acids***
- These deficiencies result in metabolic, digestive, immune and neurological problems (vision, speech, attention, and socialization weaknesses).
- Nutritional supplementation leads to behavioral and cognitive improvement.
- Children with ASD often suffer from **impaired methylation, decreased glutathione, and oxidative stress**
- Supplementation with ***vitamin methyl-B12, folinic acid, and trimethylglycine*** is beneficial.
- Supplementation with ***Magnesium and vitamin B6*** reduce symptoms of hyperexcitability, improve speech/communication, social interaction, and stereotype behavior.

ASD: AMINO ACIDS

- The levels of 14 organic acid compounds in ASD children are elevated.
- ***High Homocysteine (Hcy)*** level contributes to the neuronal damage, associated with aggression/irritability.
- Supplementation of vitamin B6, B12, and folate lowers the levels of Hcy in blood.
- ***Glutamate*** (associated with aggression/irritability) is increased and ***Glutamine*** is decreased in ASD children.
- Other amino acids which are increased in ASD children are:
  - ***taurine,***
  - ***lysine***
  - ***aspartic acid.***



ASD: GLUTEN AND CASEIN

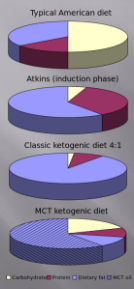


- Some ASD children suffer from deficiency of digestive enzymes transforming gluten and casein to amino acids.
- Increased gut permeability enables leaking gluten and casein into the blood stream, and passing the brain-blood barrier.
- In the brain they directly regulate signal transduction, causing disruption to the operation of the nervous system.
- In some patients elimination of gluten/casein from the diet results in disappearance of the symptoms of ASD.

ASD: KETOGENIC DIET

- The **ketogenic diet** is a high-fat, adequate-protein, low-carbohydrate diet.
- It forces the body to burn fats rather than carbohydrates.
- Normally, the carbohydrates are converted into glucose, which fuel brain functions.
- When carbohydrates are deficient, the liver converts fat into fatty acids and ketone bodies leading to ketosis.
- The ketone bodies pass into the brain and replace glucose as an energy source.

ASD: Ketogenic Diet



- KD contains a 4:1 ratio of Fat to Protein and Carbohydrates by excluding high-carbohydrate foods, while increasing high-fat food (nuts, cream and butter).
- Metabolic benefits of the KD are not solely due to increased fat.
- High-fat, sufficient-carbohydrate (i.e. non-ketogenic) diet worsens ASD core behaviors.
- Metabolic changes in blood within 2 days, behavioral effects at least 1 week.

ASD: KD- Key Mechanisms

1. improves mitochondrial function
- In the gestational valproic acid model, KD treatment normalized dysfunctions in mitochondrial respiration

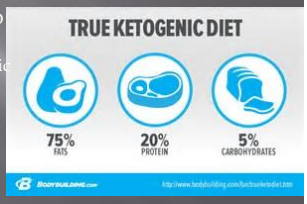
2. reduces inflammation
- Low dietary carbohydrate and limited protein forces nervous tissue to rely on ketone bodies for energy. Ketone bodies lower inflammation. KD has neuroprotective and disease-modifying effects. ***Ketone bodies: Acetoacetate, beta-hydroxybutyrate and acetone.***
- Reduces core ASD symptoms subsequent to MIA (Maternal Immune Activation). MIA- acute inflammatory event during the first 2 trimesters- a physiologic response to infection that increases the risk of persistent autistic behaviors in the offspring.
- MIA-induced inflammation triggers an increase of proinflammatory factors and activates immune cells bathing the fetus in proinflammatory compounds and antibodies and increasing the likelihood of the child developing ASD.

3. increases adenosine
- KD increases brain adenosine levels and signaling; it shows an inverse relationship between adenosine and symptoms of ASD.
- Abnormalities in purine metabolism are common, and a purinergic treatment is effective in alleviating symptoms.

