Diet and Behaviour
Myth or Science?

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Hyperactivity Attention Deficit Disorder (ADHD)

- The current term for behavioural disorder in children
- Food as an etiological factor in behavioural disorders has been considered for decades
- Lack of agreement as to the disorder that is being studied when the role of food is being considered
Hyperactivity Attention Deficit Disorder (ADHD)

- Early studies regarded behavioural disorders as due to brain damage ("minimal brain damage" (MBD)) and foods were not implicated in the etiology of this condition.

- Confusion as to which aspects of behavioural disorder were due to neurological and which to environmental factors.
Hyperkinetic Reaction of Childhood

- Hyperkinesis recognized in the DSM-II in 1968
- Hyperactivity considered to be due to neurological dysfunction
- Also determined to occur without any evident pathology
- More than 90 different terms used to describe hyperactive children
- Neurological impairment demonstrated in less than 5 percent of hyperactive children
Current Designations of ADHD

Several subcategories of ADHD are now recognized, for example:

- ADHD alone
- ADHD with oppositional defiant disorder
- ADHD with conduct disorder
- ADHD with thought/mood disturbance
- ADD without hyperactivity
- Learning disability without ADHD
There is no consensus that these are scientifically divisible conditions on a physiological basis.

Physiological responses are important when investigating the effect of diet on behaviour.
Environmental Factors in ADHD

- Environmental factors were considered in opposition to the use of stimulant drugs
  - Claims that hyperactivity was a perception created by intolerant teachers and parents
- The hypothesis of neurological deficit as a cause was opposed by some authorities
- The idea that diet may play a role in hyperactivity became very popular in the 1970s with the trend towards healthy lifestyle and "natural foods"
Environmental Factors In ADHD

- Dietary components as a cause of aberrant behaviour had been suggested since the 1920s
- Reactions to wheat and corn as a cause of fatigue, irritability and behaviour problems advanced by Randolph in 1940s
Suggested Dietary Factors Affecting Behaviour

- Pharmacologically active chemicals
- Allergens: release inflammatory mediators that affect the central nervous system
- Nutritional deficiency
- Stress or food phobia may trigger neuropeptides that lead to the release of inflammatory mediators
Hyperactivity and Diet

- Benjamin Feingold hypothesised that hyperactivity is caused by a toxic reaction to food dyes, artificial flavours and natural salicylates
- Claimed that 70% of hyperactive children improved when these eliminated from the diet
- Became a popular concept with parents
Hyperactivity and Diet

- Several scientific studies refuted this claim.
- The idea that food components can cause hyperactivity then fell into disrepute in medical circles.
- However, all the studies indicated that a SMALL NUMBER OF CHILDREN DID IMPROVE ON A RESTRICTED DIET.
Hyperactivity and Allergy

- Great Ormond Street Children's Hospital trials:
  - "Few foods diets" designed to investigate the role of food components in childhood migraine resulted in improvement in behaviour
  - The same diets were then used in studies on hyperkinesis
Hyperactivity and Allergy

- Double-blind placebo-controlled cross-over food challenge indicated that:
  - certain foods
  - food additives
  - natural chemicals in foods
- Caused deterioration in behaviour in a significant percentage of atopic children
Foods Implicated in the London Study

- Forty six foods including:
  - Milk and dairy products
  - Eggs
  - Wheat and other grains
  - Fruits
  - Nuts
  - Seeds
  - Soya
  - Meats
  - Fish
Foods Implicated in the London Study

Food additives:
• Food dyes, especially tartrazine
• Artificial flavours, especially glutamates
• Preservatives, especially benzoates and nitrates
Details of the Study

- Characteristics of the subjects:
  - "Overactivity" with somatic complaints:
    - Migraine
    - Seizures
    - Abdominal pain
  - Headaches improved in 93% of children with severe and frequent migraine
Study Outcomes

- Patients with epilepsy who also suffer from migraine and/or hyperkinetic syndrome respond to dietary treatment:
  - Of 45 epilepsy subjects, 25 recovered and 11 improved

- Hyperkinetic subjects' behaviour:
  - 82% improved on diet
  - 27 of 76 (35%) recovered completely
Study Details (Continued)

- On challenge, foods provoked symptoms after a time lapse of a few minutes to 7 days
- The average time interval was 2-3 days after eating the test food
Study Details (Continued)

