UNIVERSITEIT
GENT

Wij en onze hersenen
Pride or prejudice ?

Prof.Dr.P.Santens

Neurologie UZ Gent

Vakgroep H&H, Fac GE

Inhoud van de lezingencyclus

9/10 - De hersenen als dynamisch orgaan: van cel tot netwerk

16/10 - De kwetsbare hersenen: tussen verlies en hoop

23/10 - Zijn wij onze hersenen ? Durf denken, en twijfelen !

11/10 - De kwetsbare hersenen: tussen verlies en hoop

The burden of neurological diseases in Europe: an analysis for the Global Burden of Disease Study 2017

Lancet Public Health 2020; 5: e551–67

Günther Deuschl, Ettore Beghi, Franz Fazekas, Timea Varga, Kalliopi A Christoforidi, Eveline Sipido, Claudio L Bassetti, Theo Vos, Valery L Feigin

Interpretation Neurological disorders are the third most common cause of disability and premature death in the EU and their prevalence and burden will likely increase with the progressive ageing of the European population. Greater attention to neurological diseases must be paid by health authorities for prevention and care. The data presented here suggest different priorities for health service development and resource allocation in different countries.

The burden of neurological diseases in Europe: an analysis for the Global Burden of Disease Study 2017

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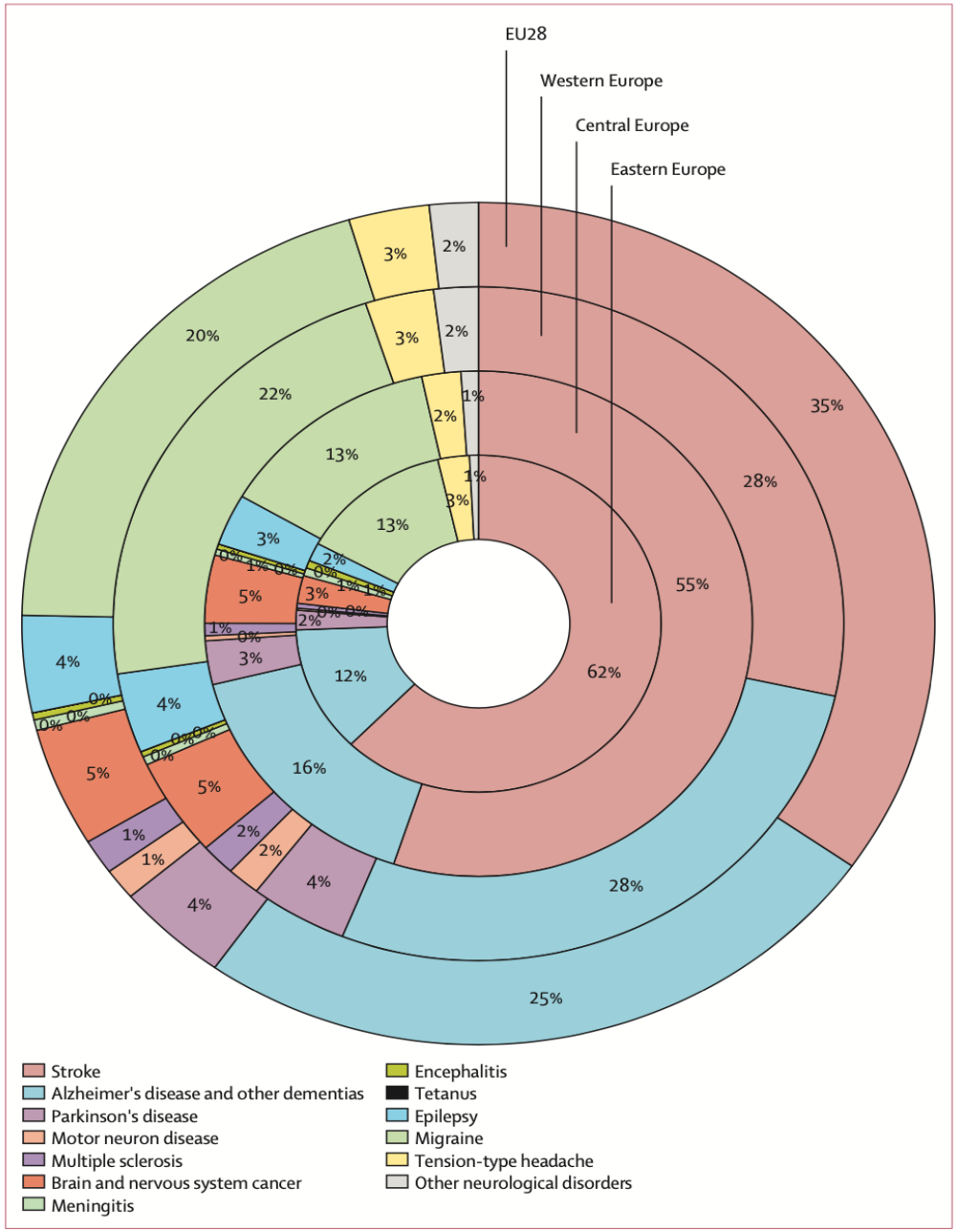


Figure 1: **Contribution of each disease to the overall burden of neurological disorders in the EU28, western, central, and eastern Europe in 2017**
Percentages represent proportion of DALYs. DALYs=disability-adjusted life-years. EU28=the 27 countries in the EU plus the UK.

"Mental disorders"

Global Burden of Disease and the Impact of Mental and Addictive Disorders

Jürgen Rehm[1,2,3,4,5,6,7] · Kevin D. Shield[2,3,6]

Table 1 Prevalence of mental and substance-use disorders 2016 per 100,000

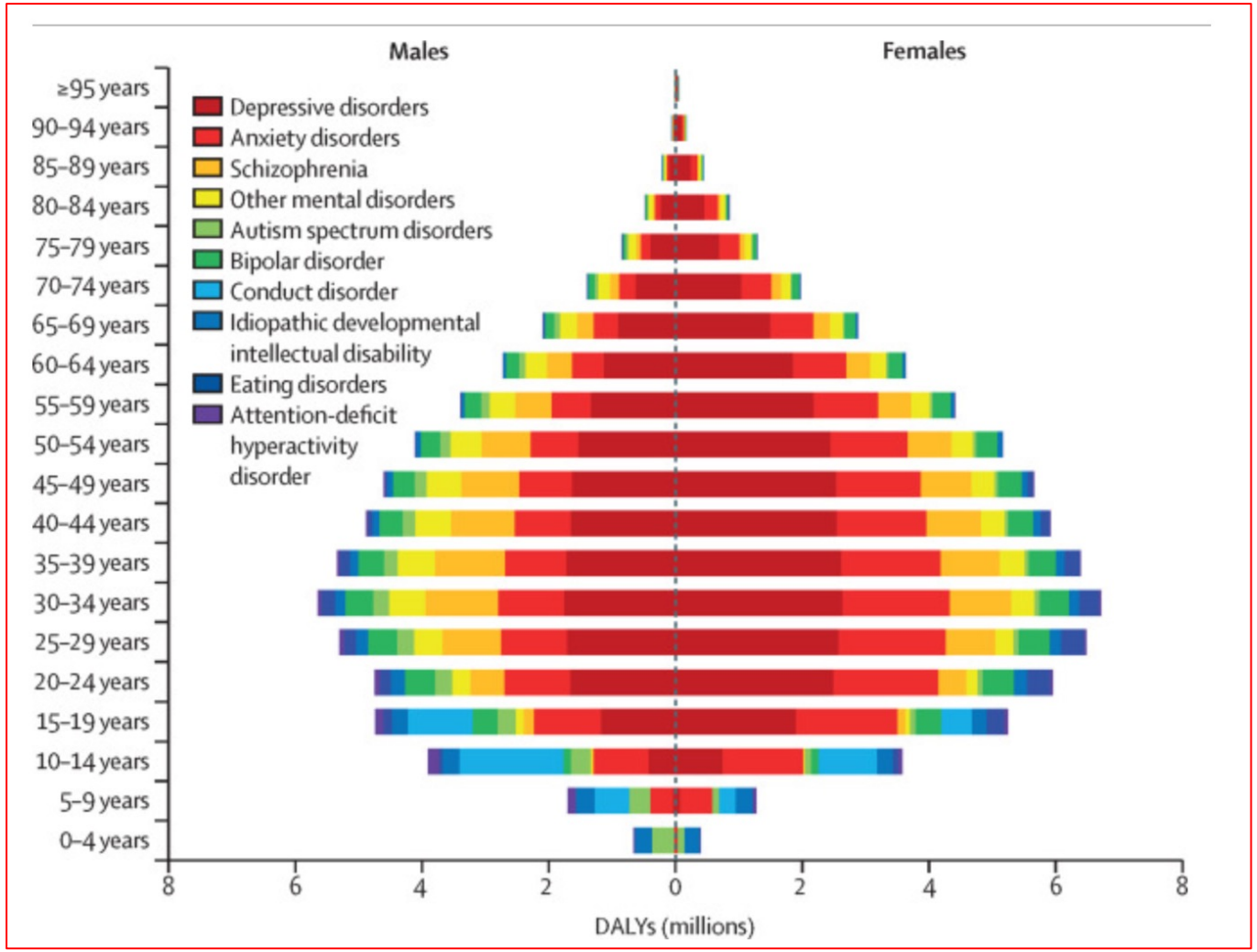
Disorder category*	Women			Men			Both sexes		
	Point estimate	Upper	Lower	Point estimate	Upper	Lower	Point estimate	Upper	Lower
Schizophrenia	283	317	251	282	317	249	282	317	250
Alcohol-use disorders	805	913	705	**1902**	**2107**	**1703**	1358	1510	1212
Drug-use disorders	615	672	566	**1070**	**1159**	**991**	844	914	780
Depressive disorders	*4428*	*4760*	*4122*	2839	3069	2635	3627	3904	3373
Bipolar disorder	*655*	*748*	*572*	534	611	467	594	679	519
Anxiety disorders	*4648*	*4984*	*4316*	2797	3012	2593	3715	3988	3454
Eating disorders	*218*	*262*	*181*	69	85	56	143	172	120
Autistic spectrum disorder	348	400	301	**1312**	**1511**	**1152**	834	957	734
Attention-deficit/hyperactivity disorder	510	560	469	**1178**	**1291**	**1084**	847	928	779
Conduct disorder	458	557	360	**865**	**989**	**740**	663	772	554
Idiopathic developmental intellectual disability	1371	1923	814	1732	2420	1058	1553	2183	940
Other mental and substance-use disorders	1582	1819	1386	**2188**	**2502**	**1911**	1887	2170	1651
Any mental substance-use disorder	14,666	15,333	14,011	15,362	16,065	14,639	15,017	15,666	14,345

*Definitions and ICD codes for the disease categories, see [29]

Italic values mark disease categories, where the point estimate for age-adjusted prevalence in women is higher than the upper uncertainty interval of men; bold values mark disease categories, where the point estimate for age-adjusted prevalence in men is higher than the upper uncertainty interval of women

Source: [28]

”Mental disorders”