4. anticonvulsant
- normalizes abnormal cerebrocortical excitation/inhibition.
- enhanced social novelty-induced neuronal activation in several brain areas–but did not normalize levels of monoamine neurotransmitters.
- ASD and epilepsy are similarly diverse and complicated

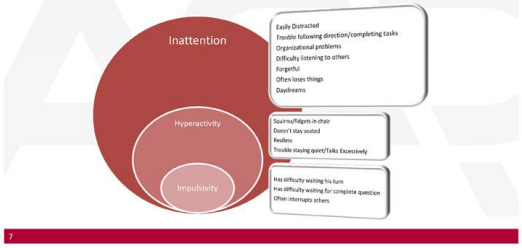
ASD: KETOGENIC DIET

- Improve:
  - ✓ core symptoms of ASD
  - ✓ symptoms of comorbidity of epileptic seizures
  - ✓ sociability
  - ✓ reduces self-directed repetitive behavior
  - ✓ normalizes play behavior in the gestational valproic acid model



Definition of ADHD

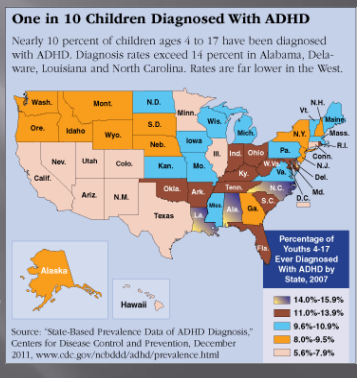
Attention deficit-hyperactivity disorder (*ADHD*) is a neurobehavioral disorder exhibited by difficulty in maintaining attention, as well as hyperactivity and impulsive behavior.



7

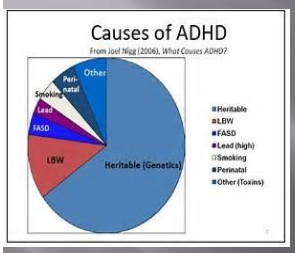
ADHD: PREVALENCE

- Worldwide 5.29% (based on 102 studies)
- Geographic differences only significant between North America and Africa, Middle East
- High solar intensity has preventive effect and explains variants in ADHD prevalence



Source: "State-Based Prevalence Data of ADHD Diagnosis," Centers for Disease Control and Prevention, December 2011, www.cdc.gov/ncbddd/adhd/prevalence.html

ADHD: CAUSES



- Combination of environmental and genetic factors.
- Neurobiology (some parts of the brain are smaller in children with ADHD)
- Genetics (ADHD tends to run in families)
- **Environmental factors: 20-30%,**
  - ✓ **can influence the severity of the disorder**
  - ✓ **modulate gene activation and deactivation (by epigenetic effect)**
  - ✓ low socioeconomic class,
  - ✓ foster placement
  - ✓ family dysfunction.
- Pregnancy-related factors:
  - ✓ low birth weight,
  - ✓ delivery complications,
  - ✓ prematurity,
  - ✓ dysmaturity,
  - ✓ prenatal alcohol and smoking exposure

ADHD: CAUSES (cont)

- A study conducted by researchers at South Hampton University in the UK and published in The Lancet in 2007 found a definitive link between children's ingestion of many commonly used ***artificial food colors***, the ***preservative sodium benzoate*** and hyperactivity.
- The British Government took actions to "Food manufacturers are being encouraged to voluntarily phase out the use of most artificial food colors by the end of 2009".
- However, in 2009 the EFSA in the UK re-evaluated the data and determined that "the available scientific evidence does not substantiate a link between the color additives and behavioral effects" for any of the dyes.
- The U.S. FDA did not make changes following the publication of the Southampton study, but following a citizen petition in 2008, the FDA reviewed the available evidence, and still made no changes.

ADHD: Artificial Food Colors(AFC)

META-ANALYSIS OF DOUBLE-BLIND PLACEBO-CONTROLLED TRIALS CONCLUDED THAT THERE IS EVIDENCE TO SUPPORT THE THEORY THAT AFC PROMOTE HYPERACTIVITY IN HYPERACTIVE CHILDREN.