- Evaluation of behaviour included:
  - Connor's rating scale
  - Independent assessment by psychiatrists and psychologists
  - Parents' observations

- Question: Did the children's behaviour improve as a result of feeling better when the physical complaints responded to diet?
Composition of the Few Foods Diet

- **Meats**: Lamb and chicken
- **Carbohydrates**: Rice and potato
- **Fruits**: Banana and pear
- **Vegetables**: Cabbage, Brussels sprouts, cauliflower, broccoli, cucumber, celery, carrot
- **Water**
- **Supplementary nutrients**: Calcium; magnesium; zinc; multivitamin
- **Duration of diet**: Four weeks
50% of 24 preschool aged (3 to 5 years) hyperactive boys improved on diet.
All foods were provided for 10 weeks for every member of the subject's household.
Nutritional deficiencies thereby controlled.
Alberta Children's Hospital Studies

- Diet eliminated:
  - Artificial colours
  - Artificial flavours
  - Monosodium glutamate (MSG)
  - Preservatives
  - Caffeine
  - Chocolate
  - Specific foods which caused an adverse reaction in individual children based on previous testing

- Restricted simple sugars
Details of Study

- Subjects selected on the basis of diagnosed hyperactivity (DSM-III)
- A few had atopic symptoms, and most came from a family with a history of allergy and intolerances
- Other symptoms improved such as:
  - Halitosis
  - Night awakening
  - Inability to fall asleep
Experimental Design Problems

- Lack of clear diagnostic criteria for the various subcategories of behavioural disorders
- Lack of diagnostic tests for food allergy and intolerance
Experimental Design Problems (continued)

- Difficulty in determining whether changes in behaviour are due to response to physical symptoms
- Difficulty in controlling the contribution of environmental factors, such as increased parental attention
- Difficulty in controlling the placebo effect
Sugar Regulation and Behaviour

"Reactive hypoglycaemia" or “Functional hypoglycaemia" (FH) blamed for a variety of behavioural problems such as:

- Irritability
- Fatigue
- Schizophrenia
- Neurosis
- Alcoholism
- Drug addiction
- Juvenile delinquency
- Anxiety
- Childhood hyperkinesis
- Lethargy
- Depression
- Suspiciousness
- Bizarre thoughts
- Hallucinations
- Mania
- Violent behaviour
Sugar and Behaviour

- No controlled studies show low blood sugar levels and impaired insulin response in conditions other than diabetes
- A small number of people shown to respond with aberrant behaviour after sugar challenge
- May be mediated by mechanisms other than impaired insulin regulation
Preliminary studies on >1,000 subjects indicate that simple sugars may be metabolized to alcohol by unusual microbial colonization of the intestine (Davies 1994)

Catecholamine control of sugar regulation may be impaired in ADHD
Connors' study (1986):
39 ADHD children challenged with sugar after a breakfast condition:
- Fasting
- Protein
- Carbohydrate

Performed worse after carbohydrate compared to fasting or protein breakfast
Catecholamines and Sugar (continued)

- Behaviour better when sucrose given after a protein breakfast, compared to behaviour after a carbohydrate breakfast
- Normal controls showed no change in behaviour in any testing modality
- Insulin levels not affected
- Cortisol and growth hormone secretion suppressed in normals, but not in ADHD children after a carbohydrate meal
Individual differences exhibited between habitual consumers and those who rarely ingest caffeine

Response to 300 mg caffeine challenge:

Regular caffeine drinkers:
  • Increased alertness
  • Decreased irritability

Non-caffeine consumers:
  • Upset stomach
  • Jitteriness
Caffeine and Behaviour

- Insomnia is a common side effect in both groups
- Methylxanthines act as competitive antagonists for adenosine receptors

- Adenosine mediates the activities of hormones such as:
  - catecholamines
  - histamine
  - glucagon
  - calcitonin
  - secretin
  - TSH
  - ACTH
  - ADH
  - LH
  - FSH
  - PTH
  - TRH
Adenosine Effects

- **ACTH**: adrenocorticotropic hormone
- **ADH**: anti-diuretic hormone (also known as **ADH**)
- **LH**: luteinizing hormone
- **FSH**: follicle-stimulating hormone
- **PTH**: parathyroid hormone
- **TSH**: thyroid stimulating hormone
- **TRH**: TSH releasing hormone
Effects of Caffeine on Children's Behaviour

