

Voeding en gedrag

Frits A.J. Muskiet

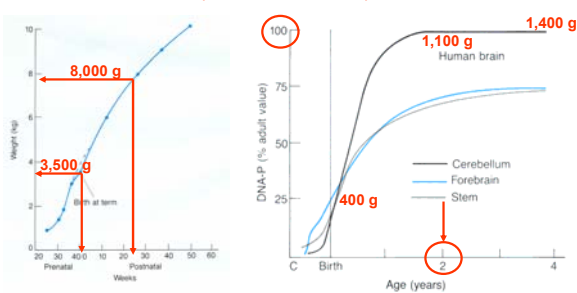
Laboratorium Centrum
Universitair Medisch Centrum Groningen
(UMCG)

Ons brein

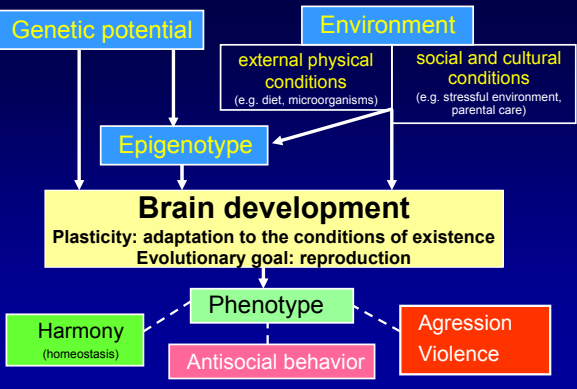
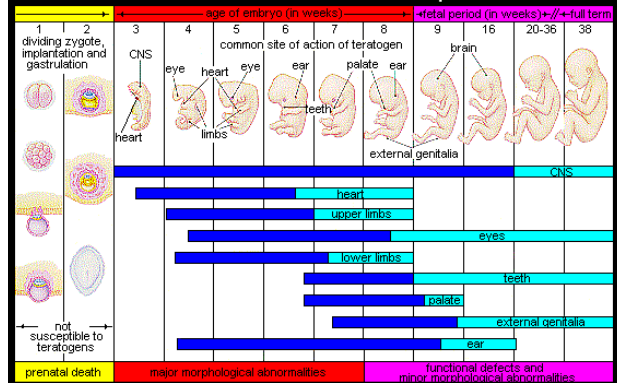


- 1.300-1.400 g
- Aantal neuronen 100 miljard
- Volume grijs/wit 1,3
- 77-78% is water
- 60% van het drooggewicht is vet
- 20% van het drooggewicht zijn essentiële vetzuren
- 8% van het drooggewicht is DHA
- 8% van het drooggewicht is AA
- DHA en AA worden selectief opgenomen
- Zitten vooral in de fotoreceptor (DHA)
- Ook in de synaptosomen (AA and DHA)

Fetal and neonatal (brain) growth (E.M. Widdowson)



Critical Periods of Human Development



Did your gene-environment interaction program you for a hawk or a dove?

	Hawk	Dove
Behavioral strategy	Fight-flight	Freeze-hide
Coping style	Proactive	Reactive
Emotional state	Aggressive and bold	Non-aggressive and cautious
Biological role	Establish territory or defend existing territory	Adopt strategy to avoid danger within territory, e.g. immobility
Exploration	Fast and superficial	Cautious and thorough
Behavioral flexibility	Rigid and routine-like	Flexible
Energy metabolism	High energy consumption	Energy conservation
Body damage (e.g. wounds, blood loss)	High risk	Low risk
Advantage according to food availability	When stable and abundant	During food scarcity
Advantage according to population cycle	When density is high	When density is low

Korte, Neurosci Behav 2005

Differences between the neuroendocrine responses of Hawks and Doves to acute threat

	Hawk	Dove
HPG-output (testosterone)	High	Low
HPA-output (cortisol or corticosterone)	Low	High
Hypothalamus (CRF mRNA)	No response	High
Hippocampus (MR mRNA)	No response, except CA1 ↑	High
Hippocampus (GR mRNA)	No response	No response
Pituitary (ACTH as % of basal)	Low	High
Adrenal cortex sensitivity	Low	High
Neurosympathetic (NE)	High	Low
Adrenomedullary (E+NE)	High	Medium
Parasympathetic (heart rate variability)	Low	High