•Population-based study with 277,3-year-old children was performed to evaluate the effect of **AFC and a benzoate** preservative on hyperactivity symptoms.

Children were divided into four groups:

The effect of FAd on hyperactivity was substantial and occurred independently of pre-existing hyperactivity or atopy.

Subgroup of children with ADHD noticeably improved on an AFC-free diet.

- 36 •children with hyperactivity and atopy
- 79 •without hyperactivity but with atopy
- 75 •with hyperactivity but without atopy
- 87 •without hyperactivity or atopy

ADHD: AFC

- **Food coloring**, or **color additive**, is any dye, pigment or substance that imparts color when it is added to food or drink.
- Color additives are used in foods for many reasons including:
- To make food more attractive, appealing, appetizing, and informative
- Allow consumers to identify products on sight, like candy flavors or medicine dosages
- 1882: German food regulations stipulated the exclusion of dangerous minerals such as arsenic, copper, chromium, lead, mercury and zinc, which were frequently used as ingredients in colorants.
- 1906: In the United States, the Pure Food and Drug Act reduced the permitted list of synthetic colors from 700 down to seven.
- The seven dyes initially approved were
- 1. Ponceau 3R (FD&C Red No. 1),
- 2. amaranth (FD&C Red No. 2),
- 3. erythrosine (FD&C Red No. 3),
- 4. indigo tine (FD&C Blue No. 2),
- 5. Light Green SF (FD&C Green No. 2),
- 6. Naphthol yellow 1(FD&C Yellow No.1)
- 7. Orange 1 (FD&C Orange No. 1).

ADHD: AFC

- Four main categories of **plant pigments** to color food
- 1. Carotenoids (E160, E161, E164),
- 2. chlorophyllin (E140, E141),
- 3. anthocyanins (E163),
- 4. betanin (E162)

- Other colorants or specialized derivatives of these core groups include:
- Annatto (E160b), a reddish-orange dye made from the seed of the achiote
- Caramel coloring (E150a-d), made from caramelized sugar
- Carmine (E120), a red dye derived from the cochineal insect, *Dactylopius coccus*
- Elderberry juice (E163)
- Lycopene (E160d)
- Paprika (E160c)
- Turmeric (E100)

- Currently permitted by FDA in food.
- **No. 1 –** Brilliant Blue FCF, E133 (blue shade)
- No. 2 – Indigotine, E132 (indigo shade)
- No. 3 – Fast Green FCF, E143 (turquoise shade)
- No. 4 – Erythrosine, E127 (pink shade, commonly used in glacé cherries)
- **No. 5–** Ilura Red AC, E129 (red shade)
- **No.** 6 Tartrazine– A, E102 (yellow shade
- **No.** 7 – Sunset Yellow FCF, E110 (orange shade)

ADHD Tx: FFA and AFC evidence-based data

- Meta-analytic review of 6 types of non-pharmacologic interventions:
  - dietary ("Few Food Diet", elimination of artificial food colors, and FFAs supplementation)
  - psychological (cognitive training, neurofeedback, and behavioral interventions)
- Statistically significant effect for supplementation with ***Omega3/Omega6 FFA*** and elimination of ***artificial food colorings*** (for food sensitive patients).

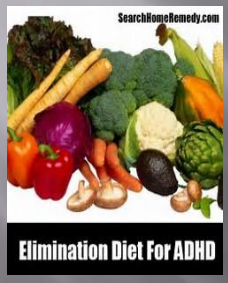
ADHD: RESTRICTED ELIMINATION DIET evidence-based data

- Researchers from the Netherlands put 50 children with ADHD on a "restricted elimination diet" which was tailored to the preferences of each child.
- Restricted Elimination Diet consists of foods with the least possible risk of allergic reaction – a combination of rice, meat, vegetables, pears and water.
- A second group of 50 children's parents were given advice on healthy eating and asked to keep a diary of everything their child ate.
- The behavior of 78% of the 41 children who completed the five-week restricted diet phase improved, while the behavior of those who were not on a special diet remained the same.
- The researchers concluded that dietary intervention should be considered in all children with ADHD if their parents are willing to follow a diagnostic restricted elimination diet for a 5-week period.

