

# HET GEWELD(DAD)IGE BREIN

*De biologie van woede en agressie*

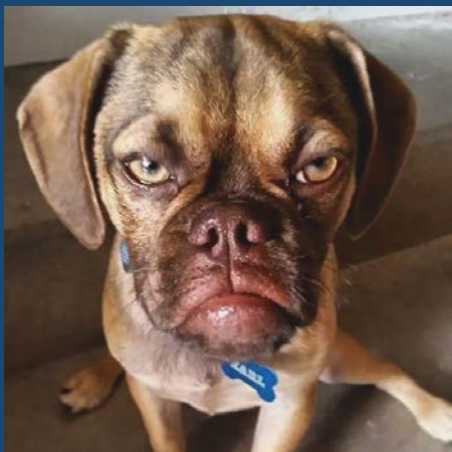


Manuel Morrens

**22 oktober, Breinwijzer VZW**



# Woede en agressie: een spectrum

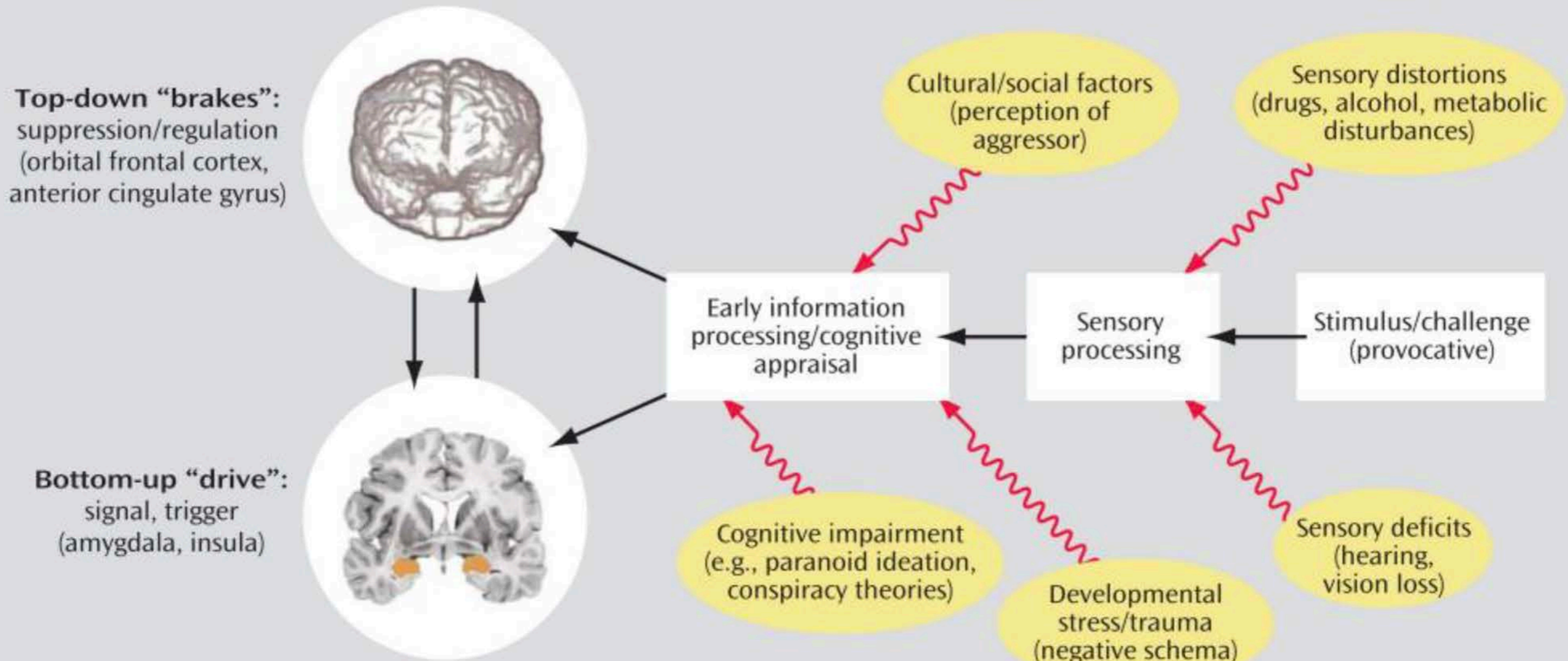


# Menselijke agressie

- Multifactorieel
  - Socioeconomische factoren
    - Armoede,...
    - Agressie meegemaakt in kindertijd
    - Hostiele omgeving
  - Culturele factoren
  - Psychologische factoren
    - Trauma, Misbruik of verwaarlozing in kindertijd
    - Persoonlijkheidsstructuur
      - Antisociale PSH, borderline PSH
      - Emotieregulatie/sensitiviteit
      - Cognitief functioneren
  - Medische factoren
    - alcohol en/of drugs
    - Hersenschade
  - Erfelijke factoren
    - Tweelingen onderzoek agressie : 44-72% heritabiliteit
    - Serotonine transporter/MAO-A



# Initiatie en modulatie van Agressie



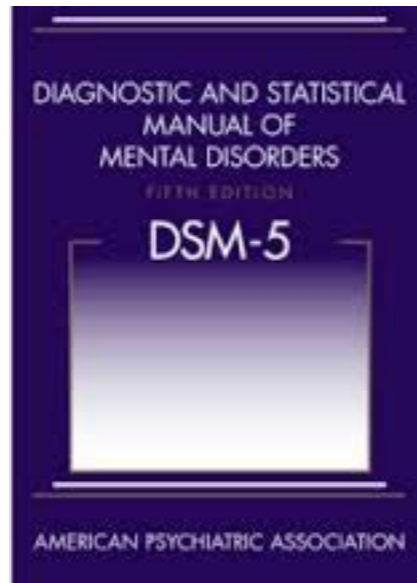
# Aspecten van agressie

- Doel van de agressie
  - Zichzelf
  - Anderen
- Vorm van agressie
  - Fysiek
  - Verbaal
  - Direct/indirect

# Aspecten van agressie

- Wereldwijd 1.43 miljoen mensen slachtoffer van geweld per jaar (WHO; excl gewapende conflicten)
  - Suicide
  - Homicide

# Woede en agressie als diagnose?



DSM-V workgroup chairmen



NO I DON'T HAVE  
PMS

# Het belang van een diagnose volgens het DSM systeem





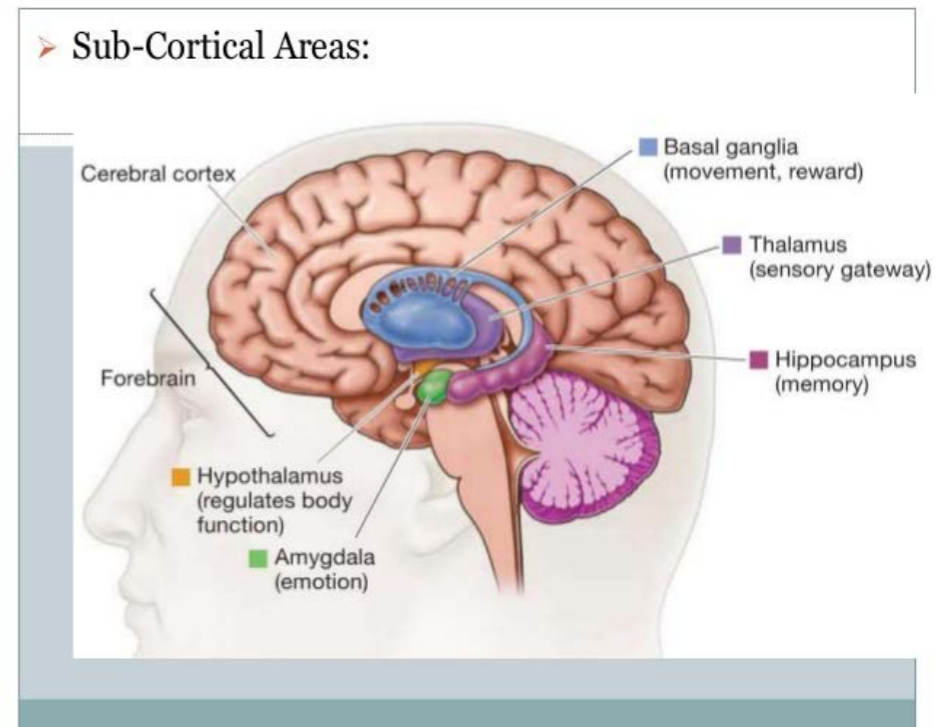
# Soorten agressie

- Aanvallende agressie
  - Voorbedacht
  - doelgericht
  
- Defensieve agressie
  - Reactief (bv op bedreigende situatie)
  - Impulsief
  - Arousal



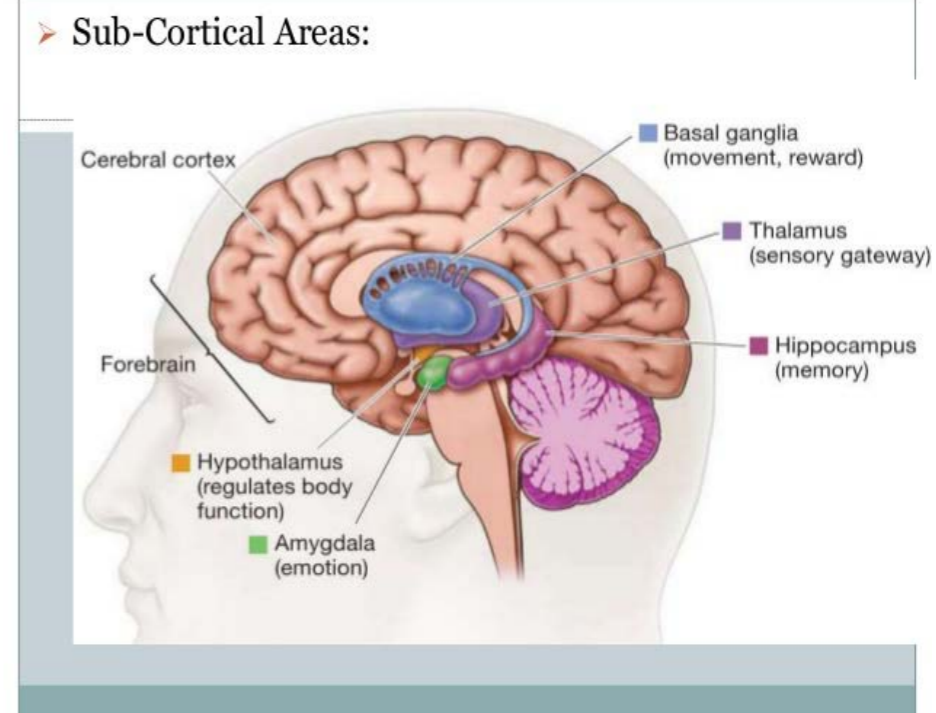
# Hersenstructuren betrokken bij agressie

- Corticale structuren
  - Orbitofrontale regio
  - Anterior cingulate cortex
- Subcorticale structuren
  - Hypothalamus
  - Amygdala
  - Limbisch systeem



# Hersenstructuren betrokken bij agressie

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# De rol van de frontale cortex bij agressie: een casus

