



## **Deliverable D.6.21 List of Seminars of patients M52**

### **Seminars for patients 2020-2023**

- 1) On **September 12 2020** we organized a similar patient meeting at Erasmus MC Rotterdam as in 2019. This meeting was attended by 11 persons, due to COVID restrictions a smaller group.
- 2) Because of further COVID-restrictions in 2020 and 2021 we did not organise more live seminars. As an alternative we organized two Teams-meetings on the same topics as the September 12-meeting.  
These meetings took place at **September 26 and October 10 2020**. The Teams meeting at September 26 had 15 participating patients, at October 10 there were 25 participants. Prof dr. Hemmo Drexhage held an updated PowerPoint presentation with the newest results on MOODSTRATIFICATION and via the Chat-function in Teams we answered questions from the participating patients and their families and partners.
- 3) In the period **2021-2022** the liaison officer held **interviews with 10 patients** about their experiences and expectations of immune-psychiatry. We used these interviews as illustrative patient-stories in our Dutch book about immune-psychiatry for the main public. This book is published in February 2023. Later on in 2023 we will organize new psycho educating patient meetings, in which we will use this new book.

Please find attached the presentations we used for the patient seminars in 2019 and 2020.



## Immuno-psihiatrie

Prof dr Hemmo A. Drexhage, arts, klinisch/medisch immunoloog

Supported by



FP7 Large scale project MOODINFLAME

FP7 IAPP project PSYCHAID

Horizon 2020 project MOODSTRATIFICATION

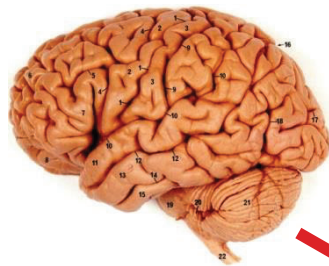


# State of the Art 1910-1930

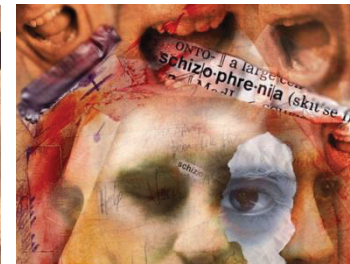
Ziekten van het Brein  
Neurologische ziekten



Emil Kraepelin (1856-1926)



“Manisch-depressives irresein”: stemmingsstoornissen

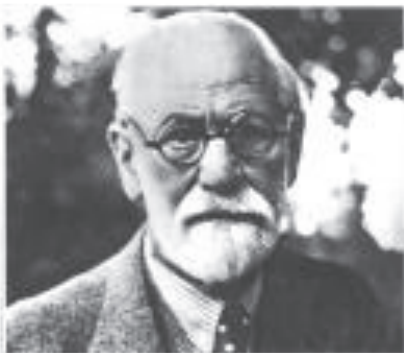


“Dementia Praecox”: Schizofrenie

# State of the Art 1945-1980



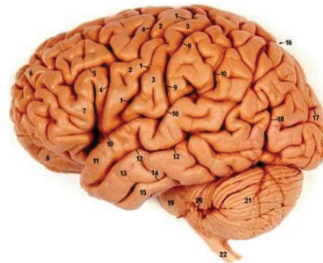
*(Kinder)trauma*



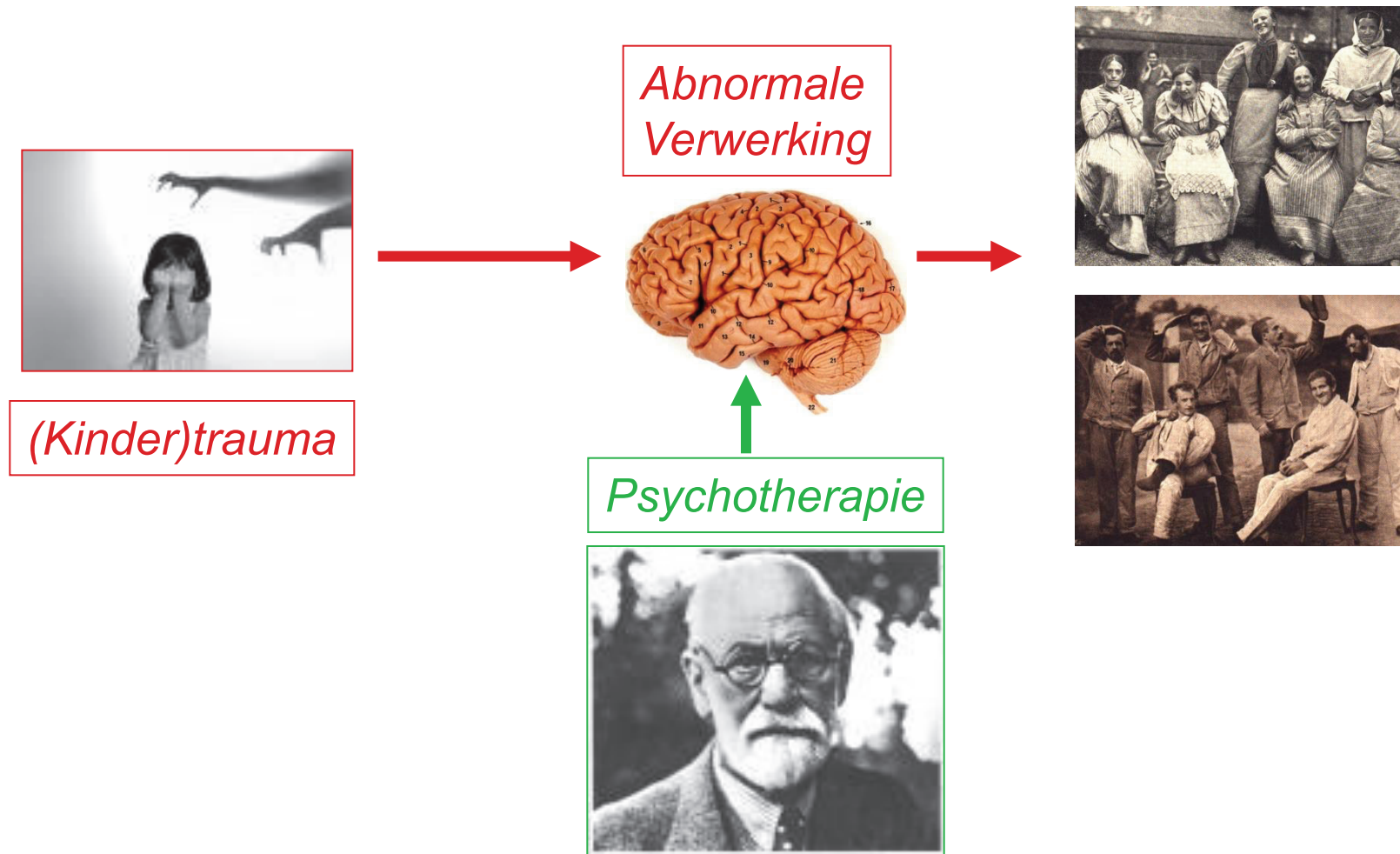
Persoonlijheidsdefect  
Geestesziekten

Sigmund Freud (1856-1939)

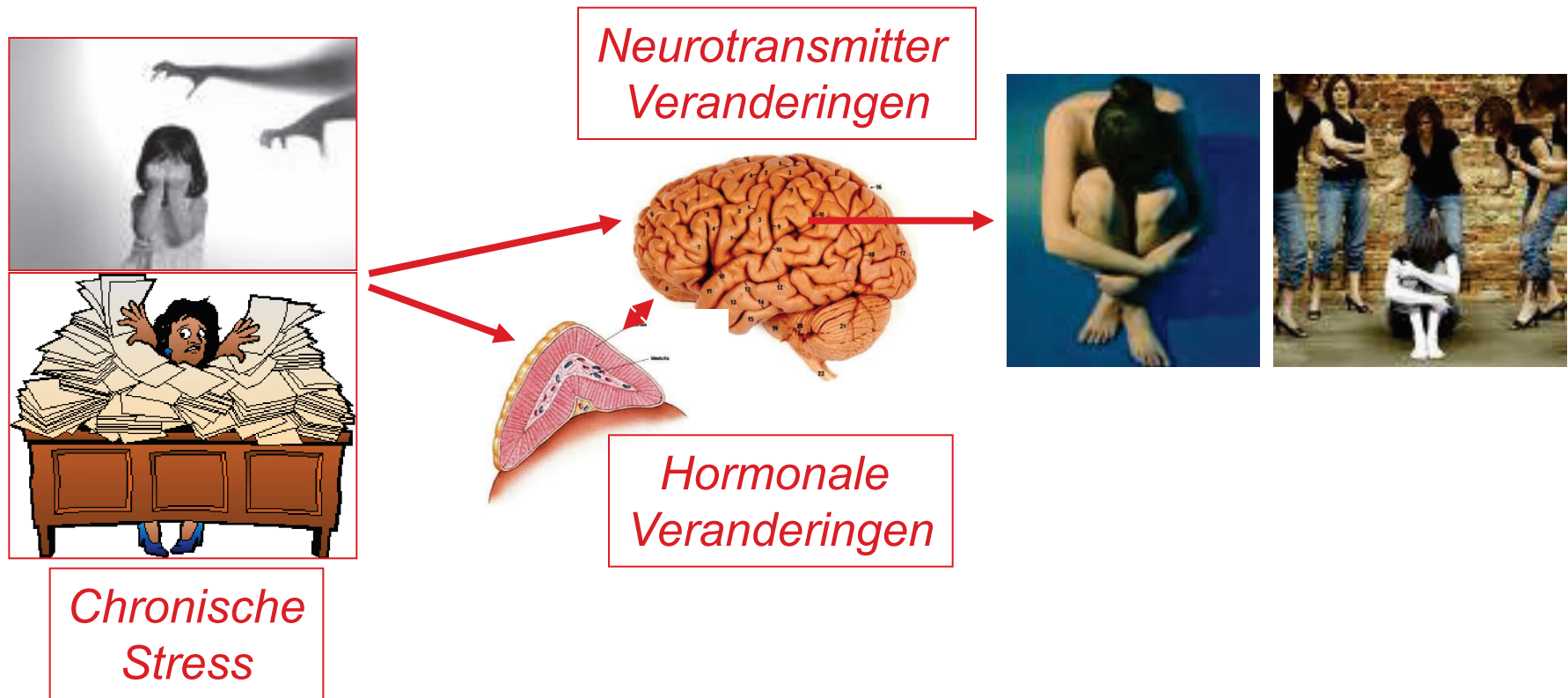
*Abnormale  
Verwerking*



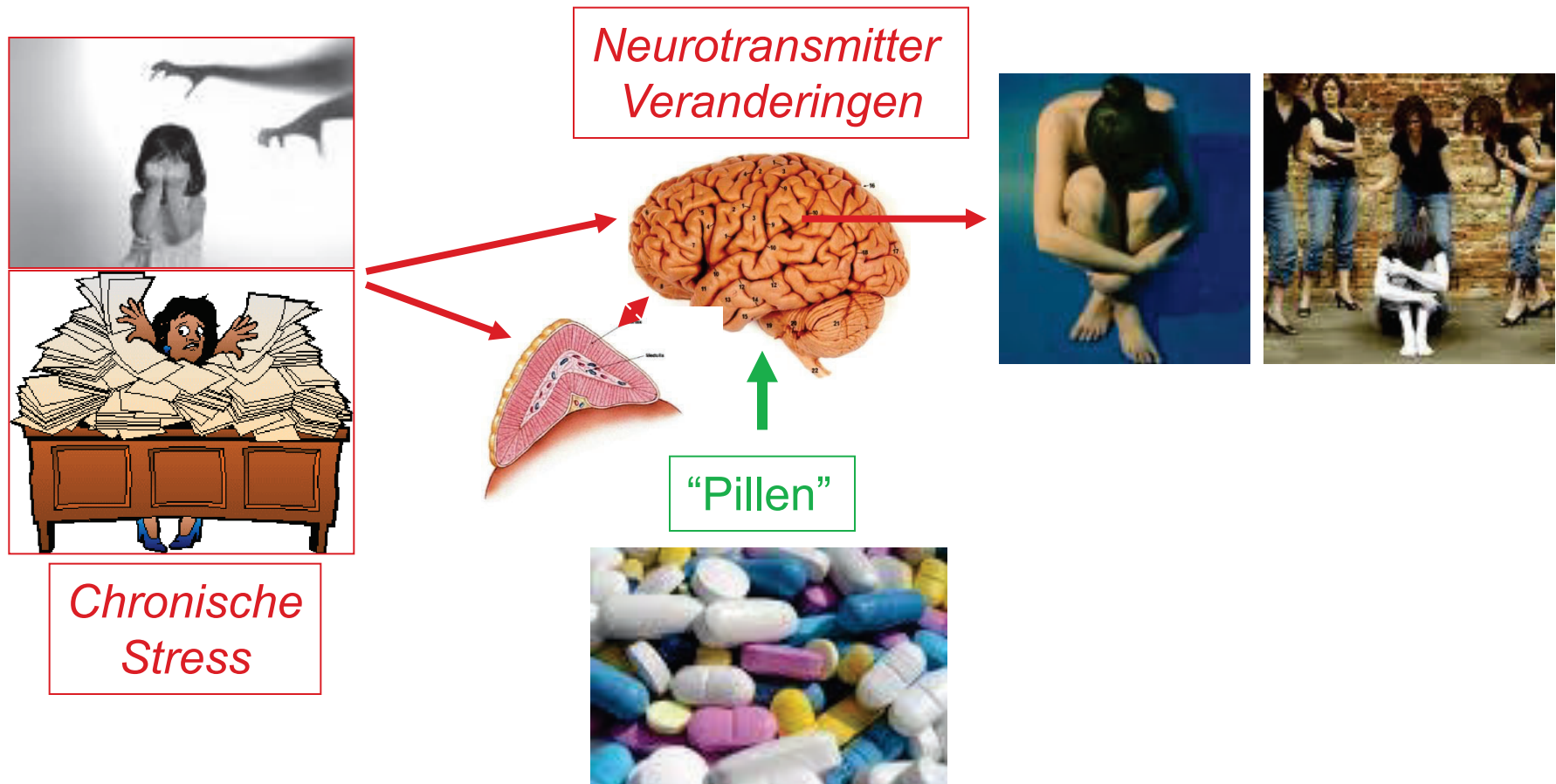
# State of the Art 1945-1980



# State of the Art 1980-2010



# State of the Art 1980-2010



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



## Cohorts

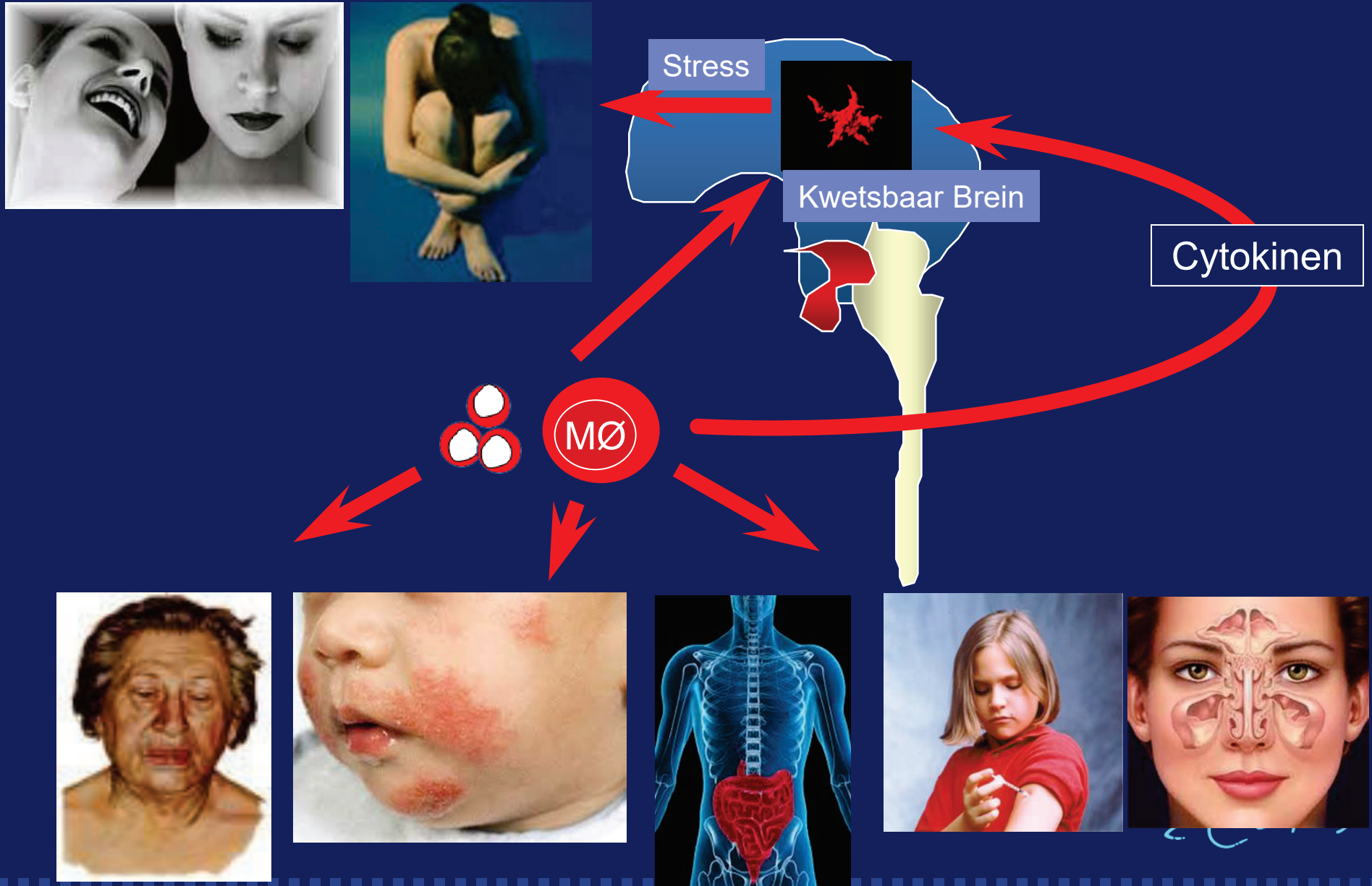


Gemeenschappelijke aangeboren aanleg?