ADHD: ELIMINATION Diet and FISH Oil evidence-based data

- Systematic review of 52 studies: 20 with avoiding food elements and 32 with increase of food elements
- ***Elimination diets and supplementation with fish oil*** are the most promising dietary interventions in reducing ADHD symptoms.
- ADHD patients with subclinical **Zinc** deficiency may benefit from supplementation.

ADHD: ELIMINATION DIET



- 3 types:
- 1. **Artificial food colorants** and other additives (natural salicylates): K- P diet, Feingold diet: studied since 1970s, has the most pronounced effect in the youngest (preschool) children.
- 2. SUGAR and artificial sweeteners.
- 3. **"Few Foods Diet"-** specific food items eliminated, vary from child to child.
- Consists of:
  - 2 types of meat
  - 2 sources of carbohydrates
  - 2 vegetables
  - 2 fruits
  - oil
  - Water
- If symptoms improved in a few weeks- reintroduction of items in a controlled way.

ADHD: Few Food Diet and Fish Oil

- Few Food Diet and Fish Oil supplementation- most data show reduce in ADHD symptoms.
- ***Few Food Diet*** is only diagnostic tool, no longitudinal studies done yet.
- ***Fish Oil*** supplementation studies showed small to modest effect in reducing ADHD symptoms with minimal inconvenience and no major side effects.
- Some study showed improvement with ***Iron, Zink, Vitamin B6 and Magnesium*** supplementations.
- Increase intake of certain nutrients (children could be deficient in) ***certain AAs, essential FAs, vitamins and minerals***

ADHD/ASD: CONCLUSION

- Multimodal treatments work best and involve a combination of biological and non-biological including nutritional approaches.
- Large variety of foods and food components can provoke or exacerbate behavioral responses, though not every child responds to the same products in a similar manner.
- Nutritional approaches are efficacious, safe and low-cost therapy that works by modulating immune system activity, and improving comorbid conditions.

Reward pathway and food

- Food is a natural reward
- Food consumption leads to dopamine production
- This activates the reward and pleasure centers of the brain
- Which in turn leads to repetition of eating a particular food in order to experience this positive feeling of gratification
- This repetitive behavior of food intake activates the reward pathways of the brain that override the signals of satiety and hunger
- Overeating and obesity are the result of this

- Food can engage similar brain reward pathways as the drugs of abuse
- Can result from casual eating or compulsive eating that leads to eventual addiction
- In human and rodent studies, dysregulated brain reward pathways may contribute to increased intake of palatable foods leading to obesity
- Overall increase in tasty and energy-rich foods that is independent of stress-induced hyperphagia or hypophagia
- Food cravings are also present

Regulation of mood, food, and obesity

- Mood: characterized by physiological arousal in the absence of a stimulus
- Emotions: short-term affective responses to a reinforcing stimuli
- Anger and joy are shown to have the strongest influence on appetite and food choice

Five way model predicting different aspects of emotional eating

- Food choice
- Food intake
- Loss of cognitive controls
- Food modulating emotions
- Emotion-congruent modulating eating

- Depending on the state of negative emotions or distress, emotional eating is triggered by food intake either increasing or decreasing

Stress and food intake

- Stress can effect feeding behavior
- In some people, there will be increased intake and in others intake will be decreased
  - This depends on the type of external or physiological stressors
- Chronic stress can lead to increased consumption of palatable and rewarding food that leads to obesity OR a diminished appetite which leads to weight loss

Mood and food intake

- Anxiety and depression often lead to increased consumption of food leading to overeating and obesity
- People suffering from depression, usually show preference to "comfort foods" that help alleviate their negative feelings
- Short term, there is some relief
- However long term, can lead to consumption of calorically rich foods ultimately leading to obesity which in turn promotes vulnerability to depression and anxiety