HPG, hypothalamic-pituitary-gonadal
HPA, hypothalamic-pituitary-adrenal

Korte, Neurosci Behav 2005

Different costs of adaptation in Hawks and Doves reflecting inefficient management of mediators of allostasis and a too frequent release of mediators of allostasis, respectively

Costs of adaptation (allostatic load)

Hawk	Dove
Mediators of allostasis inefficiently managed	Mediators of allostasis released too often (surplus)
Violence/impulse control disorders	Anxiety disorders
Hypertension/cardiac arrhythmias/sudden death	Weight loss/metabolic syndrome
Atypical depression	Melancholic depression
Chronic fatigue states/hypersomnia	Psychotic states/insomnia
Inflammation/autoimmune disease	Infection

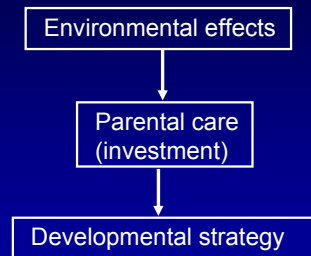
Allostasis: the ongoing adaptive efforts of the body to maintain stability (homeostasis) in response to stressors

Korte, Neurosci Behav 2005

INHOUD

- Verzorging door de ouders
- Vitamine D
- Visolievetzuren
- Folaat (foliumzuur)
- Glucose en aandacht
- Gevangenisonderzoek

The origin of phenotypic plasticity variation in parental care is the mediator

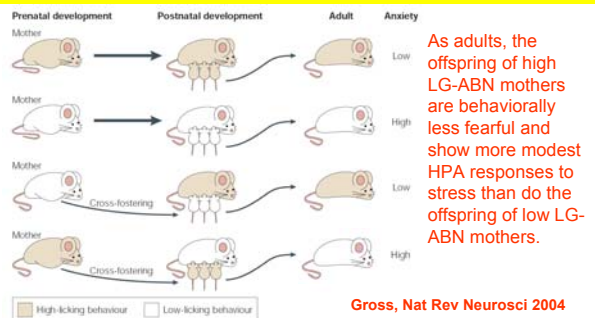


Zhang, Ann NY Acad Sci 2004

Behavior of fostering mother alters newborn gene expression via epigenetics



Rats raised by mothers displaying low licking-and-grooming behavior exhibit more anxiety-related behavior than rats raised by high licking-and-grooming mothers



(Non-Lamarckian) trans-generational inheritance of phenotype

Your maternal grandmother

Your mother

Environmental influences

Half you (maternal part)

Half of your DNA has been exposed to the environmental conditions in the uterus of your maternal grandmother.

Marks are unstable!

Half of your DNA has been exposed to the environmental conditions in the uterus of your maternal grandmother

Brain Food

- Folate *
- Essential fatty acids (DHA) *
- Retinoids (vitamin A) *
- Vitamin D *
- Iron *
- Protein-energy *

- Iodine
- Glucose/exercise

* Candidate nutrient deficiencies that might explain intrauterine risk of schizophrenia development

Brown, Schizophr Bull 2008

Age/gender adjusted RR of first contact for schizophrenic disorders for ethnic minorities in The Hague 1997-1999

	1 st + 2 nd generation 15-54 years	1 st generation 15-54 years	2 nd generation 15-29 years
Natives	1.0	1.0	1.0
Surinamese	3.7	3.2	5.5
Netherlands Antilles	2.2	2.9	NA
Turks	0.6	0.8	NA
Moroccans	5.0	4.5	8.0
Others (West/non West)	2.0	1.1/2.4	1.7

Yellow: not significant

Seltén, Br J Psychiatr 2001

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Vitamin D is a neuroactive nutrient

Gestational vitamin D deficiency causes permanent changes in the developing rat brain.