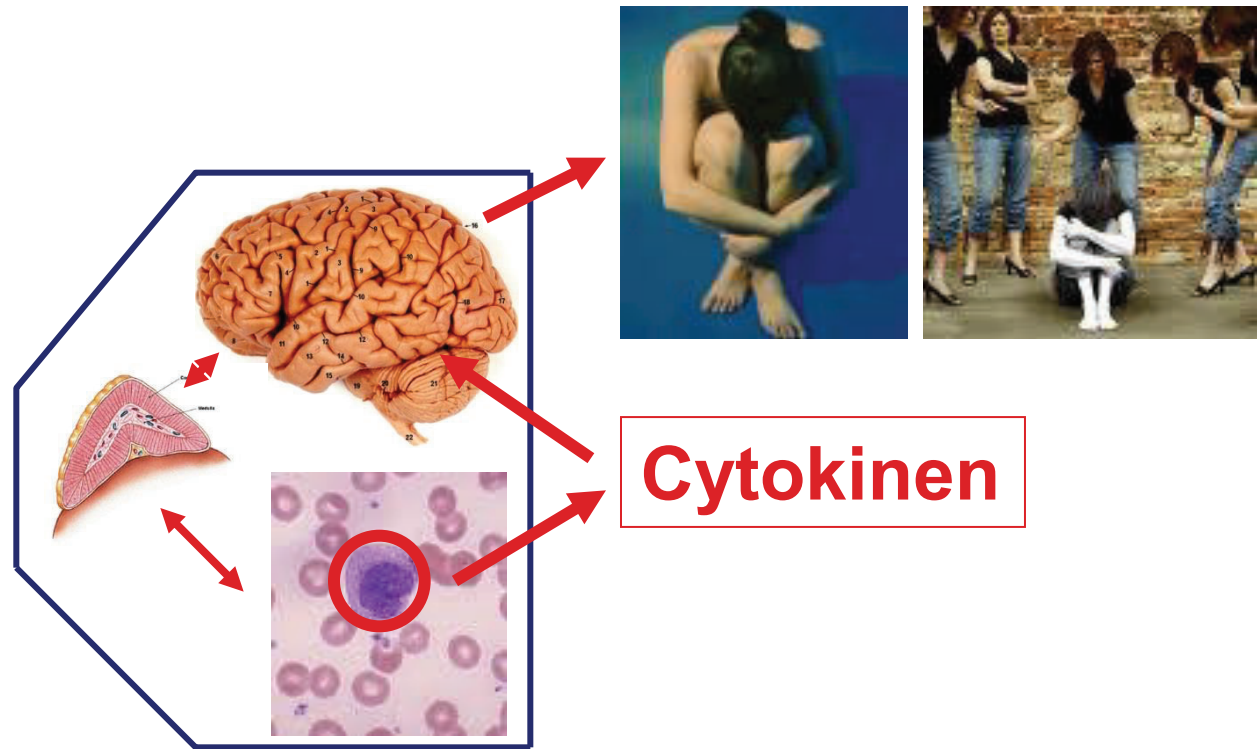
Population-wide



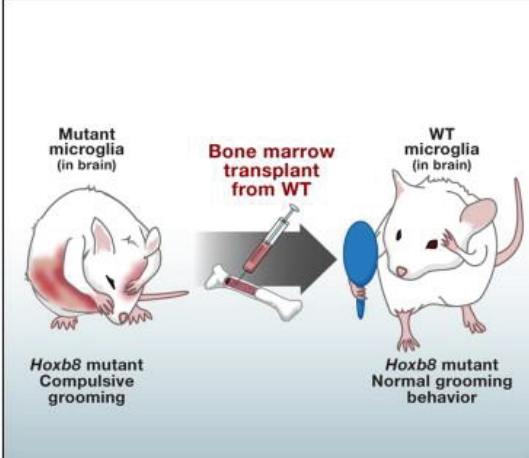
# Afweer systeem, afweer cellen en afweer stoffen centraal



# Nieuwe Inzichten: Immunologie



# Nieuwe Inzichten: Microglia

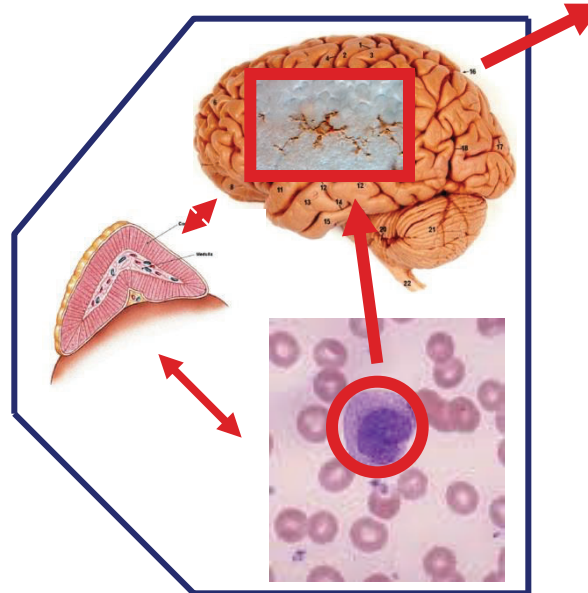


Mutant microglia (in brain) → Bone marrow transplant from WT → WT microglia (in brain)

*Hoxb8* mutant Compulsive grooming → *Hoxb8* mutant Normal grooming behavior

**Cell**

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

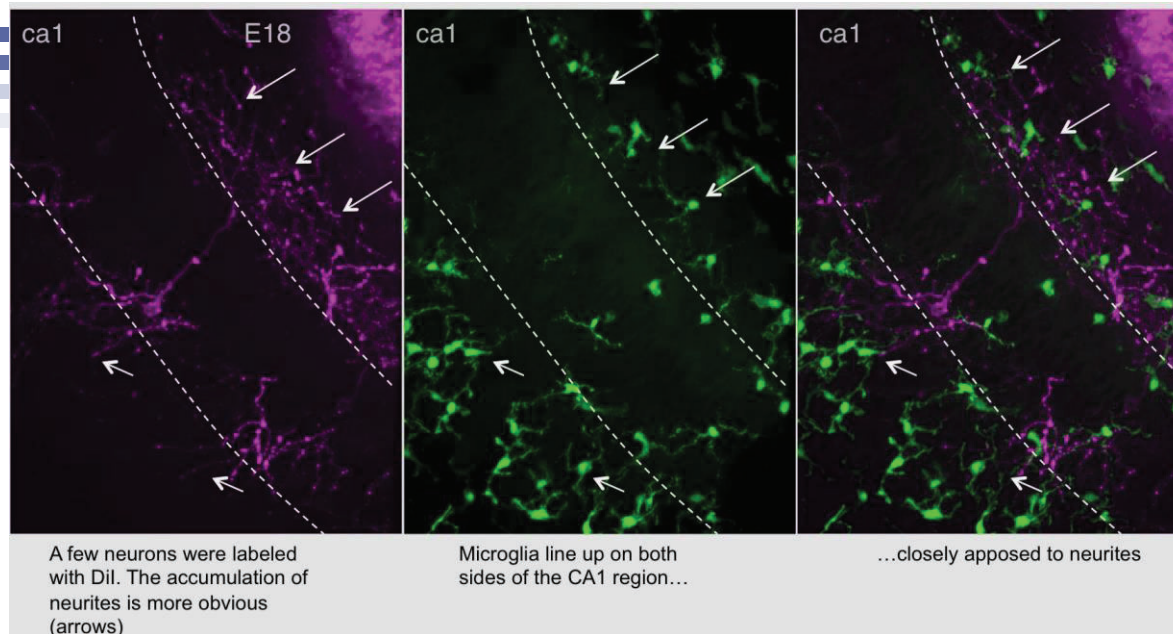


Published online 27 May 2010 | **Nature** | doi:10.1038/news.2010.268

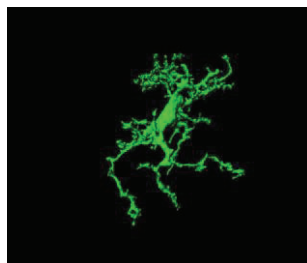
**News**

**Key to psychological disorder may lie in the immune system**

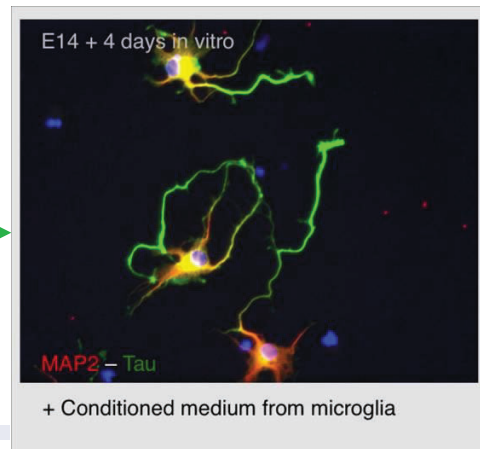
# Nieuwe Inzichten: Microglia

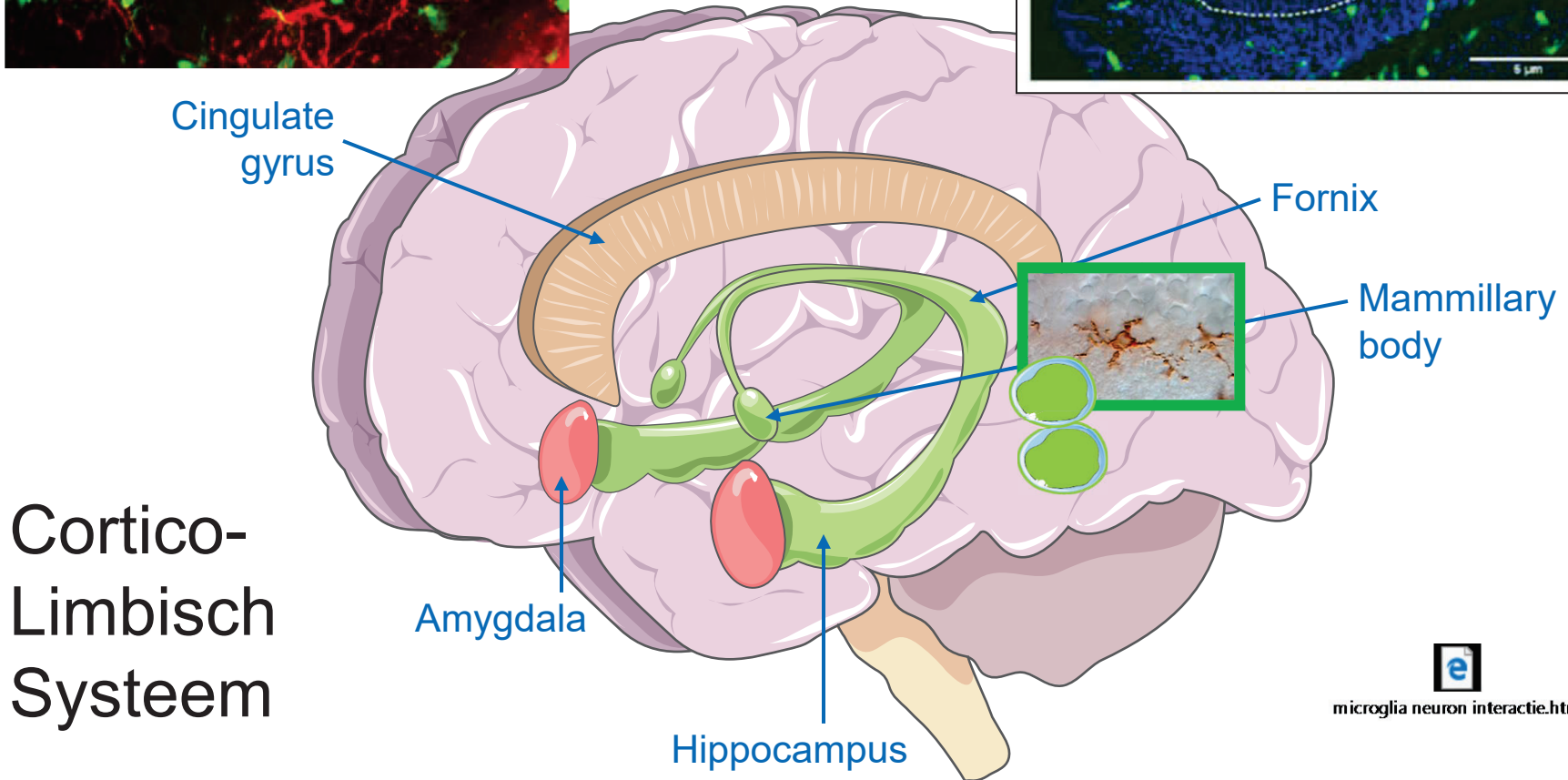
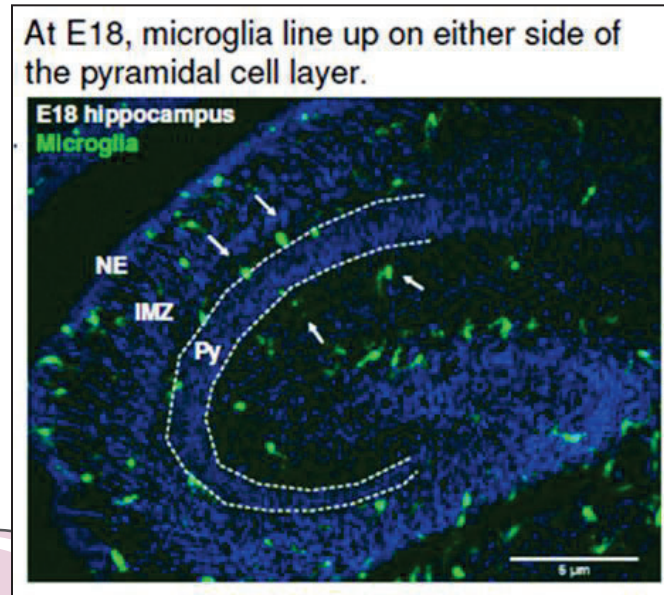
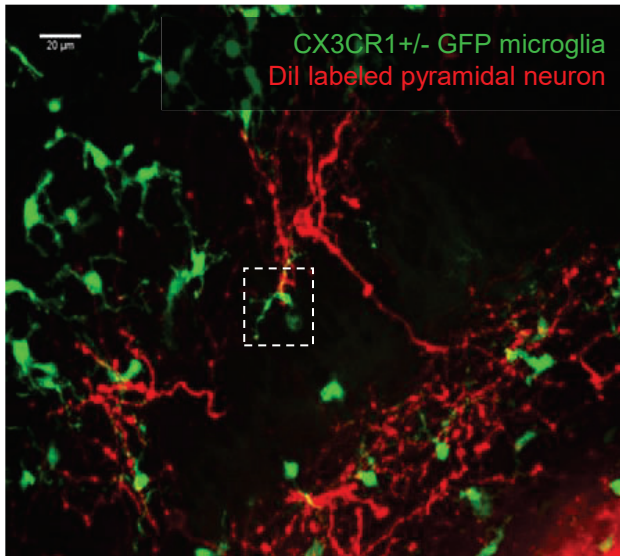


