





Immuno-psychiatrie

Prof dr Hemmo A. Drexhage, arts, klinisch/medisch immunoloog
 Professor emeritus ErasmusMC, Rotterdam

Supported by




FP7 Large scale project MOODINFLAME
 FP7 IAPP project PSYCHAID
 Horizon 2020 project MOODSTRATIFICATION








State of the Art 1910-1930






Ziekten van het Brein
Neurologische ziekten






Emil Kraepelin (1856-1926)

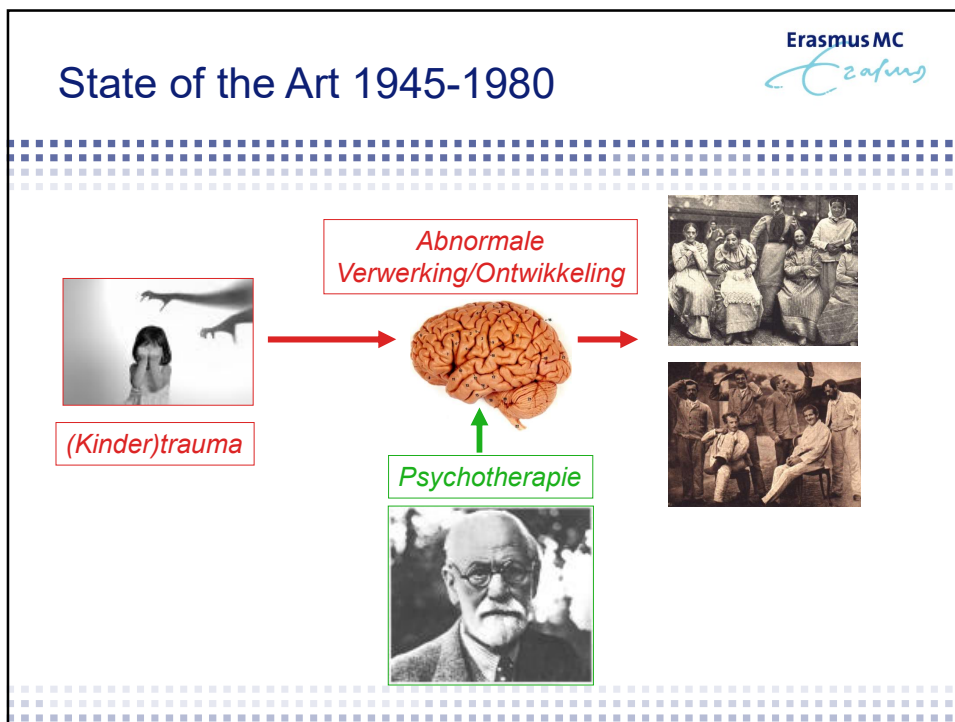
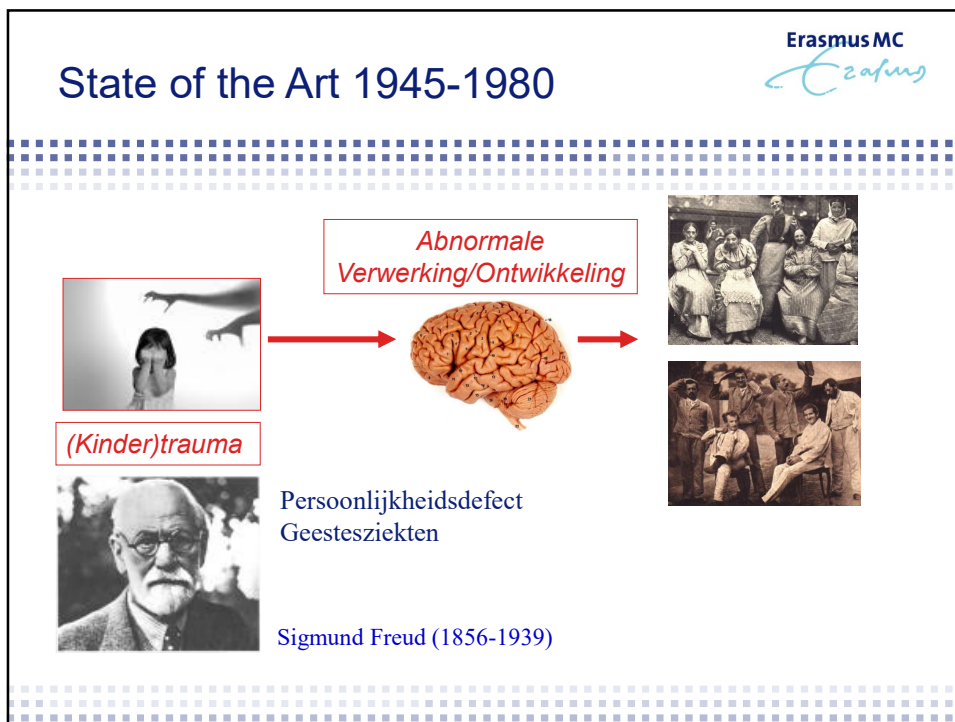