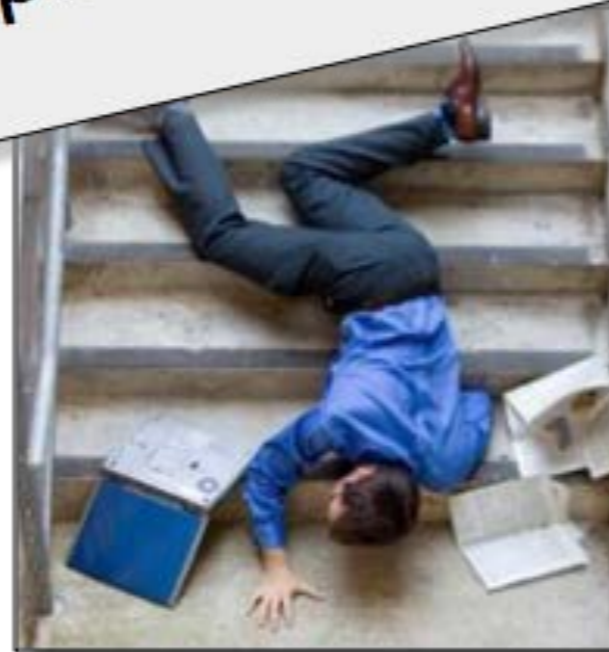


Het geval van Phineas Gage

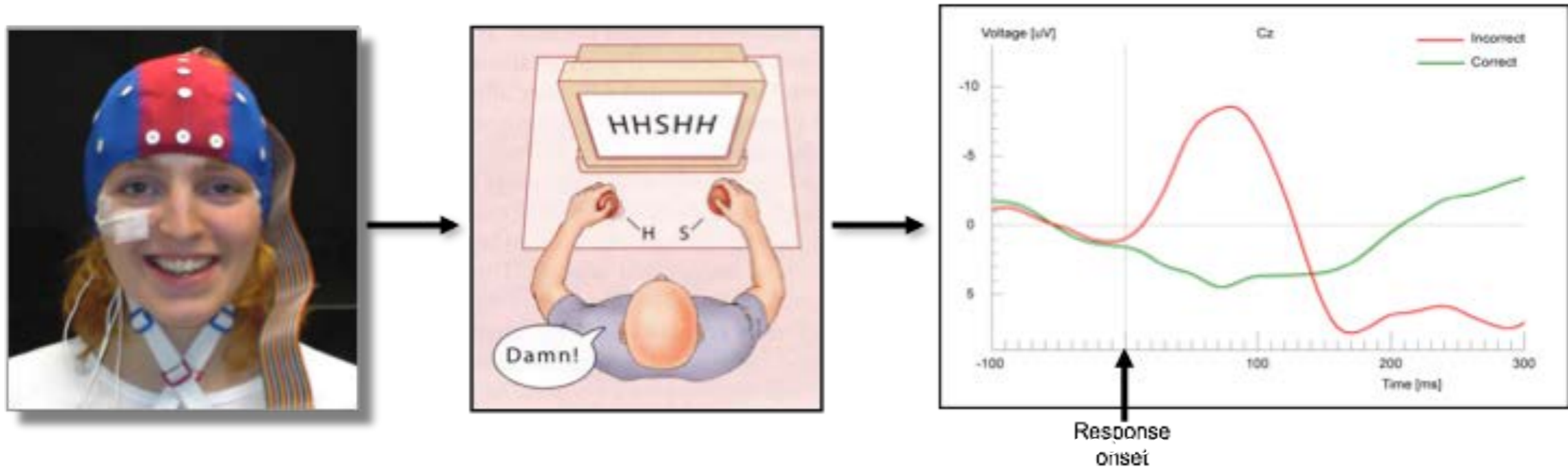
# Frontale controle en fouten



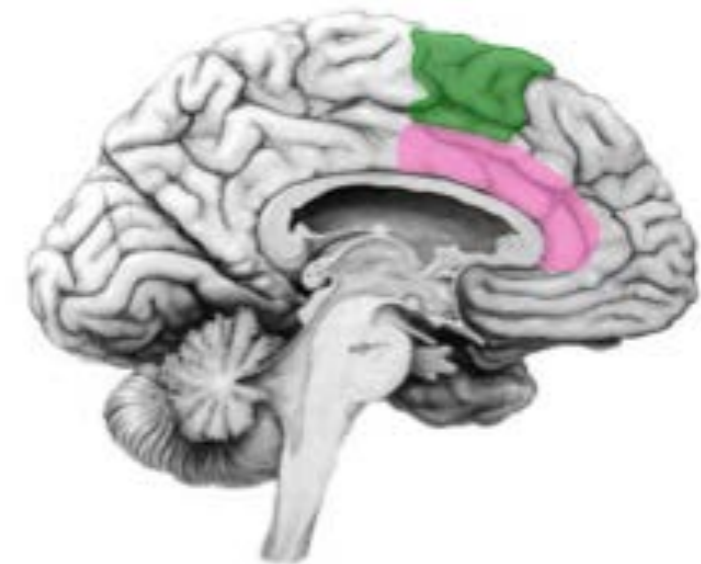
People make errors!



# Hoe de hersenen fouten detecteren



Error-related negativity (ERN) (Falkenstein et al, 1991; Gehring et al., 1993)  
Followed by positive component: error positivity or Pe  
ERN also for unaware errors, Pe only for aware errors  
(Nieuwenhuis et al., 2001)  
Crucial role for posterior medial frontal cortex (pmFC), including pre-SMA and ACC



# Foutdetectie in een sociale context

Flexibly adapt own actions in response to other's people's intentions and actions in order to reach...  
...a common goal (cooperation)  
...an individual goal (competition)

Monitor own actions and errors.

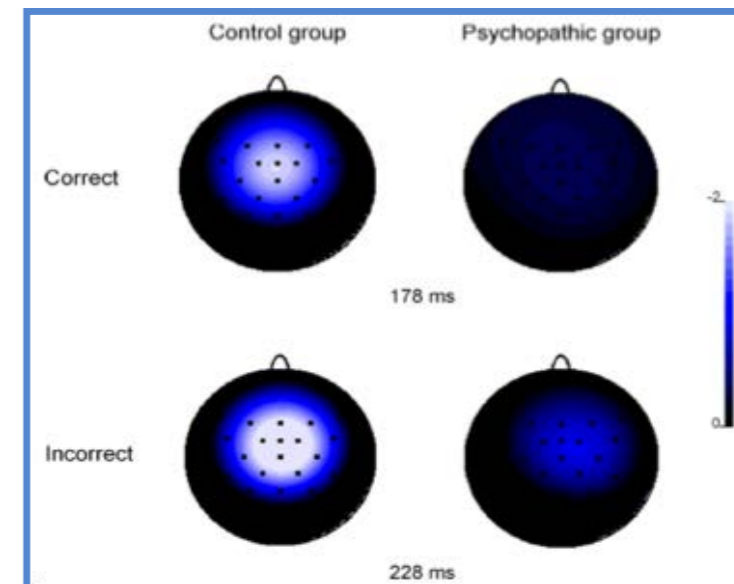
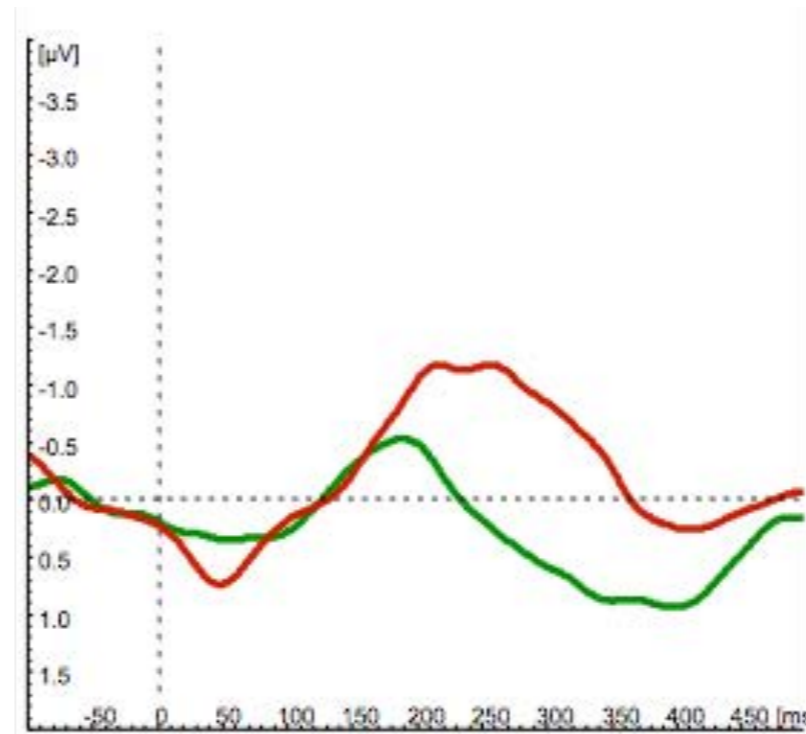
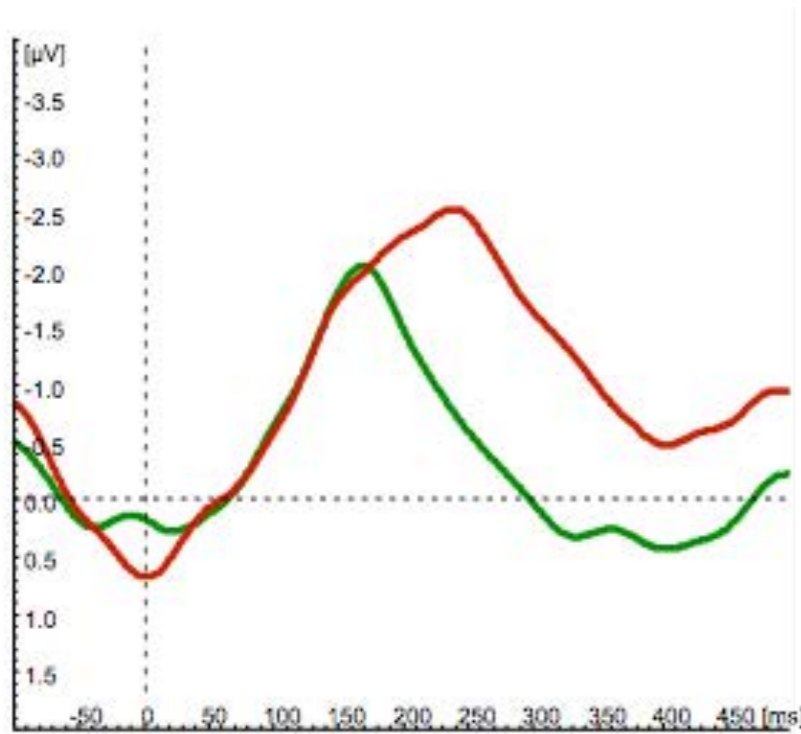
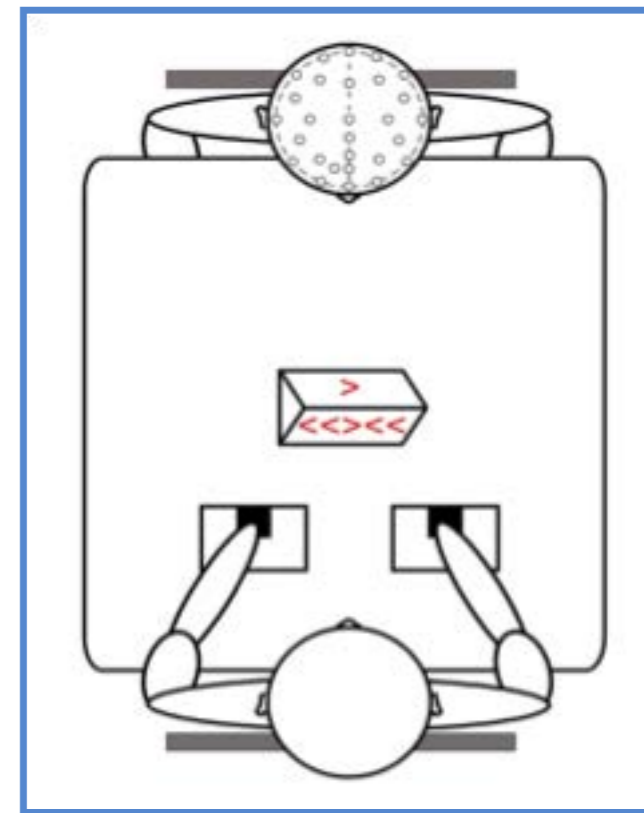
Monitor actions and errors of person one is interacting with.

Incorporate the context of the interaction.