Microglia helpen neuronen te groeien in de hippocampus, een deel van het emotionele integratie systeem, waar o.a. stress verwerkt wordt



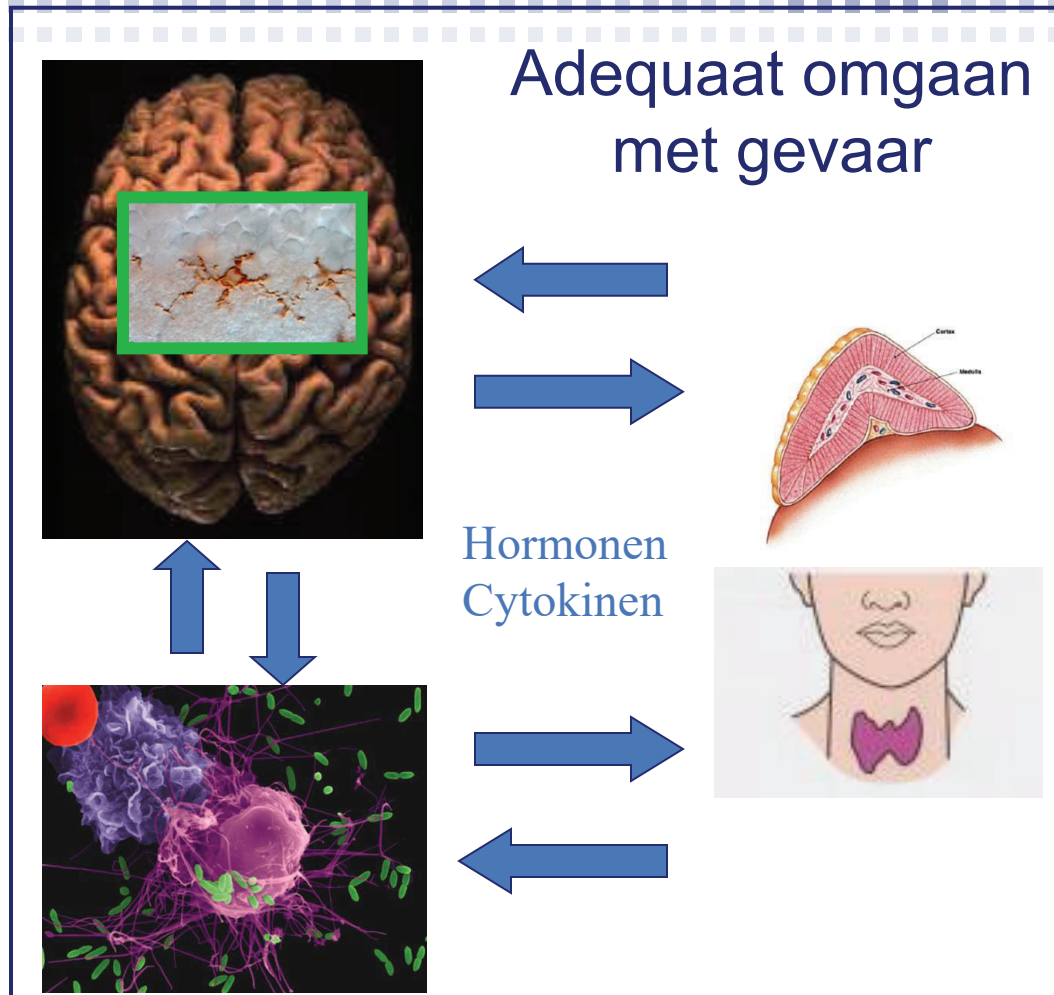
Resting microglia



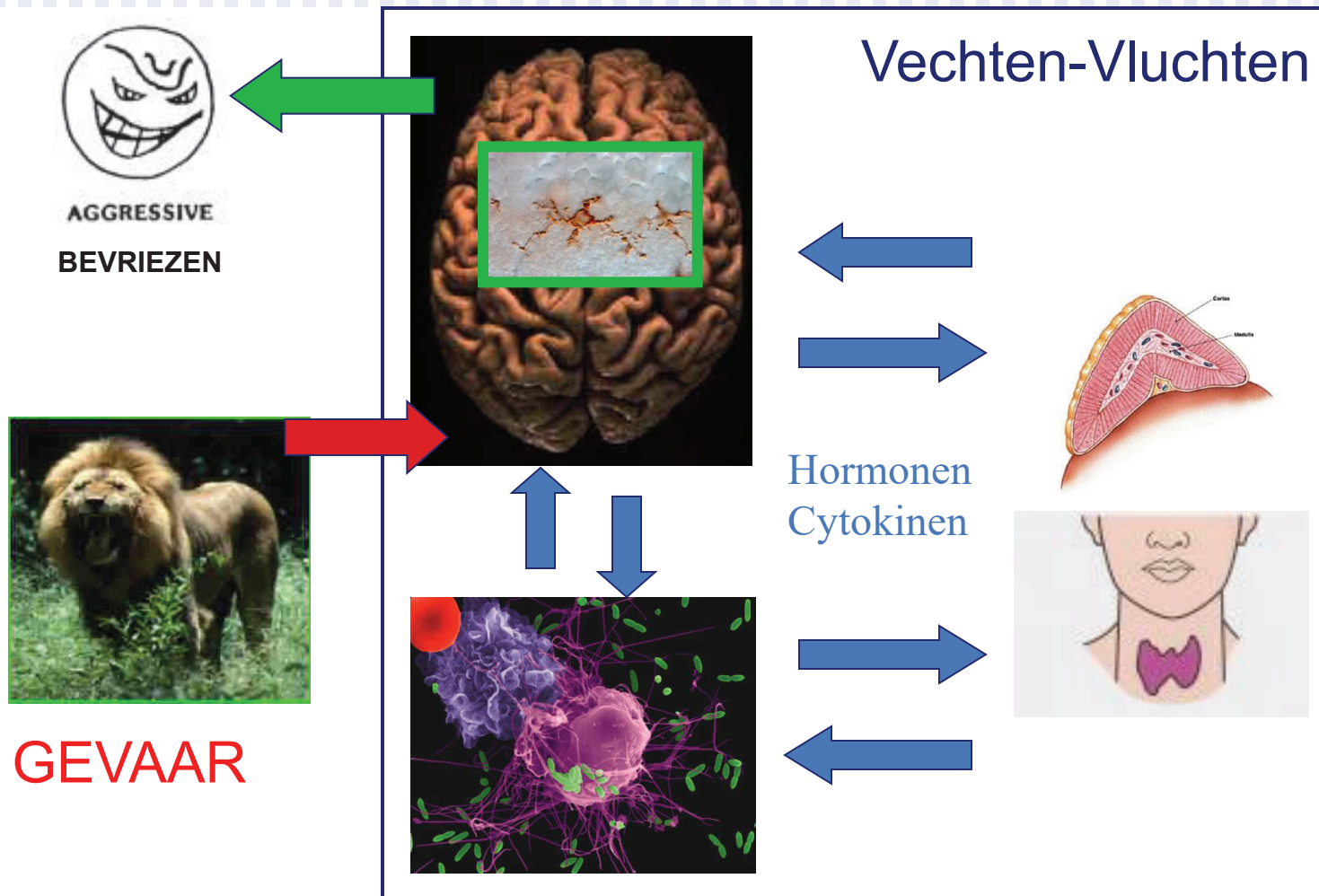


Cortico-  
Limbisch  
Systeem

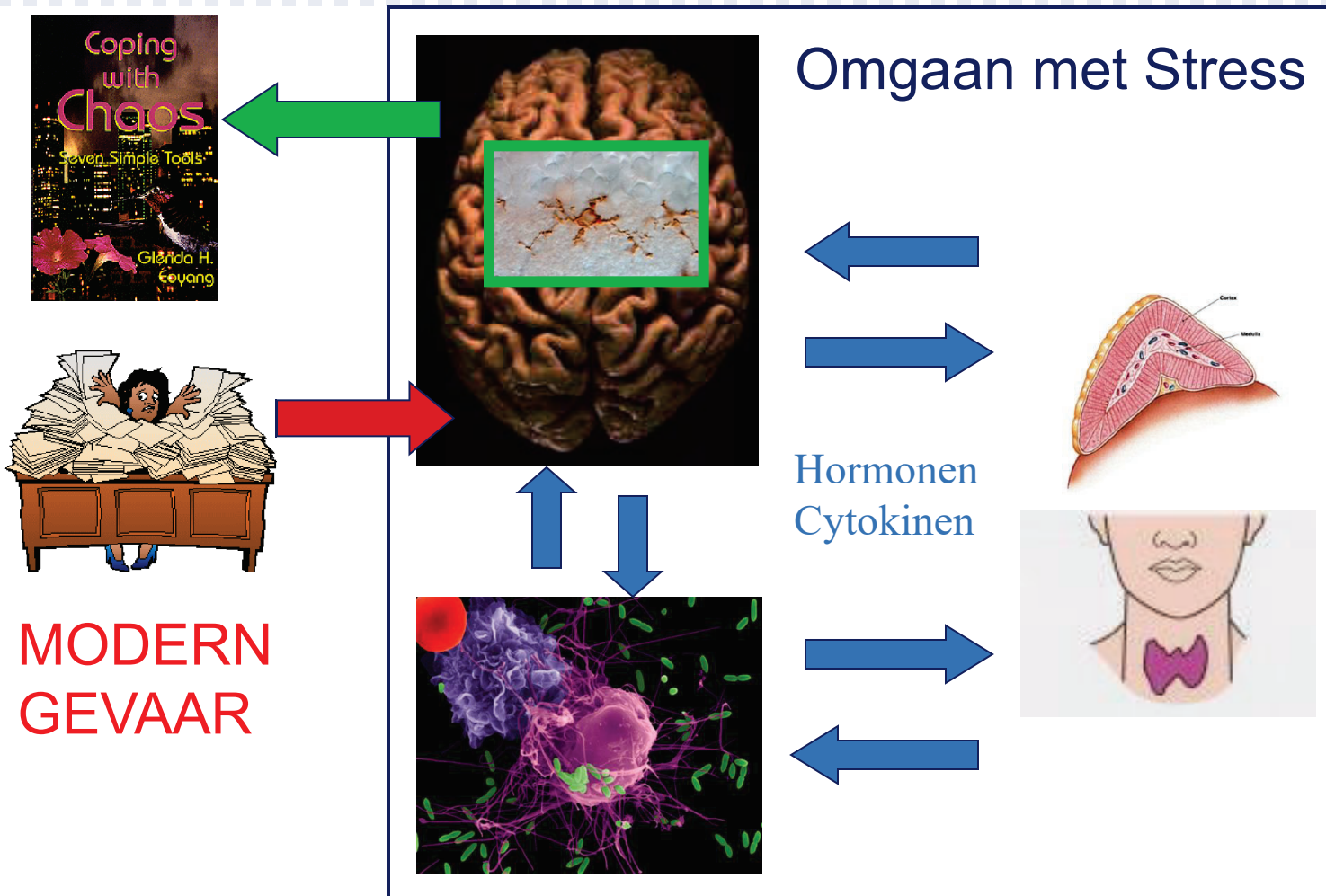
# Het Neuro-Immuno-Endocriene Systeem



# Het Neuro-Immuno-Endocriene Systeem

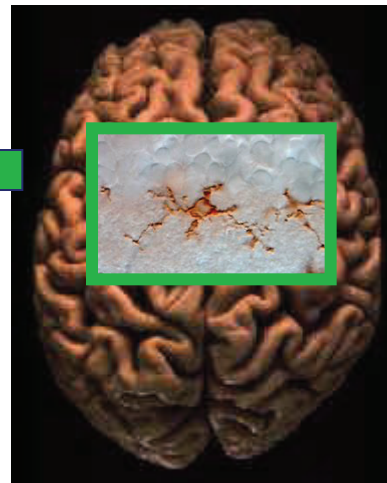
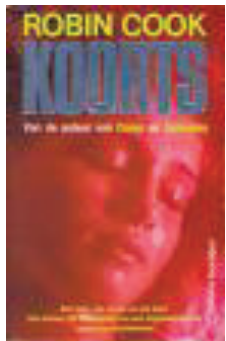


# Het Neuro-Immuno-Endocriene Systeem





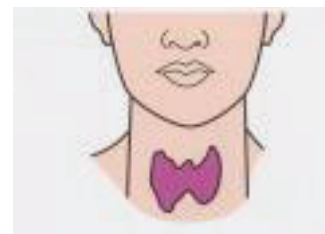
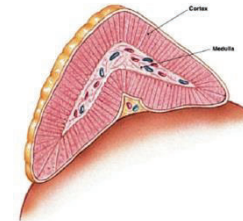
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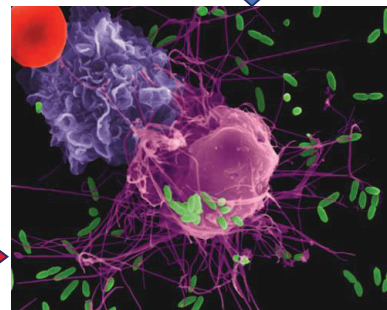
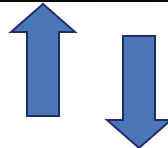
De koortsreactie