Aandoeningen van de hersenen

Aangeboren – congenitaal

Verworven

- Niet-aangeboren hersenletsels
- Degeneratieve aandoeningen

Aandoeningen van de hersenen

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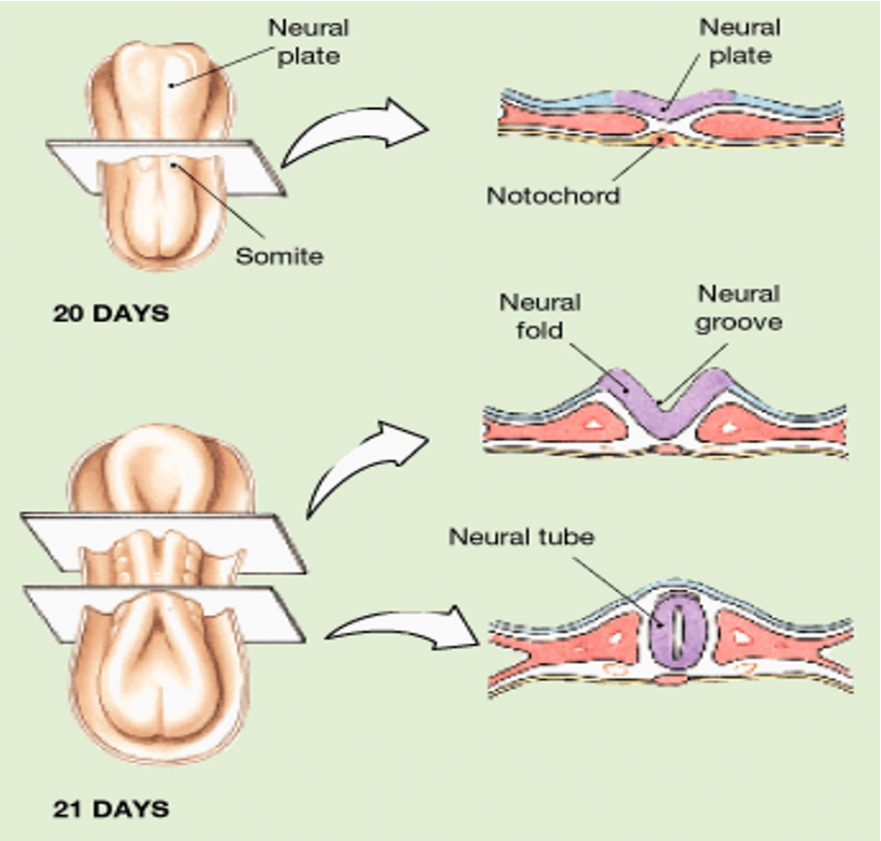
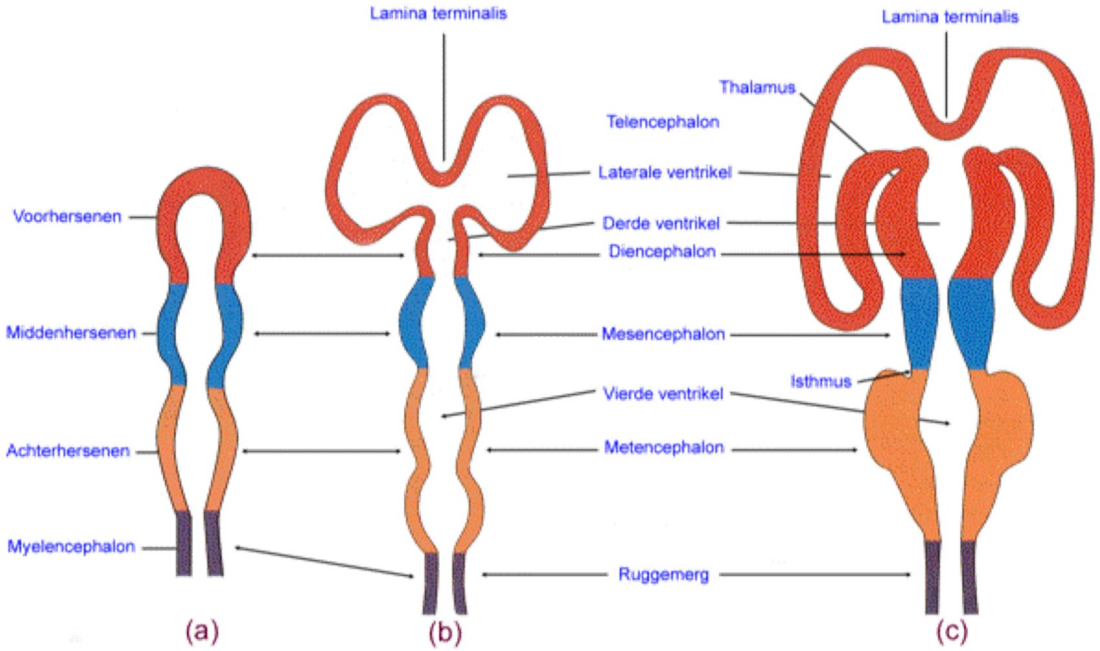
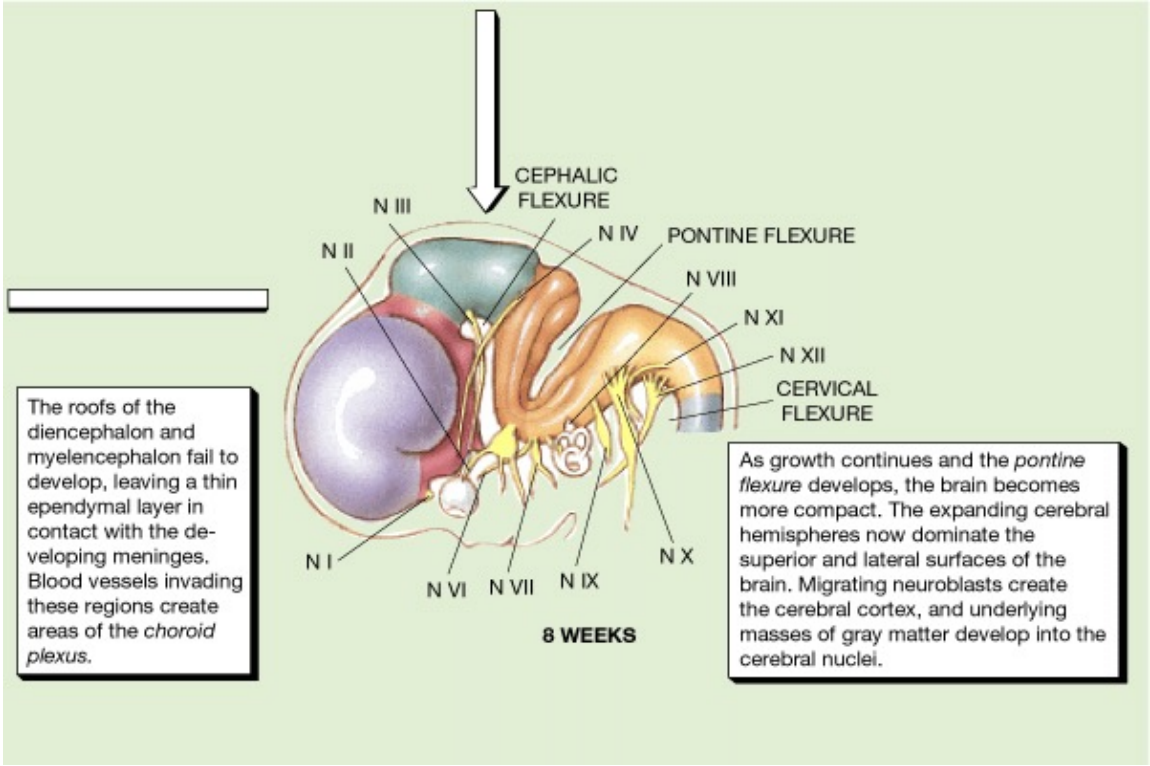
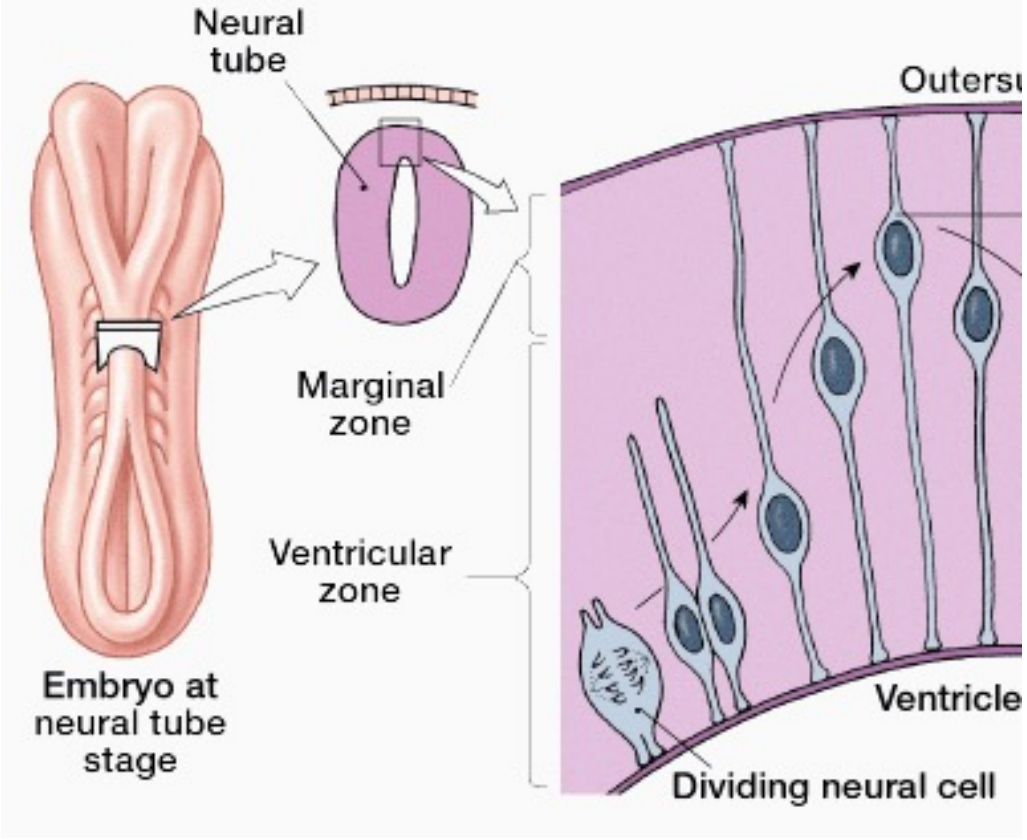
De ontwikkeling van de hersenen



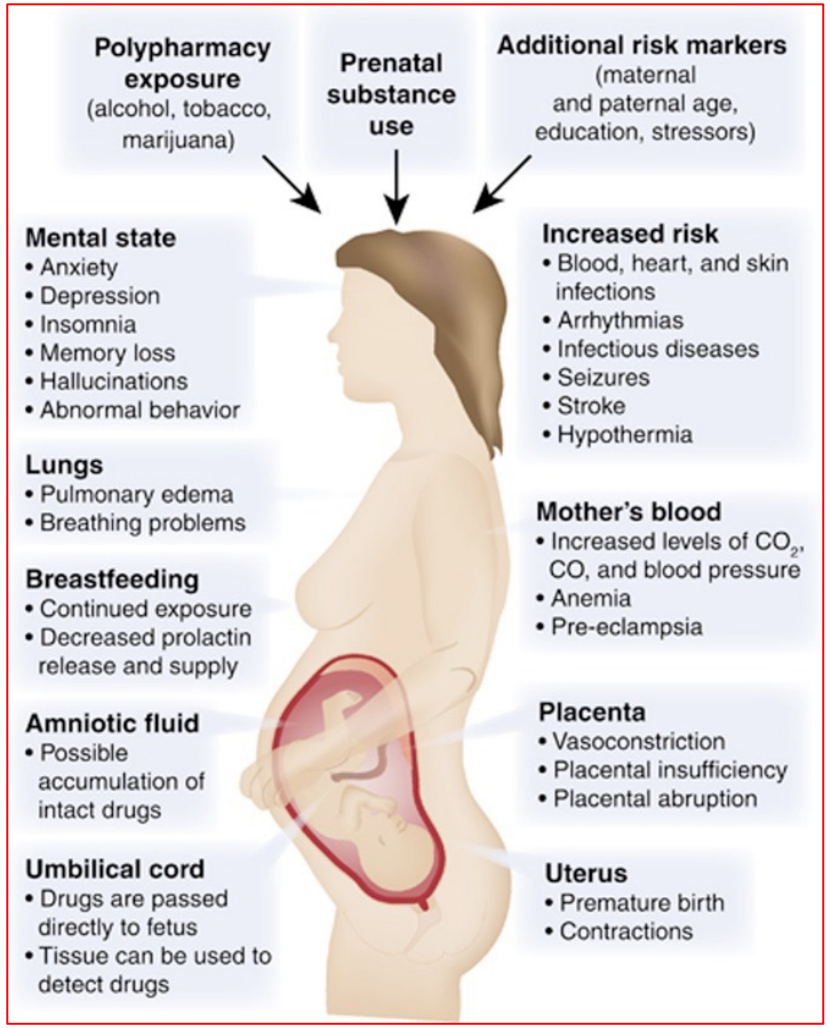


De ontwikkeling van de hersenen

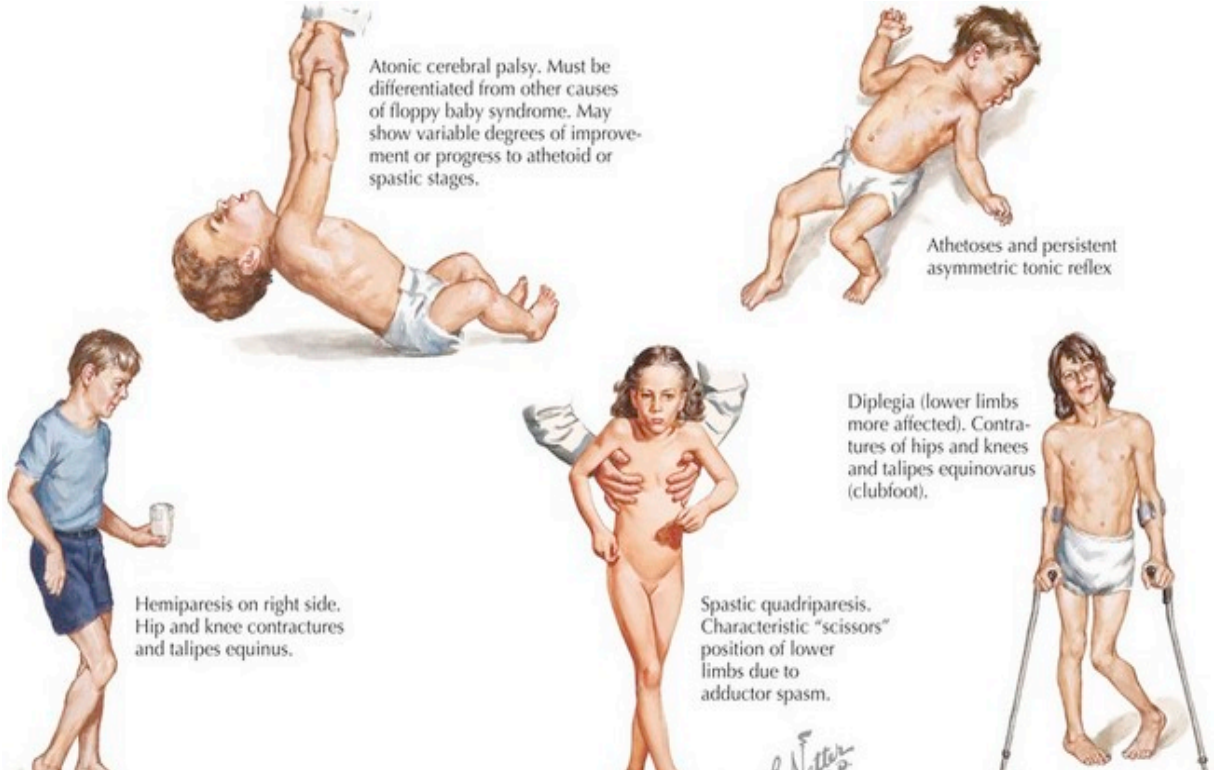




Invloeden op de ontwikkeling van de hersenen



Cerebral palsy - hersenverlamming



- Prematuriteit, laag geboortegewicht, meerlingenzwangerschap
- Zuurstoftekort : placentaire problemen, langdurige of moeilijke bevalling, meconiumaspiratie, longproblemen
- Prenatale/perinatale infectie of intoxicatie
- Postnatale problemen : geelzucht, infecties, traumata, zuurstoftekort,…