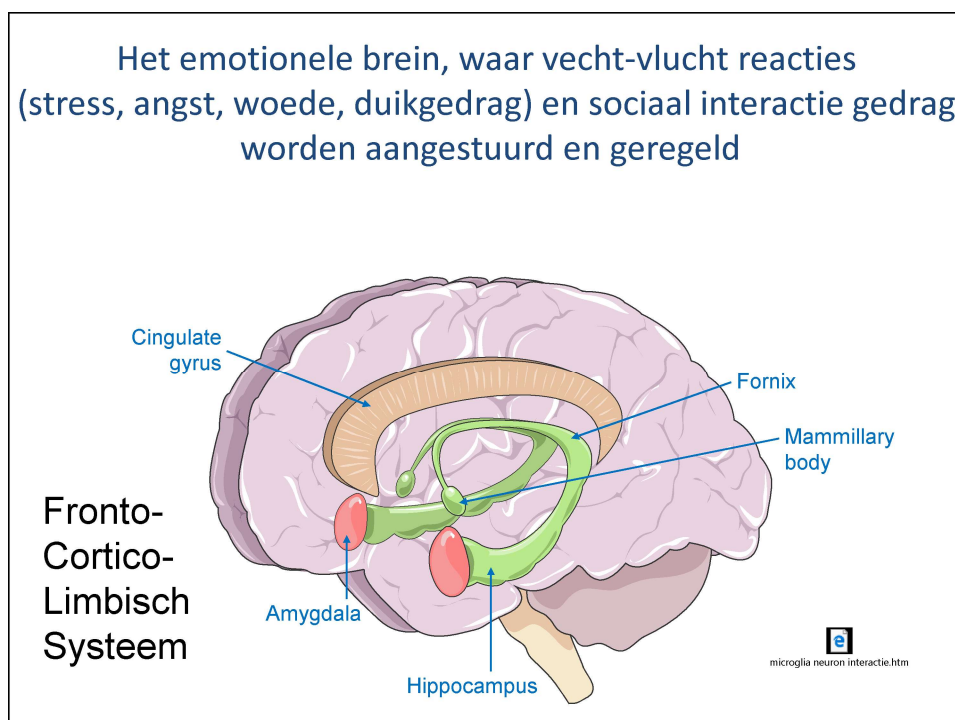
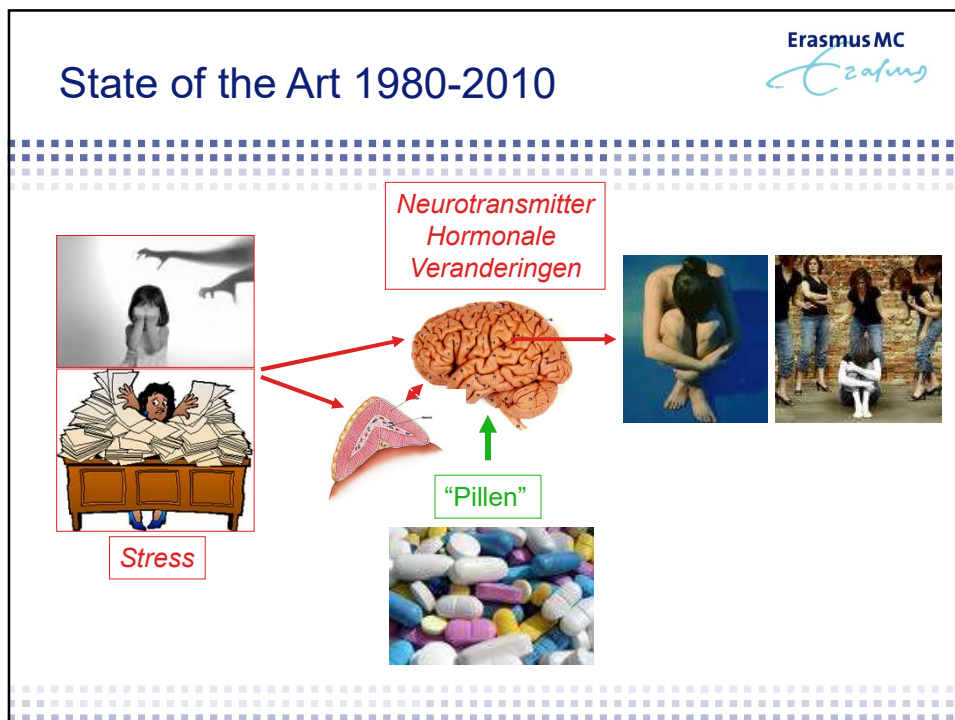




"Manisch-depressives irresein": stemmingsstoornissen

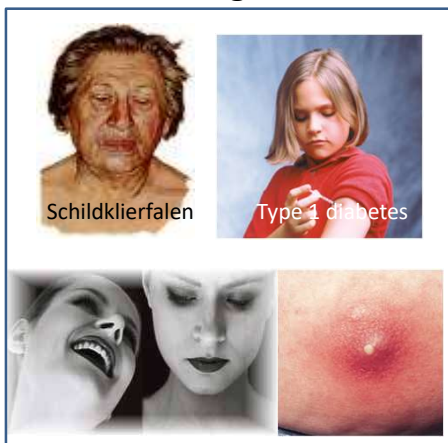




"Dementia Praecox": Schizofrenie





Infecties en auto-immuun ziekten komen 3-4 maal zoveel voor bij psychiatrische patiënten en hun eerste graad verwanten (familiaal)