Hormonen  
Cytokinen

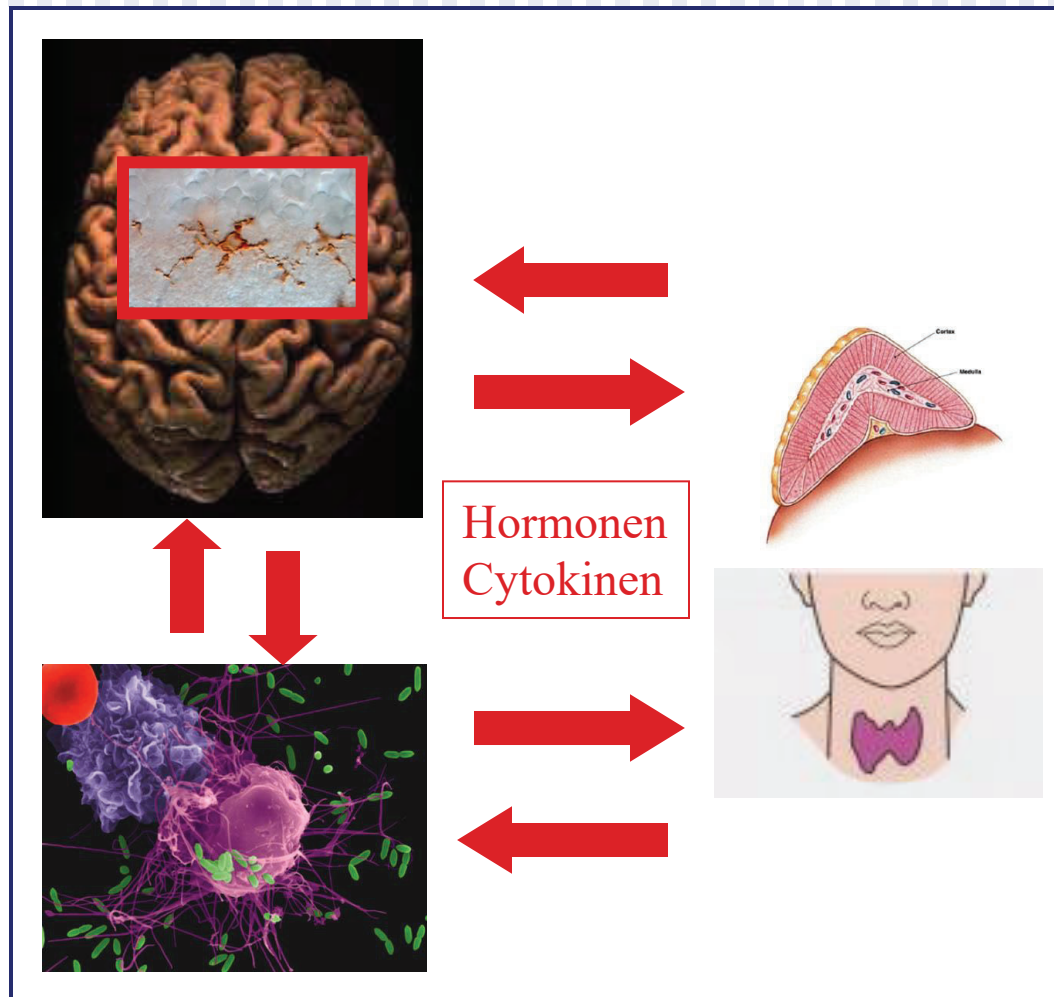


GEVAAR

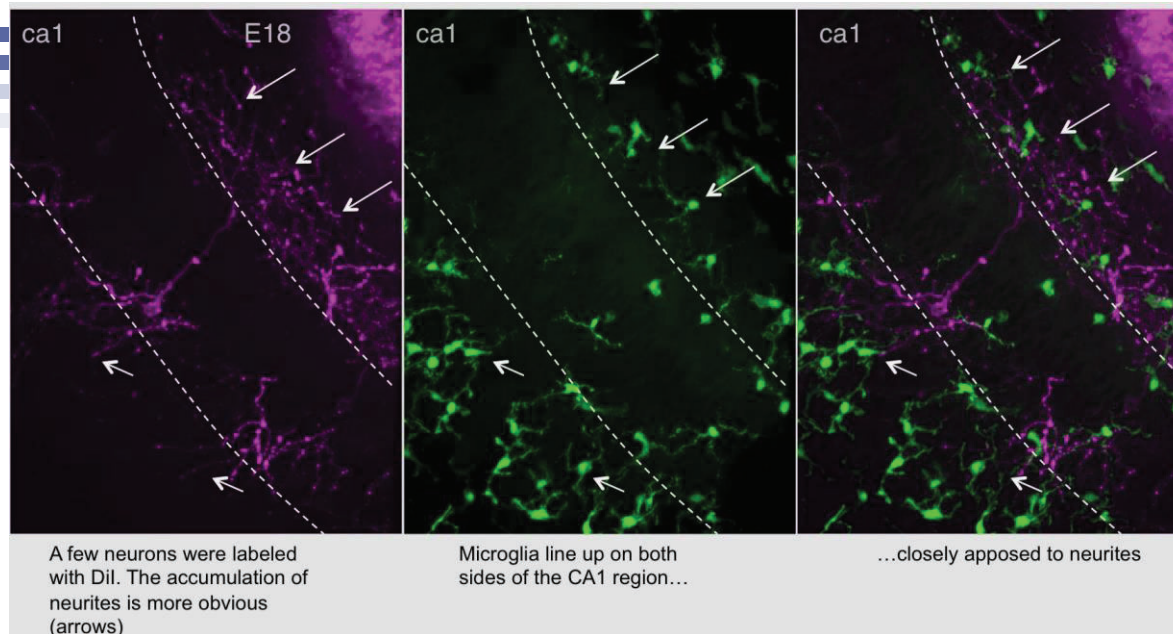


# Het Neuro-Immuno-Endocriene Systeem

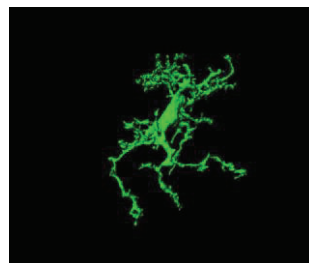
## In de fout



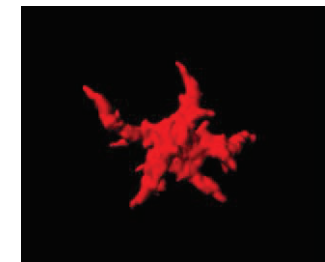
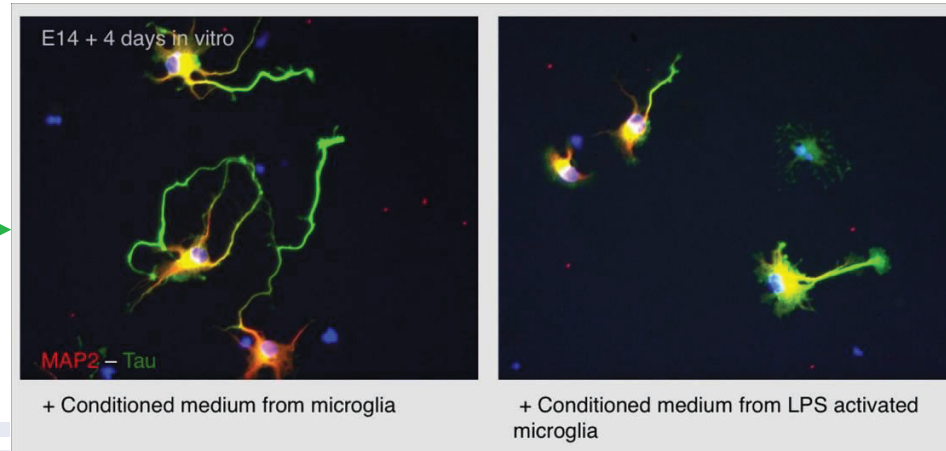
# Nieuwe Inzichten: Microglia



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



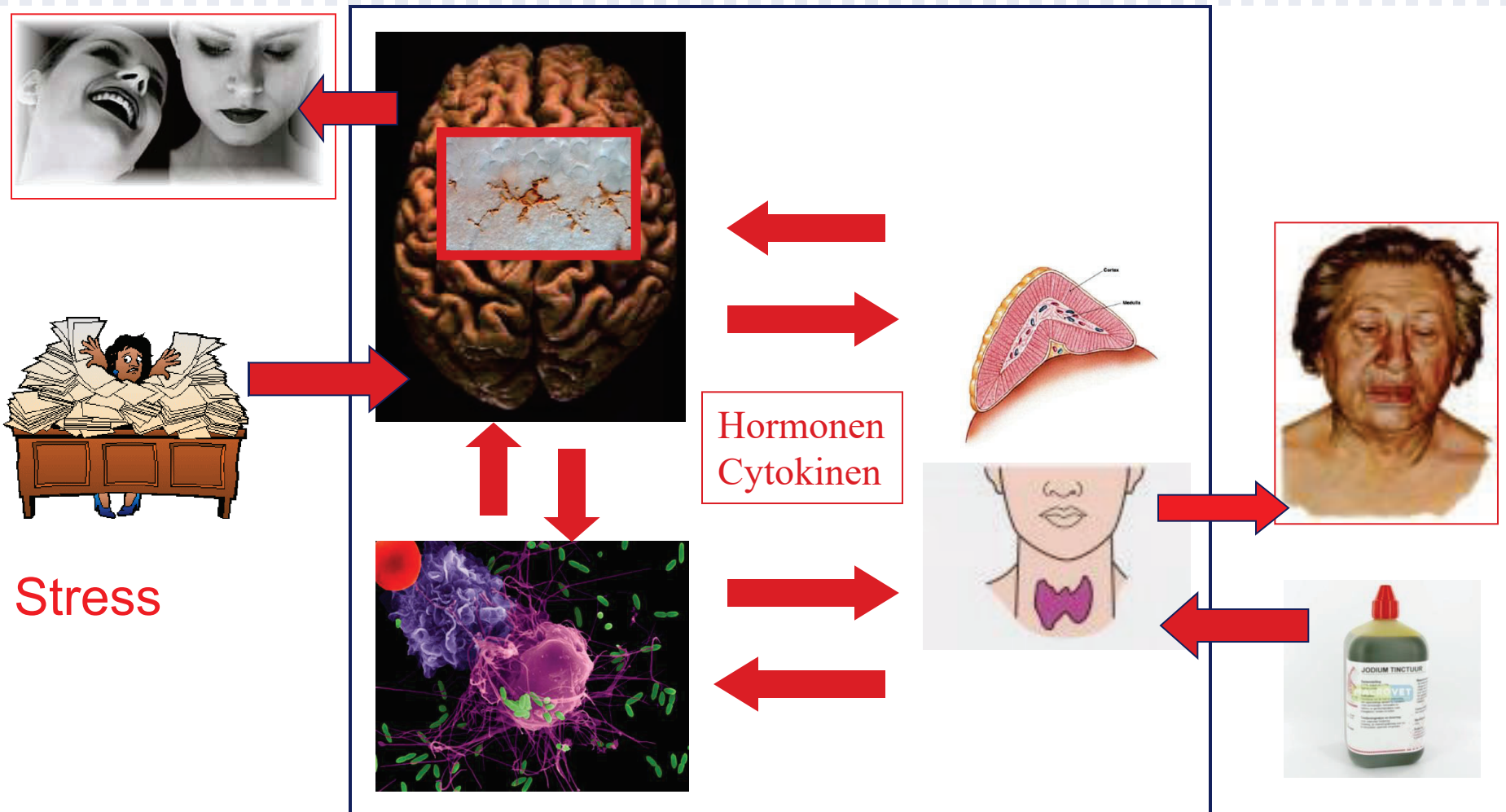
Resting microglia



Inflamed microglia

# Het Neuro-Immuno-Endocriene Systeem

## In de fout

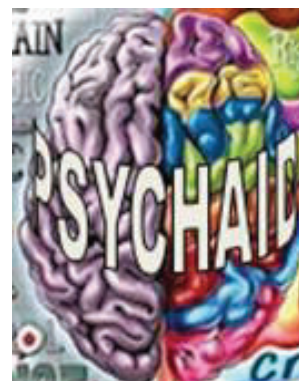


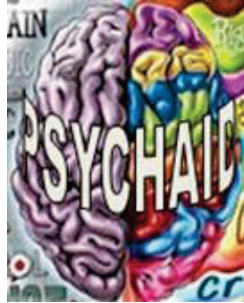
# Conclusies

- Een flink deel van 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.

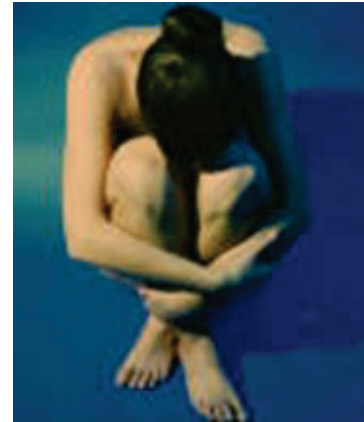
## Consequenties

- 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

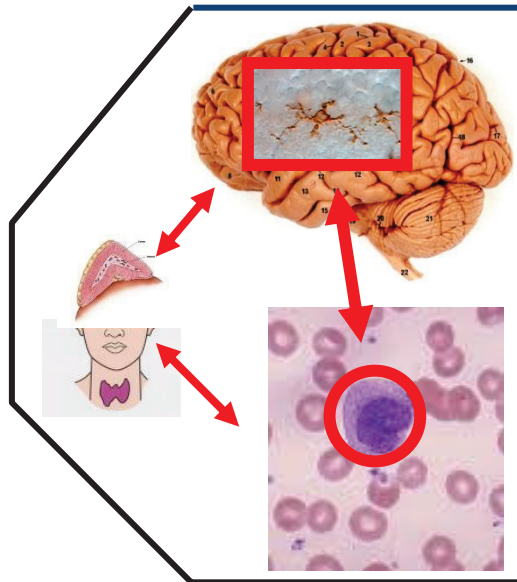




400 bipolaire  
patienten



800 depressieve  
patienten



600 gezonden

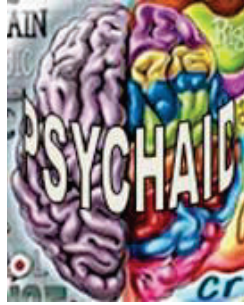


80 schizofrene  
patienten

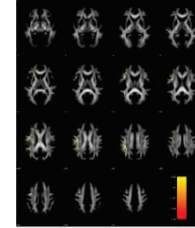
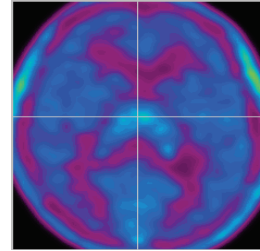
25 partners  
12 landen



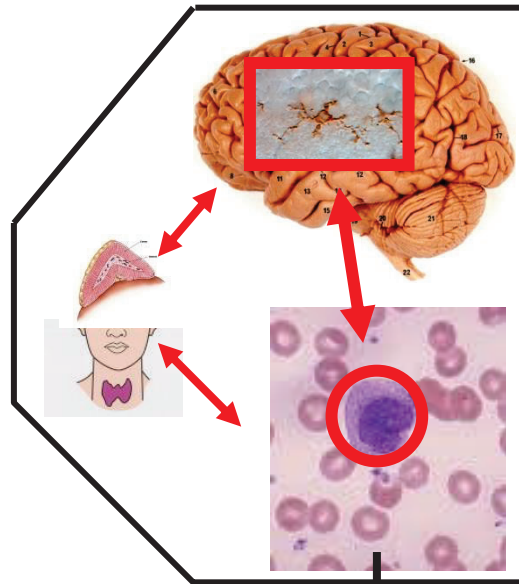
3 modellen



## Nieuwe generatie hersen scans voor o.a. microglia



## Evenwichts Interacties



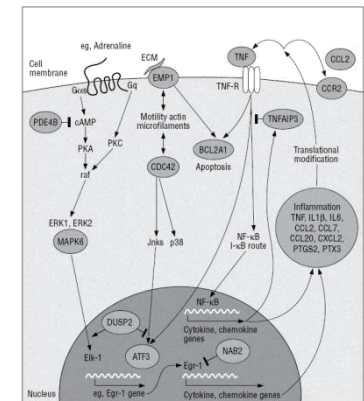
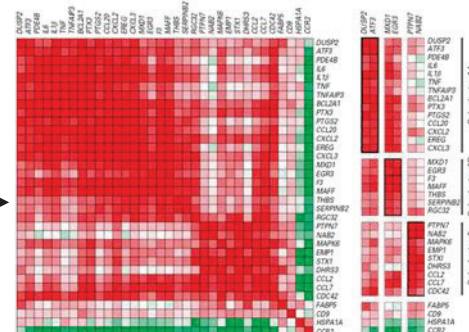
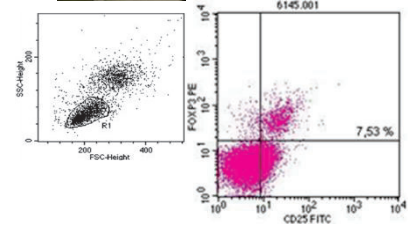
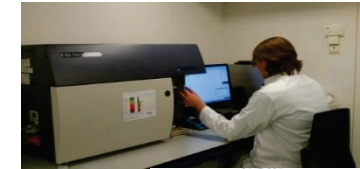
Nieuwe generatie bloed testen