**Central role for action-monitoring and error-detection processes**

# ERN in observed errors



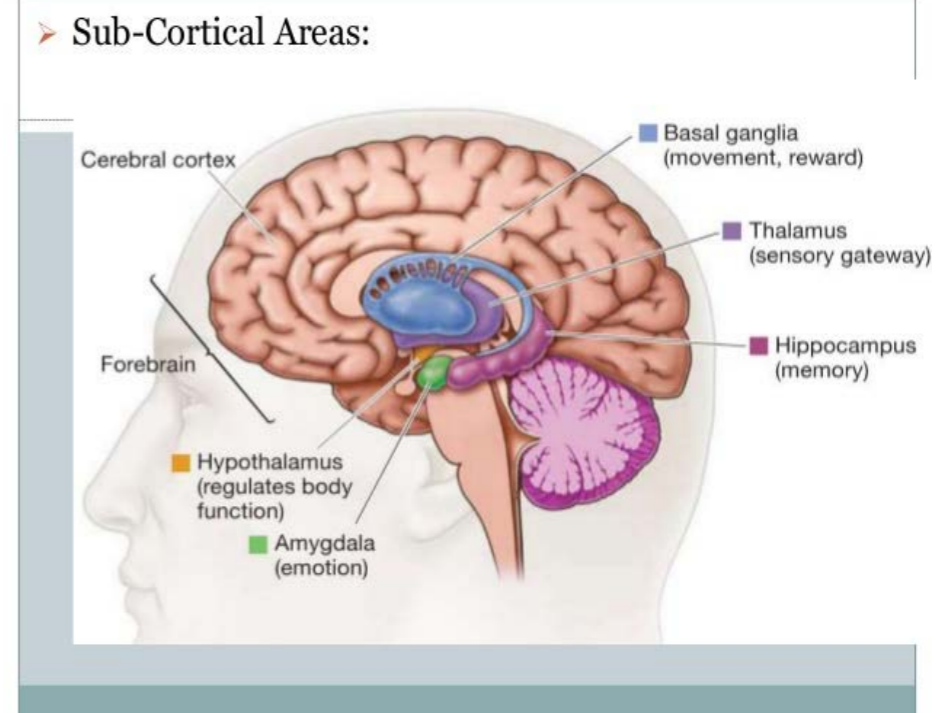
Individuals with psychopathy display reduced ERP amplitudes in response to other's actions.



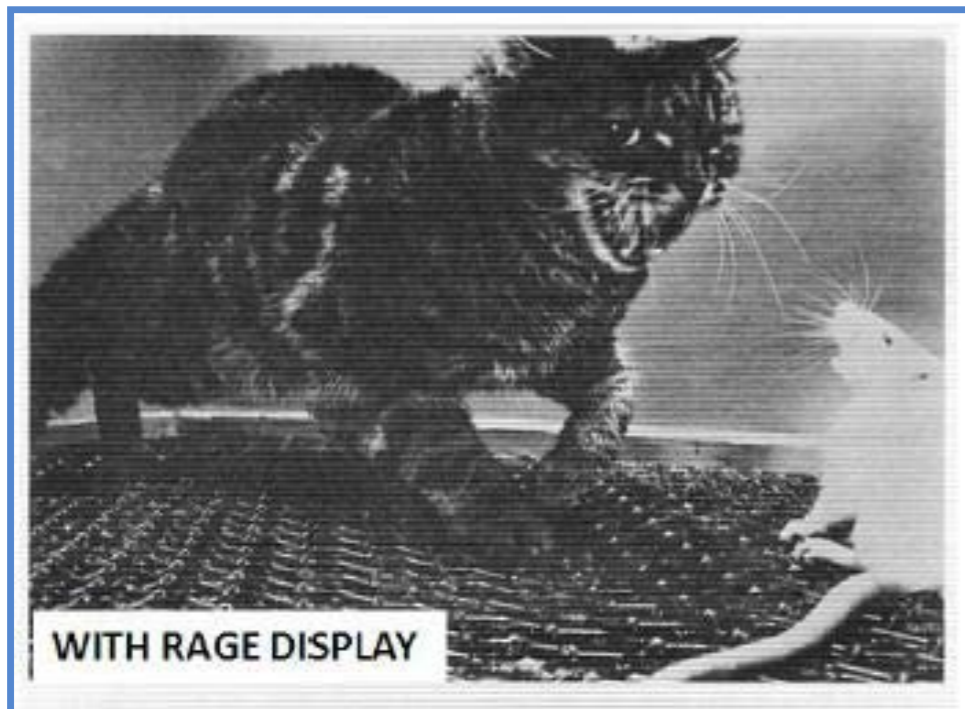
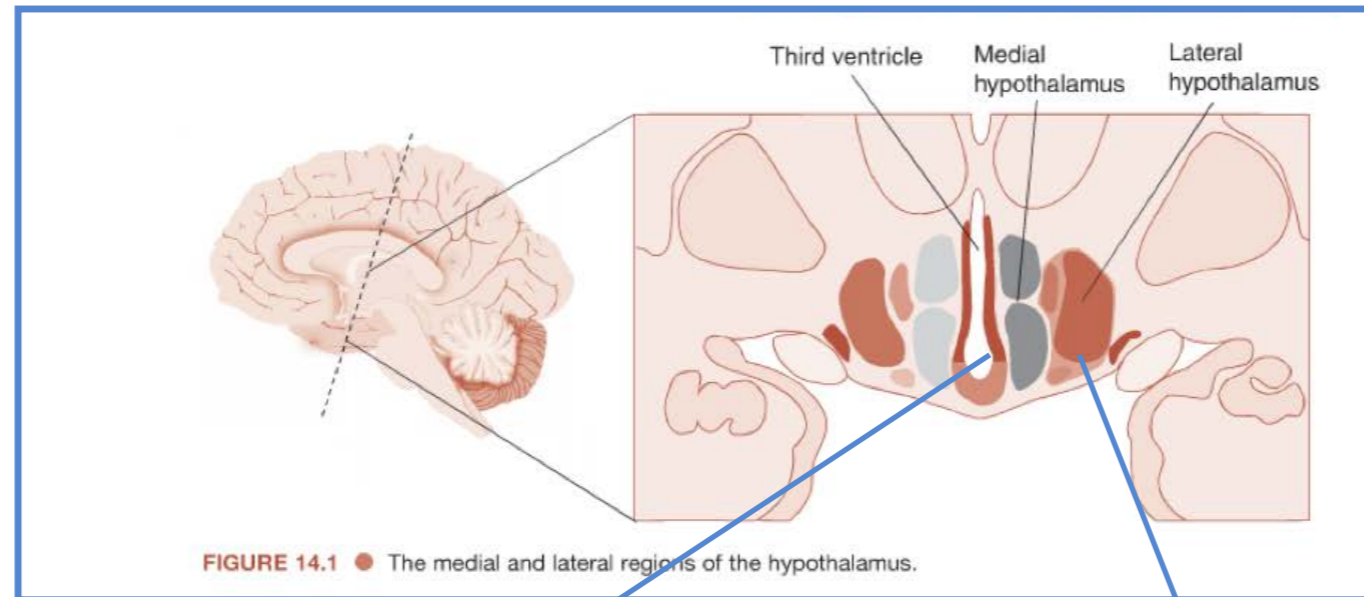
# Hersenstructuren betrokken bij agressie

- Corticale structuren
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  - Anterior cingulate cortex

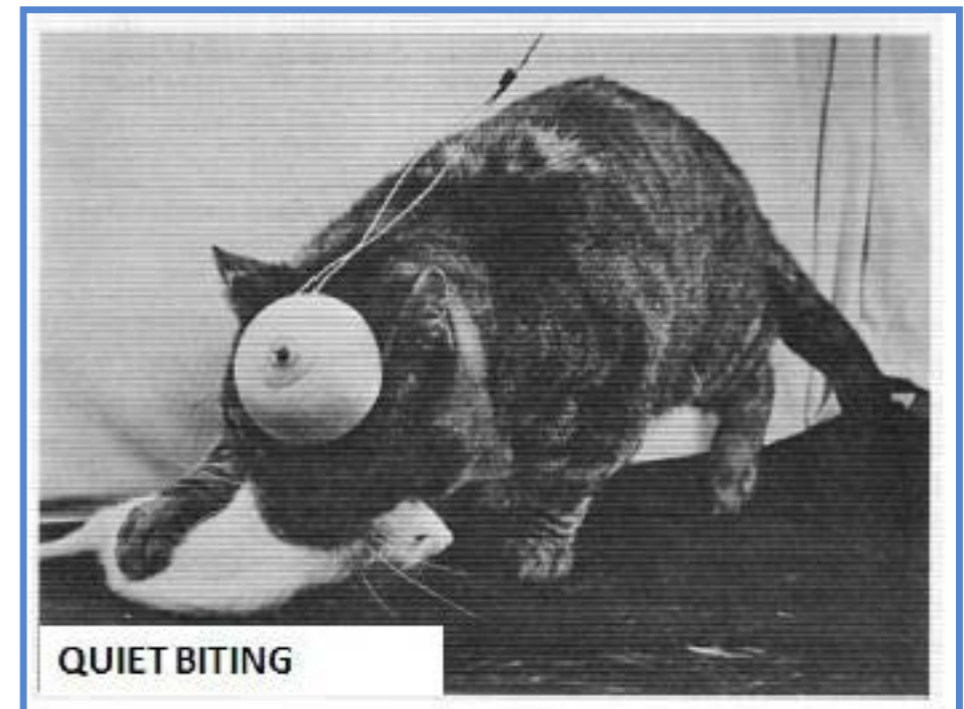
- Subcorticale structuren
  - Hypothalamus
  - Amygdala
  - Limbisch systeem



# Hypothalamus en agressie



Stimulatie mediale hypothalamus



Stimulatie laterale hypothalamus

# Aanvallende vs defensieve agressie

**TABLE 14.1**

**The Different Features of Predatory and Defensive Aggression**

|                       | <b>Predatory Aggression</b>                   | <b>Defensive Aggression</b>                    |
|-----------------------|---|--|
| CNS location          | Lateral hypothalamus                          | Medial hypothalamus                            |
| Sympathetic tone      | Calm  | Autonomic arousal                              |
| Behavior              | Stealthy movement, bite to back of rat's neck | Hissing, arching back, paw swipe, piloerection |
| Evolutionary function | Hunting                                       | Protection                                     |
| Quality               | Hidden, premeditated                          | Overt, reactive                                |

CNS, central nervous system

# Chronic high frequency stimulation of the posteromedial hypothalamus in facial pain syndromes and behaviour disorders

A. Franzini<sup>1</sup>, C. Marras<sup>1</sup>, G. Tringali<sup>1</sup>, M. Leone<sup>2</sup>, P. Ferroli<sup>1</sup>, G. Bussone<sup>2</sup>, O. Bugiani<sup>2</sup>, and G. Broggi<sup>1</sup>