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Aandoeningen van de hersenen

Aangeboren – congenitaal

Verworven

- Niet-aangeboren hersenletsels
- Degeneratieve aandoeningen

Niet-aangeboren hersenletsels

- Beroerte
- Trauma
- Acuut gebrek aan zuurstof of glucose
- Infectie en ontsteking
- Intoxicaties
- …

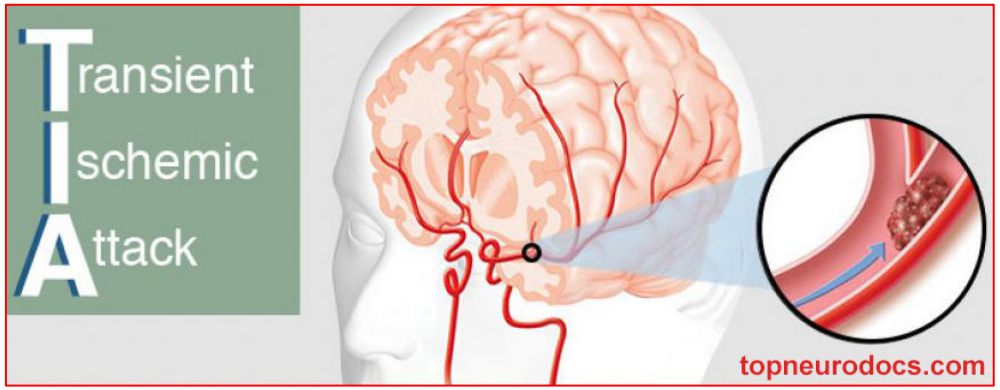
Kenmerken van NAH

- Vaak gevolg van acute gebeurtenis/letsel.
- Gevolgen dikwijls langdurig of zelfs permanent
- Veranderingen in verschillende gebieden:
  - Motorisch: kracht, mobiliteit, handigheid, spreken, slikken,…
  - Zintuiglijke functies: blindheid, verlies gezichtsveld, gehoorsstoornissen, evenwichtsproblemen, reukstoornissen, pijn, gevoelsverlies,…
  - Emotie en gedrag: persoonlijkheidsverandering, apathie, agressie, ontremd gedrag, depressie…
  - Cognitie: geheugen en concentratie, taal, redeneren en plannen, oriëntatie,…
  - Epileptische aanvallen

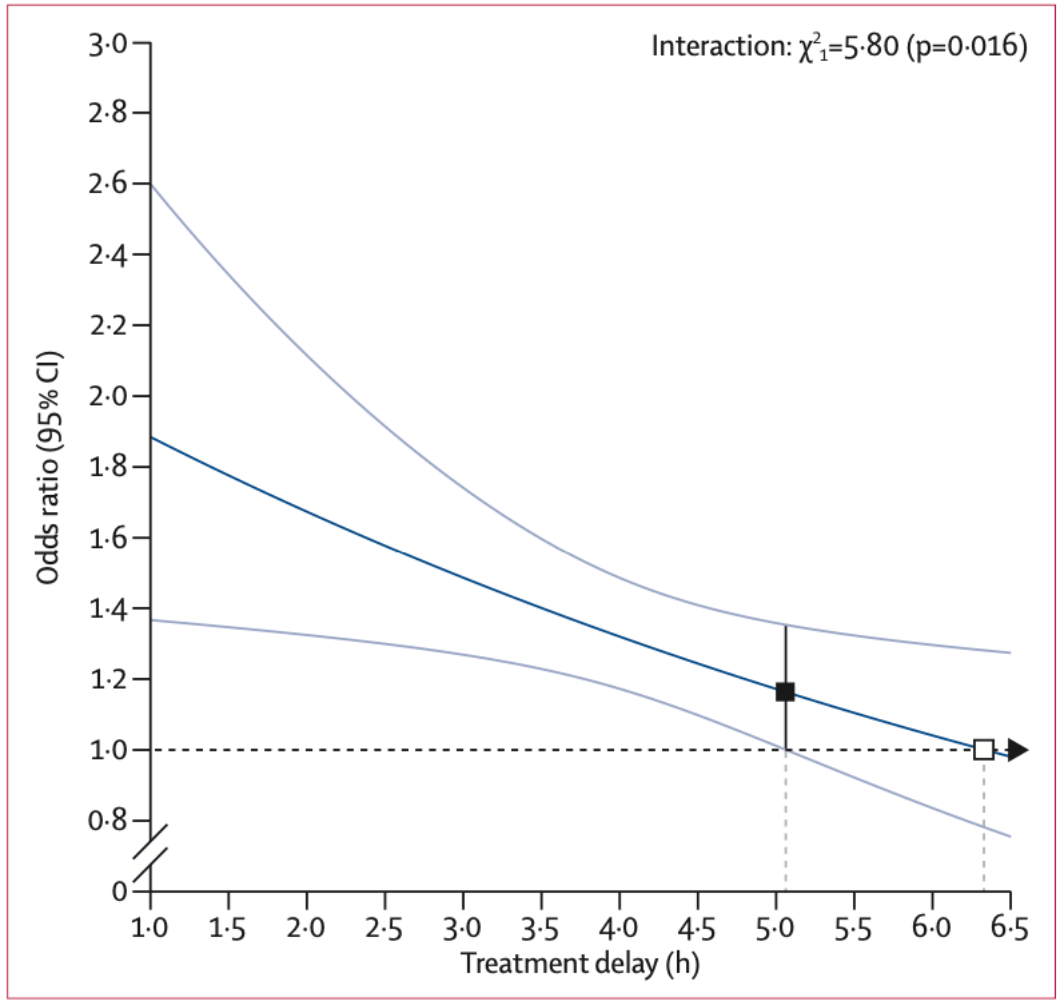
Beroerte (Cerebrovasculair accident – CVA)

Thrombose – 80%

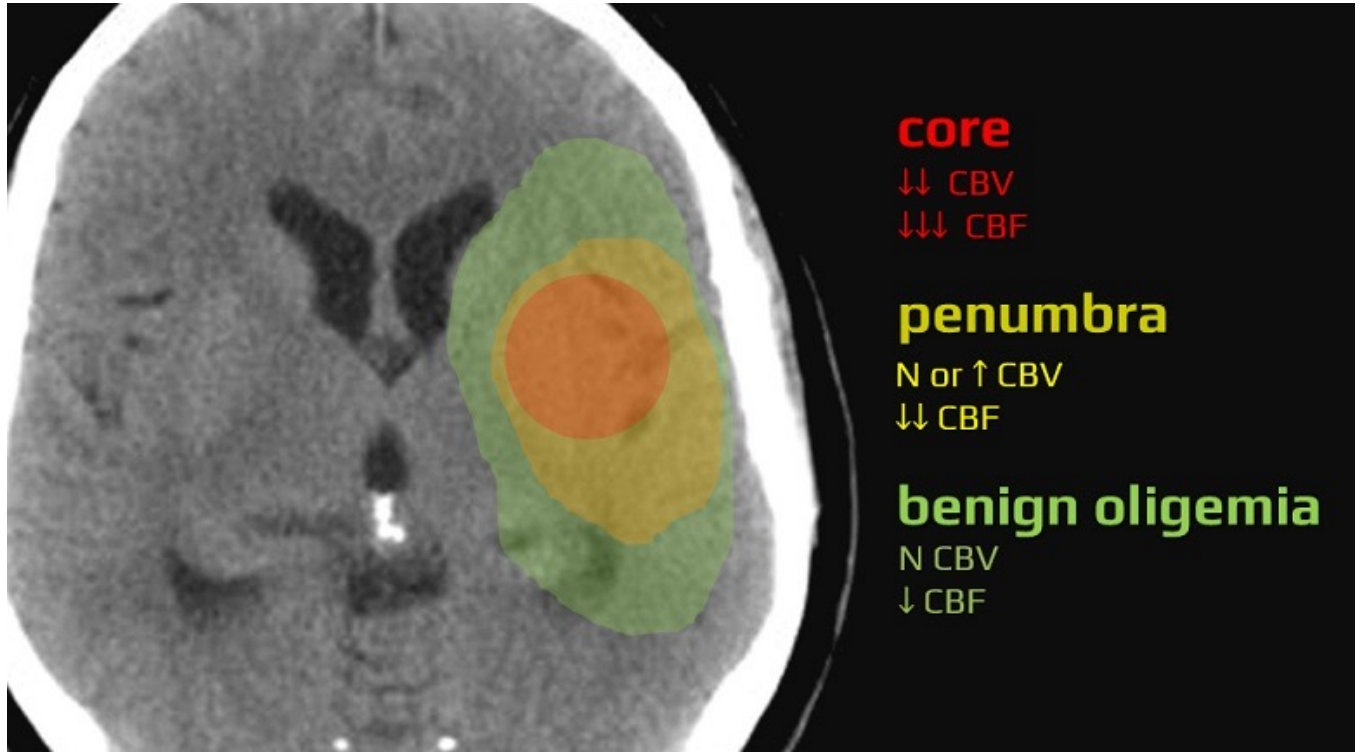
Bloeding – 20%

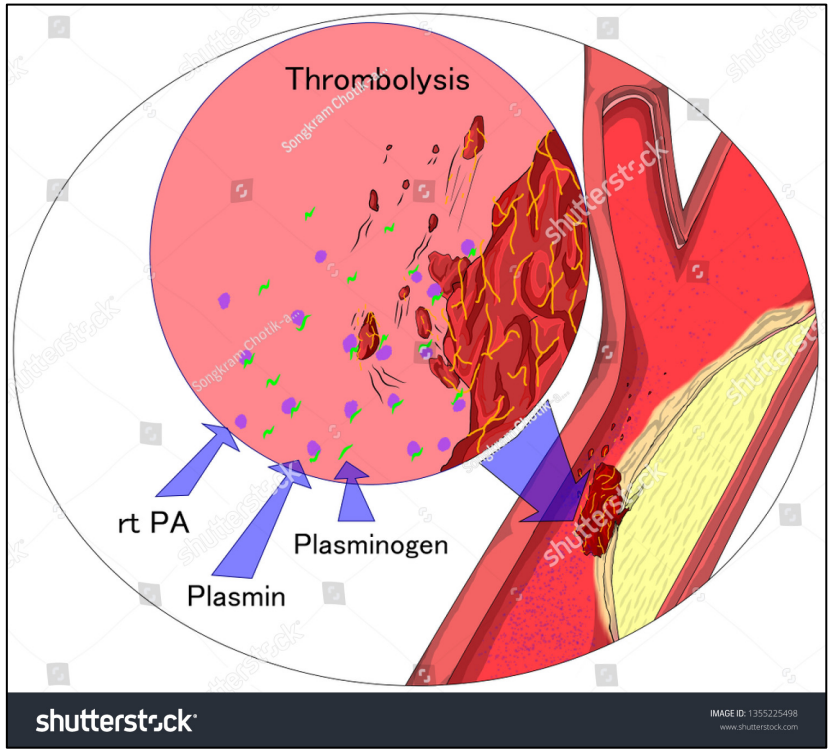


Beroerte (Cerebrovasculair accident – CVA)

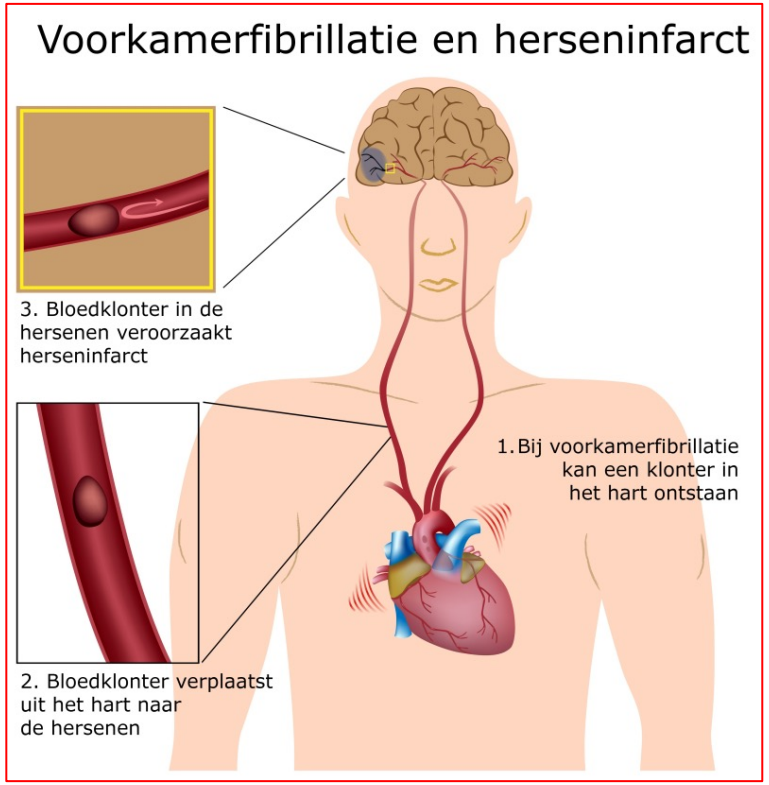


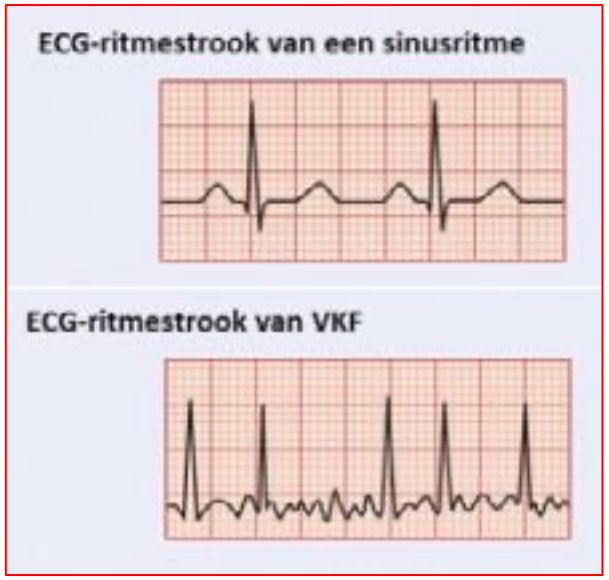
Beroerte (Cerebrovasculair accident – CVA)