Genomics

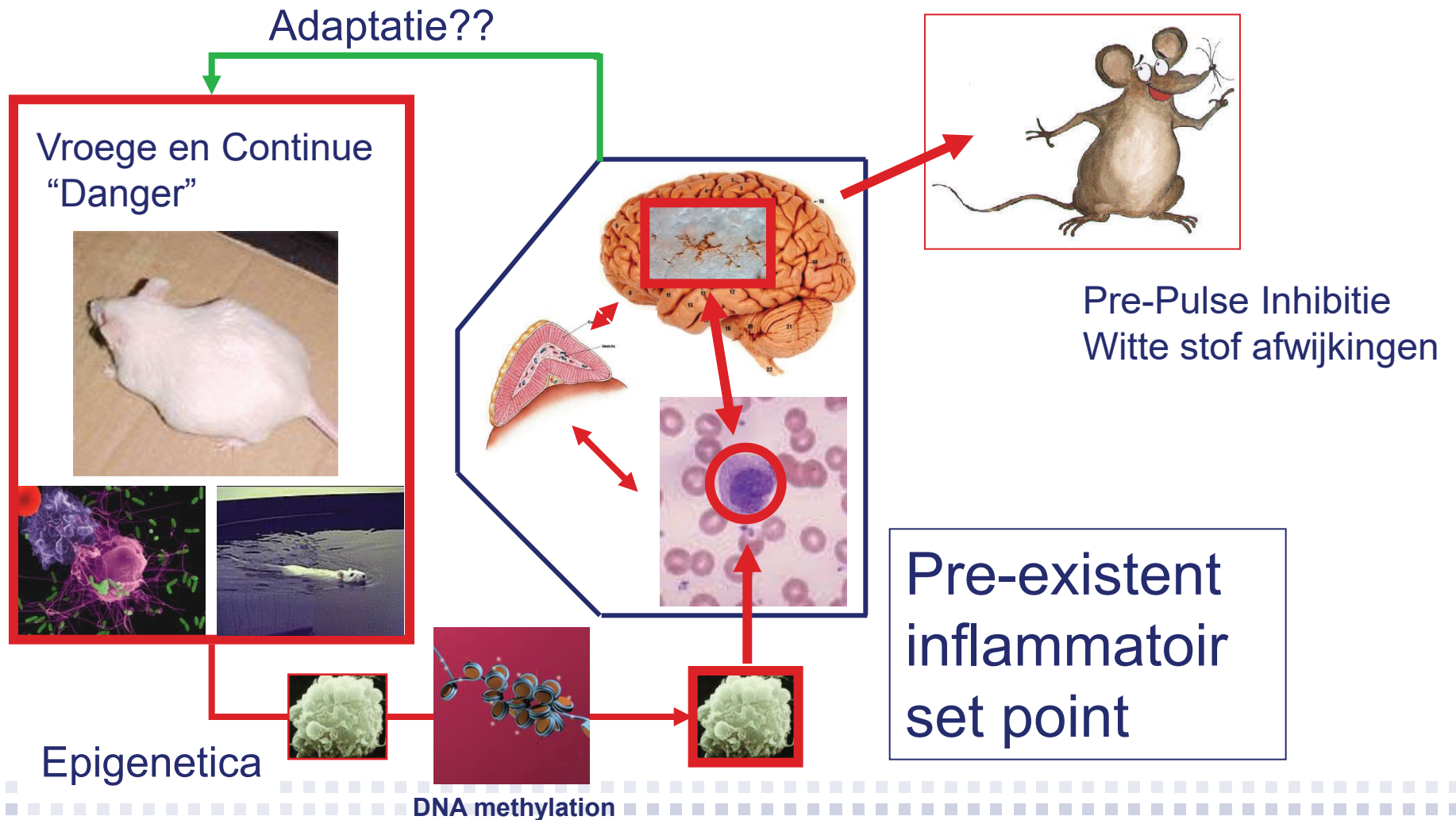


- Monocytes
- T cellen
- Cytokines, hormonen, groei factoren

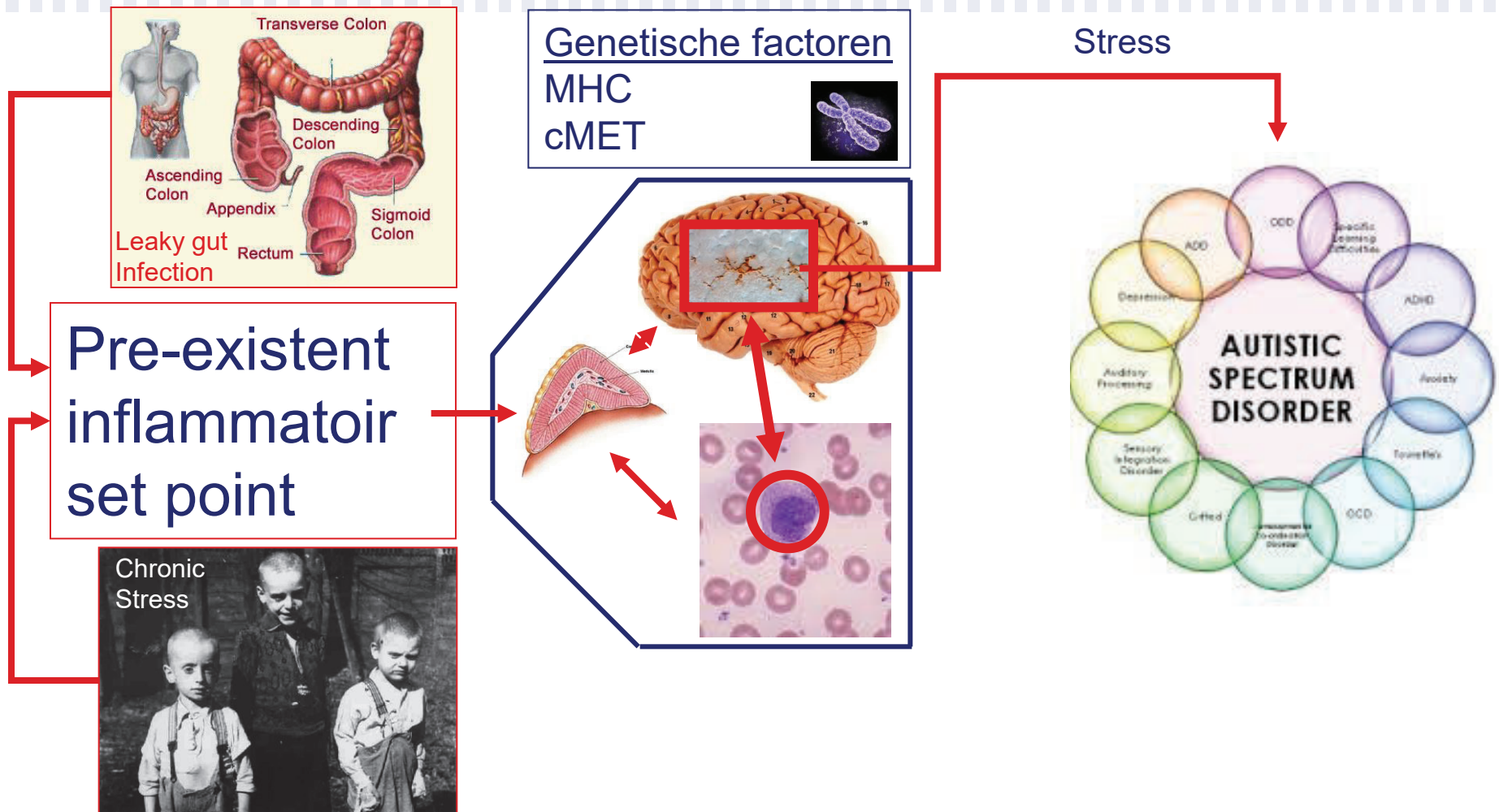




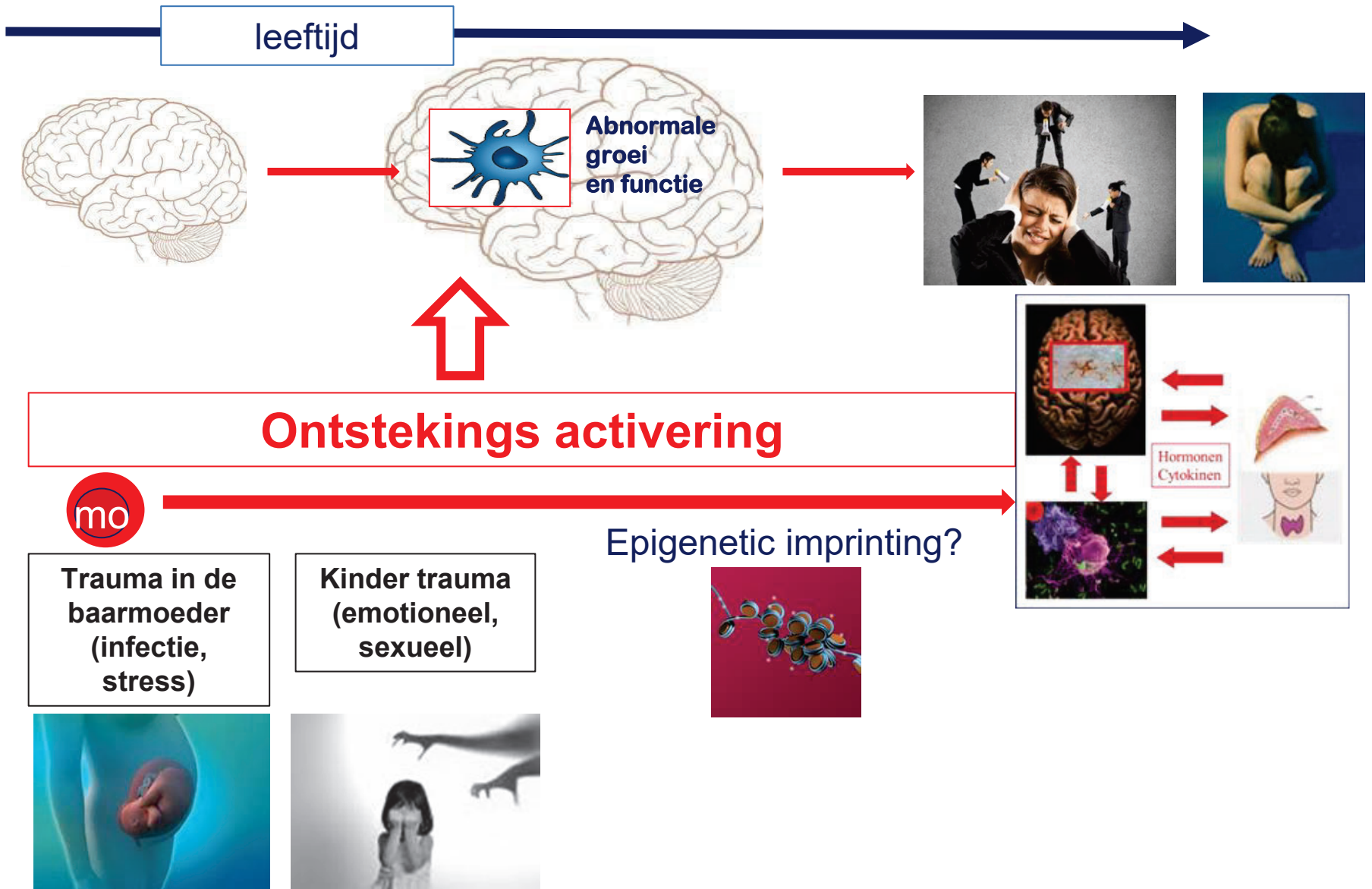
# Inflammatoir Set-point (MIA model)



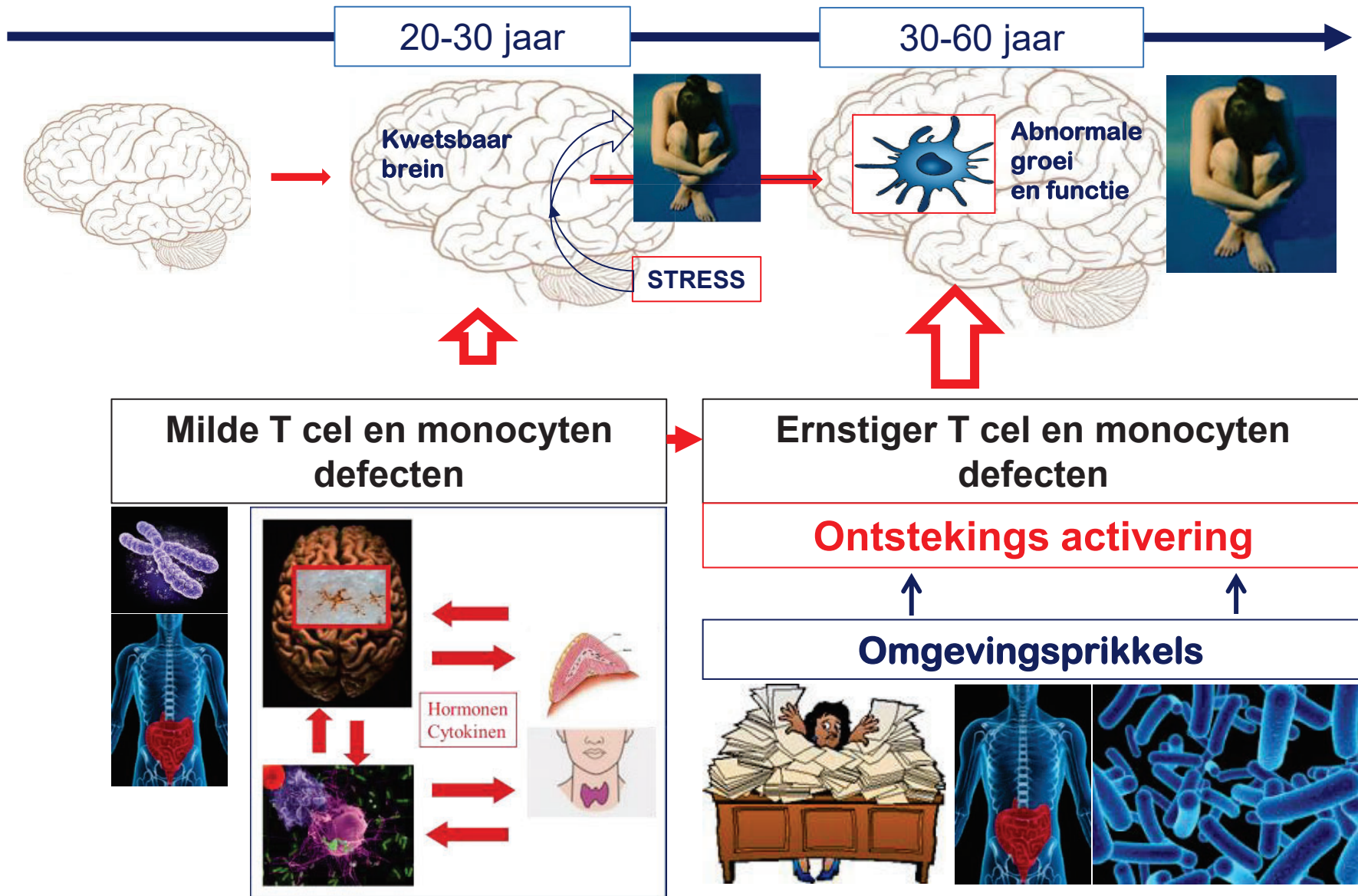
# Inflammatoir Set-point model (ASD)



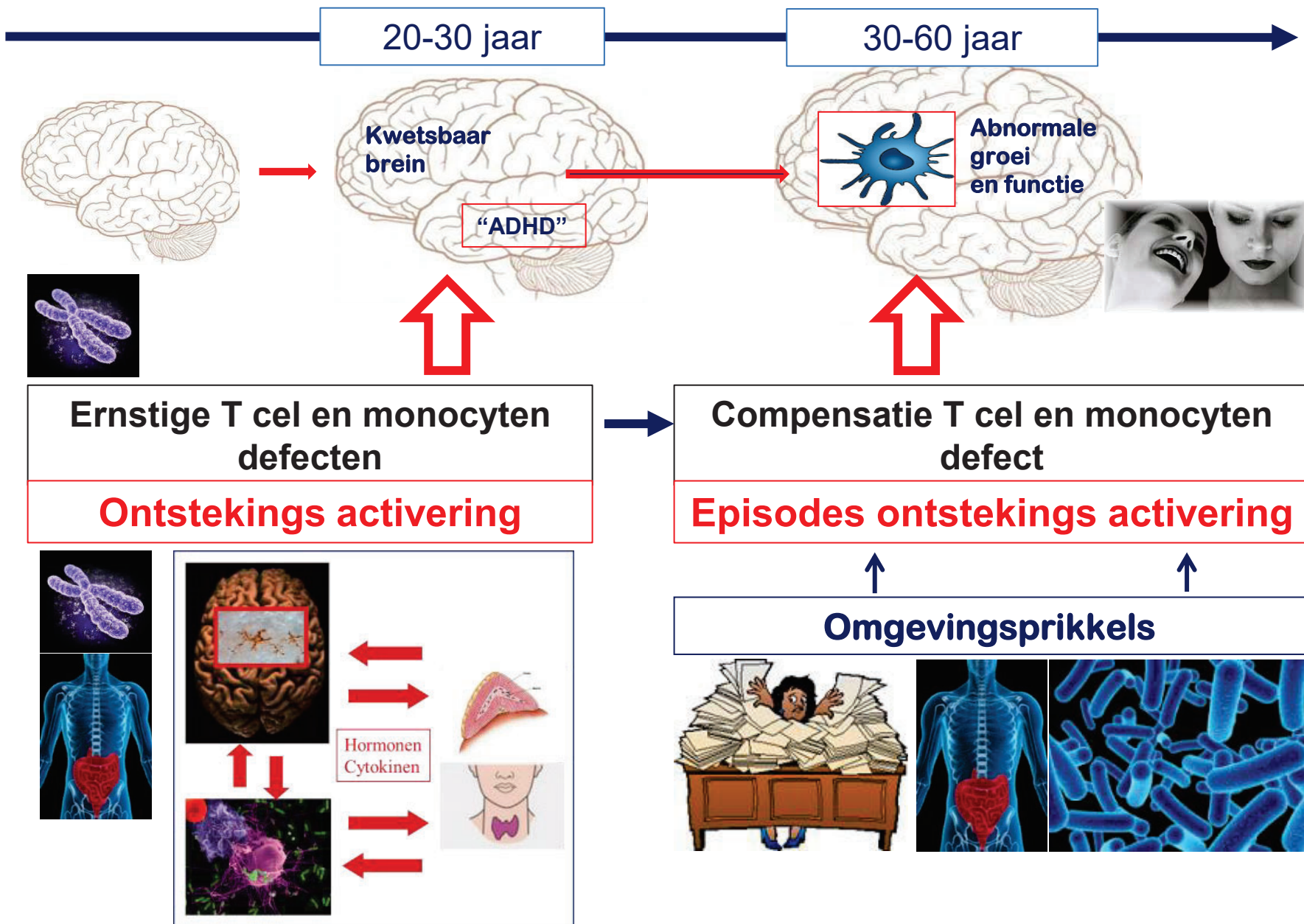
# TRAUMA MODEL (Autisme, Schizofrenie, Ernstige Depressie)