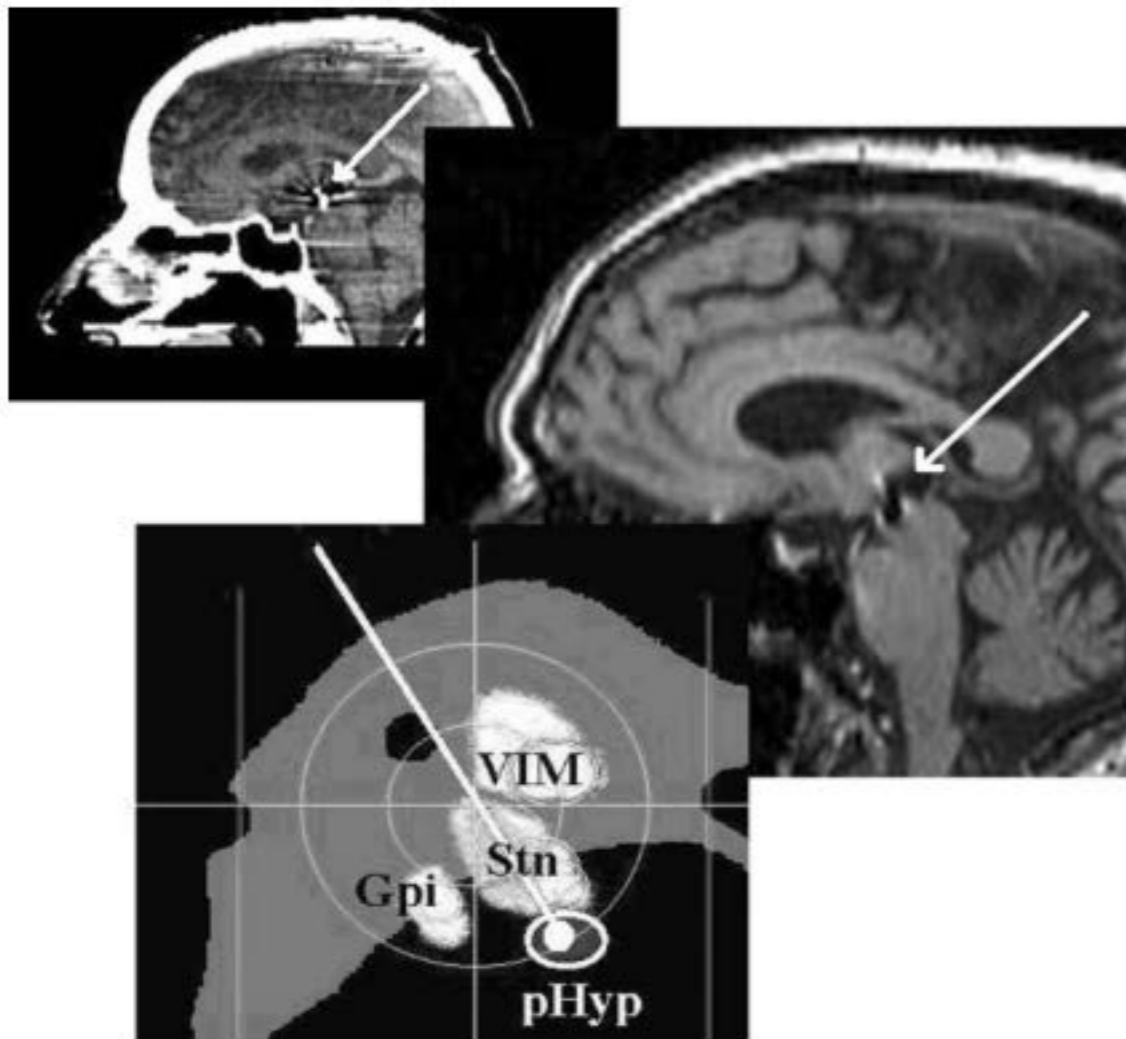


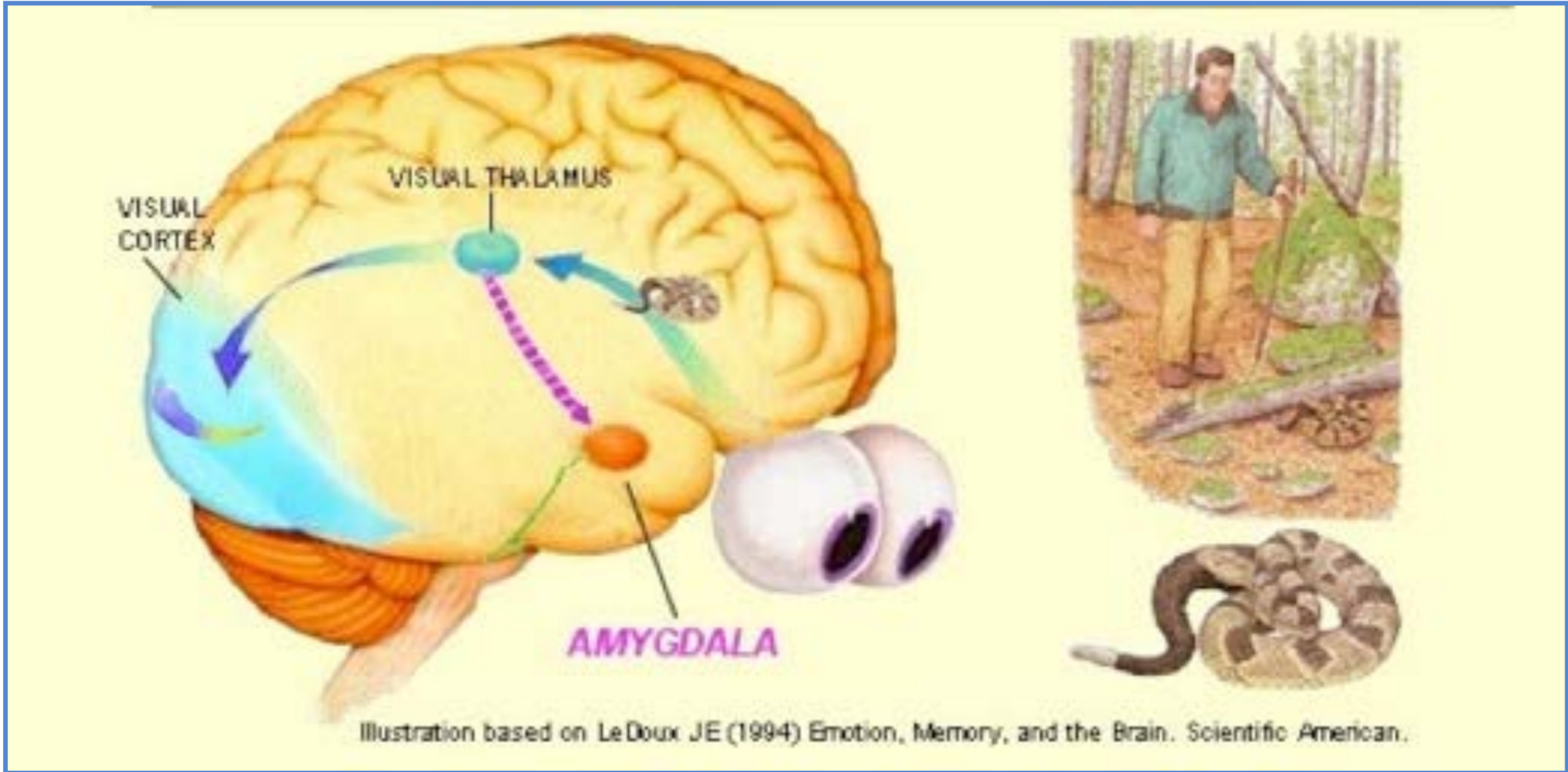
Fig. 3. Sagittal CT and MRI slices showing the active contact of the electrode stimulating the posteromedial hypothalamus (*white arrows*). The inferior box shows the target on the ventriculogram registered to the bicommissural system



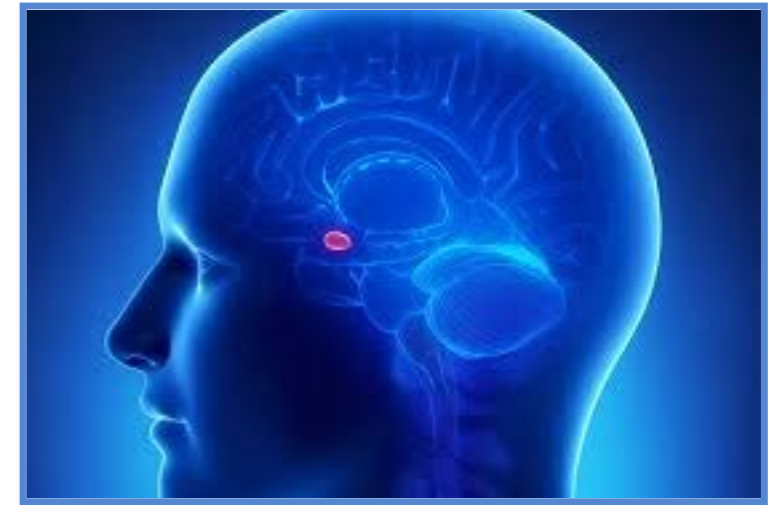
HFS of the PMH successfully controlled violent and disruptive behaviour in patients refractory to the conventional sedative drugs.



# Rol van amygdala



## Rol van de amygdala



- Historische ingrepen van bilaterale amygdalotomie:  
=> Afgevlakt: noch angstig, noch agressief
- Overactivatie amygdala geassocieerd met verhoogde defensieve agressie

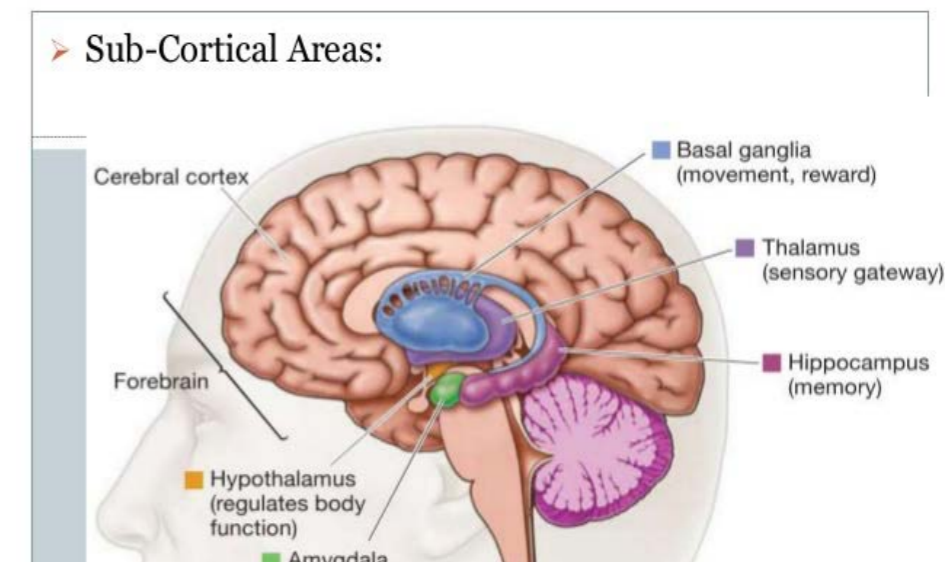
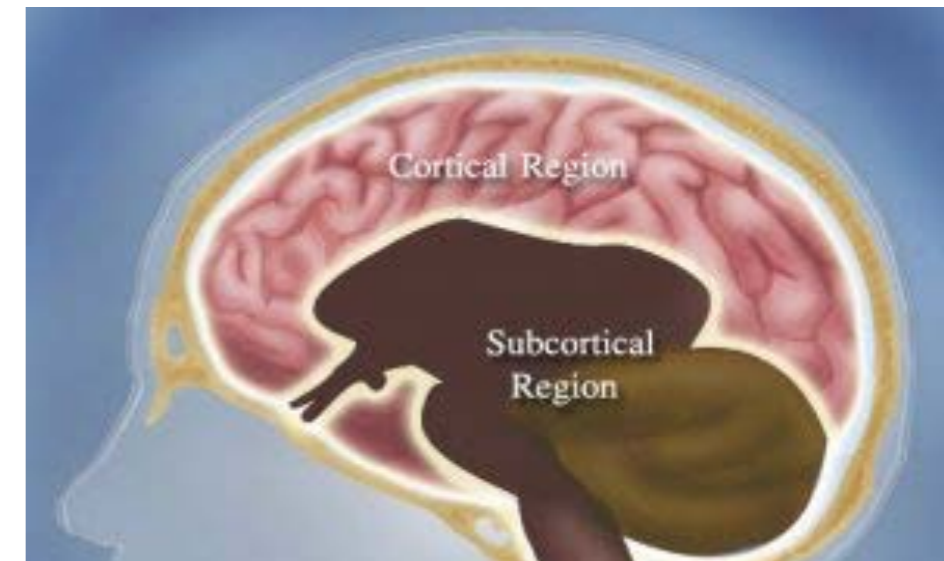
Amygdala lijken rol te spelen in inschatting of situatie bedreigend is.