- Findings show that prolonged high-fat foods leads to negative emotional states, increased stress sensitivity, and altered basal corticosterone levels
- Altered serum cortisol level, HPA axis, and food intake have been associated with depression
- Glucocorticoids regulate reward and emotional processes through their receptors in the midbrain and limbic circuits

Vitamins

- Vitamin B12
- Folic acid
- Vitamin D
- Thiamine
- Niacin
- Calcium

Vitamin B12

- Cobalamin
- Water soluble vitamin
- Key role in the brain and nervous system
- Affects DNA synthesis, fatty acid/amino acid metabolism, formation of red blood cells
- Essential nutrient that cannot be produced in the body
- Found in: meat, fish, dairy products

Vitamin B12 Deficiency

- Can cause severe and irreversible damage to the brain and nervous system
- Symptoms include: Fatigue, lethargy, depression, poor memory, headaches, cognitive impairment, weakness, peripheral neuropathy
- This damage can be more severe in elderly due to less ability to absorb
  - Can even lead to symptoms of mania and psychosis
- Other clinical manifestations: hyperpigmentation, vitiligo, jaundice, anemia, thrombocytopenia

Psychiatric symptoms of Vitamin B12 deficiency

- Psychosis
- Depression
- Mania
- Cognitive impairment
- Delirium

Folic acid

- One of the B vitamins
- Essential to the body in order to make DNA, RNA, and for amino acid metabolism
- Required for the synthesis of SAMe (S-Adenosyl Methionine) which is needed for the synthesis of key neurotransmitters required in mood regulation
- Not produced by humans
- Found in: Dark green leafy vegetables, fruits, beans, nuts, dairy products, avocadoes, liver, spinach
- Recommended daily intake: 400 micrograms
- Signs and symptoms of deficiency manifest after 4 months

Folate deficiency

- Very common in excessive alcohol use and pregnancy
- Pregnant women are recommended to increase their daily intake of folate due to the risk of neural tube defects
- Clinical manifestations: megaloblastic anemia, glossitis, nausea and vomiting, diarrhea, thrombocytopenia, angular stomatitis

Psychiatric symptoms of Folate deficiency

- Depression
- Cognitive decline
  - Impairment in attention, visual spatial memory, abstract reasoning

Thiamine

- Vitamin B1
- Essential nutrient
- Found in food and used as a dietary supplement
- Needed for the metabolism of carbohydrates
- Found in: whole grains, meat, and fish

Thiamine Deficiency

- Beriberi, Wernicke-Korsakoff syndrome, optic neuropathy
- Symptoms early in the disease:
  - Fatigue
  - Irritability
  - Poor memory
  - Sleep disturbances
  - Chest pain
  - Anorexia
  - Abdominal pain
  - Constipation

Psychiatric symptoms of Thiamine deficiency

- Peripheral neuropathy
- Pain
- Paresthesias
- Degeneration of the myelin
- Wernicke's Encephalopathy:
  - Triad = Opthalmoplegia, Ataxia, and Confusion

Vitamin D

- Fat soluble
- Responsible for maintaining normal blood levels of calcium and phosphorus
  - Helps the body absorb calcium to maintain strong bones
- Most important form in humans:
  - Vitamin D3 = Cholecalciferol
  - Vitamin D2 = Ergocalciferol
- Sources of Vitamin D: sunlight, fish, eggs, fortified milk
  - Even just 10 minutes of sun exposure a day helps!

Risk factors associated with Vitamin D deficiency

- Age > 65
- Insufficient sunlight
- Breastfeeding
- Dark skin
- Malabsorption diseases
- Obesity
- Use of certain medications that alter vitamin D metabolism (anticonvulsants and glucocorticoids)
- Hepatobiliary disease
- Renal disease

Vitamin D Deficiency

- Rickets
  - Childhood disease
  - Soft, weak, deformed long bones
  - Found in lower income countries
- Osteomalacia
  - Adult disease
  - Softening of the bones that leads to bending of the spine, bow legs, proximal muscle weakness, bone fragility
  - Increased risk of fractures

How does Vitamin D effect the brain?