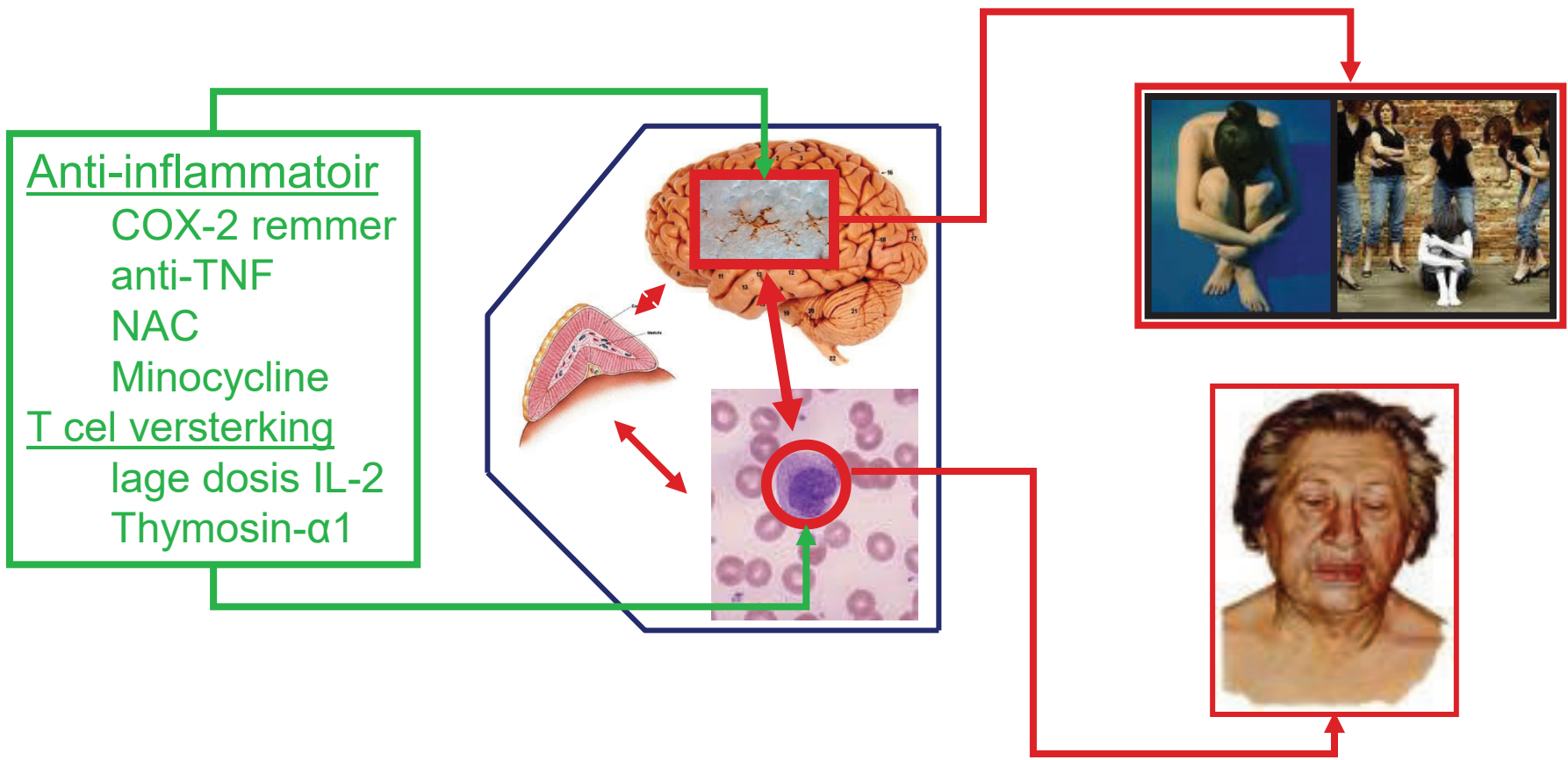
# IMMUUN DEFECT MODEL (Ernstige Depressie)



# Gecompenseerd immuun defect model (Bipolaire stoornis)



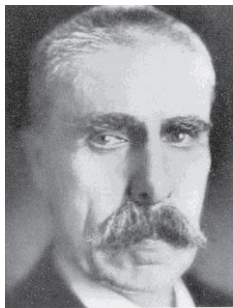
# Immuun Abnormaliteiten (Therapie)



# Therapie nieuw??

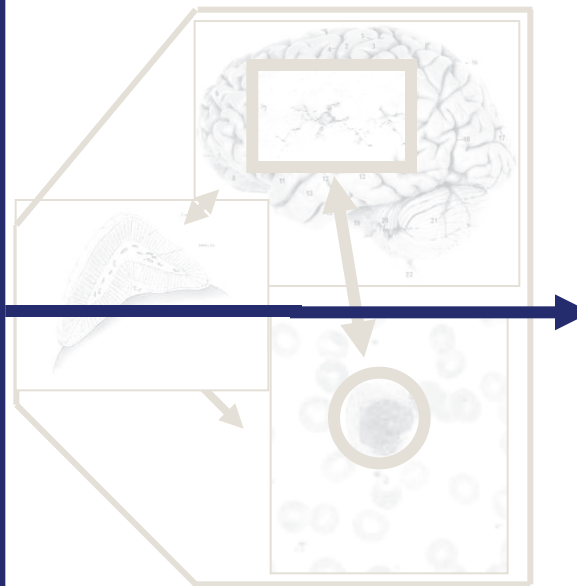


Robert Koch (1890):  
Tuberculine  
Malaria



*Wagner-Jauregg*

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









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## 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







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## State of the Art 1910-1930







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Ziekten van het Brein  
 Neurologische ziekten






Emil Kraepelin (1856-1926)



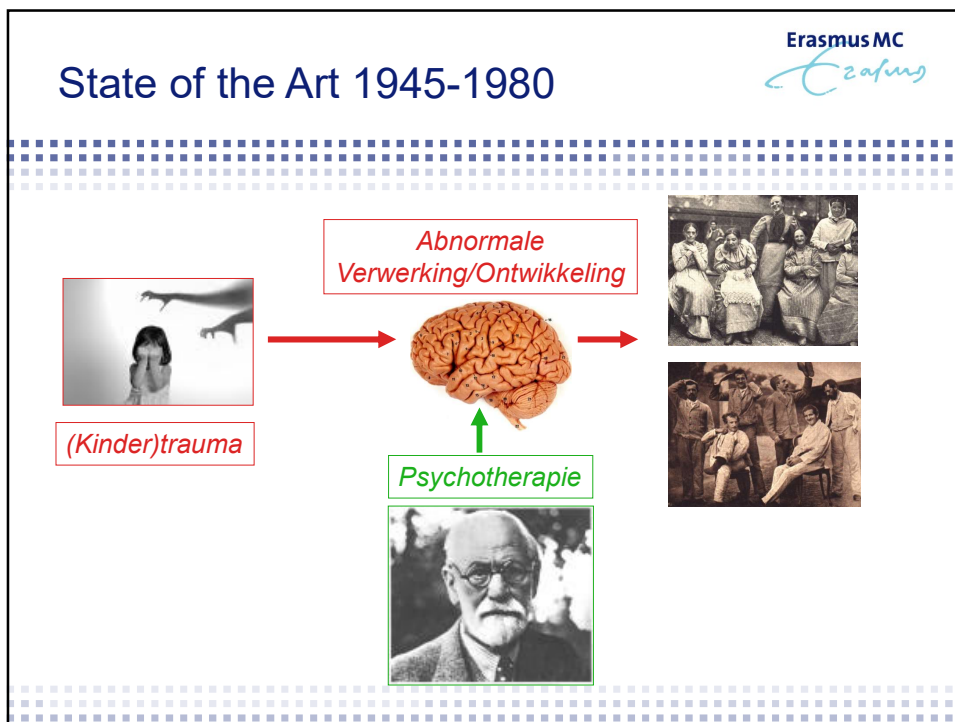
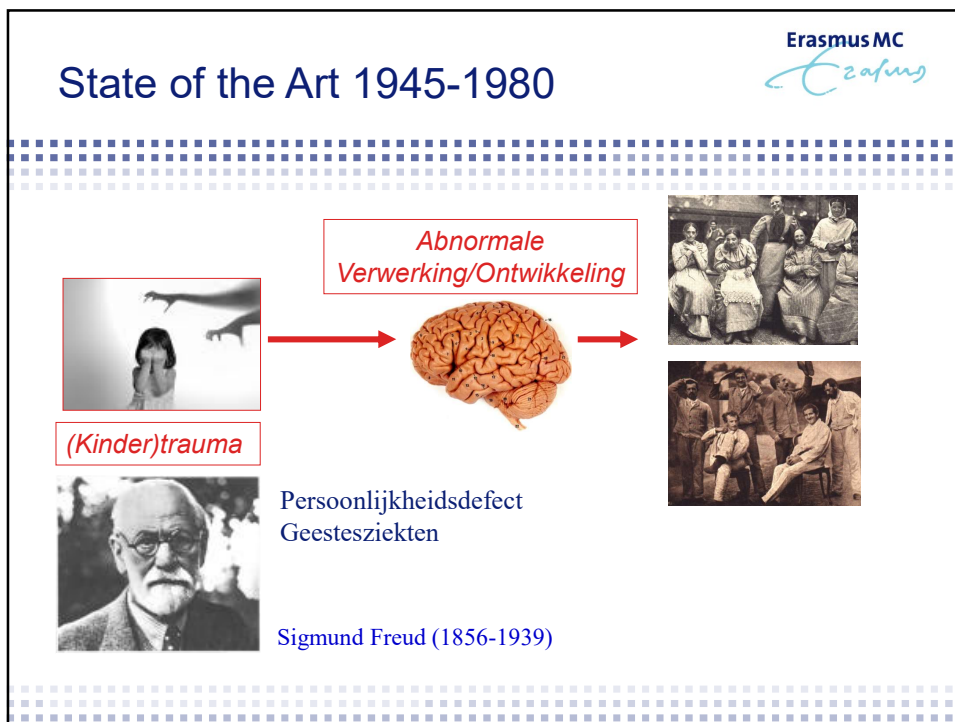




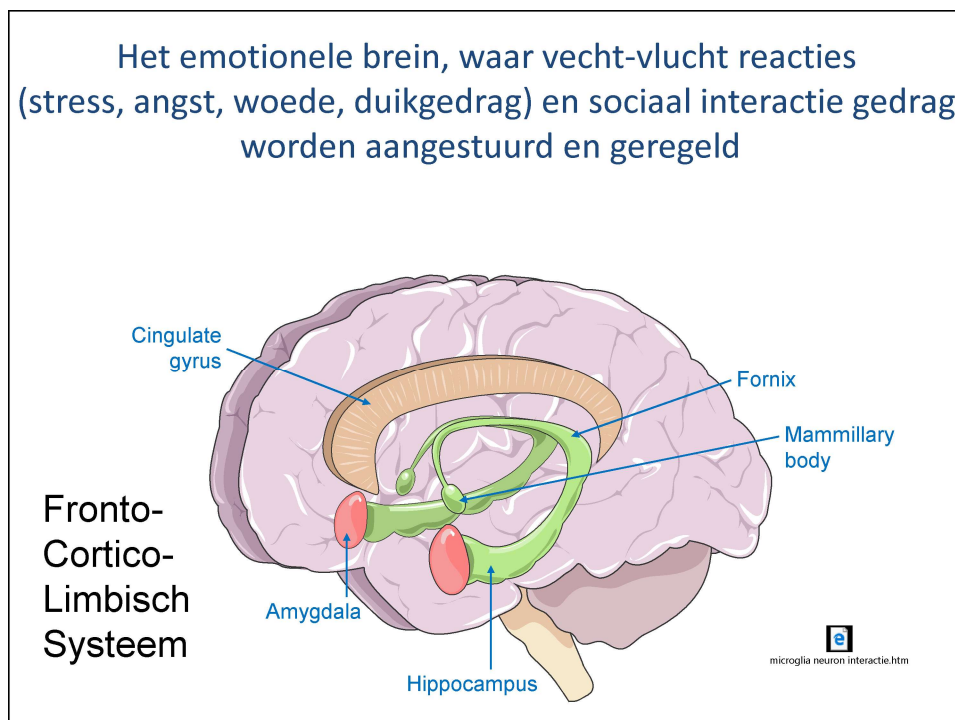
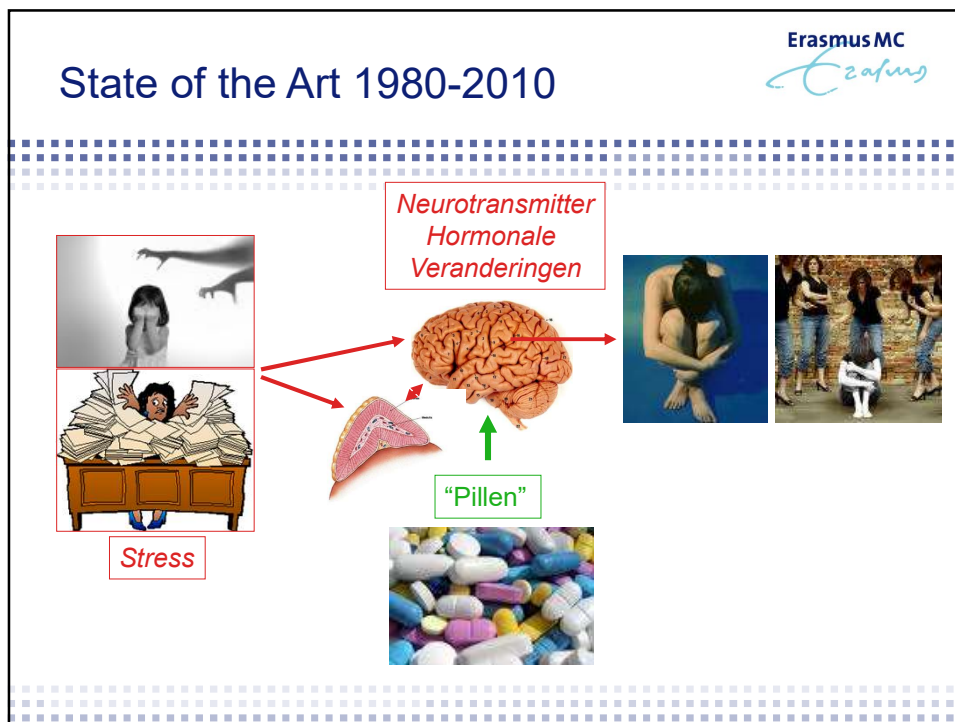
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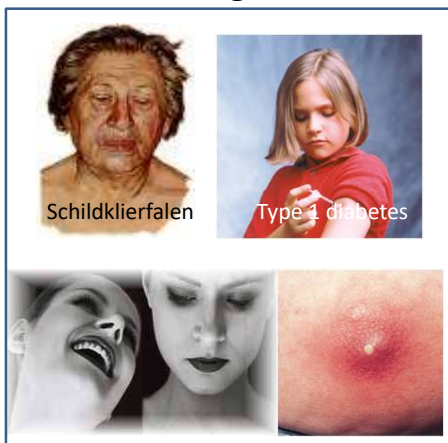
“Dementia Praecox”: Schizofrenie