# Hersenstructuren betrokken bij agressie

- Corticale structuren
  - Orbitofrontale regio
  - Anterior cingulate cortex

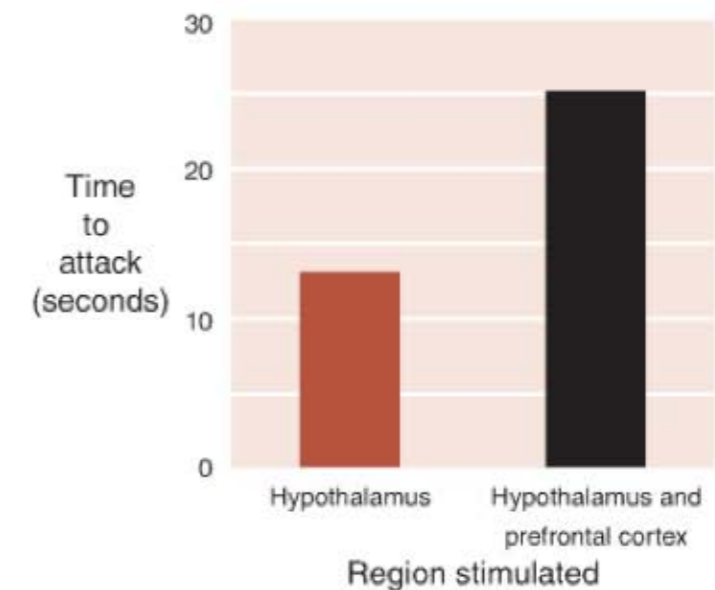


- Subcorticale structuren
  - Hypothalamus
  - Amygdala
  - Limbisch systeem



# Inhibitorische functie van de PFC

- PFC speelt rol in:
  - Gedragsregulatie
  - Inhibitie van sociaal ongepast gedrag
  - Complex gedrag plannen
  - Besluitvorming
  - expressie van persoonlijkheid

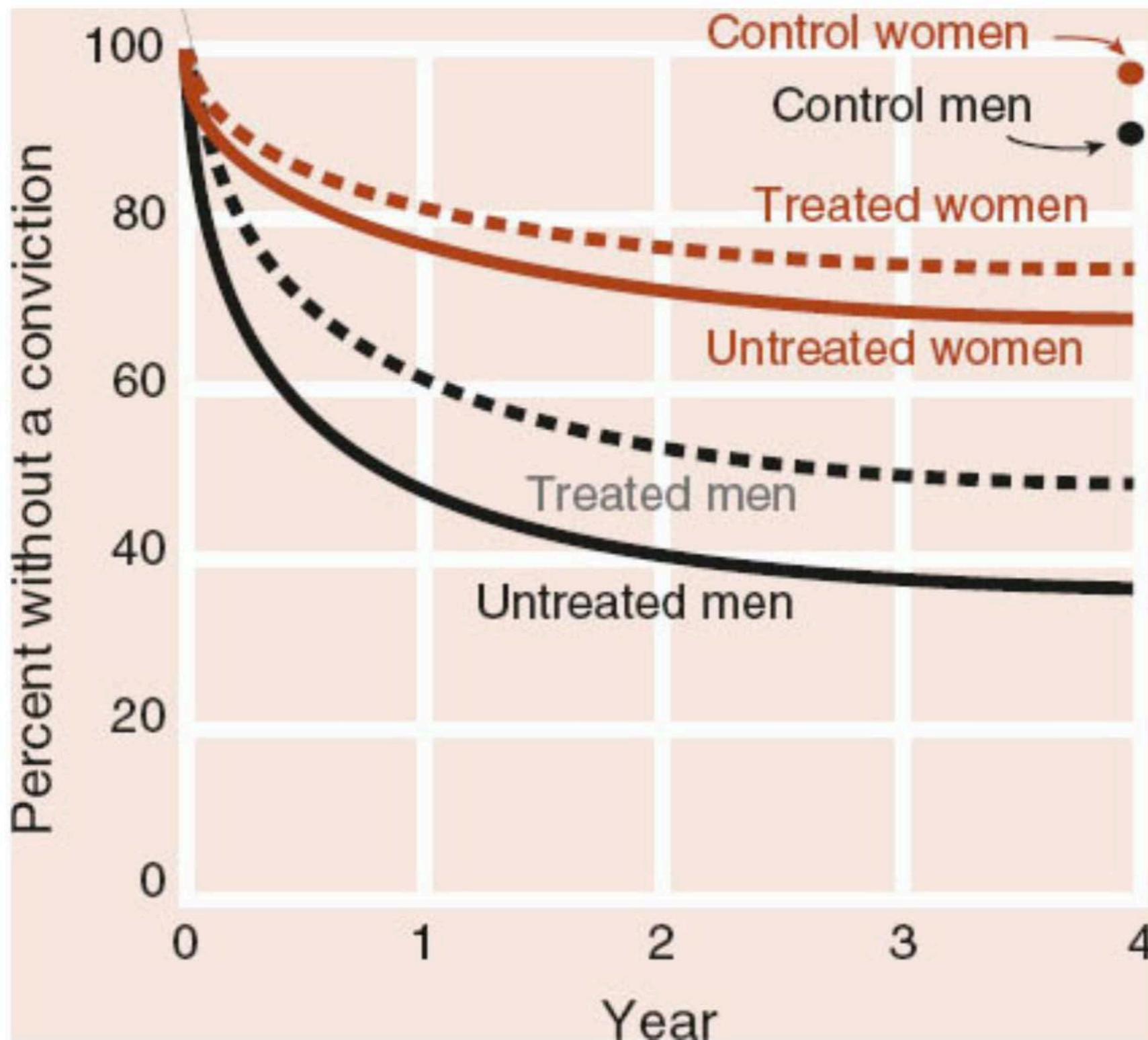


**FIGURE 14.5** ● The time it takes a cat to attack a rat after the hypothalamus is stimulated is greatly increased when the frontal cortex is simultaneously stimulated. (Adapted from Siegel A, Edinger H, Dotto M. Effects of electrical stimulation of the lateral aspect of the prefrontal cortex upon attack behavior in cats. *Brain Res.* 1975;93:473-484.)



# Corticale-subcorticale structuren ikv psychiatrische aandoeningen

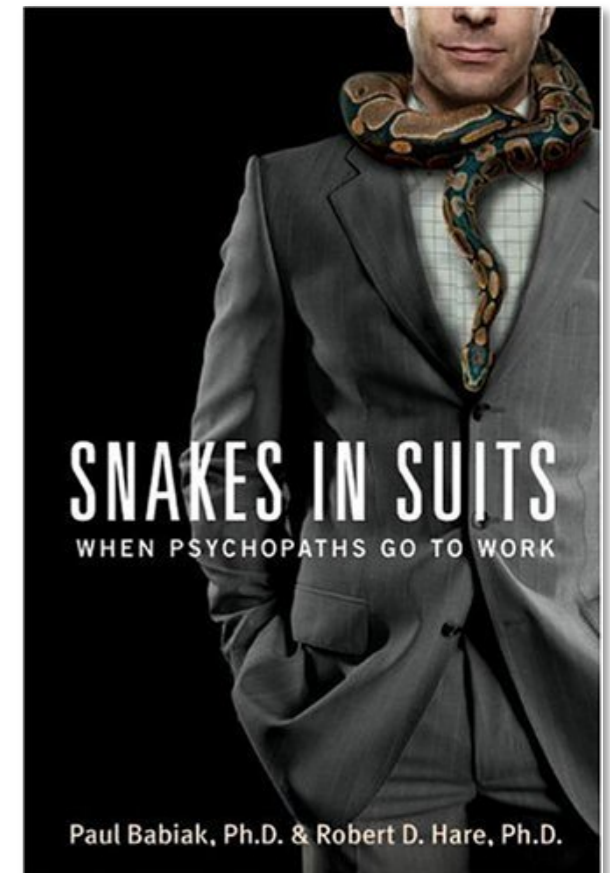
|  | Frontal inhibition | Limbic irritability | Striatal hyperactivity |
|--|--------------------|---------------------|------------------------|
| ADHD   | ↓                  |                     |                        |
| Borderline personality disorder/PTSD/substance abuse | ↓                  | ↑                   |                        |
| Antisocial personality disorder                      | ↓                  | ↓                   |                        |
| Psychosis  | ↓                  |                     | ↑                      |



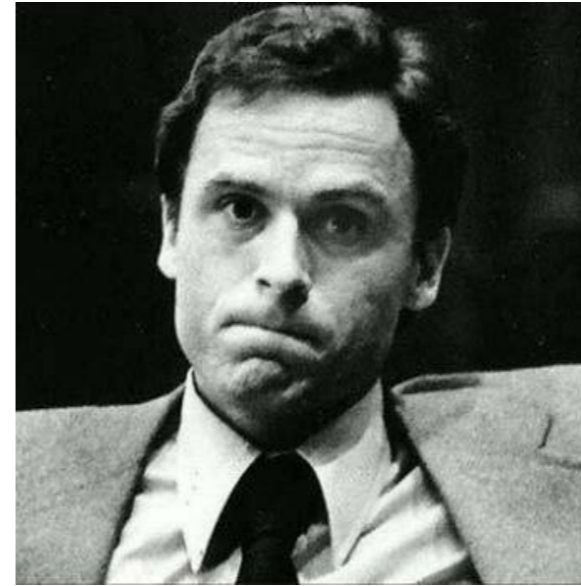
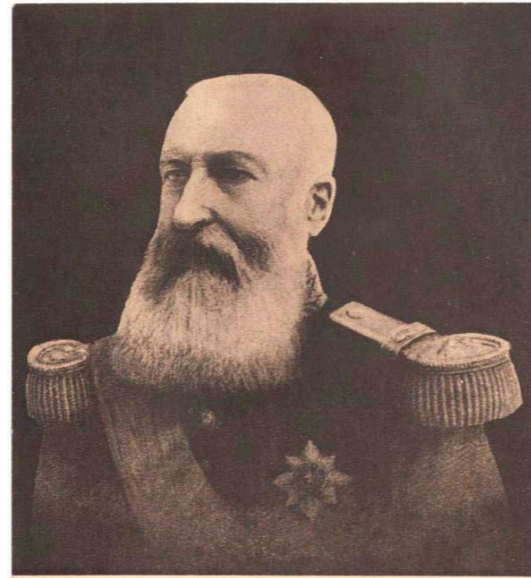
ADHD is geassocieerd met meer veroordelingen wegens agressie. Echter, behandeling voor ADHD verlaagt aantal veroordelingen

# Psychopathie

- Agressieve factor
  - Impulsieve agressie
  - Misdaden
- Emotionele oppervlakkigheid
  - Oppervlakkig
  - Egocentrisch
  - Gebrek aan schuldgevoelens
  - Gebrek aan empathie
  - manipulatief