Beroerte Risico en preventie





Aandoeningen van de hersenen

Aangeboren – congenitaal

Verworven

- Niet-aangeboren hersenletsels
- Degeneratieve aandoeningen

Degeneratieve aandoeningen

Chronische en progressieve aandoeningen

Verlies van zenuwcellen in min of meer typische gebieden/netwerken

Klassieke en typische symptomen en verloop, maar vele varianten

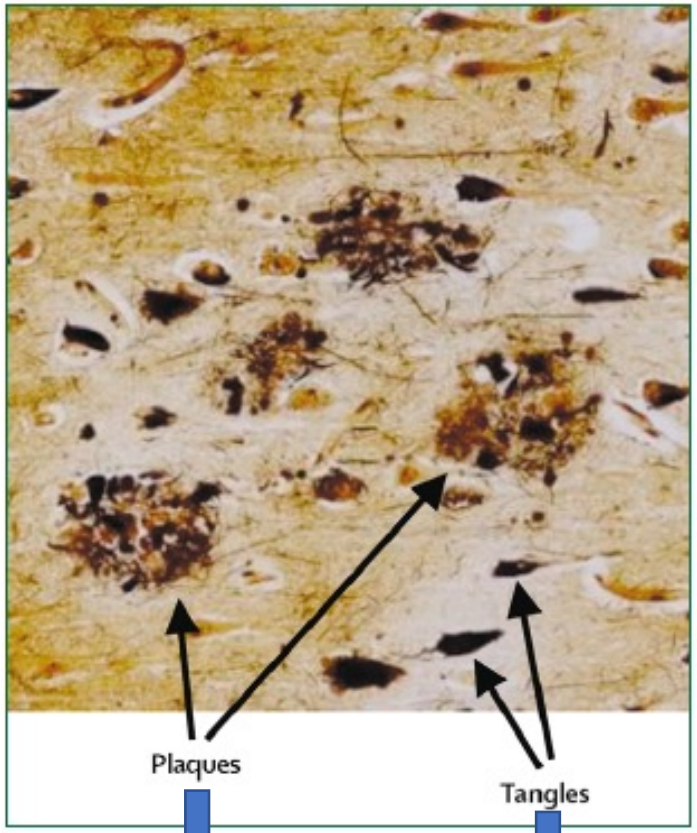
Pathologische veranderingen
- Verlies van zenuwcellen
- Stoornissen in neurotransmitter systemen
- Stapeling van pathologische eiwitten
  - binnen/buiten de cel

Momenteel enkel symptomatische behandelingen

“Dementie”

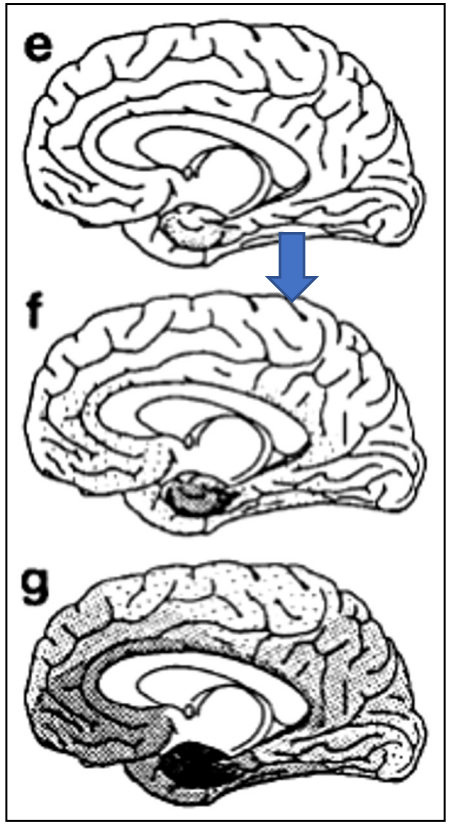
- Geheugenstoornis
- En een of meer andere cognitieve stoornissen
  - afasie (taalstoornis)
  - apraxie (klungelen)
  - agnosie (herkennen)
  - uitvoerende functies (plannen, organiseren)
- En negatieve invloed op het dagelijks functioneren, werk, sociale activiteiten en relaties
- En geen delier

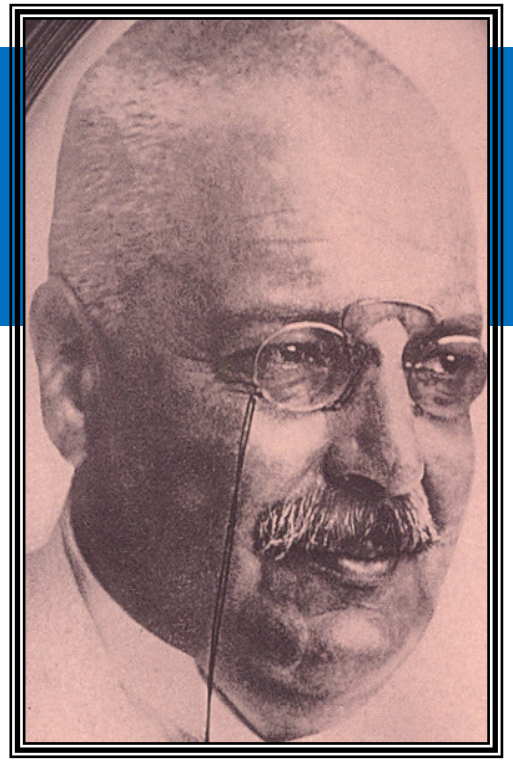
De ziekte van Alzheimer



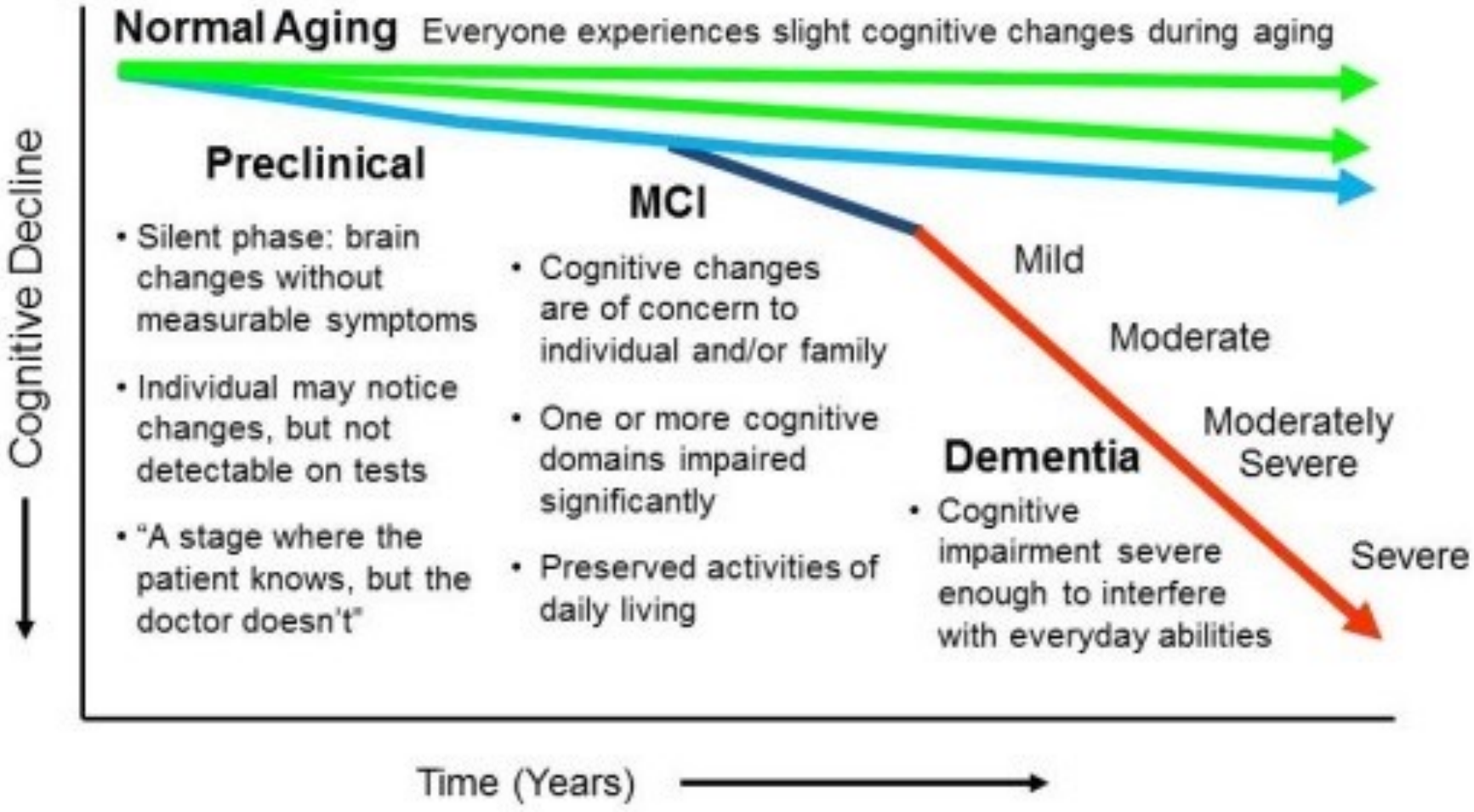
Beta-amyloid

Tau





De ziekte van Alzheimer



De ziekte van Alzheimer

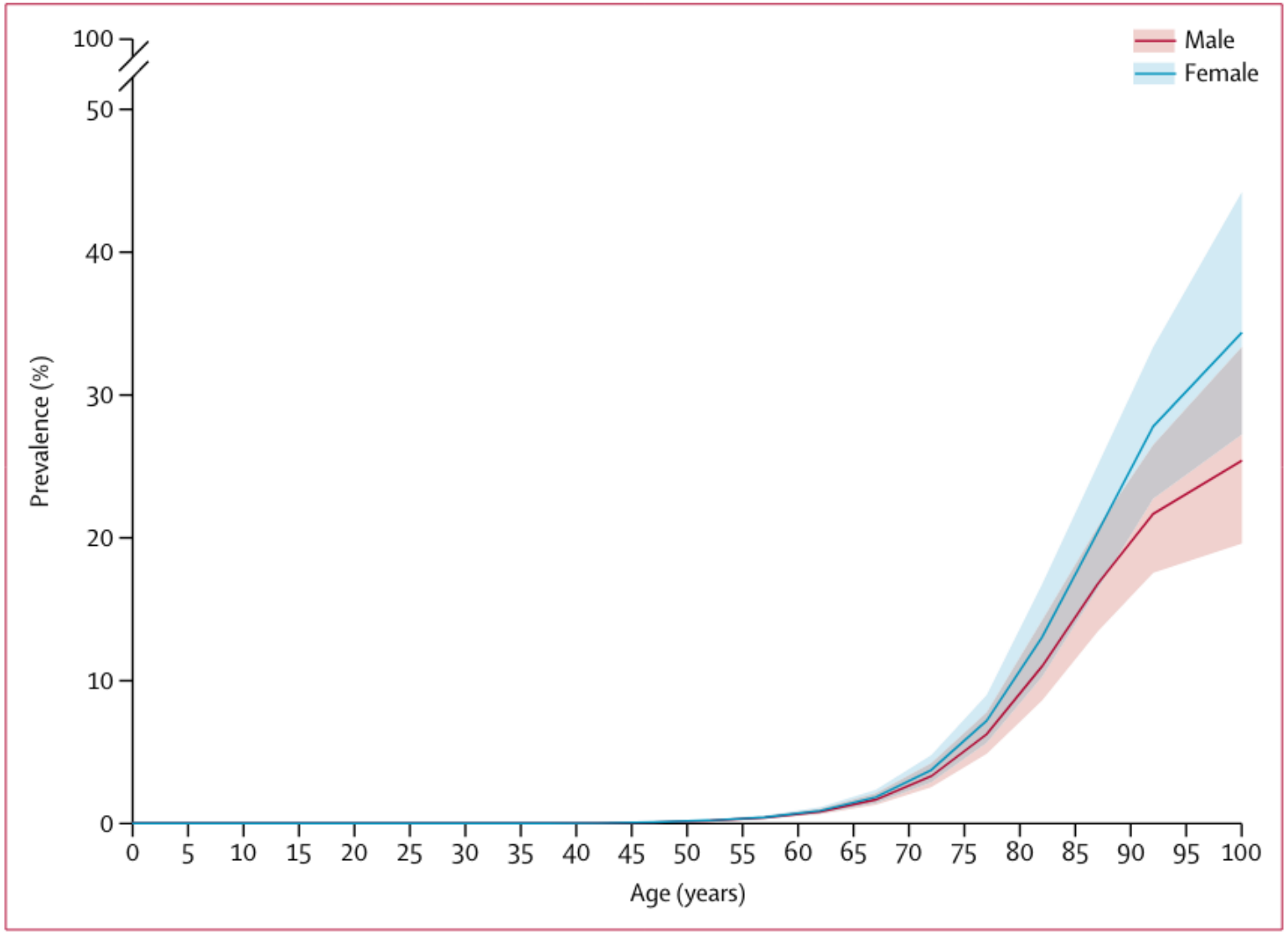
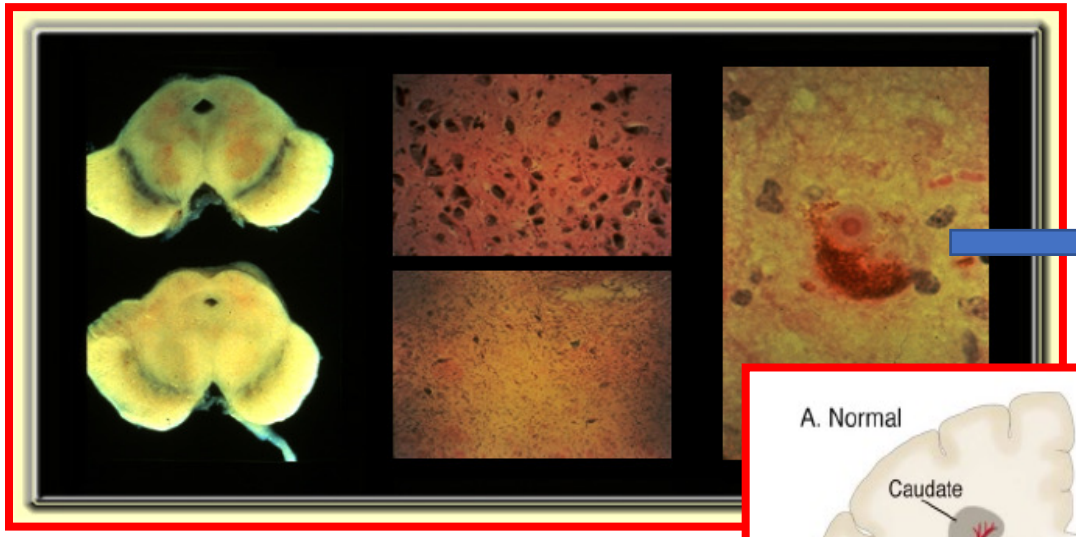
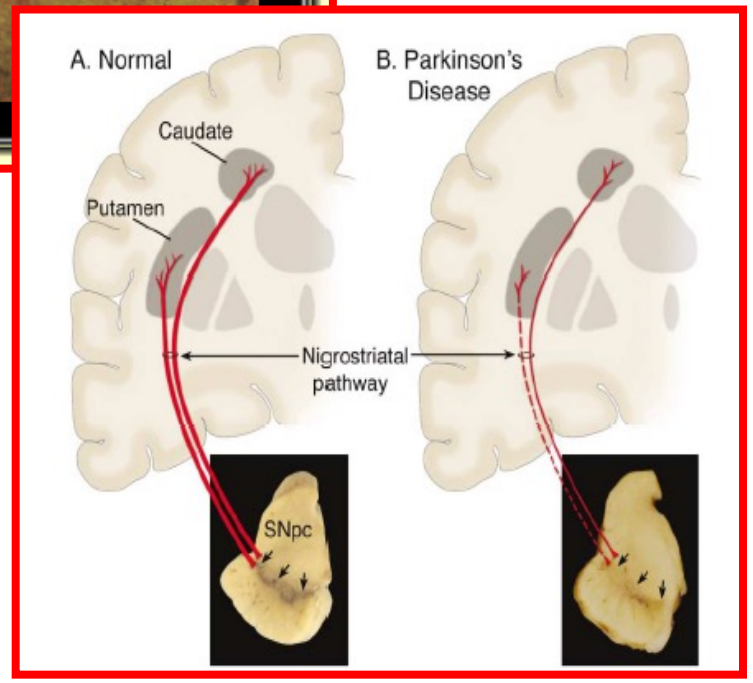