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



Schildklierfalen

Type 1 diabetes



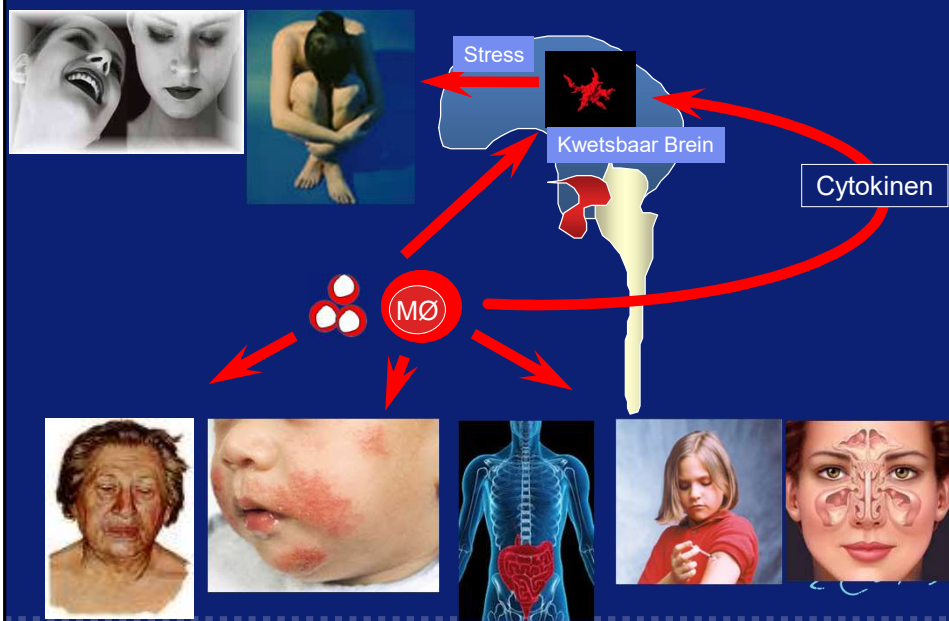
Cohorts



Population-wide

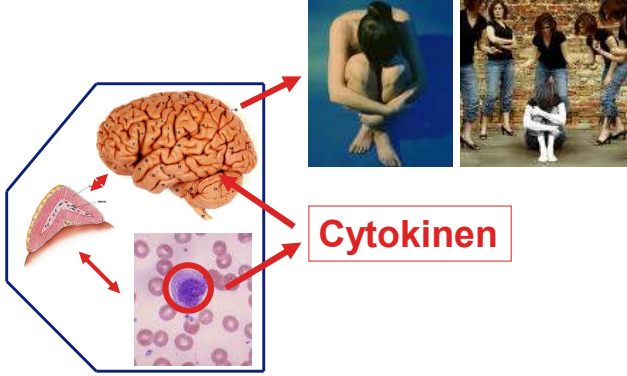
**Gemeenschappelijke aangeboren aanleg?**

**Afweer systeem, afweer cellen en afweer stoffen centraal**



ErasmusMC  
*Erasmus*

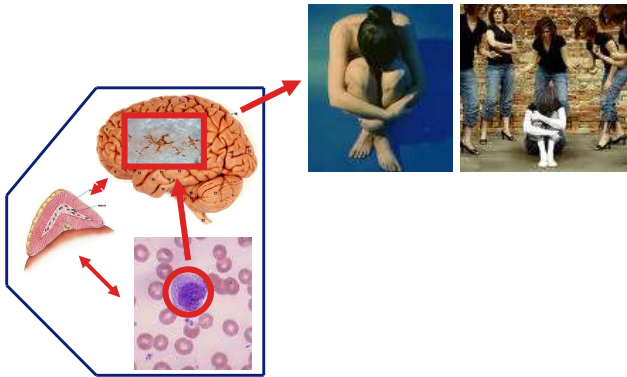
## Nieuwe Inzichten: Immunologie



**Cytokinen**

ErasmusMC  
*Erasmus*

## Nieuwe Inzichten: Microglia

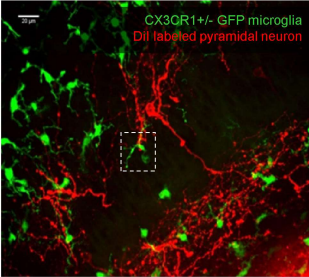


**Cell**

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

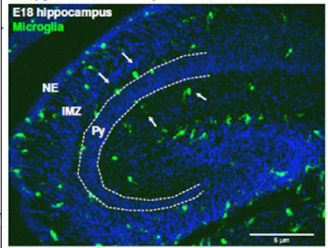
**News**  
**Key to psychological disorder may lie in the immune system**



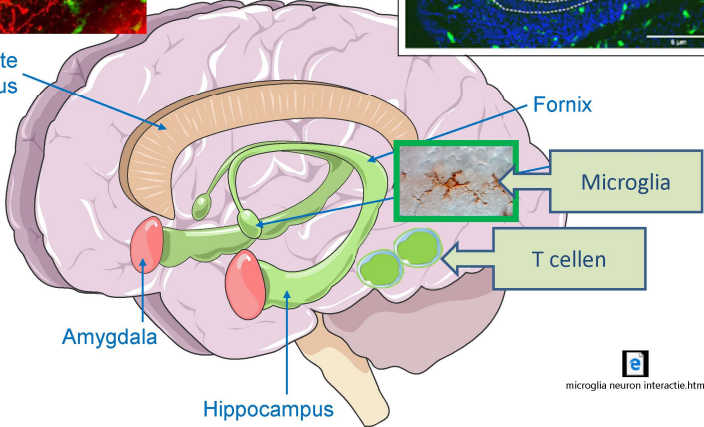
CX3CR1+/- GFP microglia  
Dll1 labeled pyramidal neuron

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  
NE  
IMZ  
Py



Cingulate gyrus      Fornix

Microglia

T cellen


Amygdala

Hippocampus

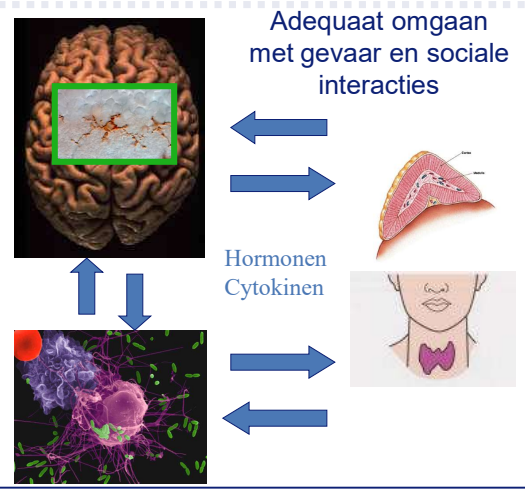
**Fronto-Cortico-Limbisch System**

microglia neuron interactie.htm

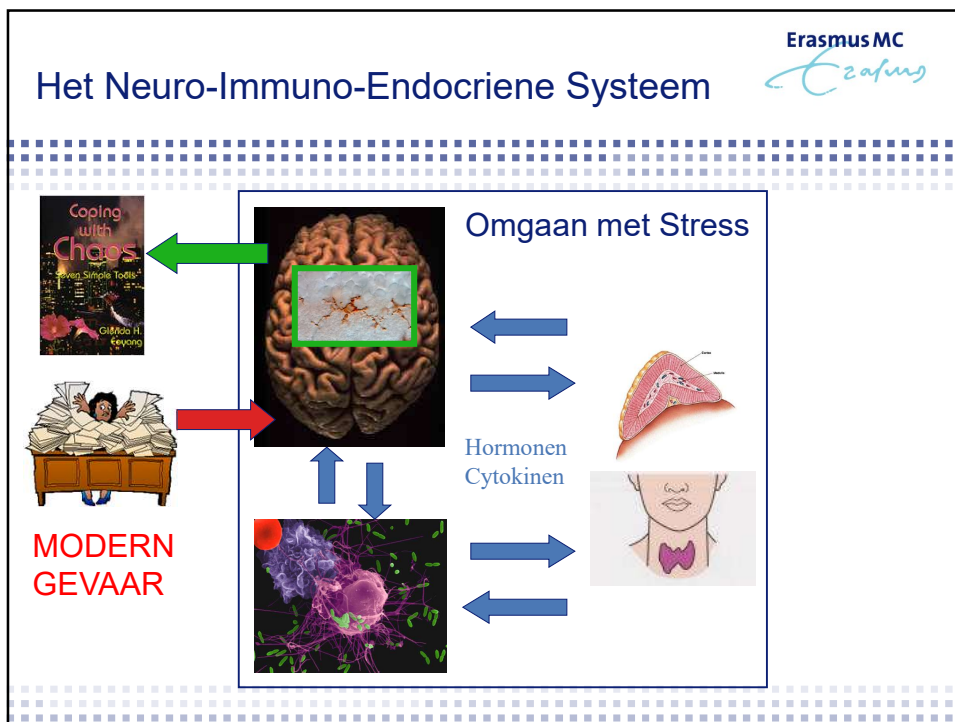
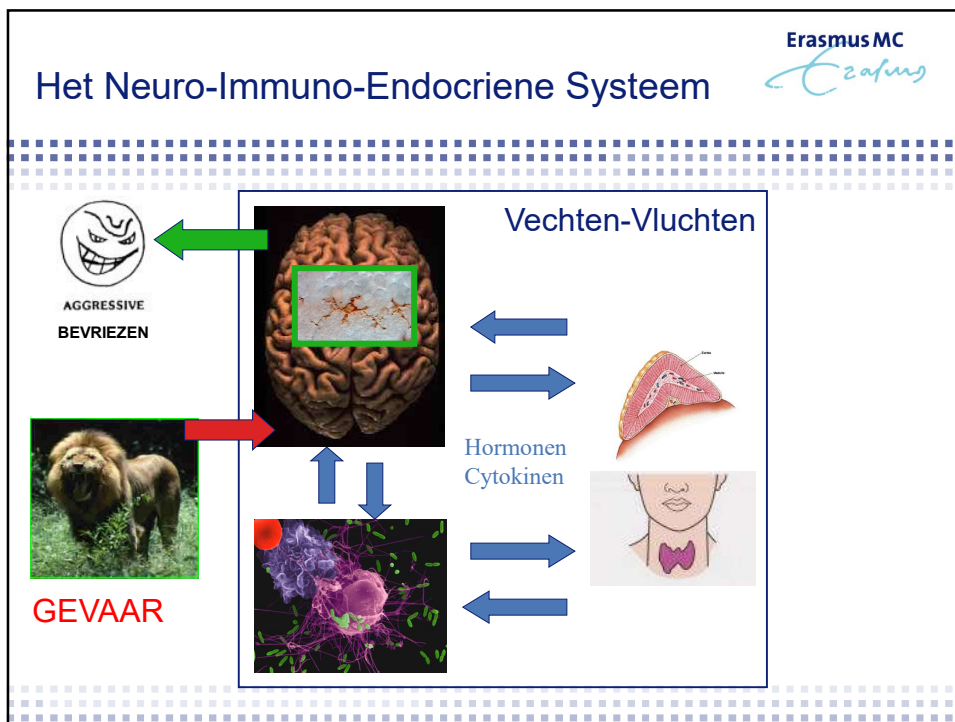
## Het Neuro-Immuno-Endocriene Systeem

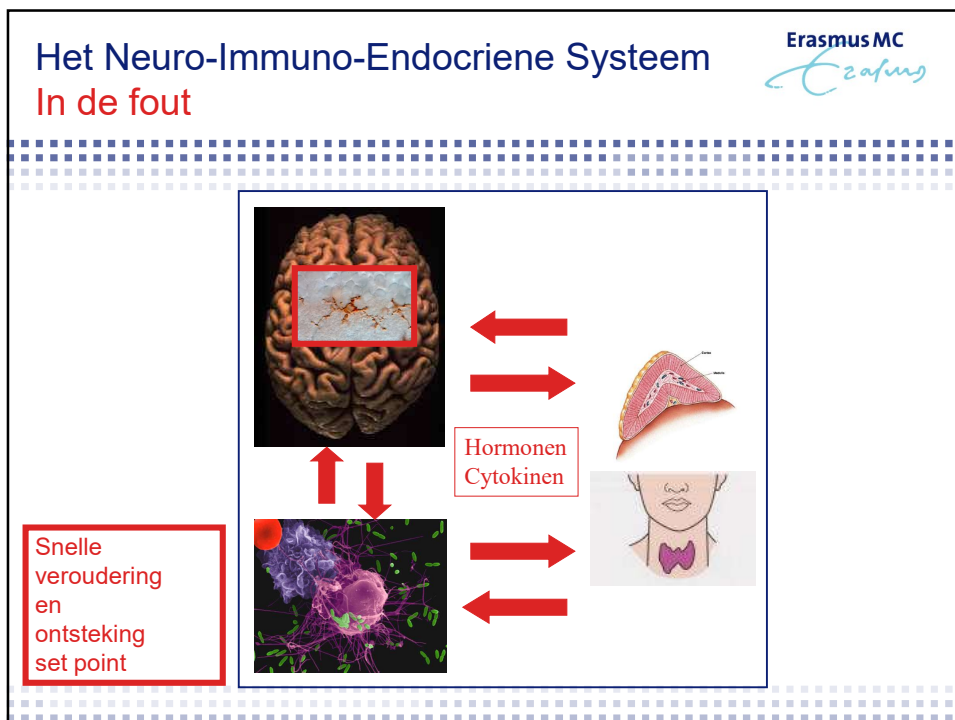
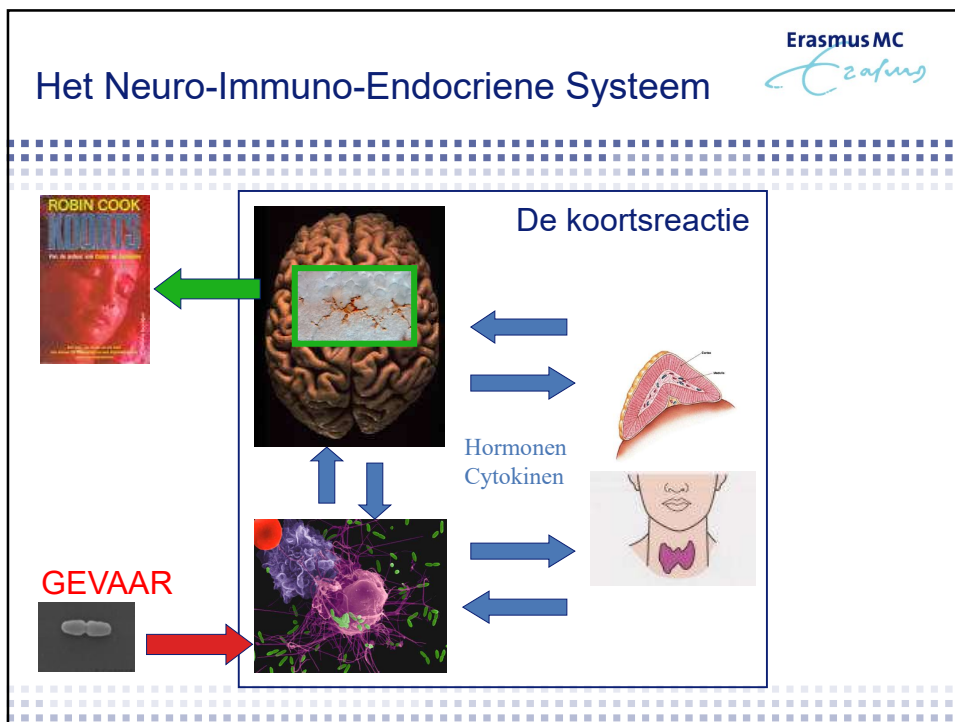


Adequaat omgaan met gevaar en sociale interacties



Hormonen  
Cytokinen

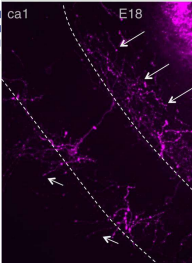






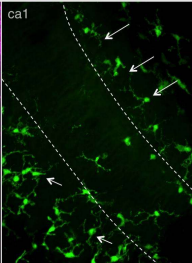
ErasmusMC  
*Erasmus*

## Nieuwe Inzichten: Microglia



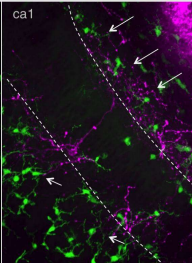
ca1 E18

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



ca1

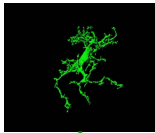
Microglia line up on both sides of the CA1 region...