# Gekende psychopaten



**Donald Trump outscores  
Hitler on psychopathic traits  
test, claims University of  
Oxford researcher**



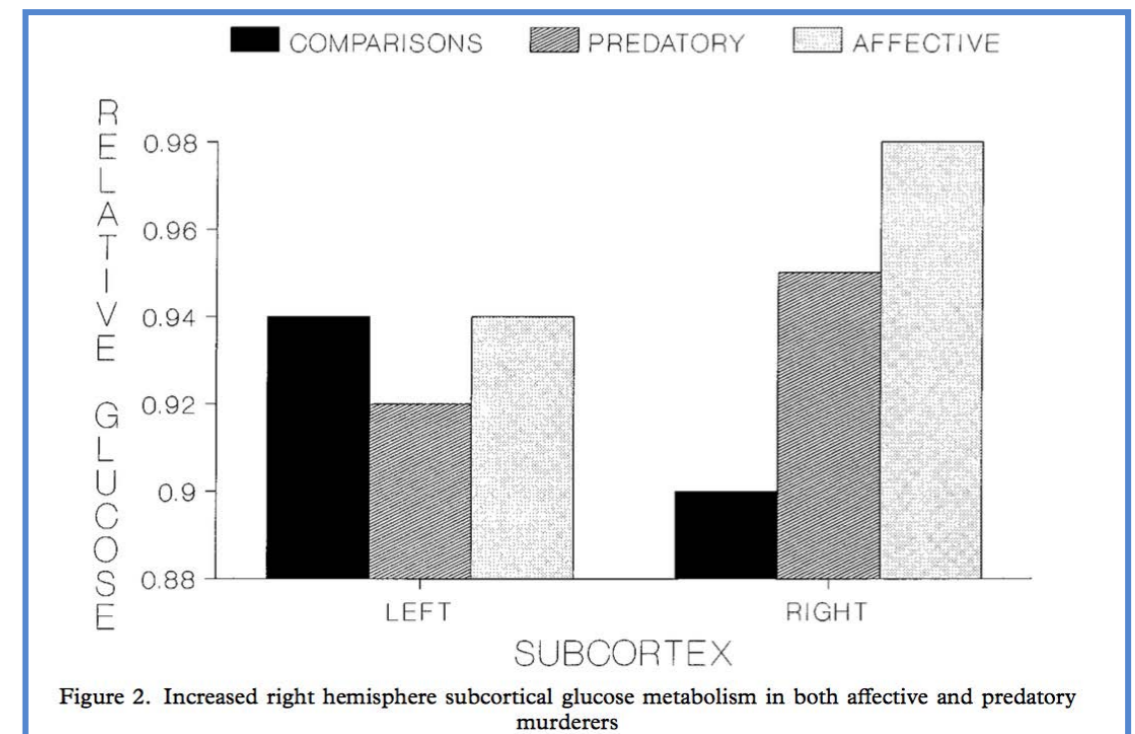
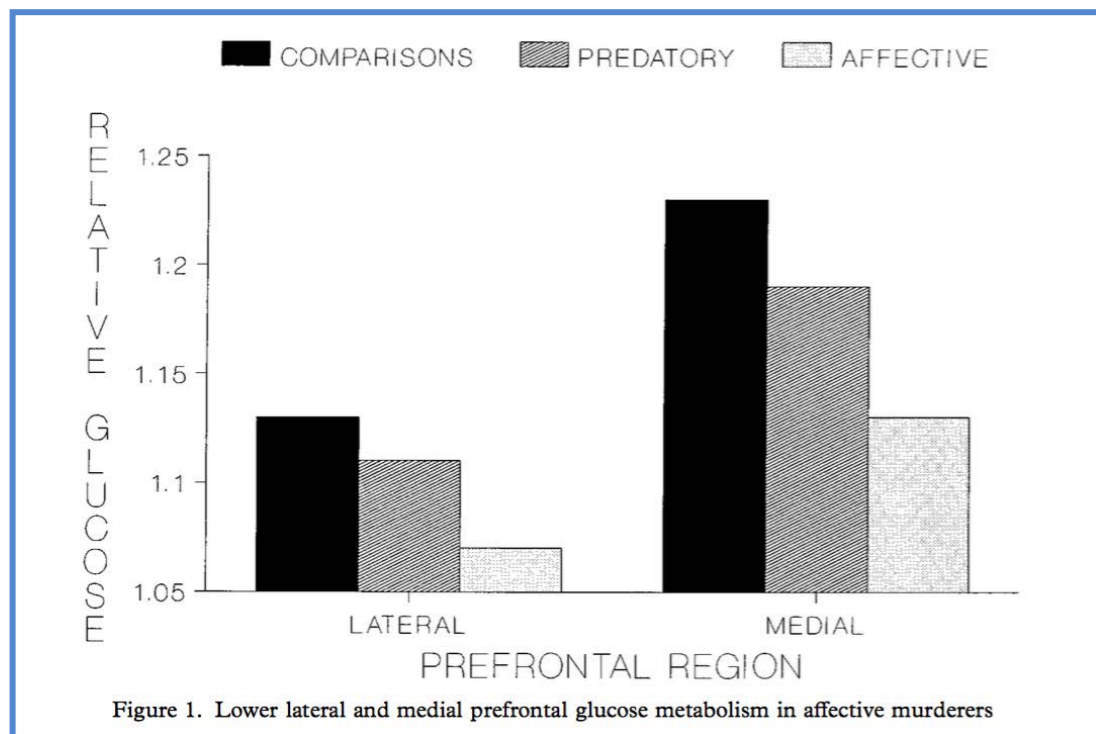
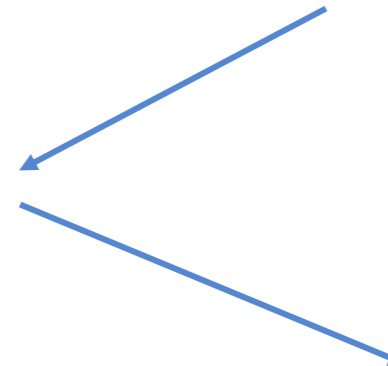
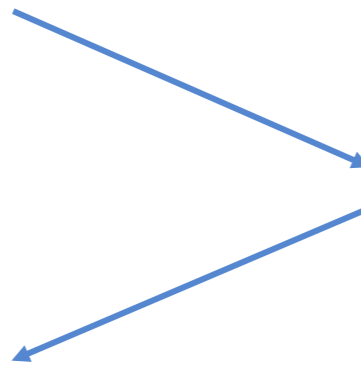
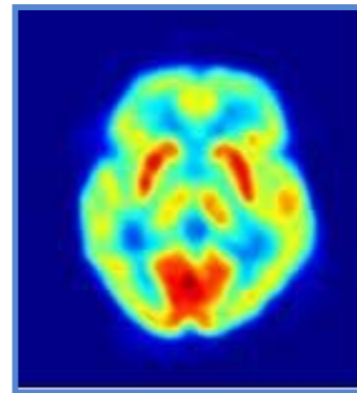
<https://www.youtube.com/watch?v=17lulasjDcU>



Affective murderers




Predatory murderers





# De neurobiologie van automutilatie bij borderline persoonlijkheid



## RISK FACTORS

  
 Genetics


  
 Trauma


  
 Female

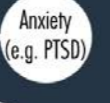
BPD has been linked to possible structural and functional changes in brain involving impulsivity, though the relationship is not fully understood yet.


## COMORBIDITY


Those with BPD are also likely to be diagnosed with other mental disorders, including:


  
 Bipolar Disorder

  
 Eating Disorders


  
 Anxiety (e.g. PTSD)


  
 Other Personality Disorders


  
 Substance Abuse

  
 Depression

## TREATMENT/RESEARCH

  
 Psychotherapy

  
 Self-Image


  
 Education

What are the biological and environmental risk factors?




How do we identify BPD earlier in children and adolescents?

## BORDERLINE PERSONALITY DISORDER (BPD)

Borderline personality disorder (BPD) is a mental disorder characterized by rapid and intense changes in emotion and unstable moods and behaviors that affects 1.6% of US adults. It was first considered to be a combination of schizophrenia and neurosis, not its own disorder, until the third edition of the Diagnostic and Statistical Manual for Mental Disorders.



### EPIDEMIOLOGY

BPD affects

1.6%

of the population


Women are **2x** more likely to have BPD than men. **75%** of those diagnosed are women, but actual rates between women and men are likely much closer as men are often misdiagnosed with PTSD or depression.


BPD has a

10%

suicide rate


## SYMPTOMS/DIAGNOSIS

  
 Normal people experience a range of emotions

  
 BPD sufferers often experience extreme mood swings, anger, and paranoia

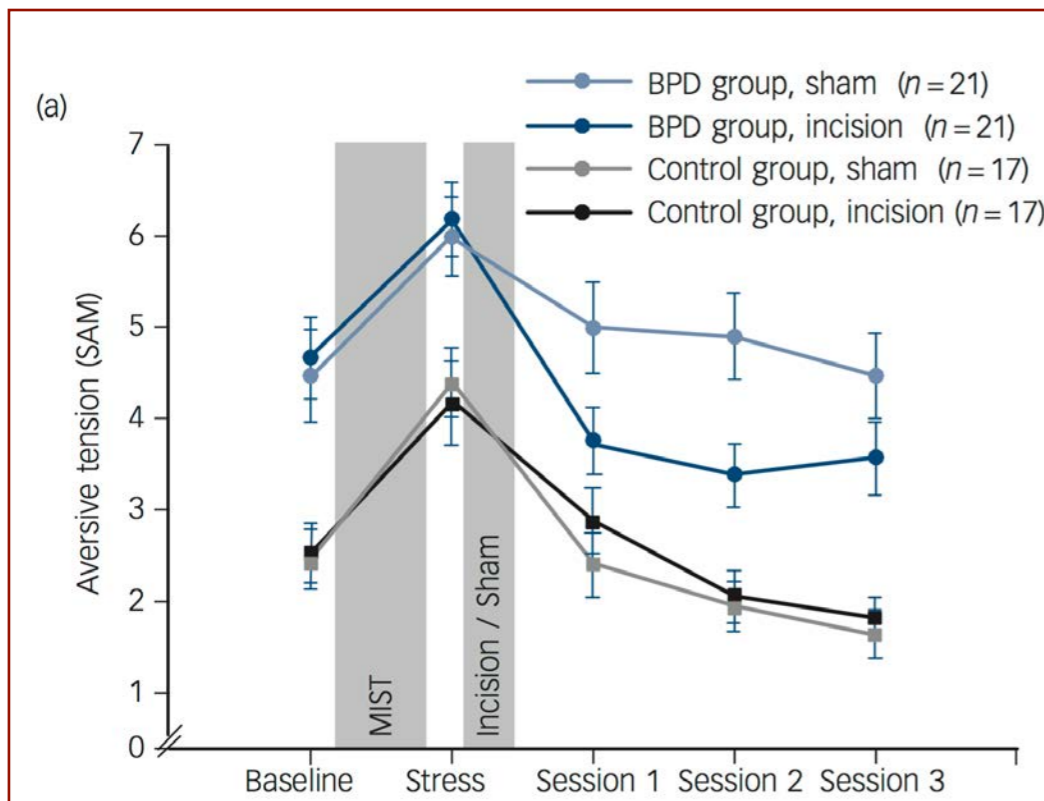
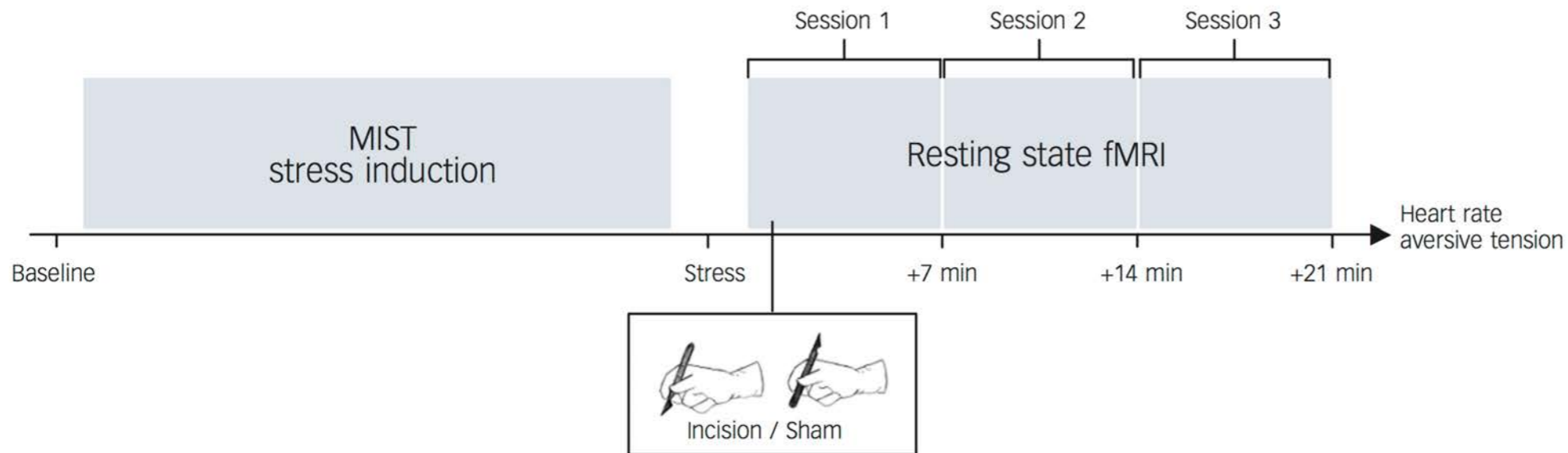
BPD is easy to misdiagnose since many symptomatic behaviors belong to more than borderline personality disorder. People must experience at least 5 of the symptoms to be diagnosed with BPD:

- Avoiding real or imagined abandonment
- Extreme positive and negative emotions
- Inconsistent self-image and identity
- Impulsive, dangerous behaviors
- Instability in mood or emotion
- Paranoia or excessive stress
- Suicidal thoughts and actions
- Difficulty controlling anger
- Feelings of emptiness



Sources: National Institute of Mental Health, Mayo Clinic, NAM, Spectrum, Optimum Performance Institute, Freepik, FlatIcon