- Region specific expression of Vitamin D receptors in the cingulate cortex, thalamus, cerebellum, amygdala, and hippocampus
- Vitamin D regulates the expression of tyrosine hydroxylase which is the rate limiting enzyme in the synthesis of dopamine, norepinephrine, and epinephrine
- Vitamin D has an important role in the CNS

Psychiatric symptoms of Vitamin D deficiency

- Depression
- Seasonal Affective Disorder
- Psychosis
  - Increased risk of psychotic symptoms and schizophrenia
- Cognitive dysfunction
  - Memory and orientation impacted

Niacin

- Vitamin B3 or Nicotinic Acid
- Essential nutrient
- Precursor of nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP)
  - NAD is important for catabolism of fat, carbohydrates, protein, and alcohol
  - NAD also helps with cell signaling and DNA repair
  - NADP is important for fatty acid and cholesterol synthesis
- Found in a variety of whole and processed foods

Niacin Deficiency

- Pellagra
  - 4 D's = Dermatitis, Diarrhea, Dementia, and Death
- Psychiatric symptoms:
  - Anxiety
  - Depression
  - Irritability
  - Poor concentration
  - Fatigue
  - Restlessness

Calcium

- Essential element
- Important component of bone and teeth
- Calcium carbonate and Calcium citrate are the forms of dietary supplementation
- Found in: dairy products (milk and cheese), seaweeds, nuts and seeds (almonds, pistachios, hazelnut), soy beans, figs, quinoa, orange juice

Hypocalcemia

- Low level of plasma calcium concentration below 8.8 mg/dL
- Common causes: hypoparathyroidism and vitamin D deficiency
  - Other causes include kidney failure, pancreatitis, rhabdomyolysis
- Treatment: supplementation

Signs and symptoms of Hypocalcemia

- Confusion
- Seizures
- Petechiae
- Tetany
- Weakness
- Hyperactive reflexes
- Laryngospasms
- Cardiac arrhythmias → prolonged Q-t interval
  - EKG

Psychiatric symptoms seen in Hypocalcemia

- Confusion
- Behavioral changes
- Psychosis
- Depression
- Irritability

Hypercalcemia

- High levels of serum calcium measured to be greater than 10.4 mg/dL
- Commonly caused by hyperparathyroidism and as a result of excessive bone resorption
  - Medications such as Lithium and Hydrochlorothiazide can also increase calcium levels
- Treatment: IV fluids, furosemide, bisphosphonates and calcitonin, and treating the underlying cause

Signs and symptoms of Hypercalcemia

- Abdominal pain
- Bone pain
- Nausea/vomiting
- Kidney stones
- Anemia
- Confusion
- Weakness
- Pruritus
- Cardiac arrhythmia → shortened Q-t interval
  - EKG