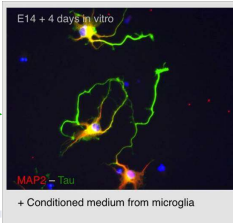
ca1

...closely apposed to neurites

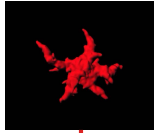
Microglia helpen neuronen te groeien in de hippocampus, het integratie centrum aan o.a. stress responsen



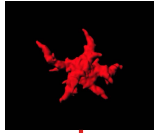
Resting microglia



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



+ Conditioned medium from LPS activated microglia




Inflamed microglia

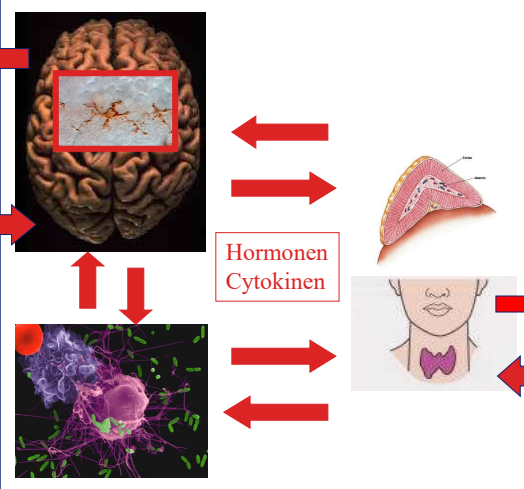
ErasmusMC  
*Erasmus*

## Het Neuro-Immuno-Endocriene Systeem


### In de fout



Stress



Hormonen  
Cytokinen

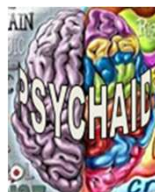



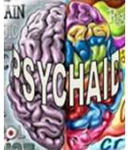


## Conclusies

- 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



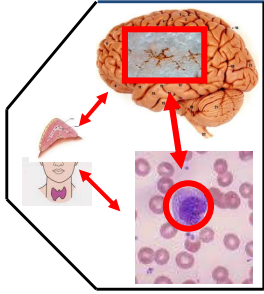
800 depressieve  
patienten




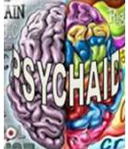

600 gezonden  
80 schizofrene  
patienten



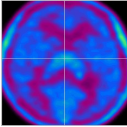
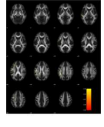

3 modellen



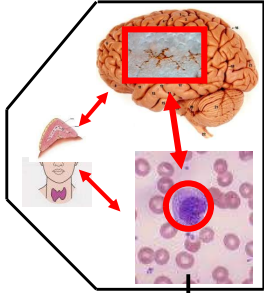

25 partners  
12 landen

Nieuwe generatie  
hersenscans voor o.a. microglia

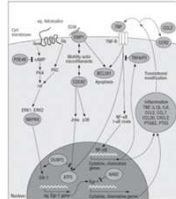

Evenwichts  
Interacties

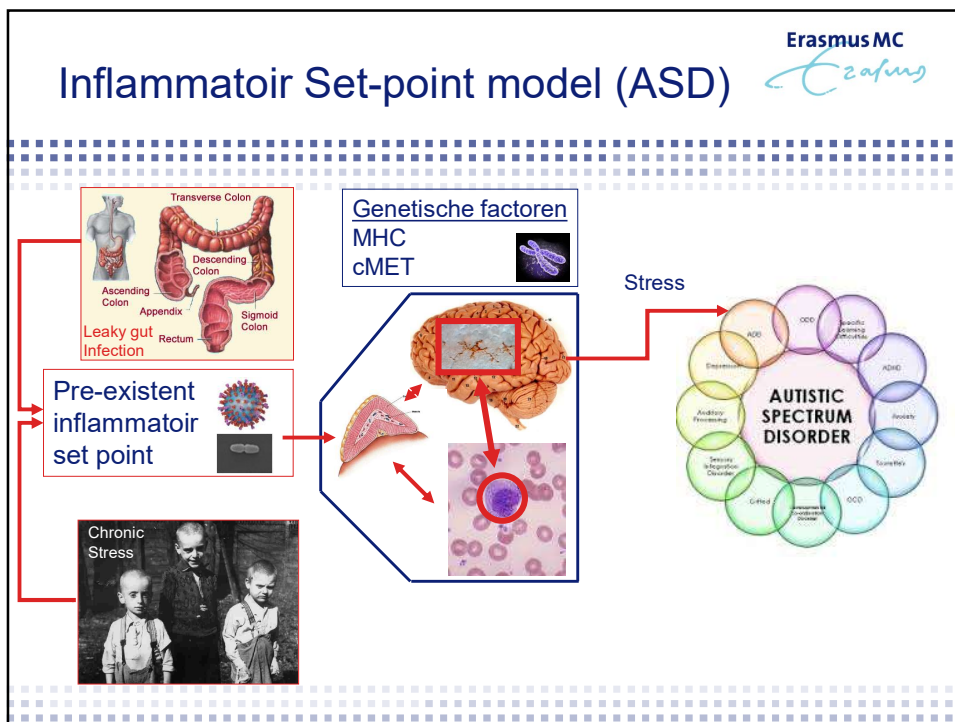
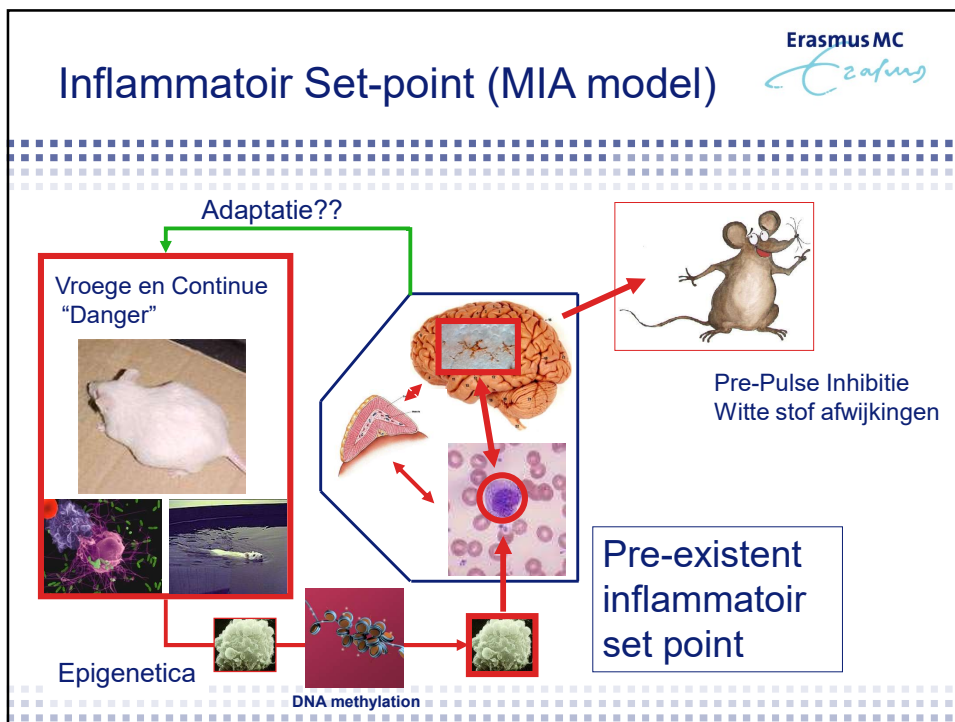



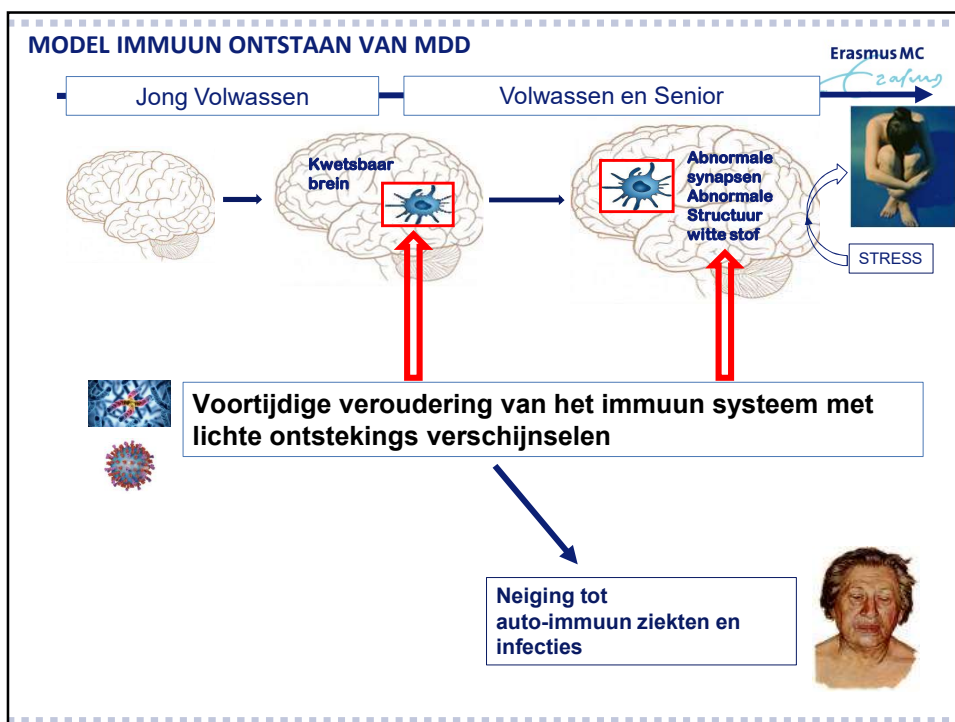
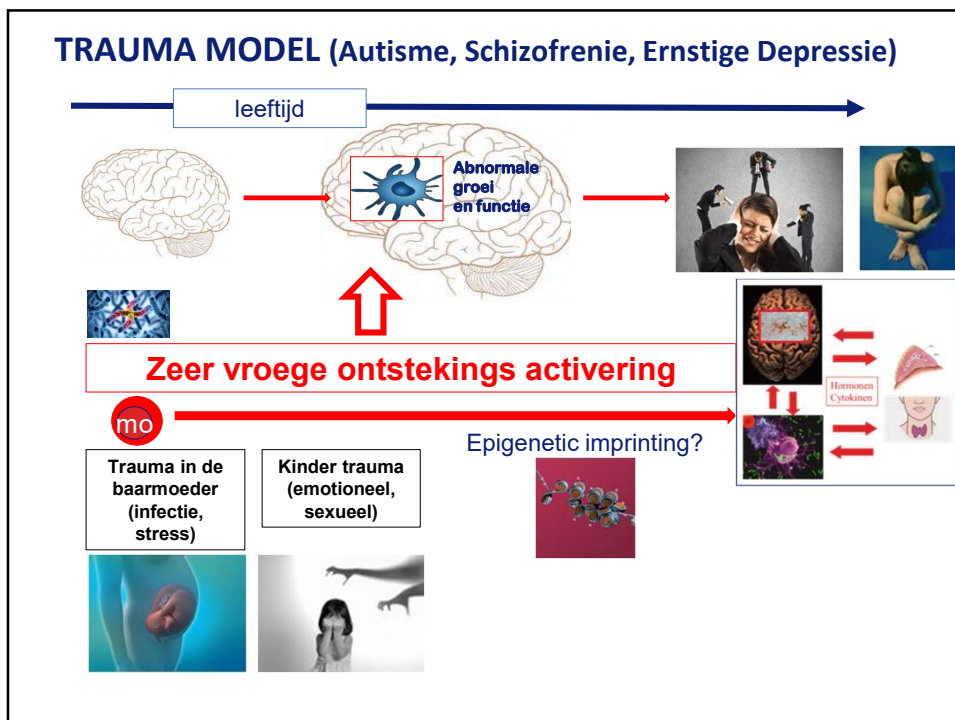
Nieuwe generatie  
bloed testen

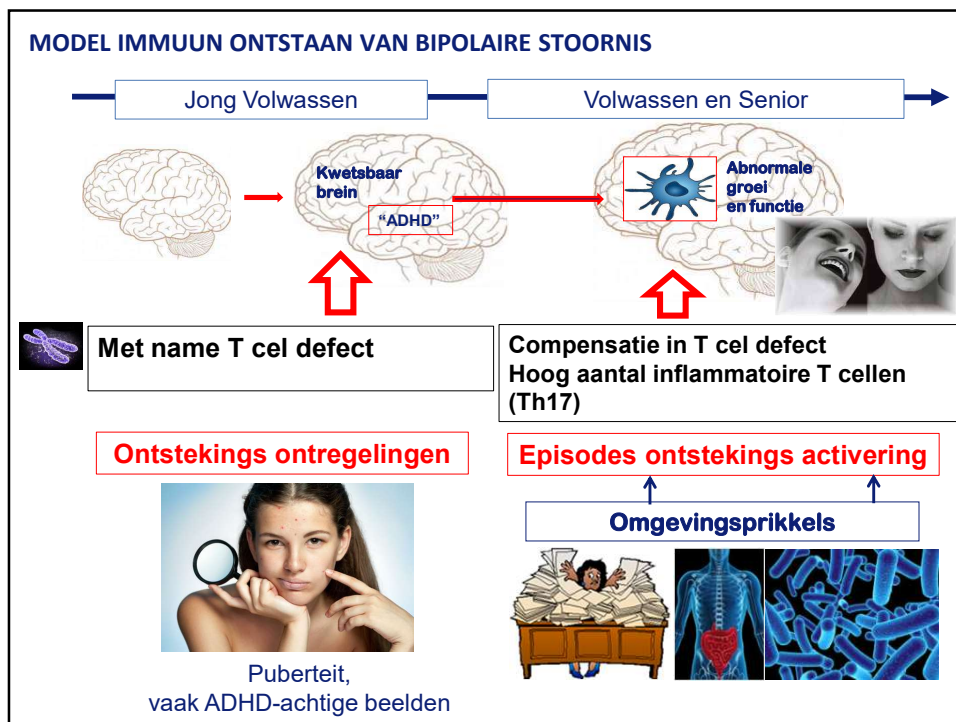
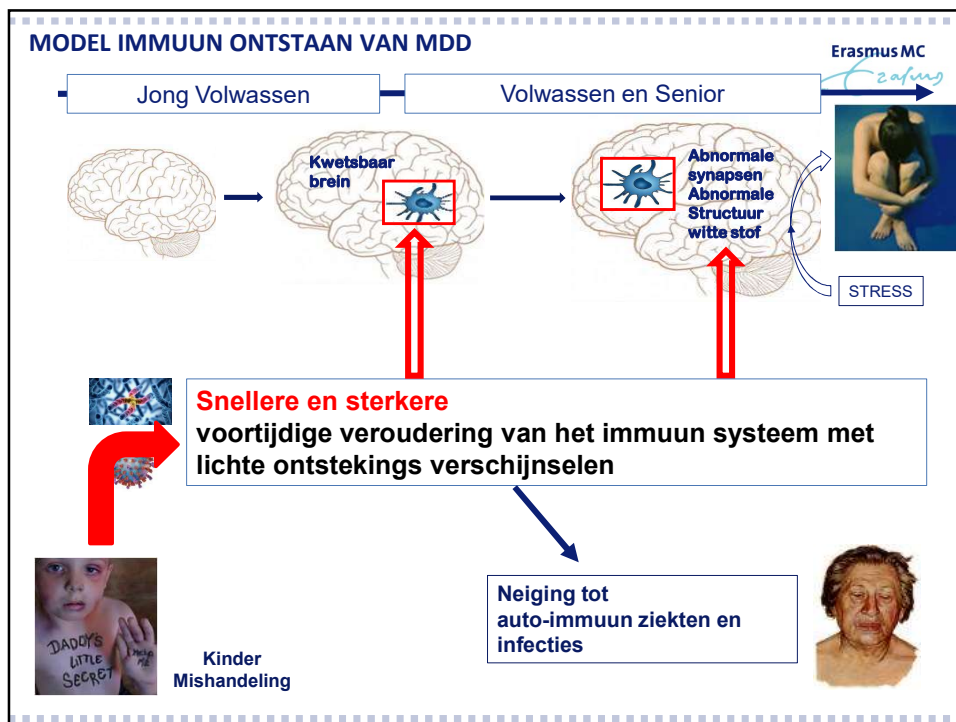
Genomics

- 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