- Caffeine detectable in umbilical cord blood and breast milk
- Rate of caffeine elimination from the body is much slower in infants than in adults
- Caffeine effects likely to last longer in children
Cola drinks may affect children in several ways:

- Direct pharmacological effect of caffeine
- Excessive sugar may affect behaviour
- Nutritional deficiency as a result of excessive intake of low-nutrient drinks
- Reaction to artificial colours, flavours, preservatives
Theories of Dietary Effects on Brain Function

- Amino acid-derived neurotransmitter levels in the brain are affected by dietary precursors:
  - serotonin (tryptophan)
  - histamine (histidine)
  - tyramine (tyrosine)

- Enzyme defects, such as phenolsulphotransferase in blood platelets may cause migraine and behaviour changes
Theories of Dietary Effects on Brain Function

- Opiate-like peptides in milk and wheat might lead to food cravings, addiction and withdrawal symptoms.
- Opiates may induce mast cell degranulation and release biogenic amines that affect brain function.
- Decreased activity of the cytochrome P-450 complex may lead to abnormal metabolism.
Nutrient Deficiency

- **Theory**
  - Elimination of foods high in sugar, artificial colours, flavours, preservatives removes a lot of "junk foods" from the diet
  - Diet becomes more nutritionally complete
  - Aberrant behaviour is the result of nutritional deficiency, especially of micronutrients such as vitamins and minerals
Micronutrient Deficiency and Behaviour

- **Iron deficiency anaemia:**
  - Restlessness, irritability, disruptive behaviour, learning disability

- **Low thiamine levels:**
  - Poor impulse control, irritability, hostility, sleep disturbances, restlessness, night terrors, insomnia, sleep-walking, fatigue, depression, headache, abdominal pain, chest pain
Micronutrient Deficiency and Behaviour

- **Zinc deficiency:**
  - Moodiness, depression, hyperactivity, irritability, photophobia, antagonism, temper tantrums, learning problems

- **Magnesium deficiency:**
  - Excessive fidgeting, restlessness, psychomotor disturbances, learning difficulties
Micronutrient imbalance

- Excessive amounts of micronutrients may also affect behaviour:
- Lead and other heavy metal toxicity
- Excessive copper may impair zinc absorption
- Excessive carbohydrate may lead to high cadmium levels: thought to impair academic performance
Movement Disorders Caused by Reactions to Foods  {Gerrard et al 1994}

- Shaking head and Headache
  - Beef
  - Pork
  - Milk
  - Potato
  - Coffee
  - Tea
  - Chocolate
  - Citrus fruit
  - Raspberry
  - Strawberry
Movement Disorders Caused by Reactions to Foods  {Gerrard et al 1994}

- Shoulder shrugging ; Hoarseness
  - Egg
  - Coffee
- Contraction of arms and legs
  Tachycardia
  Chest pains
  Indigestion
- Aspartame
Study Details

- Foods identified by elimination and placebo-controlled double blind challenge
- Allergy skin tests all negative, indicating the reactions were probably not caused by IgE-mediated Type I hypersensitivity
- Accompanying physical symptoms also cleared when foods were eliminated
- Conclusion: movement disorders triggered by an action on dopamine and other neurotransmitter pathways in the brain
Immune System and CNS Interactions

- In disease, dysregulation in one system can result in effects in the other.
- Such interaction has been demonstrated in allergy.
- The key event in allergy is release of inflammatory mediators from mast cells.
- Activation of mast cells can occur in response to a variety of triggers.
Mast Cell Activators

- Allergen-specific IgE is the major mast cell activating factor in classical allergy (Type I hypersensitivity)

- Other antibody classes (IgM; IgG) in response to specific antigen activate mast cells via the anaphylatoxins produced in the complement cascade
Mast Cell Activators (continued)

- Food components can activate mast cells in the absence of antibody (sulphites; lectins)
- Neuropeptides (e.g. vasoactive intestinal peptide (VIP); Substance P) can stimulate mast cell release of histamine, leukotrienes and other mediators of allergy
Pavlovian Conditioned Release of Inflammatory Mediators

- Release of inflammatory mediators from mast cells shown in animal experiments:
  • Rats sensitized to egg albumin and conditioned to a audio-visual stimulus released Mast Cell Protease II in response to the a-v stimulus alone
  • Guinea pigs sensitized to bovine serum albumin and conditioned to an olfactory stimulus released histamine in response to the odour alone