Schildklierfalen

Type 1 diabetes



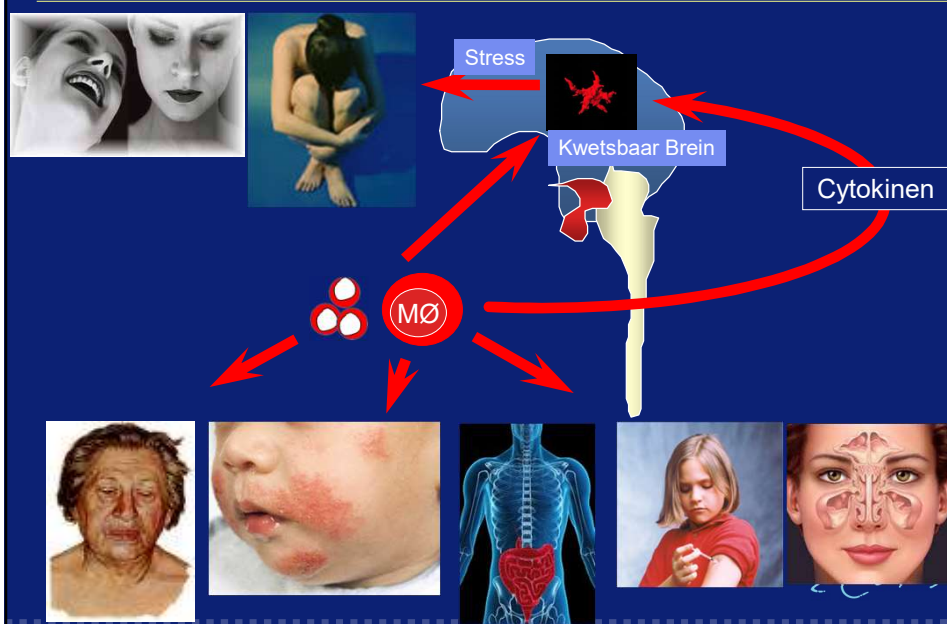
Cohorts



Population-wide

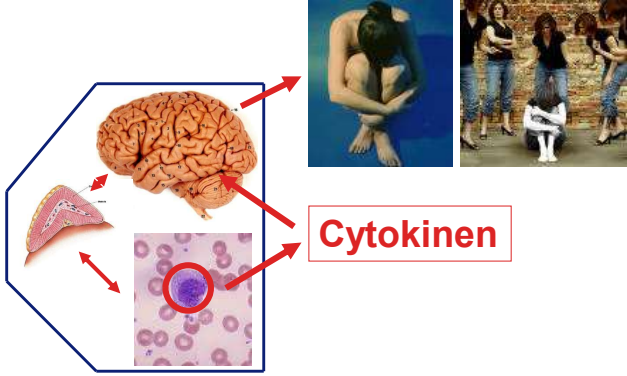
Gemeenschappelijke aangeboren aanleg?

Afweer systeem, afweer cellen en afweer stoffen centraal



ErasmusMC
Erasmus

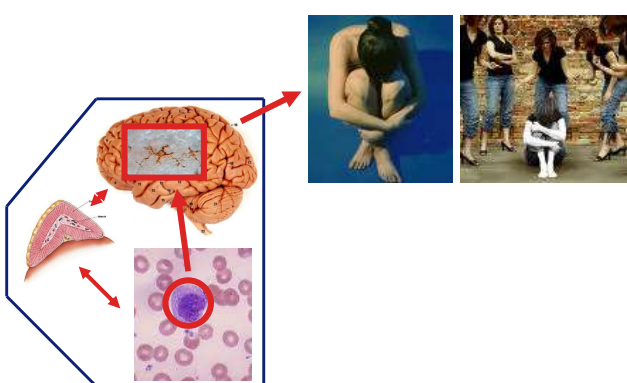
Nieuwe Inzichten: Immunologie



Cytokinen

ErasmusMC
Erasmus

Nieuwe Inzichten: Microglia

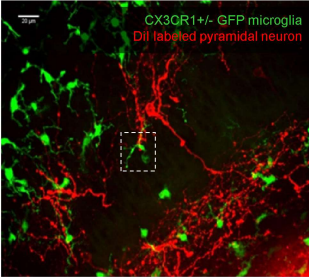


Cell

Bone-marrow transplants cure obsessive-compulsive behaviour in mice. *Mario R. Capecchi*

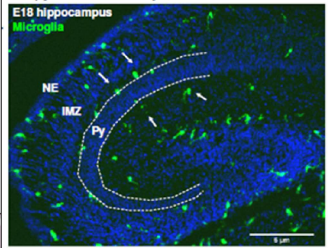
Published online 27 May 2010 | **Nature** | doi:10.1038/news.2010.268

News
Key to psychological disorder may lie in the immune system



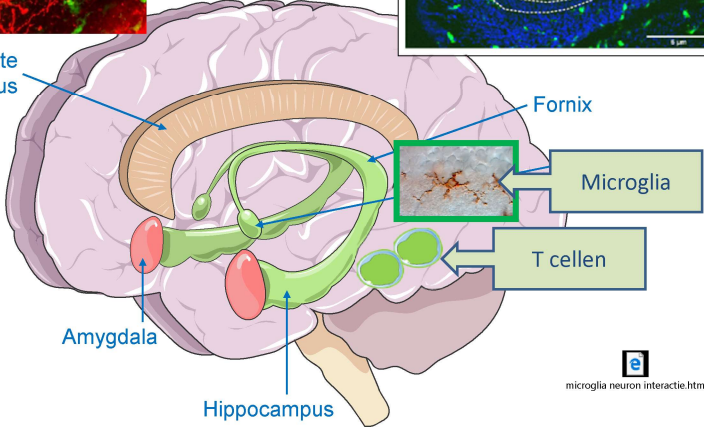
CX3CR1+/- GFP microglia
Dll1 labeled pyramidal neuron

Microglia en T cellen helpen neuronen te groeien in de hippocampus, een deel van het emotionele integratie systeem, waar o.a. stress verwerkt wordt



At E18, microglia line up on either side of the pyramidal cell layer.