There is ample biological evidence to suggest an important role for vitamin D in brain development and function

Deficiency alters brain gene and protein expression

Deficiency disrupts the balance between neuronal stem cell proliferation and programmed cell death in the offspring

Deficiency has been associated with impaired cognition, depression, bipolar disorder, and schizophrenia

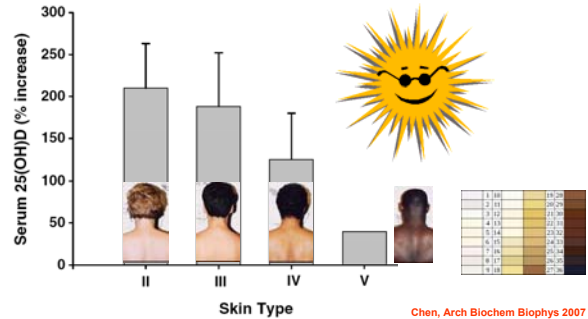
Kiraly, ScientificWorldJournal 2006; McCann, FASEB J 2008; Levenson, Nutr Rev 2008; Cherniack Curr Psychiatry Rep 2009

Schizophrenia prenatal vitamin D insufficiency hypothesis

1. 5–8% excess schizophrenic births in winter/spring at high latitudes
2. Sharp schizophrenia increase in early gestation during the Dutch Hunger Winter (confirmed in China)
3. Association between short birth interval and offspring schizophrenia (might be folate but also vitamin D insufficiency)
4. Excess of schizophrenia and schizophrenia births in urban centers
5. Schizophrenia excess in dark-skinned immigrants in northern European countries
6. Protective factor of ethnic density (ethnic food availability?)
7. North–south gradient in schizophrenia prevalence rates
8. Less severe course in the developing countries (generally located in lower latitudes).

Dealberto, Med Hypotheses 2007

Serum 25(OH)D in volunteers with different skin types after weekly exposure to simulated sunlight for 12 weeks



Chen, Arch Biochem Biophys 2007

Serum 25(OH)D, vitamin D deficiency and percentage undetectable 25(OH)D in pregnant women of several ethnic backgrounds living in The Hague, NL

	25(OH)D concentration ¹	25(OH)D deficiency ²	25(OH)D under the detection limit ³
Western (reference) (n = 105)	52.7 ± 21.6 ⁴	8 (8)	1 (1)
Turkish (n = 79)	15.2 ± 12.1 ⁵	66 (84) ⁶	17 (22) ⁶
Moroccan (n = 69)	20.1 ± 13.5 ⁵	56 (81) ⁶	3 (4)
Other non-Western (n = 105)	26.3 ± 25.9 ⁵	62 (59) ⁶	9 (9) ⁷

¹ Means compared by using ANOVA and Dunnett's test; vitamin D data were log transformed and weighted by inverse cell variances.

² Deficiency = < 25 nmol 25(OH)D/L.

³ Means compared by using logistic regression.

⁴ Under the detection limit = < 7 nmol 25(OH)D/L.

⁵ ± SD (all such values).

⁶ p ≤ 0.001.

⁷ p ≤ 0.05.



Van der Meer, AJCN 2006

Symptomen vitamine D deficiëntie

In kinderen (rachitis)

- Rusteloosheid, slecht slapen
- Laat zitten, kruipen, lopen, sluiten fontanel
- Vervormde schedel en andere botten
- Spierzwakte, groeivertraging, abnormale ontwikkeling tanden
- Late effecten: convulsies, fracturen, tetanie/spasmen

In volwassenen (osteomalacie)

- Pijn ("mij pijn mij moe"), botpijn, zwakte en gevoeligheid
- Spierzwakte (benen, traplopen), botfracturen

In volwassenen (osteoporose)

- Vroeg: spier en gewrichtspijn
- Laat: dunne, zwakke en broze botten, fracturen, rugpijn, verlies van lengte, deformatie wervelkolom

Not many foods are rich vitamin D sources

Food	Vitamin D (µg/100 g)
Eel	25.6
Pike-perch	24.6
Herring	15.4
Salmon	12.4
Egg yolk	7.8
Tuna	7.2
Cod	7.0
Egg	2.8
Liver, beef	0.8
Butter	0.3



Lamberg-Allardt Prog Biophys Mol Biol 2006

Suppletie adviezen NL Gezondheidsraad dd 30 09 2008

10 microgram vitamine D per dag*

- kinderen tot 4 jaar
- personen met een donkere huidskleur
- personen die onvoldoende buitenkomen
- vrouwen die een sluier dragen
- vrouwen die zwanger zijn of borstvoeding geven
- vrouwen vanaf 50 jaar
- mannen vanaf 70 jaar

20 microgram vitamine D per dag*

- personen met osteoporose of die in een verpleeghuis wonen
- vrouwen vanaf 50 jaar
 - met een donkere huidskleur
 - die onvoldoende buitenkomen
 - die een sluier dragen
- mannen vanaf 70 jaar
 - met een donkere huidskleur
 - die onvoldoende buitenkomen