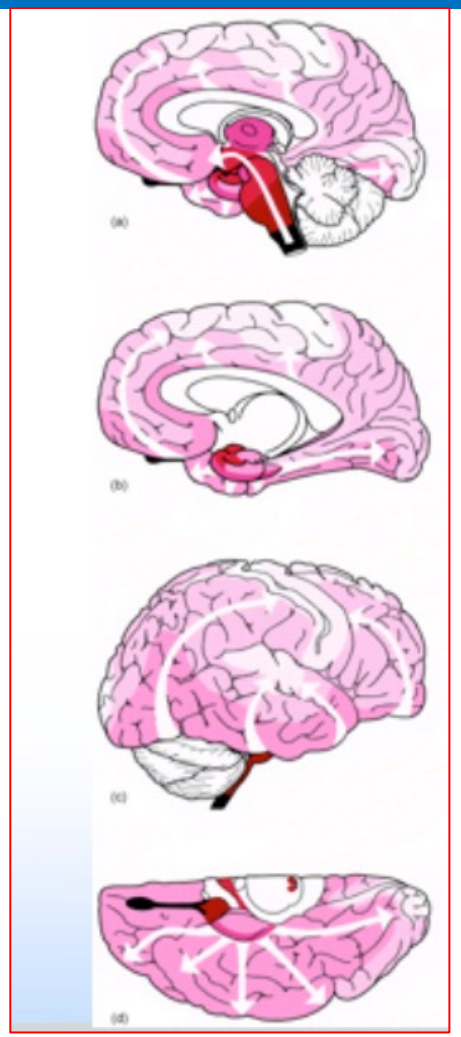
***Figure 3*: Global age-standardised prevalence of Alzheimer's disease and other dementias by sex, 2016**
Prevalence expressed as the percentage of the population that was affected by the disease. Values are plotted at the midpoint of 5-year age categories. Shading indicates 95% uncertainty intervals.

De ziekte van Parkinson

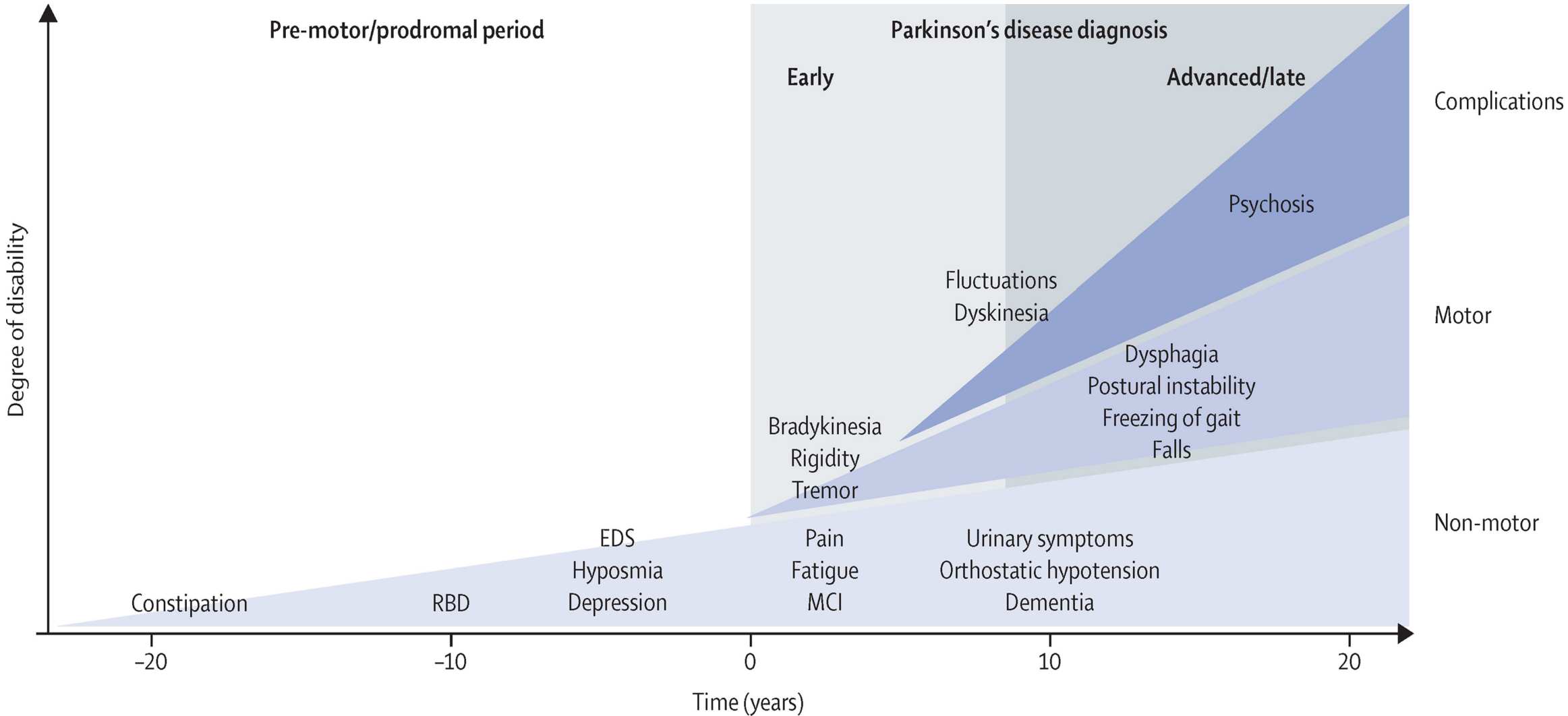


Alfa-synucleine





De ziekte van Parkinson



Behandeling van neurodegeneratieve ziekten

Symptomatische behandelingen

Ziekte modificerende behandelingen

- De ziekteprocessen stoppen of vertragen
- De resterende hersenen en neuronen beschermen
- Herstellen van opgelopen schade

Neuromodulatie

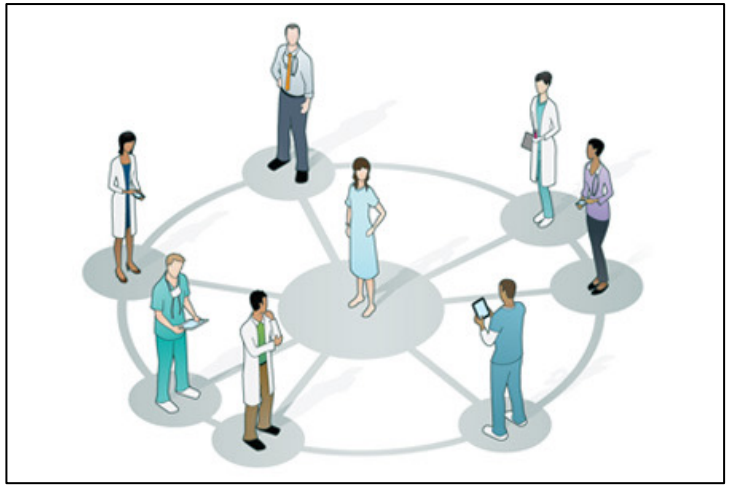
Symptomatische behandelingen

Farmacologische behandelingen:

Gebaseerd op neurotransmitter deficiënties

Bv. tekort aan dopamine bij ziekte van Parkinson: dopaminerge medicatie
Bv. tekort aan acetylcholine bij ziekte van Alzheimer: cholinesteraseremmers

Niet-farmacologische behandelingen:



Paramedische behandelingen
Interprofessionele revalidatie

Behandeling van neurodegeneratieve ziekten

Symptomatische behandelingen

Ziekte modificerende behandelingen

- De ziekteprocessen stoppen of vertragen
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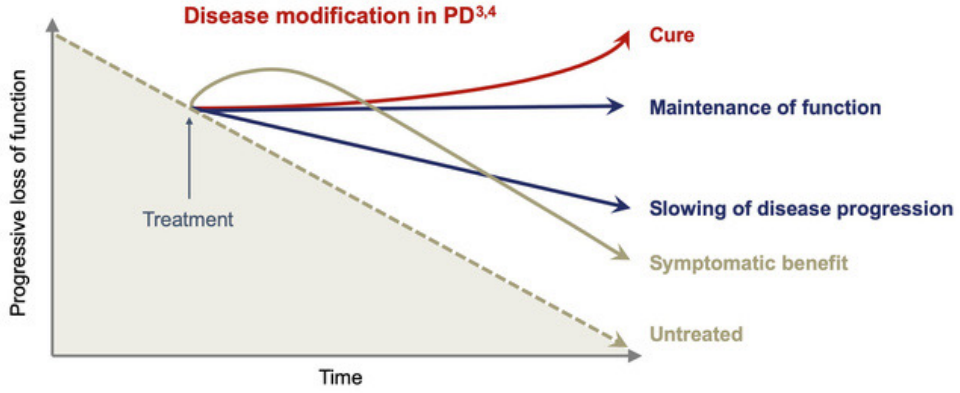
- Herstellen van opgelopen schade

Neuromodulatie

Ziekte modificerende behandelingen

The 'holy grail' – a disease-modifying drug

- One of the greatest unmet needs in the treatment of PD is a disease-modifying therapy that reduces the rate of neurodegeneration seen in PD, or stops the process altogether[1,2]



1. Kalia et al. Mov Disord 2015;30(11):1442–1450; 2. Lang & Espay. Mov Disord 2018;33(5) 660–677;
2. Adapted from: Lang. Nat Med 2010;16(11):1223–1226; 3. Adapted from: Van Dam & De Deyn. Nat Rev Drug Discov 2006;5(11):956–970