E18 hippocampus
Microglia



Cingulate gyrus

Fornix

Microglia

T cellen


Amygdala

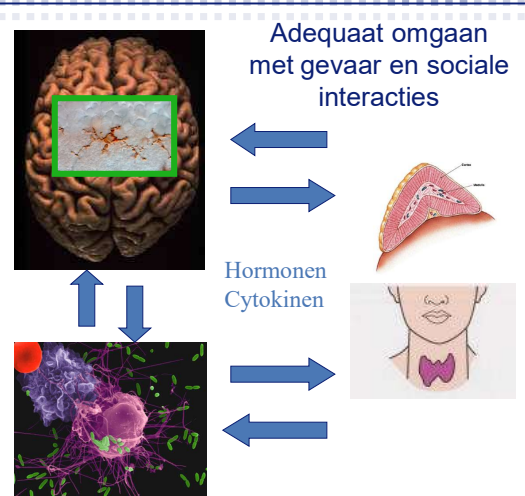
Hippocampus

Fronto-Cortico-Limbisch Systeem

microglia neuron interactie.htm

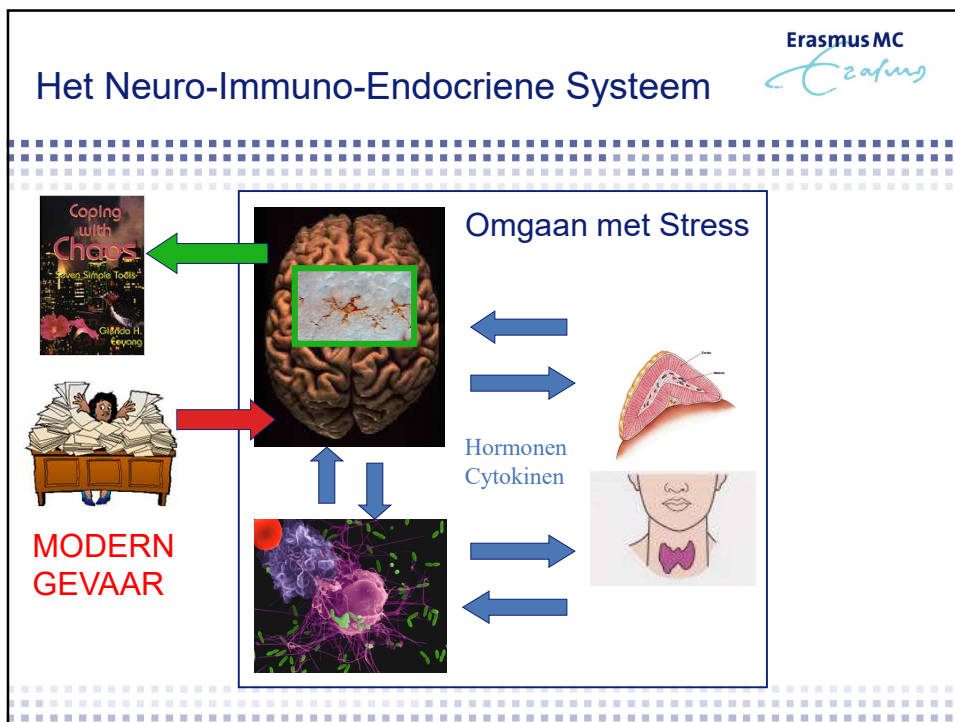
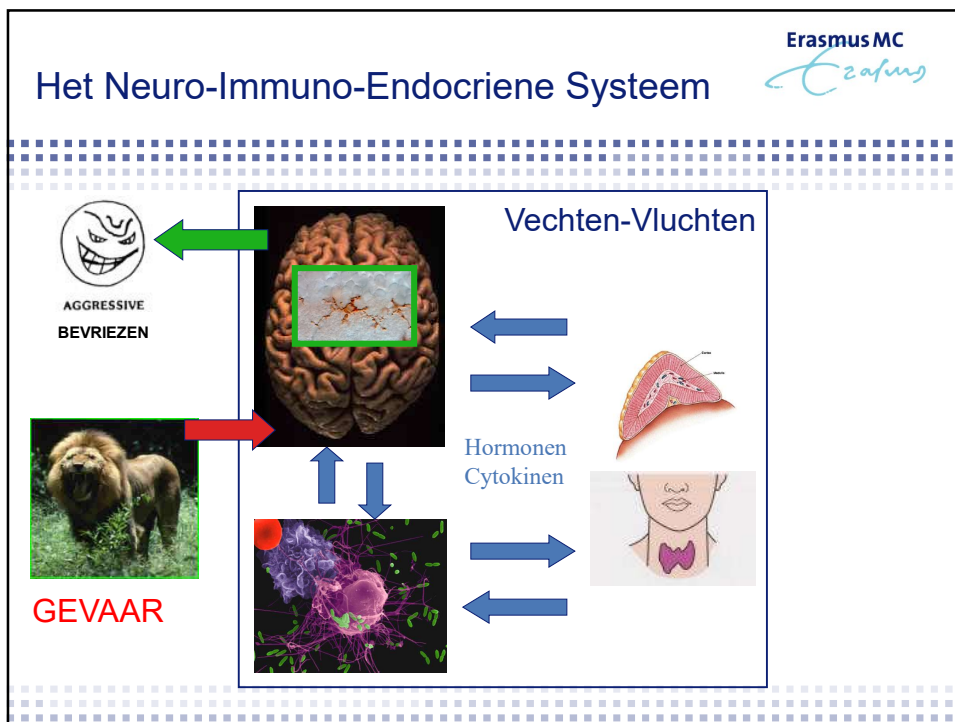
Het Neuro-Immuno-Endocriene Systeem