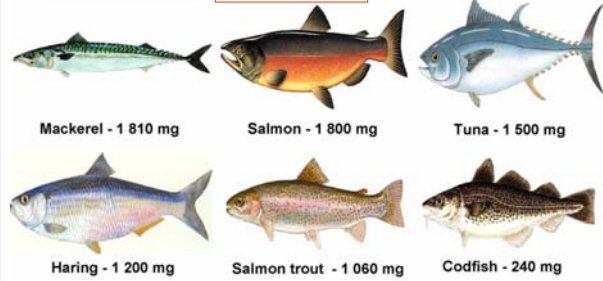
*In combinatie met voldoende calciuminname

Voeding Nu 2008;10:14-16

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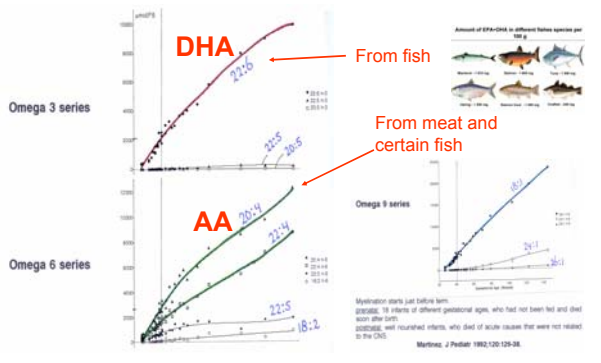
- Verzorging door de ouders
- Vitamine D
- **Visolievetzuren**
- Folaat (foliumzuur)
- Glucose en aandacht
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EPA and DHA per 100 g fish

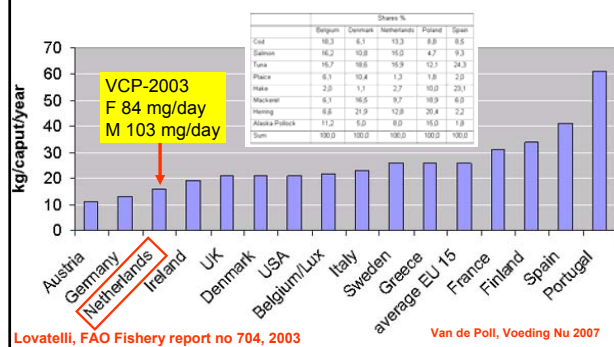


Fedacko Pathophysiology 2007

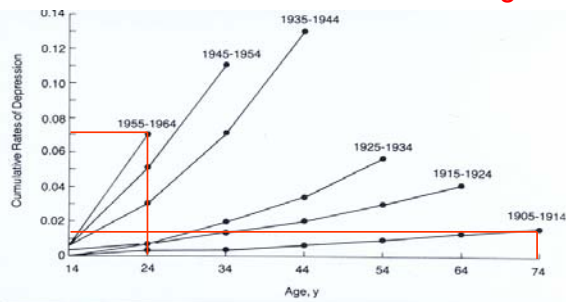
Pre and Postnatal Forebrain development



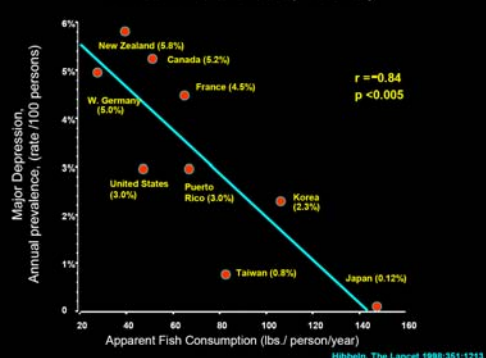
Fish consumption in EU and USA 1994-1998



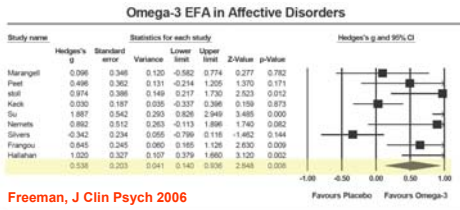
Cumulative rates of major depression for USA birth cohorts as a function of age