- **Question**: Can a similar conditioned response occur in humans?
Anecdotal Reports of Conditioned Response In Humans

- From the Allergy Nutrition Clinic, Vancouver

- Case 1: 22 year old male: previous anaphylactic reactions to peanut

- Experienced severe urticaria starting on the face and spreading to whole body within 15 minutes of standing next to a child spreading peanut butter on a cracker
Anecdotal Reports of Conditioned Response
In Humans

- **Case 2**: 21 year old male: previous anaphylactic reactions to peanuts and nuts
  - Experienced symptoms of severe anaphylactic reaction on several occasions when told by his friends that he had consumed nuts as an ingredient in a meal
  - No nuts were present.
Case 3: Kindergarten-aged child strongly skin test positive to peanut

"Became ill; experienced breathing difficulty" after observing another child eating a peanut butter sandwich on the other side of a classroom
Alternative Explanations for Responses

- Inhalation of volatilized peanut antigen
  (Case 1: Case 3)
- Anxiety attack mimics symptoms of anaphylactic reaction
  (Case 2; Case 3)
- Food phobia and stress response activates mediator release via neuropeptides
  (Case 3)
Alternative Explanations for Responses

- Mediator release is the key event in clinical expression of allergy symptoms, whatever the initial triggering mechanism may be.

- **Dilemma:** If a sensory signal is responsible for mediator release, double-blind food challenges would be invalidated because of the absence of the sensory signal.
Current Thinking on the Link Between Diet and Behaviour

- Allergy symptoms will cause a child to feel ill, miserable, irritable, restless, have difficulty sleeping, and difficulty concentrating: Removal of the allergen will lead to improvement in behaviour.
- Debilitating allergy symptoms may induce social exclusion: The child responds with frustration and antisocial behaviour.
Current Thinking on the Link Between Diet and Behaviour

- Inflammatory mediators cross the blood/brain barrier and induce behavioural changes via CNS stimulation: Removal of the allergen eliminates the inflammatory mediators

- Natural chemicals in foods and food additives have a direct pharmacological effect on CNS functions
Reasons for Improvement on Diet

- Exclusion of food allergens leads to remission of allergy symptoms:
  - The child feels better and behaviour improves

- Removal of excess sugar and additives eliminates "junk food" from the child's diet:
  - A more nutritious diet reduces behavioural effects due to malnutrition
Reasons for Improvement on Diet

- A specially formulated diet requires extra care and attention, which is focused on the child:
- A change in status and family dynamics may have a positive effect on the child's behaviour
Dietary Management in Behaviour Disorders

- A small number of behaviourally disordered children will respond positively to dietary manipulation.
- The opportunity to improve the quality of life of the child and family justifies lifestyle and dietary changes.
Dietary Management in Behaviour Disorders

The best candidates for dietary intervention are children with:

- poor eating habits
- physical as well as behavioural symptoms
- family history of adverse reactions to foods, additives, stimulants and environmental factors
Dietary Guidelines

- Initial elimination diet removes food allergens suspected on the basis of:
  - history
  - appropriate tests
  - careful record of food intake and symptoms
- All food additives and caffeine are removed
- Simple sugars are restricted
Dietary Guidelines

- A nutritionally complete diet is prescribed, using nutrients from alternate sources
- Elimination diet is followed for four weeks
- If improvement is achieved, sequential incremental dose challenge identifies specific triggers of adverse reactions
The Test Diet

Eliminate the most likely food allergens:

- Milk and dairy products
- Wheat and corn
- Peanut
- Apple
- Orange, grapefruit
- Tomato
- And any other suspected individual food allergens
The Test Diet (continued)

- Eliminate food additives, especially:
  - Artificial colours
  - Artificial flavours
  - Preservatives:
    - Benzoates
    - BHA and BHT
    - Nitrates and nitrites
    - Propyl gallate
    - Sulphites
  - Aspartame
The Test Diet (continued)

- Eliminate foods high in related naturally occurring chemicals:
  - Benzoates
  - Caffeine
- Use simple sugars in moderation.
- Dilute fruit juices half and half with water
- High sugar foods should be consumed at the end of a meal, not as between-meal snacks
Food should be taken every 2 – 2½ hours

Divide meals into six feedings

Avoid highly-perfumed products