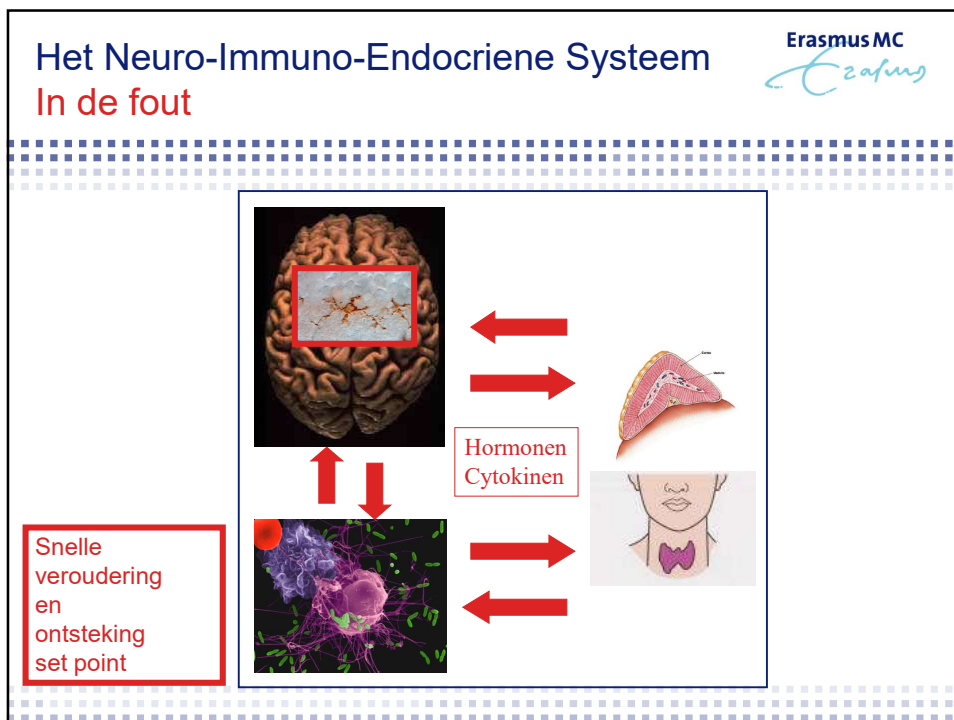
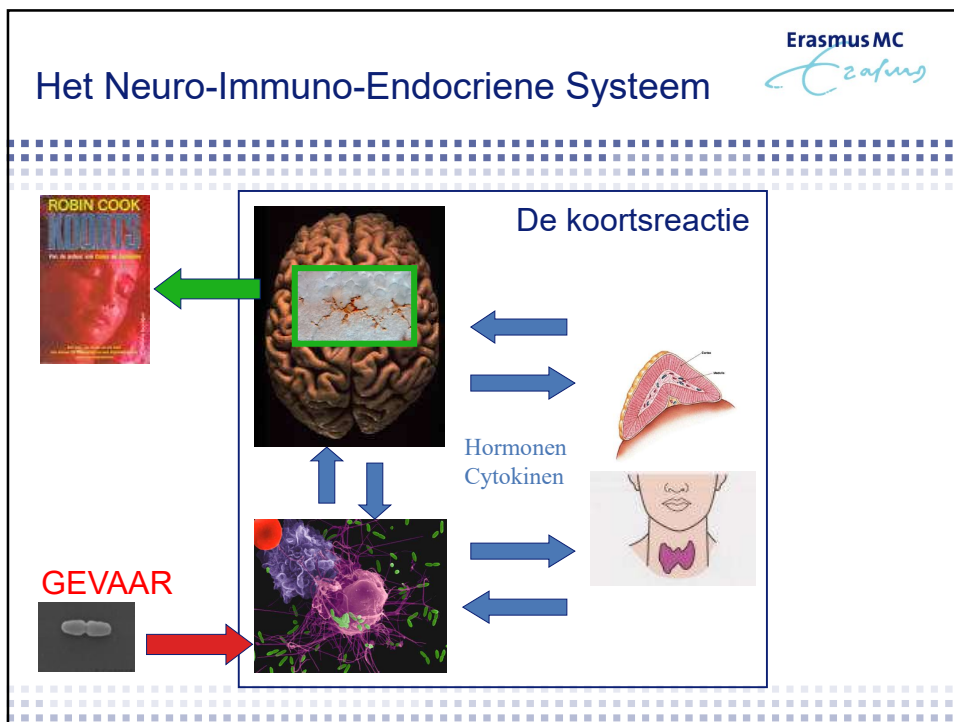




Adequaat omgaan met gevaar en sociale interacties

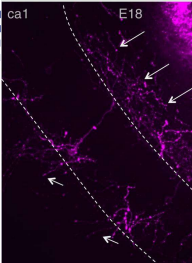
Hormonen
Cytokinen





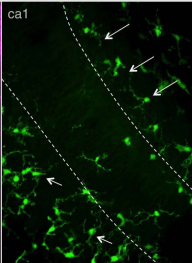
ErasmusMC
Erasmus

Nieuwe Inzichten: Microglia



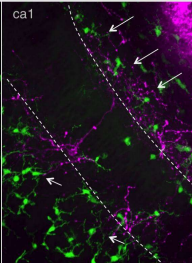
ca1 E18

A few neurons were labeled with DII. The accumulation of neurites is more obvious (arrows)



ca1

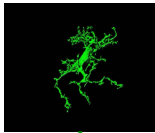
Microglia line up on both sides of the CA1 region...



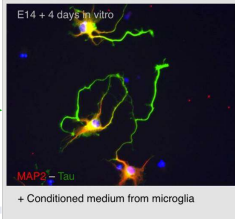
ca1

...closely apposed to neurites

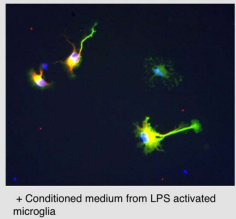
Microglia helpen neuronen te groeien in de hippocampus, het integratie centrum aan o.a. stress responsen