Fish Consumption and Major Depression Annual Prevalence by Country



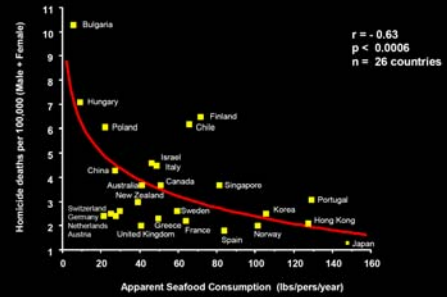
Recent meta analysis of RCTs showing beneficial effects of LCPw3 in patients with affective disorders (i.e. combined unipolar and bipolar depression)



Results highly heterogeneous (Freeman et al., 2006b; Lin and Su, 2007). More large scale RCTs needed to identify favorable target subjects, therapeutic dosages and LCPw3 compositions (Lin and Su, 2007). 1-2 g LCPw3/day effective (Ross et al., 2007)

Lin and Su, 2007
Ross et al, 2007
Sinclair et al, 2007

Homicide Mortality Rates¹ and Seafood Consumption



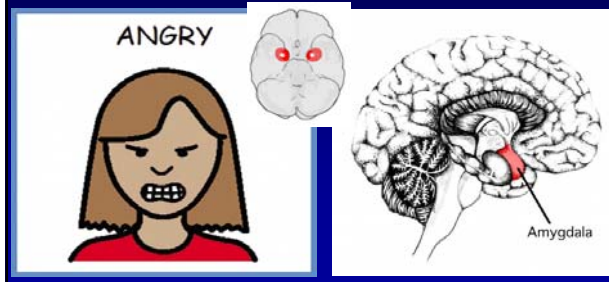
¹World Health Statistics Annual 1995, WHO, Geneva Switzerland Hibbeln, JR World Rev Nutr Diet, 2001; 68; 41-46

De amygdala legt verbanden tussen informatie die van verschillende zintuigen afkomstig is en koppelt deze aan emoties. Bij iedere nieuwe situatie bepaalt het individu welke emotionele reactie het meest zinvol is. Daarbij reageert de amygdala bijvoorbeeld ook op de gezichtsuitdrukking van soortgenoten. De reactie van de amygdala op prikkels die angst veroorzaken, kan snel en volledig automatisch (d.w.z.reflexmatig) plaatsvinden.

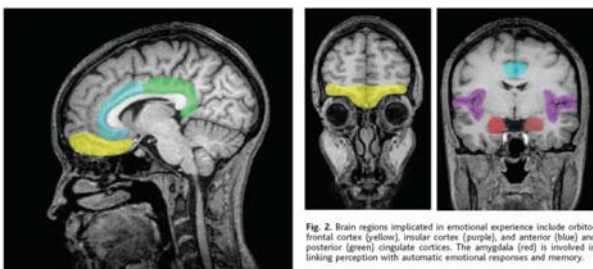
Met name de rol bij angst-reacties is bekend, maar de amygdala lijkt ook betrokken te zijn bij andere emoties. Het gaat dan om gebieden als angst, agressie, seksueel gedrag en conditionering.

Door een bepaalde situatie een emotionele waardering te geven (en als zodanig in het geheugen vast te leggen), kan het individu een toekomstige soortgelijke situatie gemakkelijker herkennen en daar gepast op reageren (bijvoorbeeld met een vecht- of vluchtreactie).

When people see a photograph of an angry or fearful face, they have increased activity in a region of the brain called the amygdala, which serves as an alarm to activate a cascade of biological systems to protect the body in times of danger

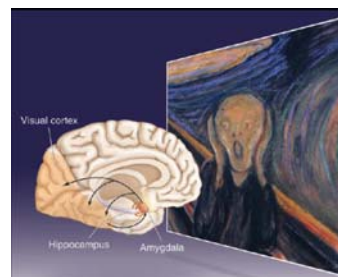


The amygdala is involved in linking perception with automatic emotional responses and memory