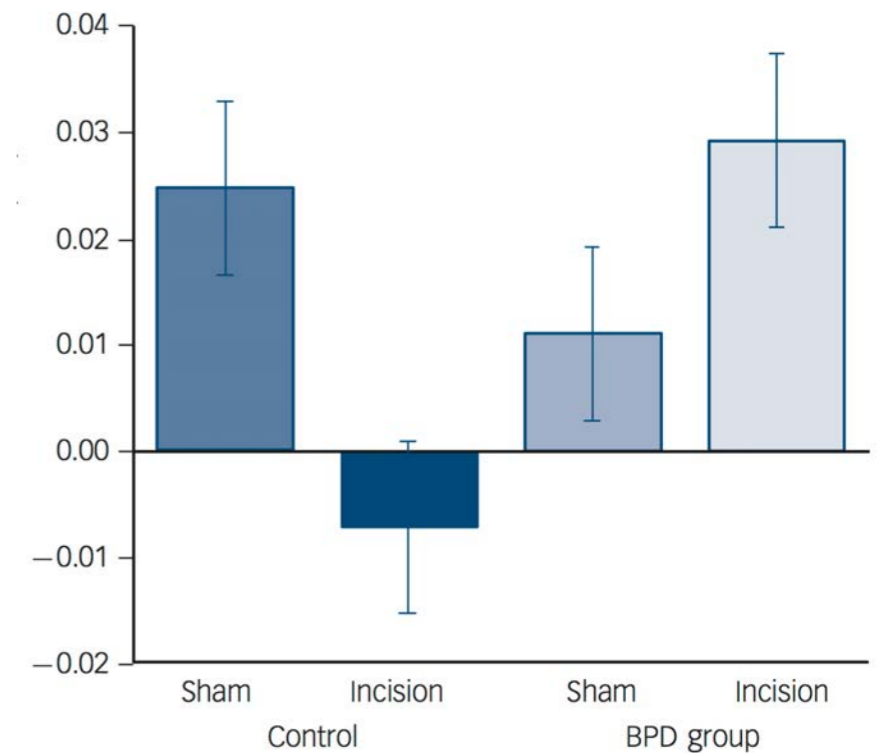
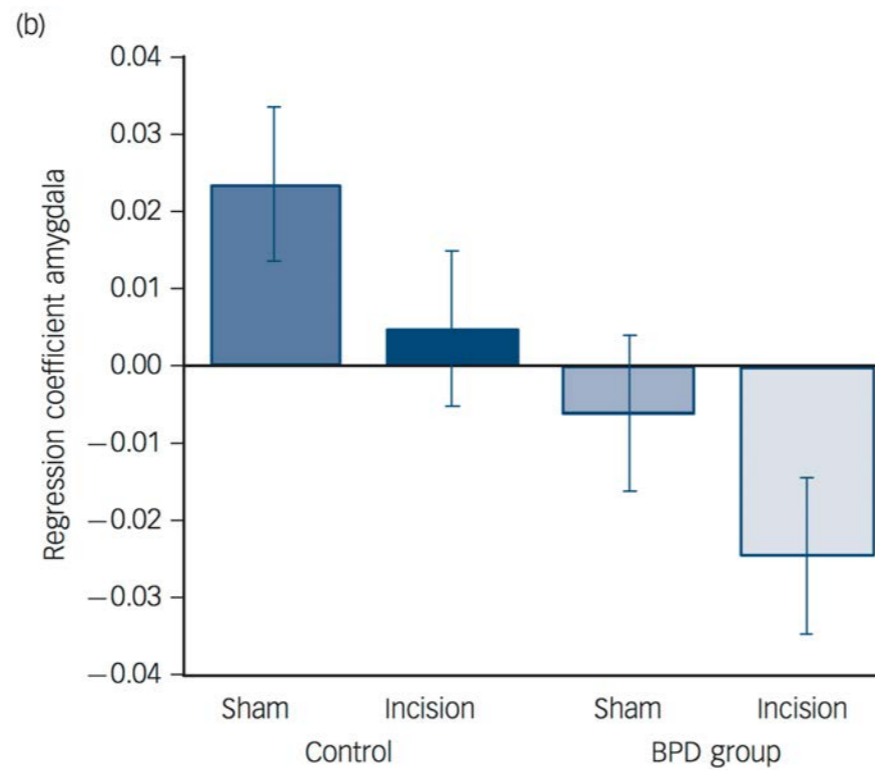
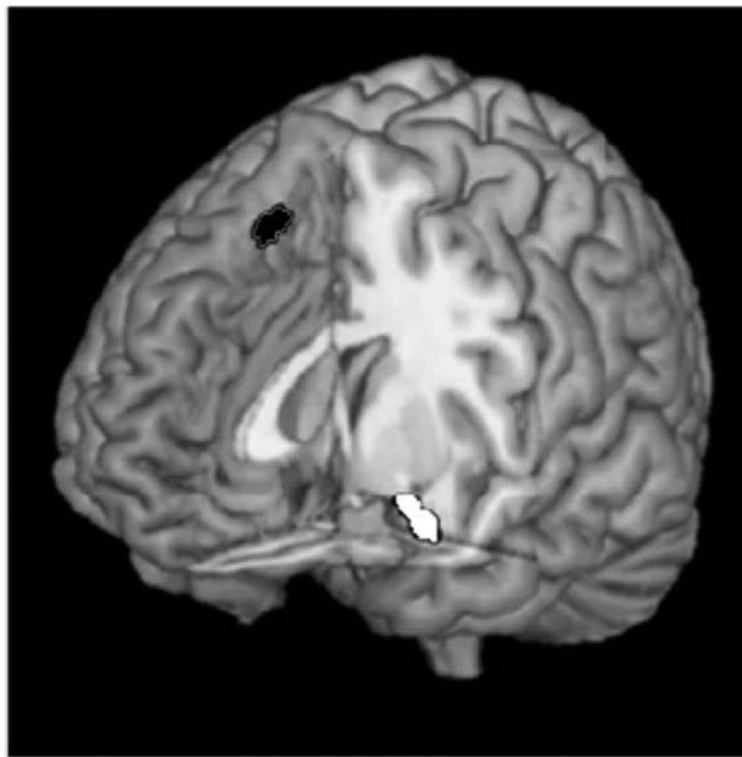
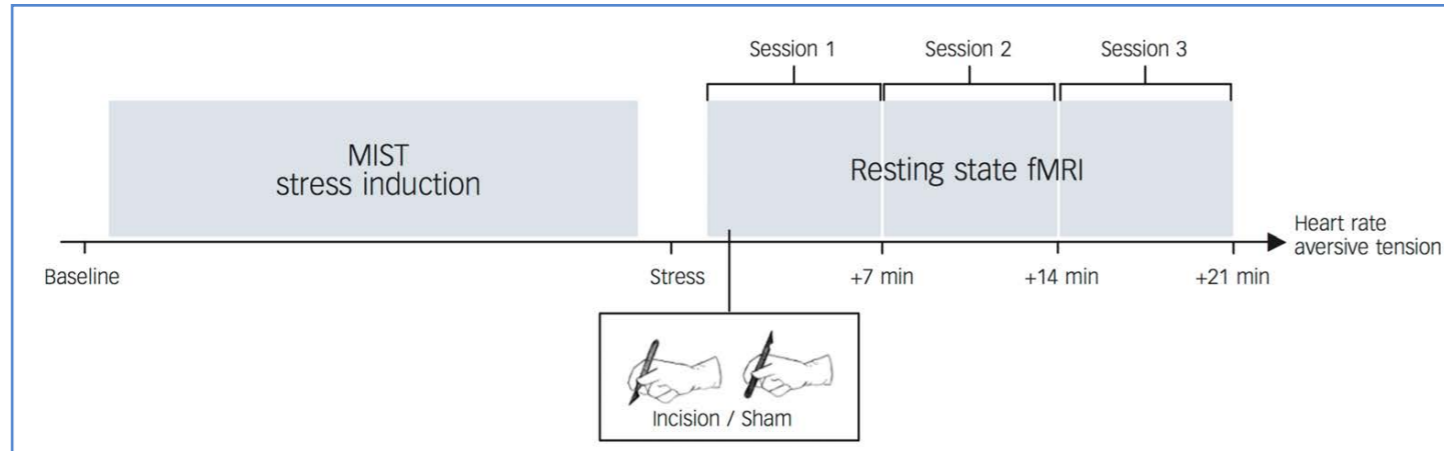
# De neurobiologie van automutilatie bij borderline persoonlijkheid



Na inductie van stress had snijden een spanningsreducerend effect bij borderline persoonlijkheden die niet in de controle conditie aanwezig was

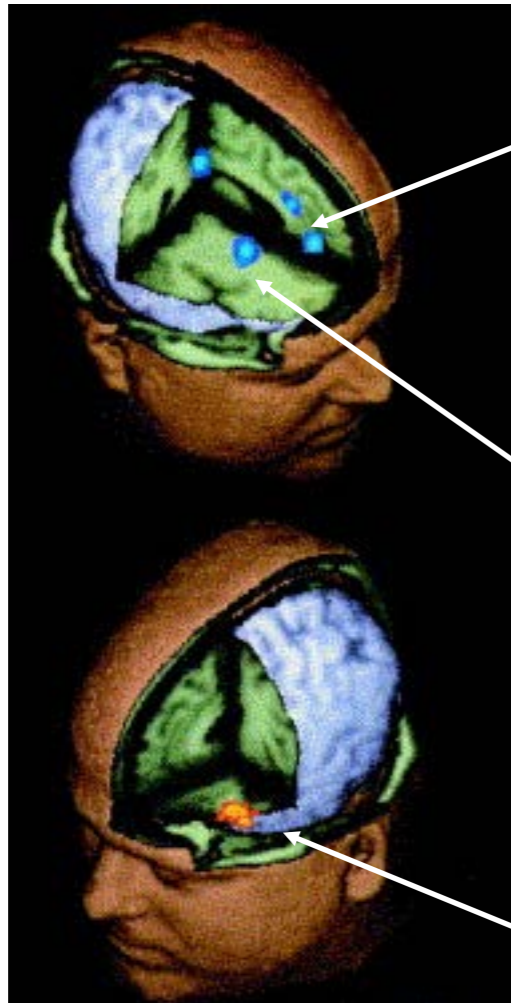


# De neurobiologie van automutilatie bij borderline persoonlijkheid



Door het snijden nam frontale activiteit toe bij BPD groep (rechts), waardoor amygdala activiteit daalde

# Verschillen in hersenactiviteit tussen criminele psychopaten en controles



Cingulate gyrus

Amygdala/  
hippocampus

Ventral striatum

inferior frontal gyrus

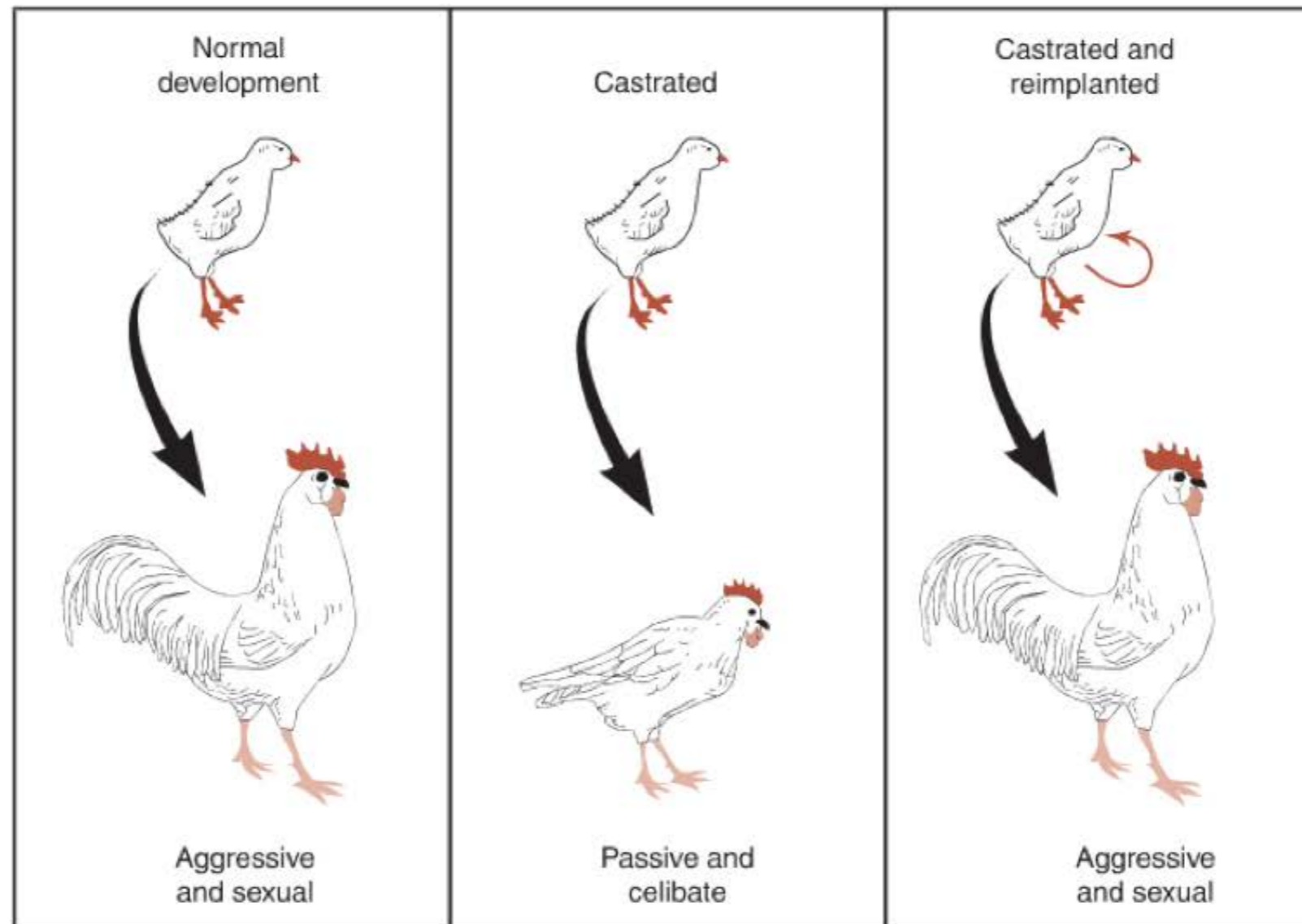


Onderactivatie van amygdala en frontale cortex bij psychopathie lijkt suggestief dat deze onderactivatie geassocieerd is met agressief gedrag