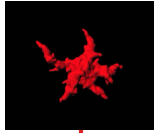
Resting microglia



E14 + 4 days in vitro
MAP2 - Tau
+ Conditioned medium from microglia



+ Conditioned medium from LPS activated microglia




Inflamed microglia

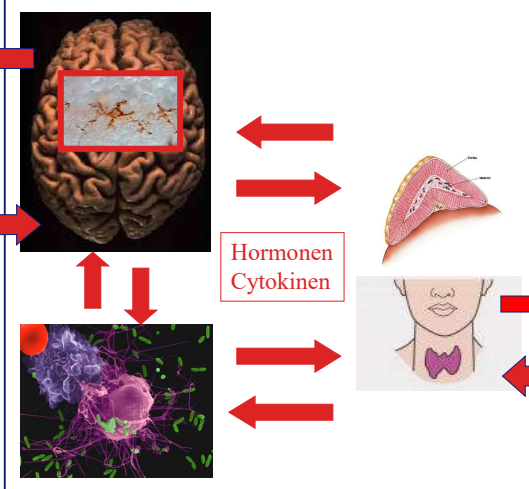
ErasmusMC
Erasmus

Het Neuro-Immuno-Endocriene Systeem


In de fout



Stress



Hormonen
Cytokinen

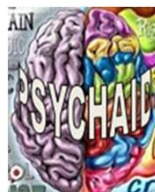



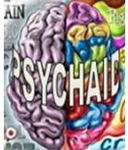


Conclusies

- Een flink deel van ernstige psychiatrische stoornissen
 - Zijn ontregelingen van het evenwicht tussen de cellen en de signaalstoffen (hormonen, cytokinen) van het immuno-neuro-endocriene systeem
 - Gaan gepaard met een verhoogde kans op auto-immuun ziekten en infecties
 - Zijn uitingen van een lichamelijk (organisch) onvermogen om zich op juiste wijze aan te passen aan “gevaar” (stress) van welke aard dan ook.


Consequenties

- Het moet mogelijk zijn om
 - testen te ontwerpen voor afweer cellen in het bloed om stemmingstoornissen vast te stellen
 - nieuwe immuun behandelingen te ontwikkelen.
- Dit werd/wordt gedaan binnen drie grote EU projecten





400 bipolaire
patienten



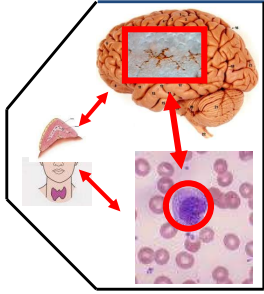
800 depressieve
patienten




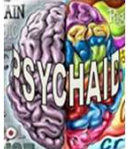

600 gezonden
80 schizofrene
patienten



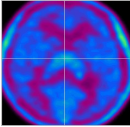
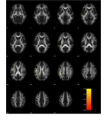

3 modellen



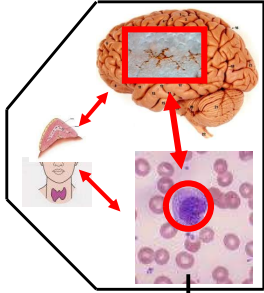

25 partners
12 landen

Nieuwe generatie
hersenscans voor o.a. microglia

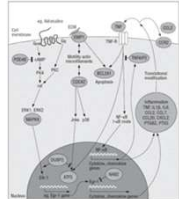

Evenwichts
Interacties

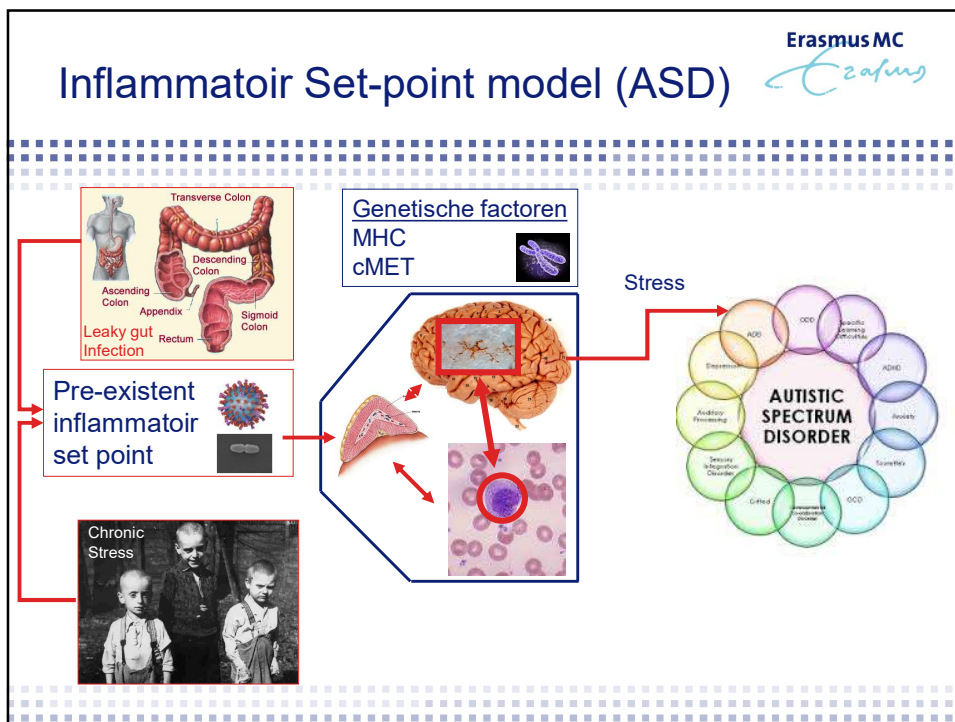
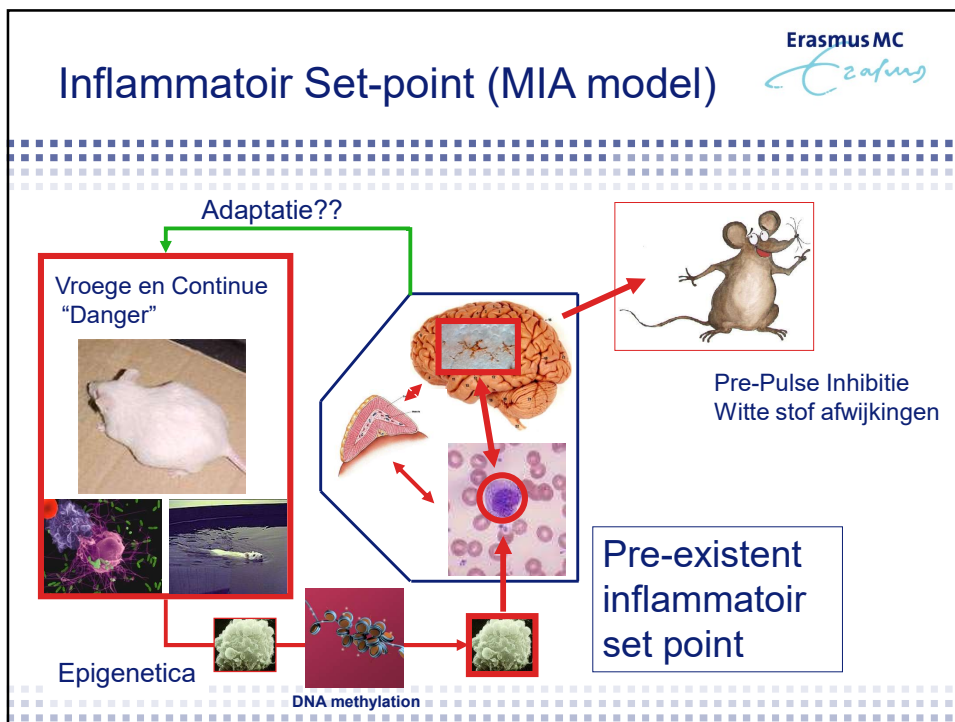