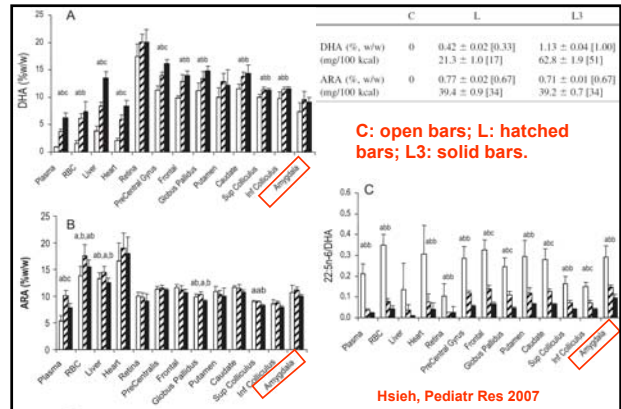
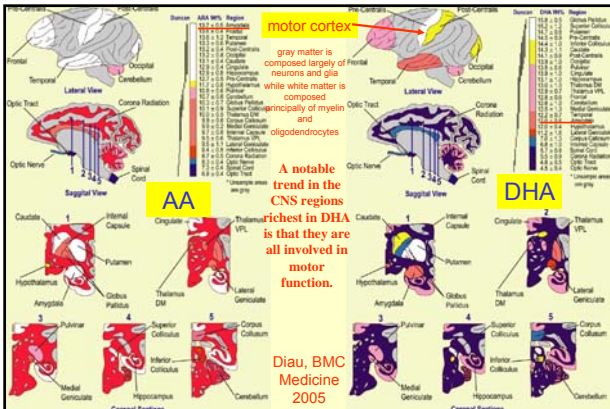
www.sciencemag.org SCIENCE VOL 298 8 NOVEMBER 2002 Dolan, Science 2002

An emotional-perceptual-memory circuit in the human brain



The amygdala (red), an anterior medial temporal lobe structure, is a crucial structure in registering emotional occurrences. Extensive connection (arrows) to visual cortex (orange) and hippocampus (blue) allows amygdala to modulate their function and facilitate perceptual and memory functions in those regions.

Dolan, Science 2002



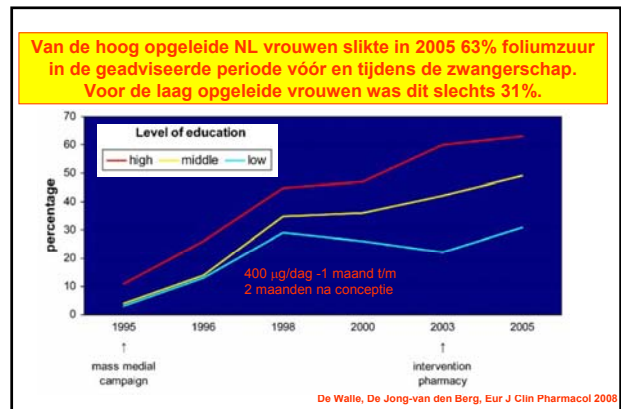
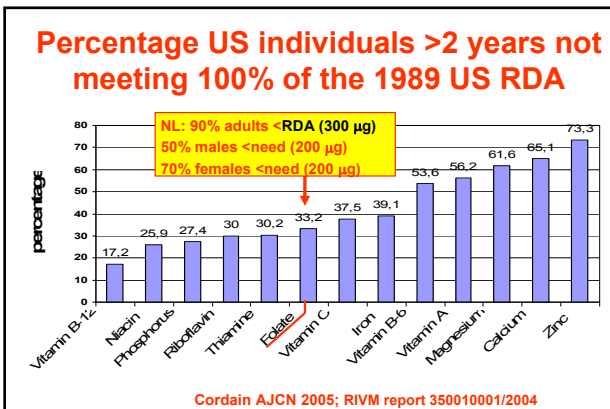
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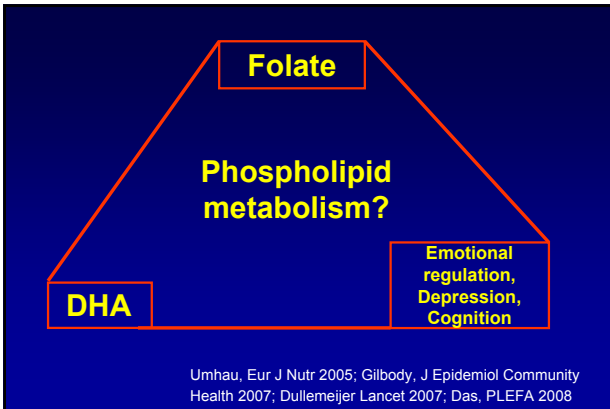
- Verzorging door de ouders
- Vitamine D
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- Glucose en aandacht
- Gevangenisonderzoek