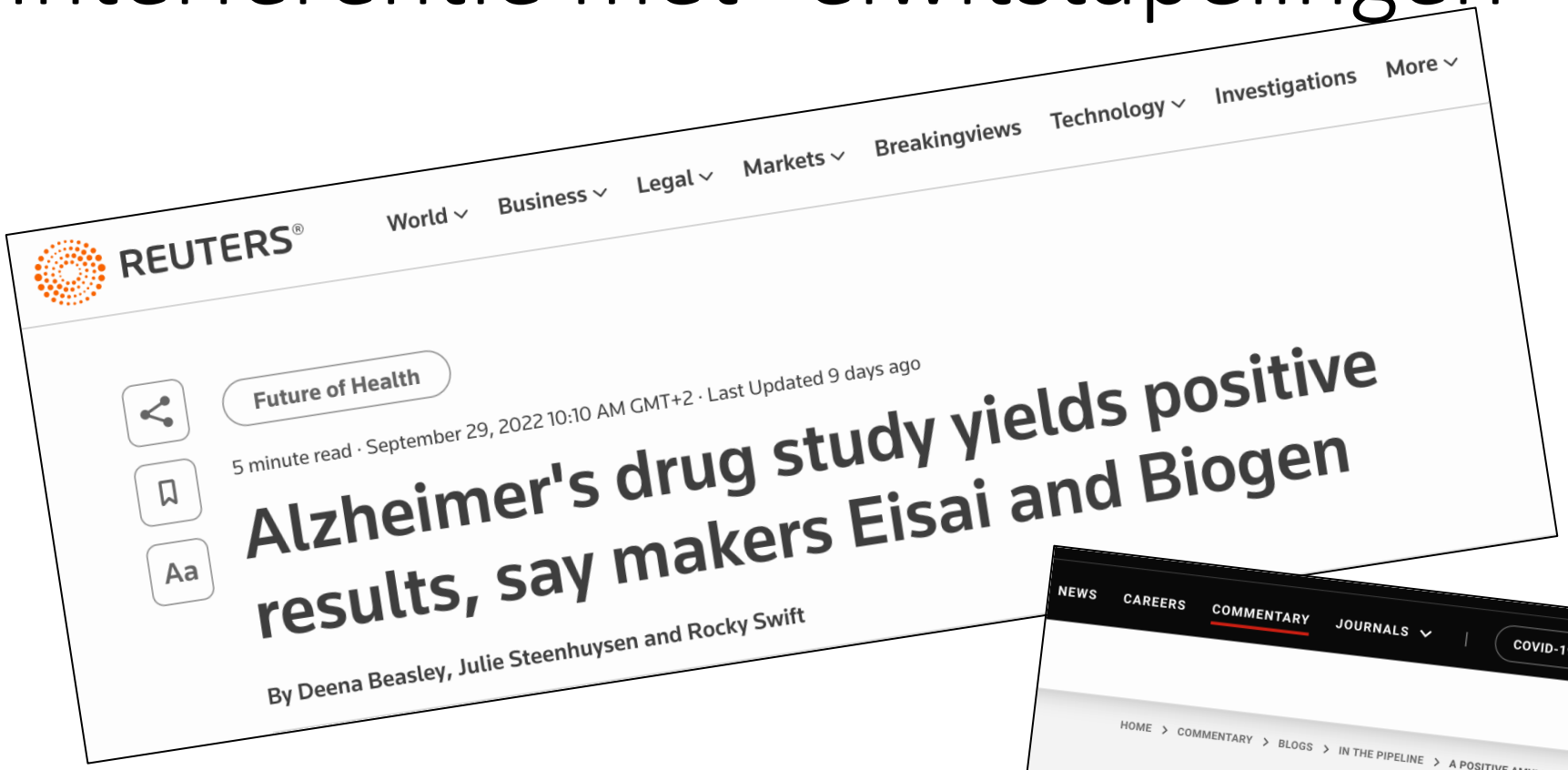
Lundbeck Institute Campus

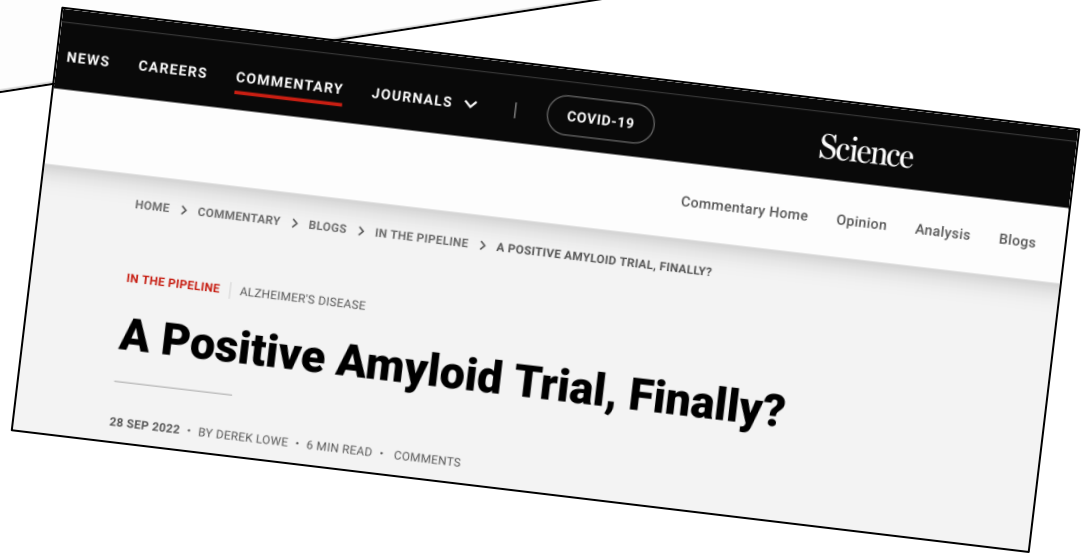
20

Interfereren met de vermoedelijke oorzakelijke processen

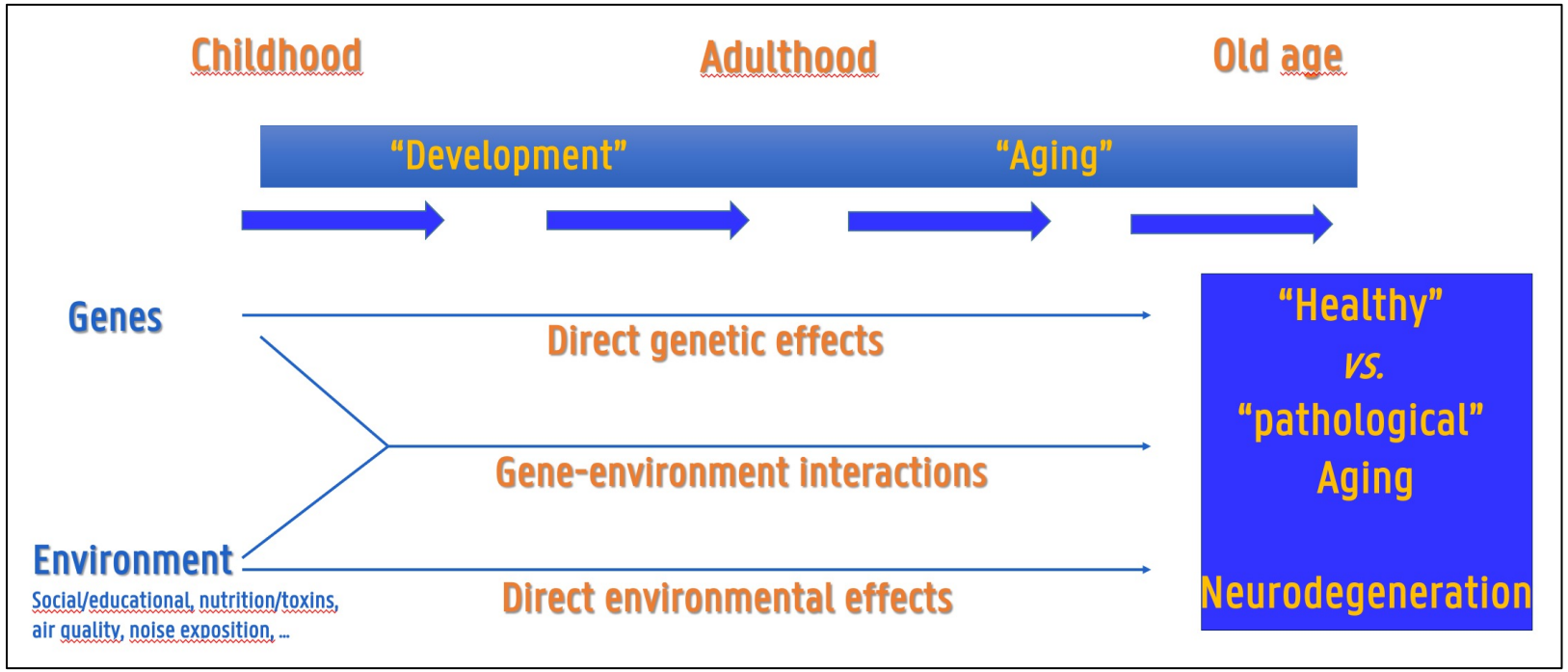
- Vroegtijdige detectie van ziekte in de presymptomatische fasen
- Onderzoek naar de oorzaken van neurodegeneratie

Interferentie met “eiwitstapelingen”





Wat is de oorzaak van neurodegeneratieve ziekten ?

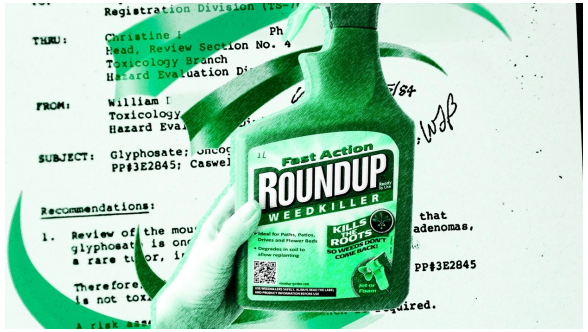


Erfelijke/familiale ziekten:
-Ziekte van Huntington
-Familiaal ZvAlzheimer
-Familiaal ZvParkinson
-.....

Erfelijke risicofactoren:
-ApoE lipoproteïne
-....

Causale omgevingsfactoren:
-Toxische stoffen bv ”schildersziekte”, zware metalen,...
-trauma

Omgevingsfactoren ?



Contents lists available at ScienceDirect

Journal of Chemical Neuroanatomy

journal homepage: www.elsevier.com/locate/jchemneu

Review

Pesticides and Parkinson's disease: Current and future perspective

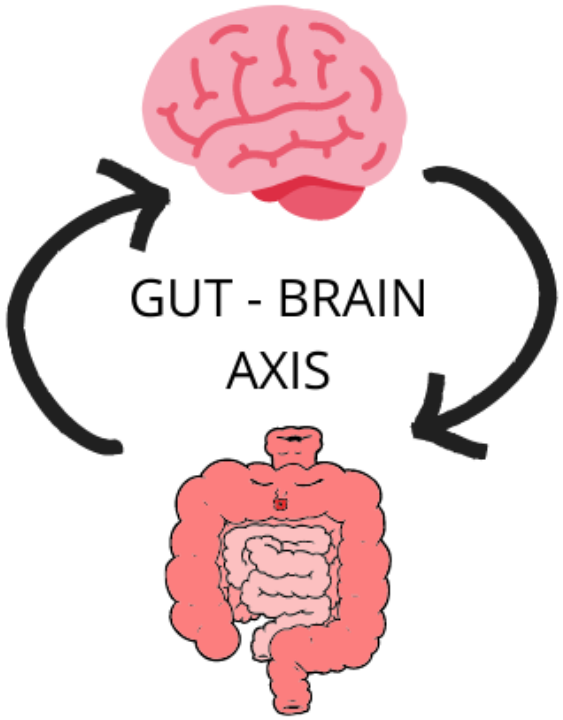
Md Shahidul Islam [a,*], Fazli Azim [b,h], Hedaeytullah Saju [c], Arman Zargaran [c], Meysam Shirzad [c], Mostofa Kamal [d], Kaniz Fatema [e], Sumbul Rehman [f], M.A. Momith Azad [g], Somayeh Ebrahimi-Barough [a]

RESEARCH ARTICLE

Fine Particulate Matter Triggers α-Synuclein Fibrillization and Parkinson-like Neurodegeneration

Xin Yuan, MD,[1] Yingxu Yang, MSc,[1] Chaoyang Liu, PhD,[2] Ye Tian, MD,[1] Danhao Xia, MD,[1] Zehua Liu, MSc,[2] Lina Pan, PhD,[1] Min Xiong, PhD,[1] Jing Xiong, PhD,[1] Lanxia Meng, PhD,[1] Zhaohui Zhang, PhD,[1] Keqiang Ye, PhD,[3] Haiqiang Jiang, PhD,[4] and Zhentao Zhang, MD, PhD[1*]