Psychiatric symptoms seen in Hypercalcemia

- Depression
- Anxiety
- Cognitive deficits
- Memory issues
- Insomnia

References

- Singh, Minati. "Mood, Food, and Obesity." *Frontiers in Psychology* 5 (2014): n. pag. Web.
- Zepf, Florian Daniel, Sean Hood, and Gilles J. Guillemin. "Food and Your Mood: Nutritional Psychiatry." *The Lancet Psychiatry* 2.7 (2015): n. pag. Web.
- Stewart, Patricia A., Susan L. Hyman, Brianne L. Schmidt, Eric A. Macklin, Ann Reynolds, Cynthia R. Johnson, S. Jill James, and Patricia Manning-Courtney. "Dietary Supplementation in Children with Autism Spectrum Disorders: Common, Insufficient, and Excessive." *Journal of the Academy of Nutrition and Dietetics* 115.8 (2015): 1237-248. Web.
- Strasser, Barbara, Johanna M. Gostner, and Dietmar Fuchs. "Mood, Food, and Cognition." *Current Opinion in Clinical Nutrition and Metabolic Care* 19.1 (2016): 55-61. Web.
- Johnson, Chwen, Sandra Hobson, Alicia C. Garcia, and June Matthews. "Nutrition and Food Skills Education: For Adults with Developmental Disabilities." *Canadian Journal of Dietetic Practice and Research* 72.1 (2011): 7-13. Web.
- Fleming, Richard K., Elise A. Stokes, Carol Curtin, Linda G. Bandini, James Gleason, Renee Scampini, Melissa C. T. Maslin, and Charles Hamad. "Behavioral Health in Developmental Disabilities: A Comprehensive Program of Nutrition, Exercise, and Weight Reduction." *International Journal of Behavioral Consultation and Therapy* 4.3 (2008): 287-96. Web.
- Jacquelyn H. Flaskerud RN, PhD, FAAN (2015) Mood and Food, Issues in Mental Health Nursing, 36:4, 307-310, DOI: 10.3109/01612840.2014.962677
- Benton, David. "Vitamins and Neural and Cognitive Developmental Outcomes in Children." *Proceedings of the Nutrition Society* 71.01 (2011): 14-26. Web.
- Fafouti, Mata, Thomas Paparrigopoulos, John Liappas, Vassilis Mantouvalos, Rika Typaldou, and George Christodoulou. "Mood Disorder with Mixed Features Due to Vitamin B12 and Folate Deficiency." *General Hospital Psychiatry* 24.2 (2002): 106-09. Web.

1. **Diet in the treatment of ADHD in children - a systematic review of the literature.**
   Nord J Psychiatry. 2015;69(1):1-18 (ISSN: 1502-4725)
   Heiskov Rytter MJ, Andersen LB, Houmann T, Bilenberg N, Hvolby A, Mølgaard C, Michaelsen KF, Lauritzen L.
2. Nutrition, immunological mechanisms and dietary modulation in ADHD Eur Child and adolescent Psychiatry, 2014
3. Schab DW, Trinh NT (2004) Do artificial food colors promote hyperactivity in children with hyperactive syndromes? A meta-analysis of double-blind placebo-controlled trials. J Dev Behav Pediatr 25:423–434
   1. ^ *"Deciphering Developmental Disorders (DDD) Projects"*. *www.ddduk.org*. *Wellcome Trust Sanger Institute*. Retrieved 2017-01-27.
   ^ *McRae, Jeremy F.; Clayton, Stephen; Fitzgerald, Tomas W.; Kaplanis, Joanna; Prigmore, Elena; Rajan, Diana; Sifrim, Alejandro; Aitken, Stuart; Akawi, Nadia. "Prevalence and architecture of de novo mutations in developmental disorders"*. *Nature*. *doi:10.1038/nature21062*.
   ^ *Ghosh, Pallab (2017-01-25). "Child gene study identifies new developmental disorders"*. *BBC News*. Retrieved 2017-01-27.
   3. Front Mol Neurosci. 2017; 10: 34.
   Published online 2017 Feb 21. doi: 10.3389/fnmol.2017.00034
   PMCID: PMC5318388
   Metabolic Dysfunction Underlying Autism Spectrum Disorder and Potential Treatment Approaches
   Ning Cheng,[1] Jong M. Rho,[1,2,3] and Susan A. Masino[1]
   4. Trends in Food Science & Technology
   Volume 49, March 2016, Pages 45–50

   Viewpoint
   Nutritional strategies and personalized diet in autism-choice or necessity?
   Joanna Kałużna-Czaplińska*, Izabela Jóźwik-Pruska
   Institute of General and Ecological Chemistry, Department of Chemistry, Technical University of Lodz, 116 Żeromskiego Str., 90-924 Lodz, Poland
   Received 20 February 2015, Revised 9 November 2015, Accepted 4 January 2016, Available online 6 January 2016
   Show more Show less http://dx.doi.org.ezproxy.med.wmich.edu/10.1016/j.tifs.2016.01.002