Schizophrenia relates to low intrauterine folate and to neural tube defects (NTDs)

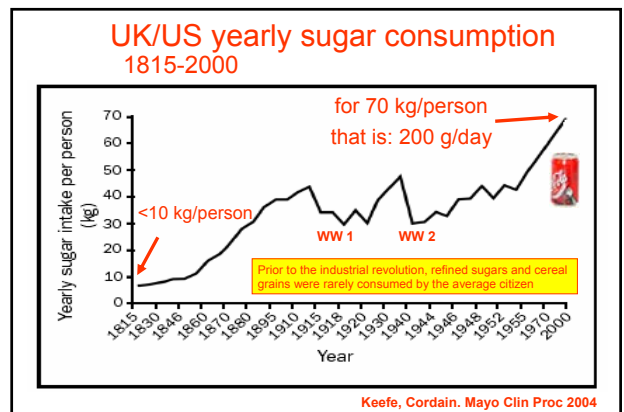
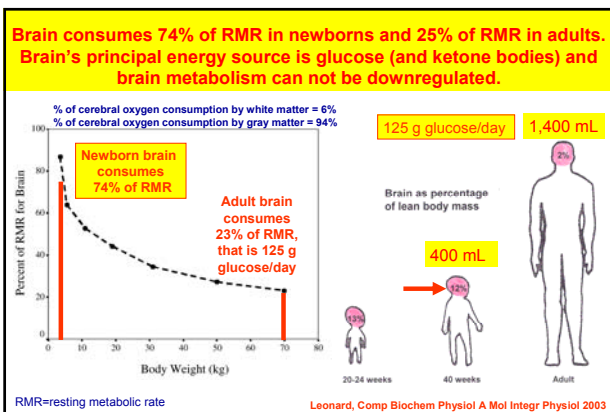
1. **Birth spacing:** short birth spacing increases schizophrenia risk (notably depletes maternal folate). Peak incidence at birth spacing of 15-20 months.
2. **Dutch hunger winter:** 2.0 times higher schizophrenia risk coincides with 2.5 times higher NTD risk in a birth cohort that was conceived at the height of the Dutch hunger winter 1944-45 (confirmed China).
3. **Seasonality:** NTD and schizophrenia conception rates coincide.
4. **MTHFR C677T homozygotes** have increased schizophrenia (meta study) and NTD (fetal genotype) risks.
5. **Immigrants** have higher schizophrenia risk and low compliance to periconceptional use of folic acid supplements.
6. **Elevated homocysteine** in the third trimester is a schizophrenia risk factor (OR=2; Brown 2007).

Muskiet, J Nutr Biochem 2006; Brown, Arch Gen Psychiatry 2007

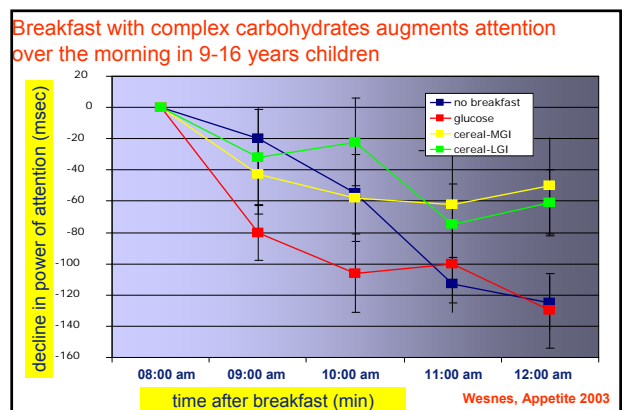




- ## INHOUD
- Verzorging door de ouders
 - Vitamine D
 - Visolievetzuren
 - Folaat (foliumzuur)
 - Glucose en aandacht
 - Gevangenisonderzoek



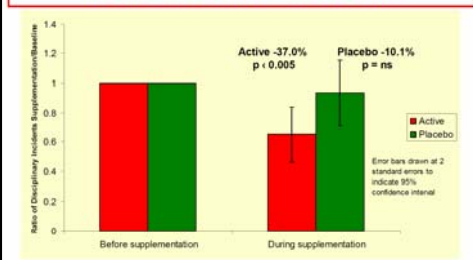
- ## Effects of hypoglycemia
- Negative mood
 - Increased tension
 - Decreased happiness
 - Drowsiness
 - Negative appraisal
 - Increased feelings of anger
- ➔ Impaired mental (cognitive) performance