Neurodegeneratie en processen buiten de hersenen: de gut-brain hypothese



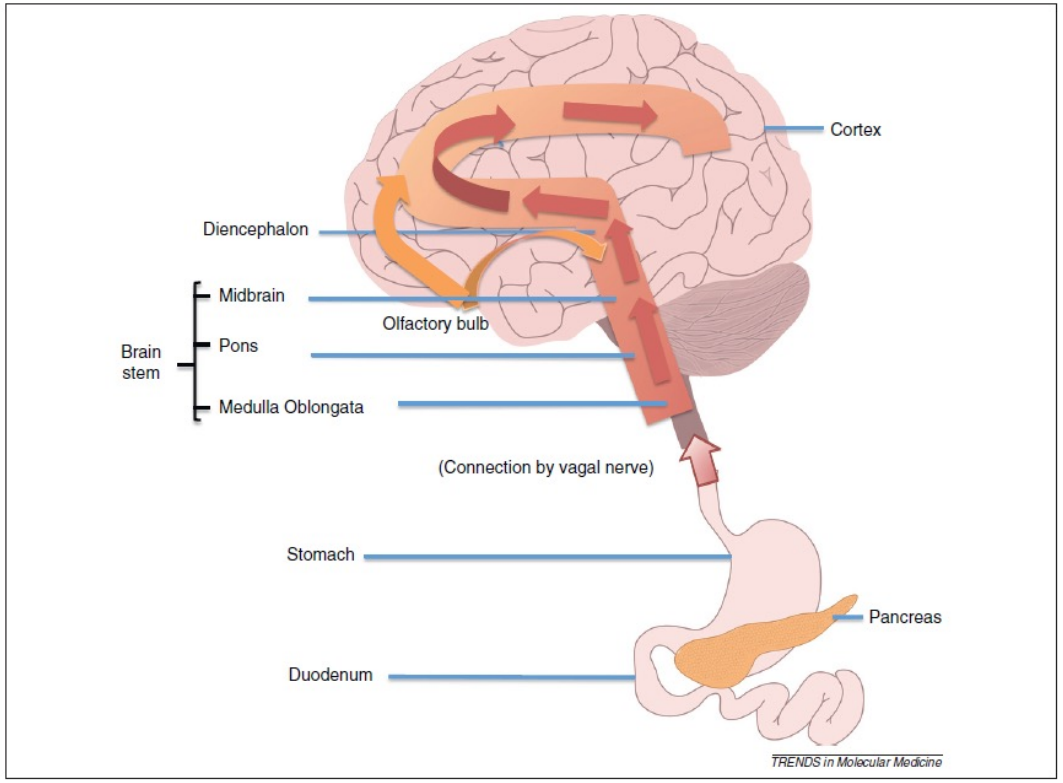
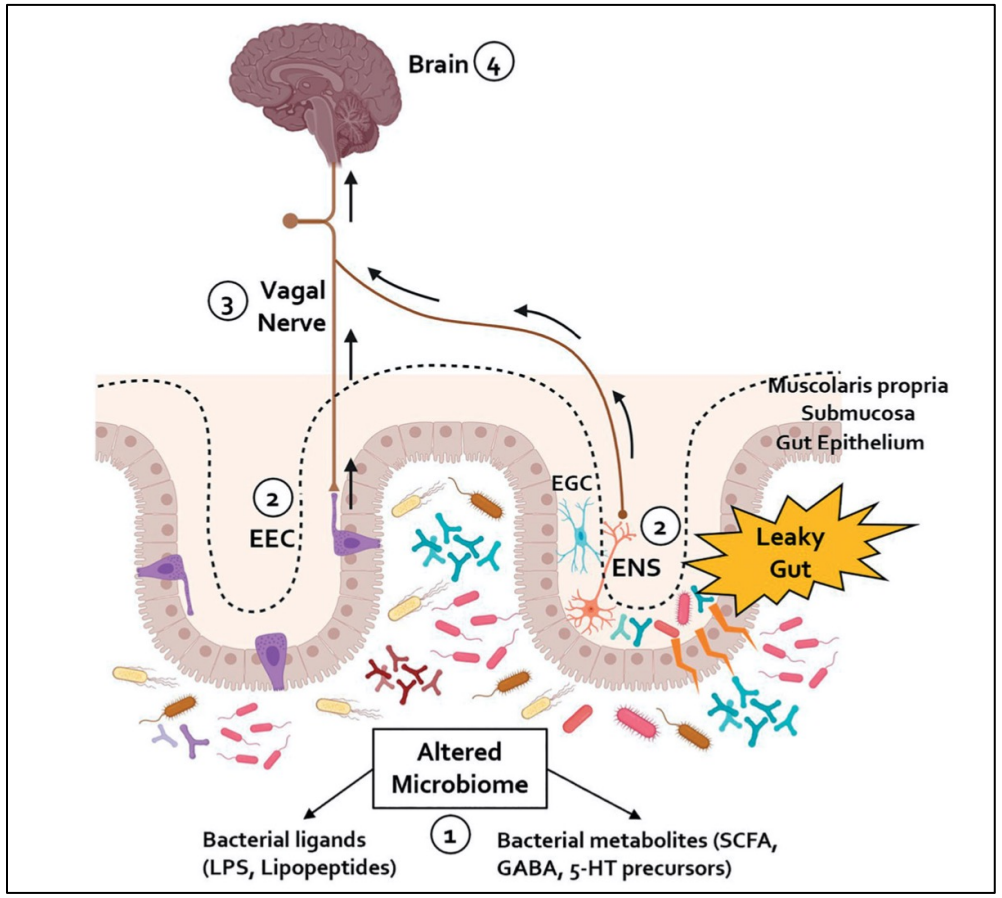


Figure 2. Spread of idiopathic PD pathology. As proposed by Braak and coauthors, Lewy body pathology may arise in the periphery/enteric nervous system, possibly in the gastrointestinal tract, and transfer to the brain stem via the glossopharyngeal and vagus nerves. Finally, it spreads to the cortex at a later stage of disease progression (red arrows). Alternatively, the pathology may initiate at the olfactory bulb and the anterior olfactory nucleus and from there spread to the midbrain and the cortex (orange arrows).

Is er een rol voor voeding en darmbacteriën ?



The Ghent University Trial in PD with Fecal Microbiota Transplantation (GUT-PARFECT)

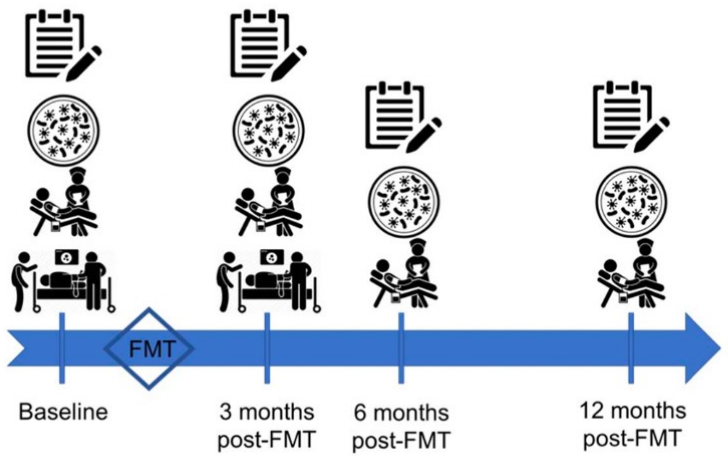


Figure 1. Overview timing of the fecal microbiota transplantation (FMT) trial. At baseline and 3, 6 and 12 months following the FMT a neurologist will score the clinical motor symptoms, clinical characteristics will be assessed via validated questionnaires, and stool and blood samples will be collected. At baseline and 3 months after the FMT, a colonoscopy will be performed to collect mucosal fecal samples (proximal colon) and gastrointestinal tissue biopsies (proximal and distal colon). Additionally, on the first five days following the FMT, candidates will collect fecal samples at home using the DiviMat system.

En wat met onze social media gewoonten ?

RESEARCH ARTICLE

Movement Disorders

CLINICAL PRACTICE

TikTok Tics: A Pandemic Within a Pandemic

Caroline Olvera, MD,* Glenn T. Stebbins, PhD, Christopher G. Goetz, MD, and Katie Kompoliti, MD

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the official journal of the european academy of neurology

SHORT COMMUNICATION

Rapid onset of functional tic-like behaviours in young adults during the COVID-19 pandemic

Tamara Pringsheim | Davide Martino

COVID-19 related increase in childhood tics and tic-like attacks

Isobel Heyman [1], Holan Liang [1], Tammy Hedderly [2]

Interactie genetica-omgevingsfactoren
Het GLORIA project

GLORIA

GHENT LONGITUDINAL OBSERVATIONAL RESEARCH INVESTIGATING AGING

Ghent, GLORIA-districts

Zwijnaarde, Gentbrugge, Sint-Amandsberg, Wondelgem & Sint-Denijs-Westrem-Afsnee (https://stad.gent/nl/binnenstad/kaart-van-de-wijk)

N=20000
Duur: 20 jaar
Leeftijden: 45+

Behandeling van neurodegeneratieve ziekten

Symptomatische behandelingen

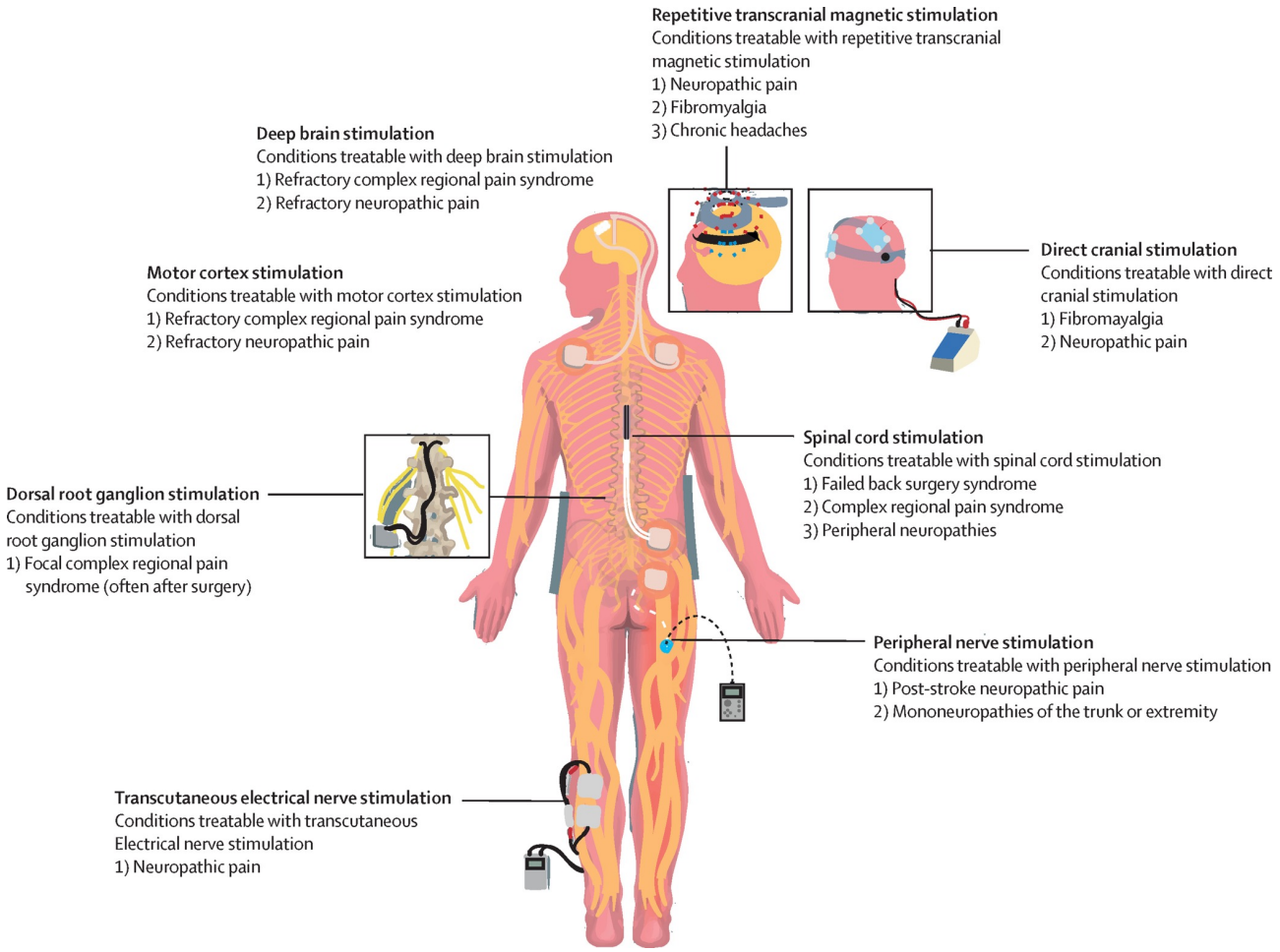
Ziekte modificerende behandelingen

- De ziekteprocessen stoppen of vertragen
- De resterende hersenen en neuronen beschermen
- Herstellen van opgelopen schade

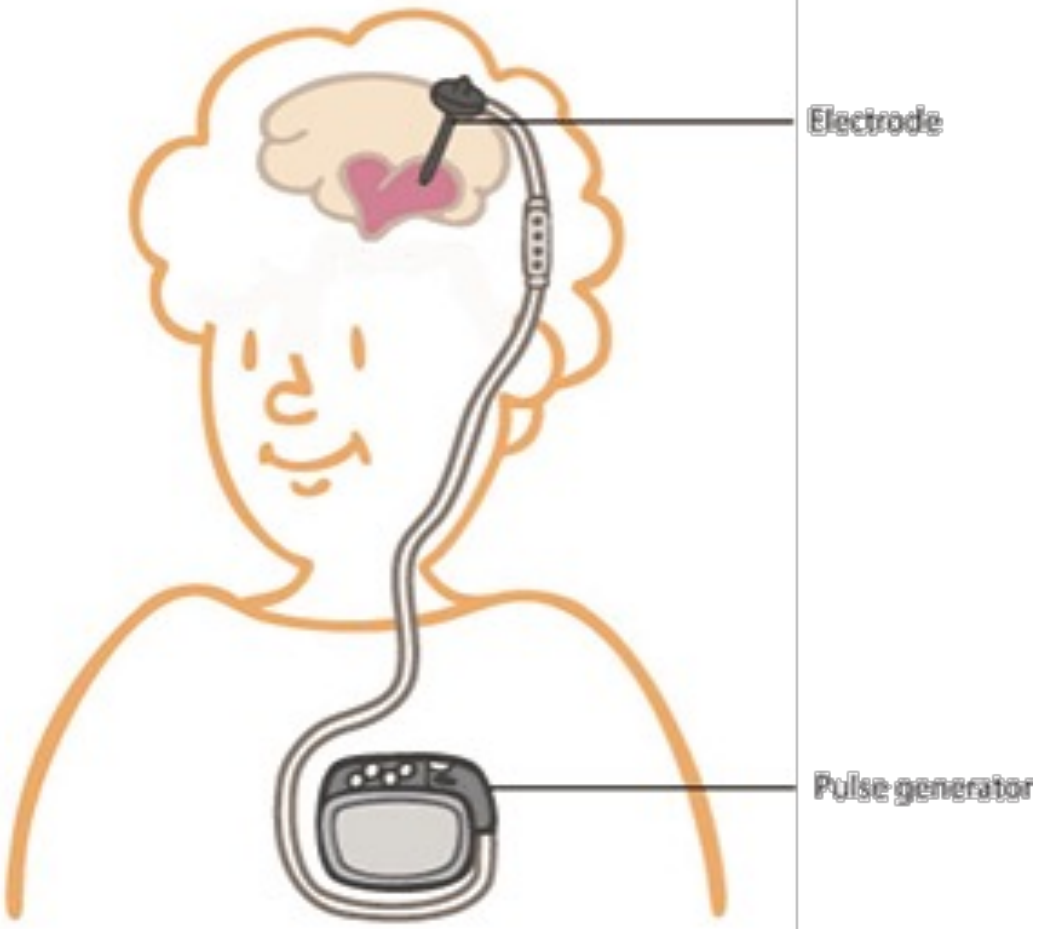
Neuromodulatie

Neuromodulatie

”Technologie die de activiteit van delen van het zenuwstelsel moduleert”