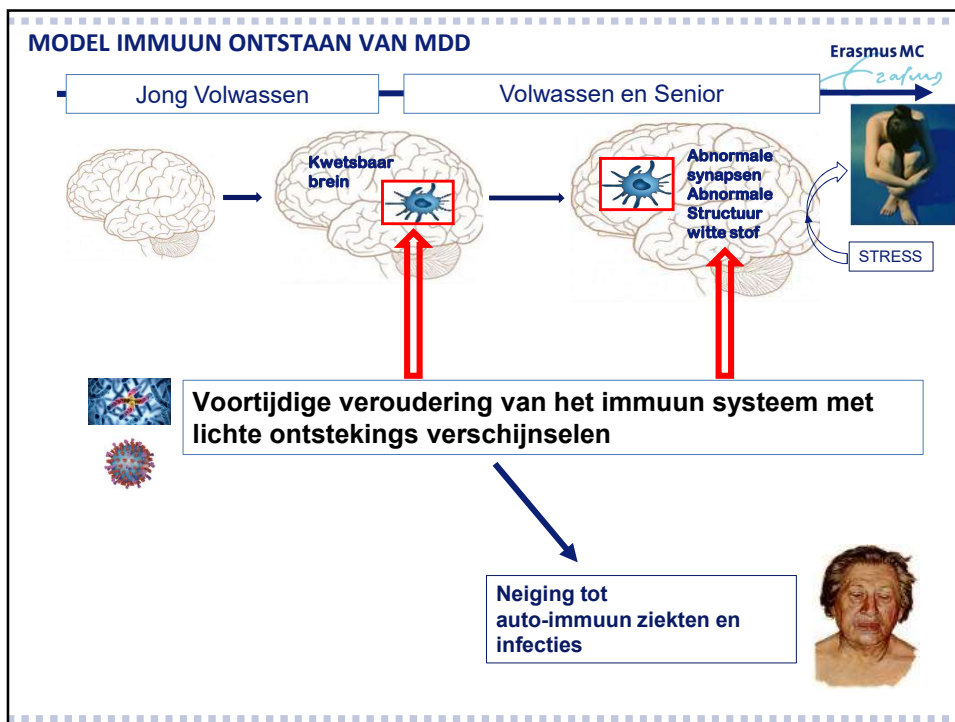
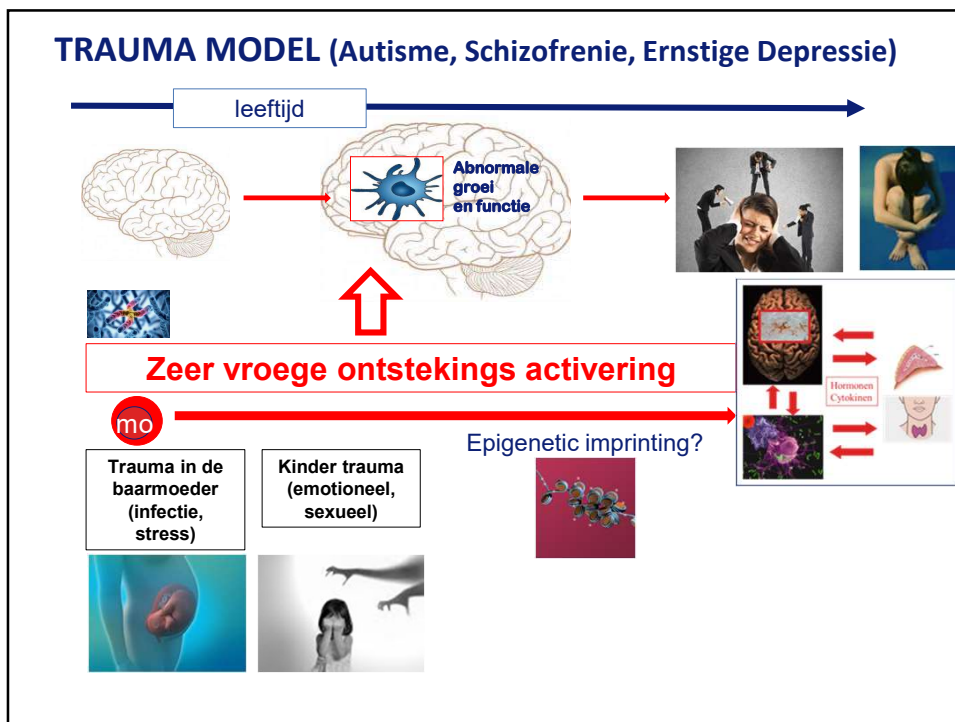
Nieuwe generatie
bloed testen