INHOUD

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- **Gevangenisonderzoek**

Reductions in felony level violent offences among prisoners in placebo controlled trial of recommended daily amounts of vitamins, minerals and essential fatty acids



338 offences among 172 prisoners over 9 months treatment in a UK maximum security prison compared to 9 months baseline. Analysis: Negative binomial mixed Poisson regression analysis
Gesch et al. Br J Psychiatry 2002, 181:22-28

LA (mg)	1260
GLA (mg)	160
EPA (mg)	80
DHA (mg)	44
Vitamin A (µg) ¹	750
Vitamin D (µg)	10
Vitamin B1 (mg)	1.2
Vitamin B2 (mg)	1.6
Vitamin B6 (mg)	2
Vitamin B12 (µg)	3
Vitamin C (mg)	40
Vitamin E (mg)	10
Vitamin K1 (µg)	-
Biotin (µg)	100
Nicotinamide (mg)	18
Pantothenic acid (mg)	4
Folic acid (µg)	400
Calcium (mg)	100
Iron (mg)	12
Copper (mg)	2
Magnesium (mg)	30
Zinc (mg)	15
Iodine (µg)	140
Manganese (mg)	3
Potassium (mg)	4
Phosphorus (mg)	77
Selenium (µg)	50
Chromium (µg)	200
Molybdenum (µg)	350

Vitamine A	2500	IE
Beta-caroten	2500	IE
(natuurlijke vorm)	2500	IE
Vitamine B1	1.2	mg
Vitamine B2	1.6	mg
Vitamine B3 (niacine)	18	mg
Vitamine B5	4	mg
Vitamine B6	2	mg
(als pyridoxal-5-fosfaat)	2	mg
Foliumzuur	400	mcg
Vitamine B12	3	mcg
Biotine	100	mcg
Vitamine C	60	mg
Vitamine D3	5	mcg
Vitamine E (α-tocopherol)	10	mg
Calcium	100	mg
Magnesium	100	mg
Zink	15	mg
Ijzer	12	mg
Mangaan	3	mg
Koper	2	mg
Kalium	4	mg
Jodium	140	mcg
Selenium	50	mcg
Chroom	200	mcg
Molybdeen	250	mcg
Docosahexaënoëzuur (DHA)	400	mg
Eicosapentaënoëzuur (EPA)	400	mg
Vitamine E	20	mg
Gammalinolenzuur (GLA)	100	mg
Vitamine E	10	mg

Gevangenis onderzoek NL

AVL: Aggressie VragenLijst;
SDAS: Social Dysfunction and Aggression Scale (vragen aan personeel);
GHQ: General Health Questionnaire-28 (algemeen welbevinden);
SCL: Symptom Check List-90 (psychische klachten)

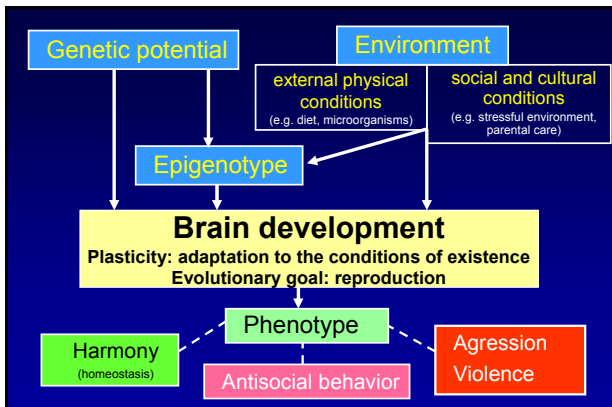
	Incidentieratio	Incidentieratio (excl. alcohol- en druggerelateerde incidenten)
Placebo	voor 9,7	8,6
Groep (n=105)	na 11,0	8,1
verandering	+ 13%	+ 23%
Supplementen	voor 11,0	8,7
Groep (n=116)	na 7,3	5,4
verandering	- 34%	- 38%

Schultemaker, Ortho 2007

Vergelijking van de resultaten van het Amerikaanse, Britse en Nederlandse onderzoek

Verschil met placebo

Schultemaker, Ortho 2007



The end