Diepe hersenstimulatie

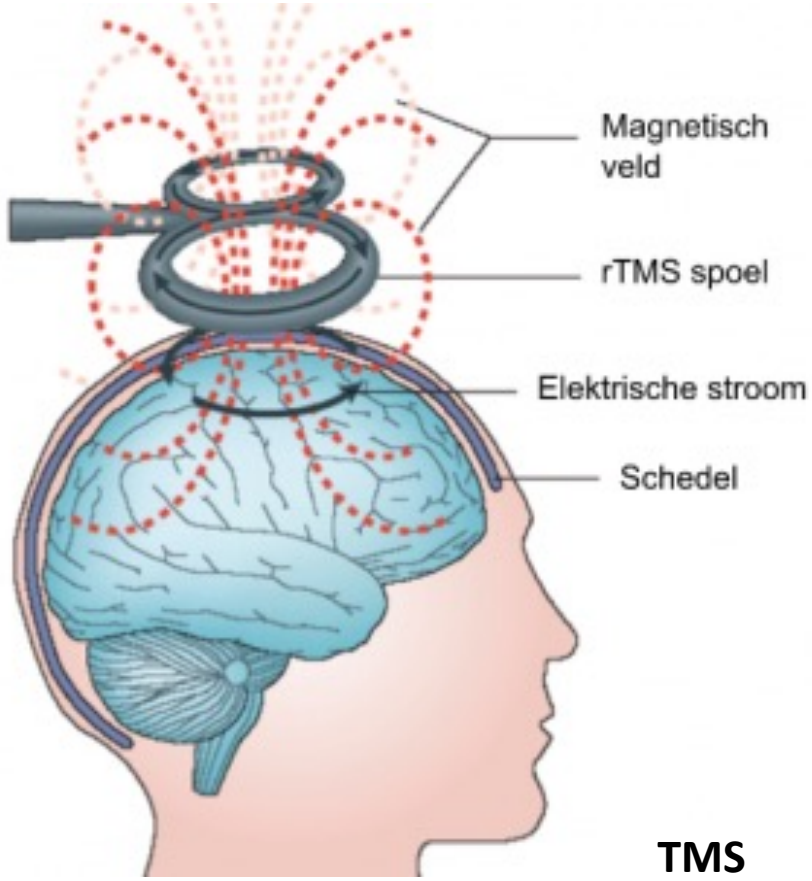


Goed geselecteerde patiënten

- Ziekte van Parkinson
- Tremor
- Bewegingsstoornissen
- Epilepsie
- Pijn

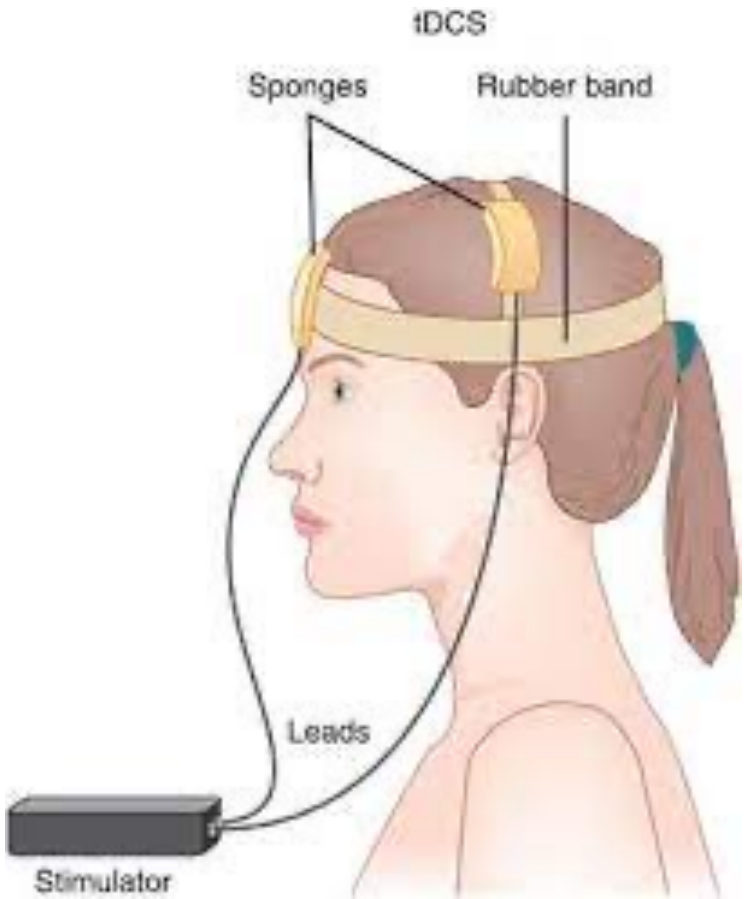
- Obsessief-compulsieve stoornissen
- Gilles de la Tourette syndroom

Transcraniële stimulatie

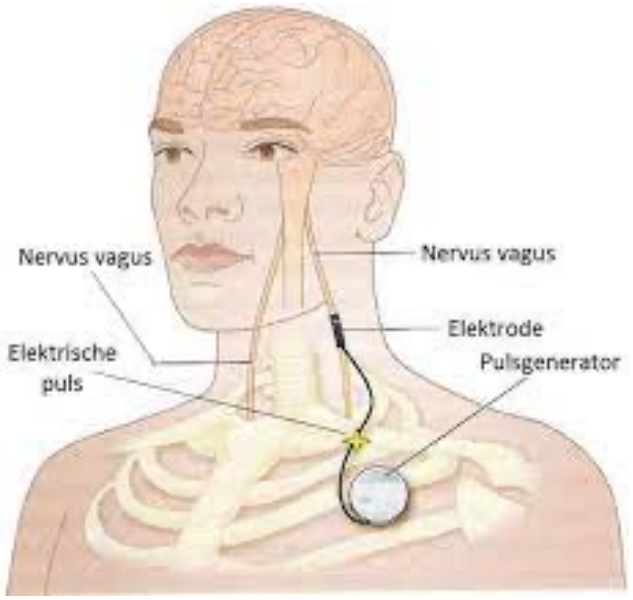


TMS

tDCS



Perifere zenuwstimulatie

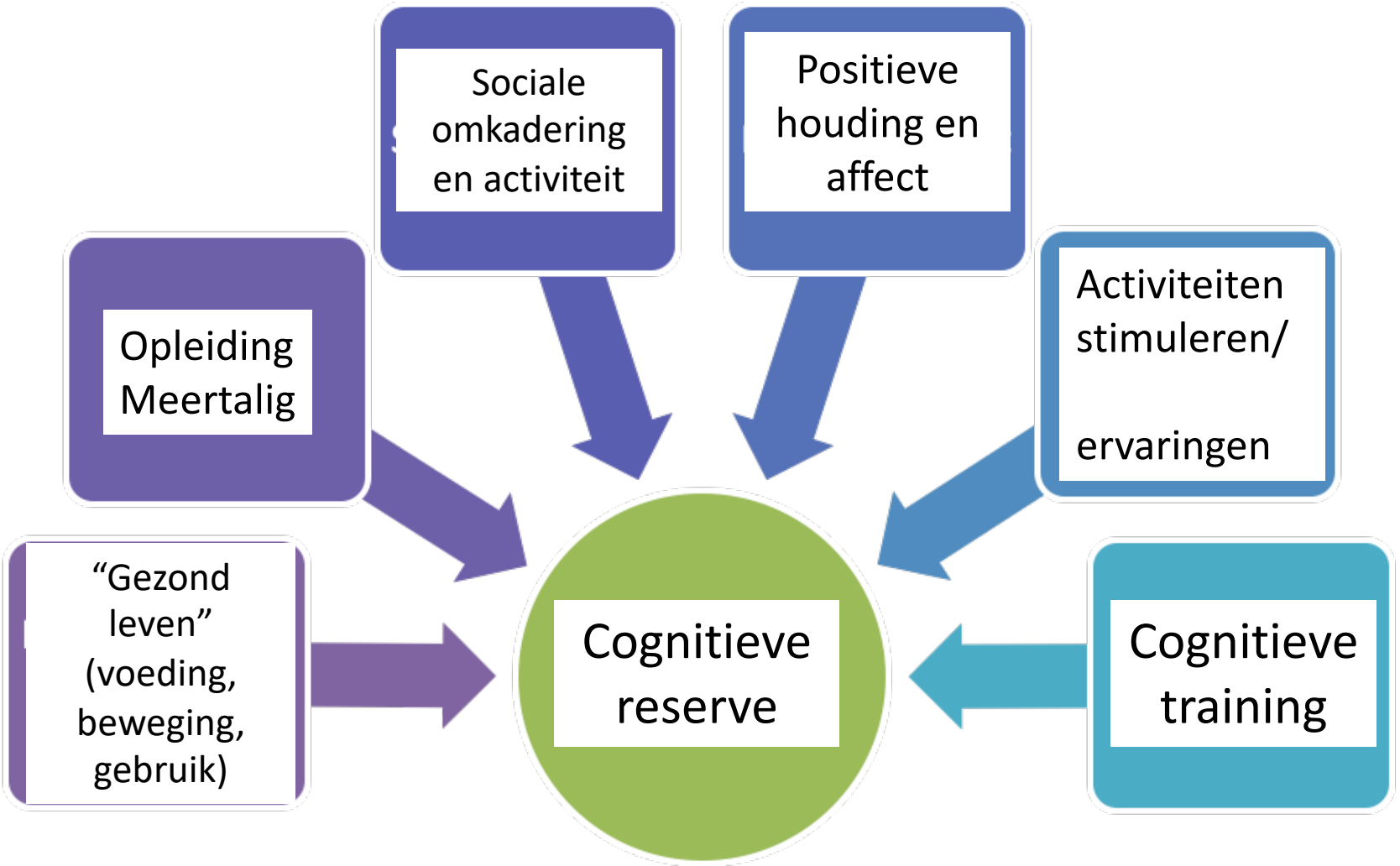
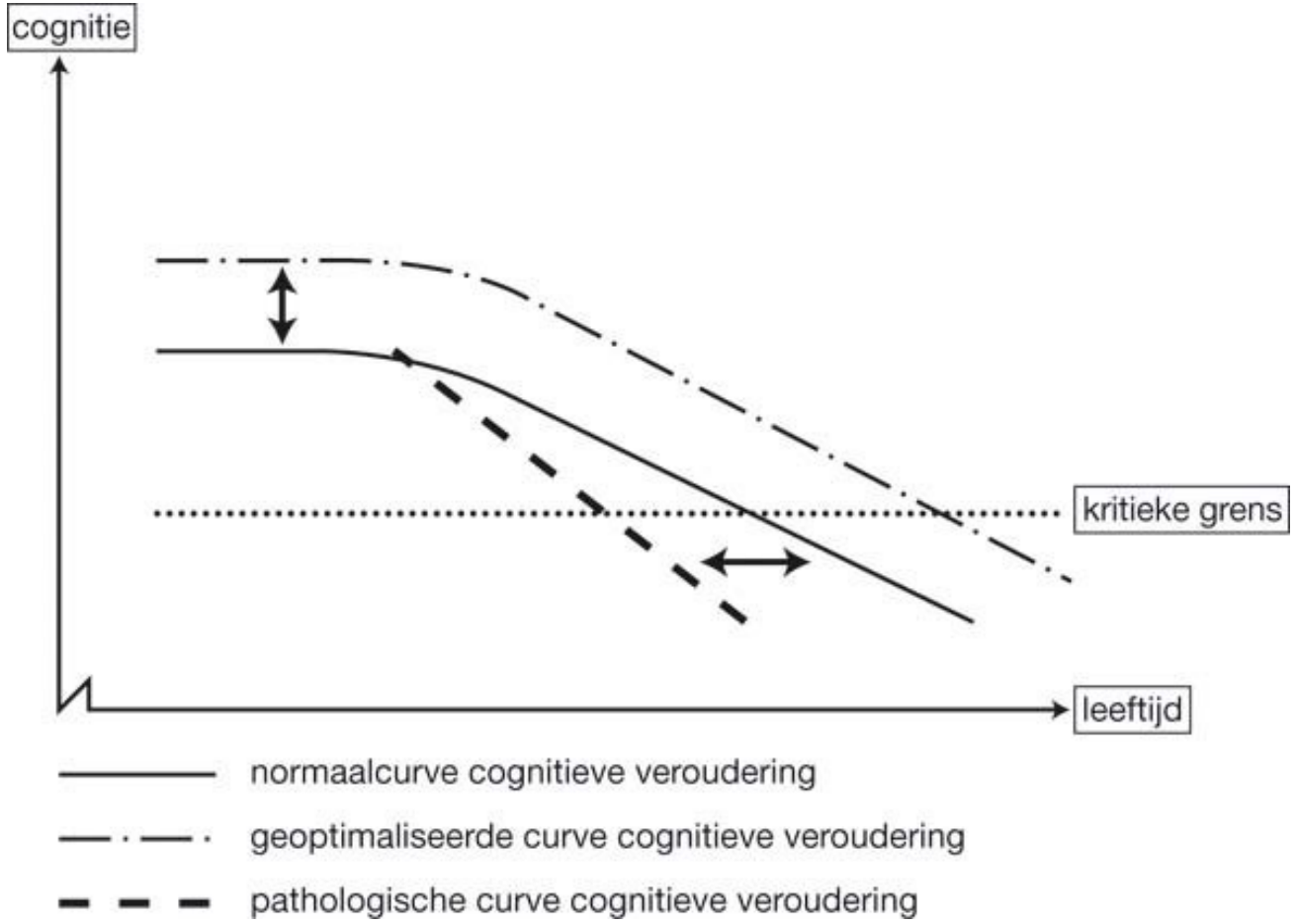


N.Vagus stimulatie

Perifere zenuwstimulatie

Ruggenmergstimulatie

Tot slot: wat kan u zelf doen voor uw hersenen?



Loont het de moeite ?