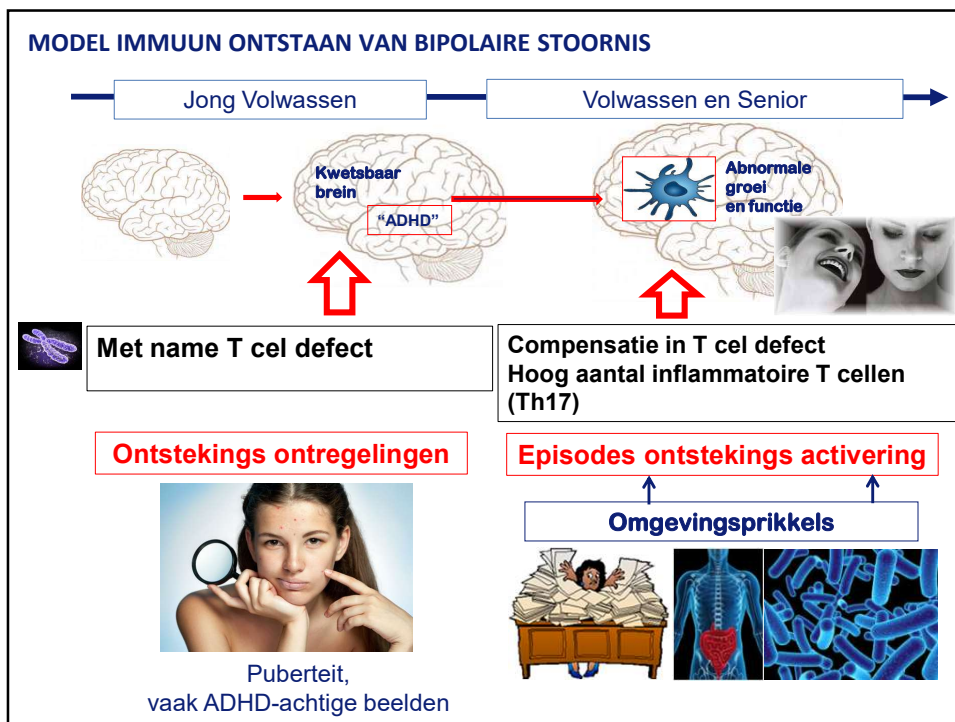
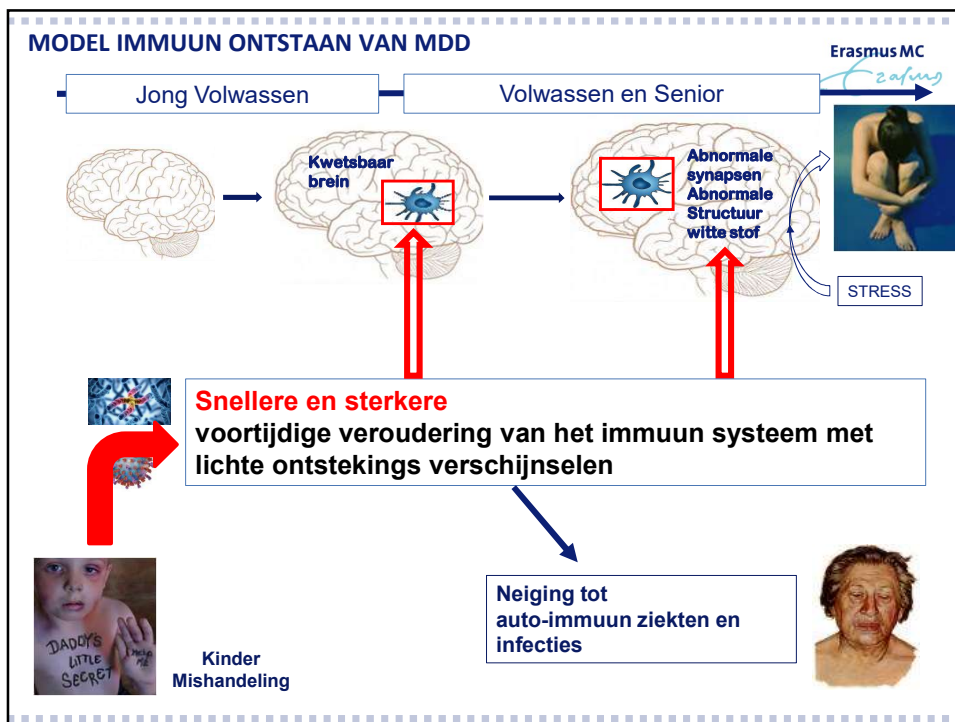
Genomics

- Monocytes
- T cellen
- Cytokines, hormonen, groei factoren







ErasmusMC
Erasmus

Immuun Abnormaliteiten (Therapie)

T cel versterking

- Sporten
- Lage dosis IL-2
- Thymosin-α1

Anti-inflammatoir

- NAC/Q10
- anti-TNF
- Minocycline
- COX-2 remmer

ErasmusMC
Erasmus

Therapie nieuw??

Robert Koch (1890):
Tuberculine
Malaria

Julius Wagner (1928)

Nobelprijs voor "malaria therapie" van "psychosen"

Het onderzoek is niet mogelijk zonder de medewerking van veel patiënten, promovendi, post-docs en samenwerkende onderzoekers