# Rol van hormonen en neurotransmitters

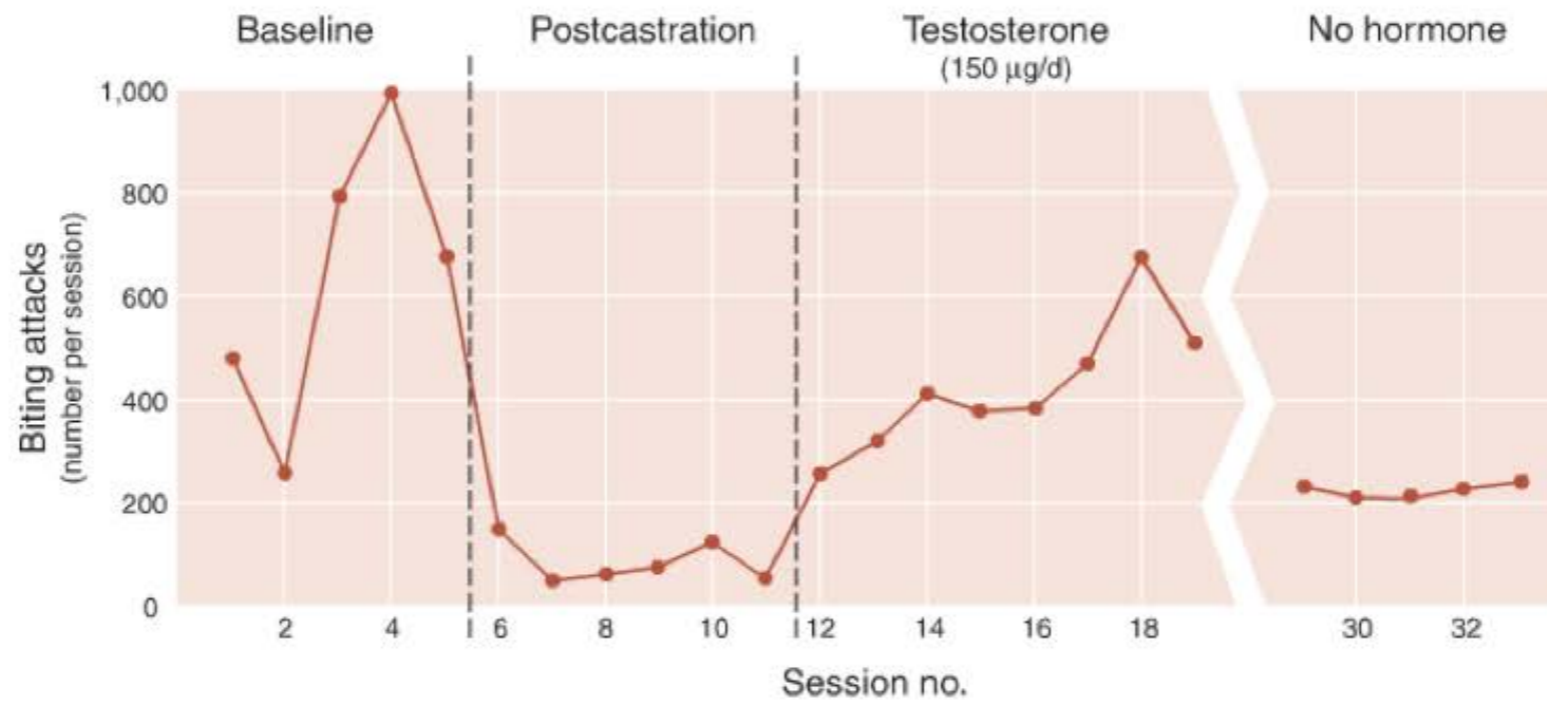
- **Geslachtshormonen**
  - Rol van testostorene
  - Agressie mannen > vrouwen
- **Neurotransmitters**
  - Serotonine (geassocieerd met impulsiviteit)
  - Dopamine (geassocieerd met beloning)

# Testosteron & agressie



**FIGURE 14.8** ● Berthold established in 1849 that a substance in the testes was necessary for the development of male behavior and body structure. (Adapted from Rosenzweig MR, Breedlove SM, Watson NV. *Biol Psychol*. 4th ed. Sunderland, MA: Sinauer; 2005.)

# Testosteron & agressie



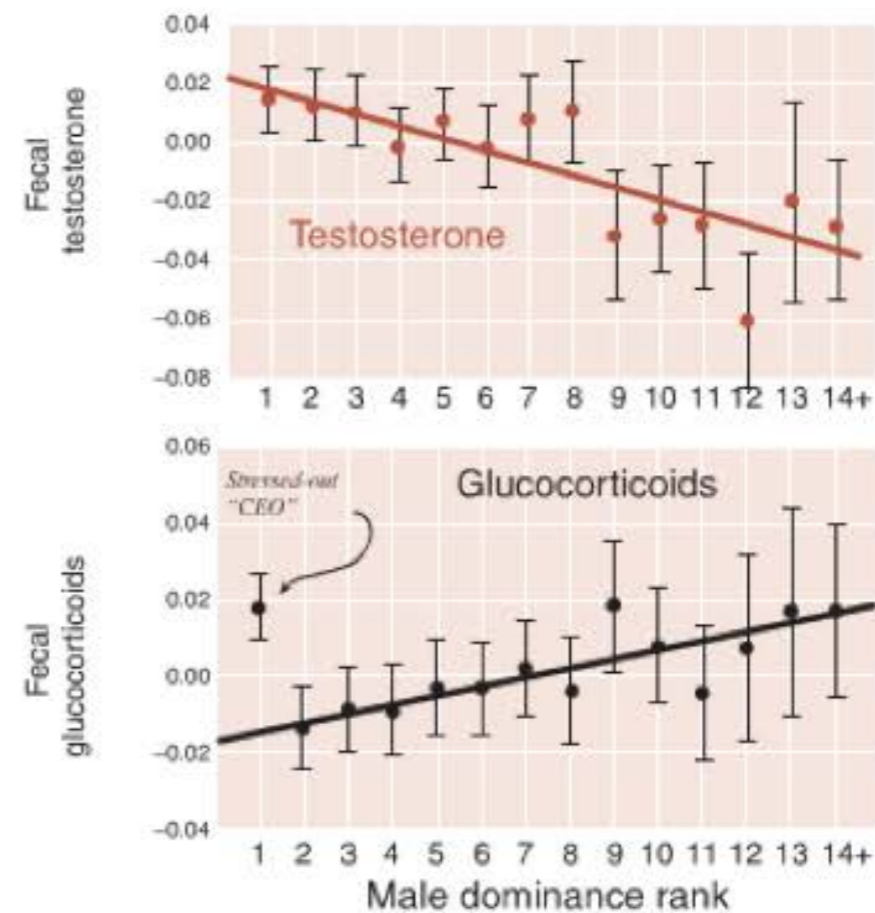
**FIGURE 14.9** ● Baseline bite attacks for male mice are markedly diminished with castration. This effect can be reversed temporarily with testosterone replacement. (Adapted from Wagner GC, Beuving LJ, Hutchinson RR. The effects of gonadal hormone manipulations on aggressive target-biting in mice. *Aggress Behav.* 1980;6:1-7.)

# Testosteron & agressie



- Groep van 125 bavianen
- 9 jaar opvolging van ranking en stress hormoon (stoelgang)
- testosteron stijgt bij opklimmen op de ladder
- Glucocorticoiden dalen bij opklimmen op de ladder

=> Testosteron lijkt meer vooral met dominantie gelinkt



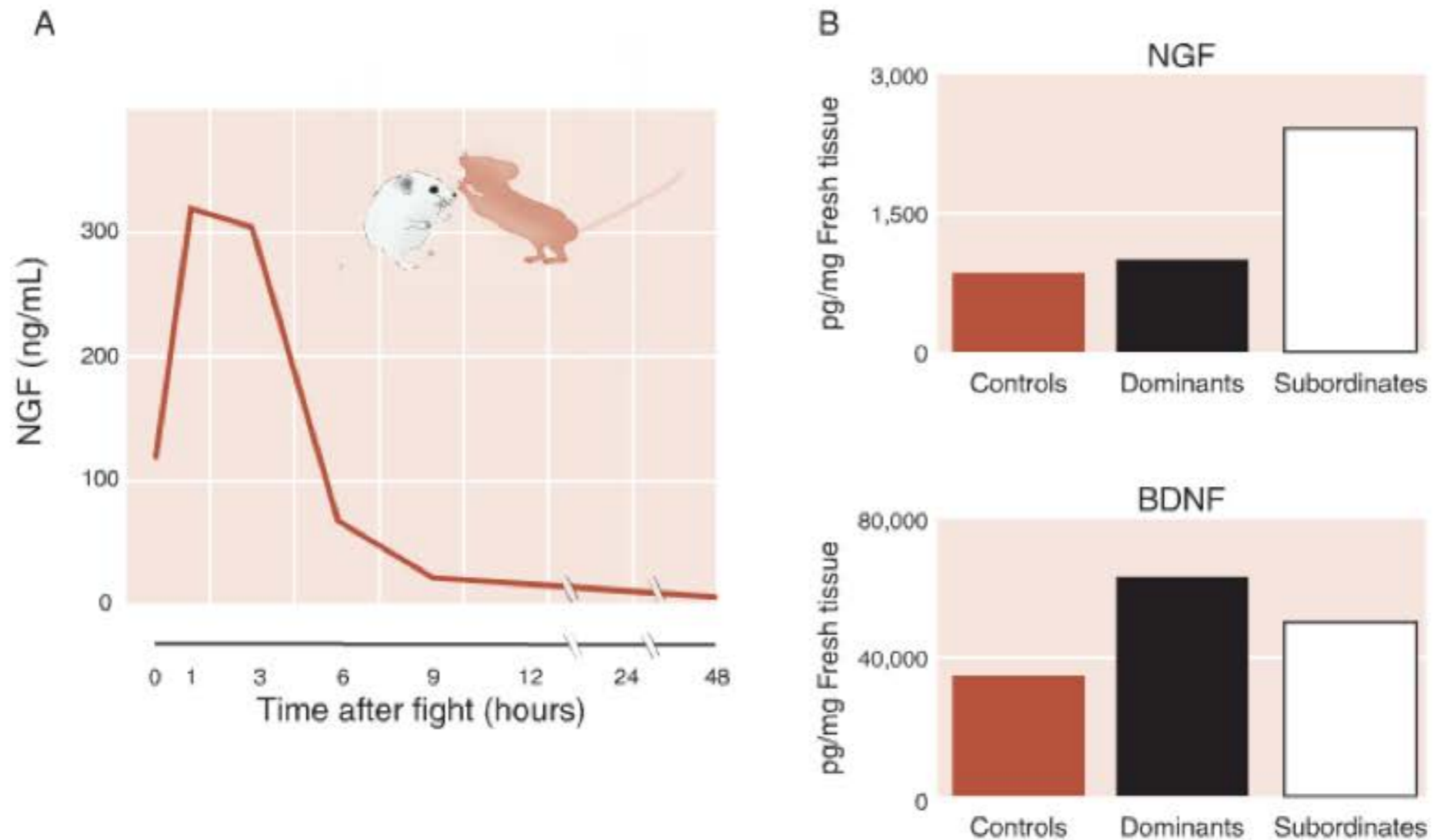
**FIGURE 14.10** ● Testosterone levels rise as baboons ascend in social rank. Glucocorticoids, with the exception of the alpha man, descend with rank. (Adapted from Gesquiere LR, Learn NH, Simao CM, et al. Life at the top: rank and stress in wild male baboons. *Science*. 2011;333:357-360.)

## Testosteron & dominantie



- Gedragsspectrum geassocieerd met dominantie lijkt mede gemedieerd door
- testosteron
  - Stemvolume
  - staren
  - zelfvertrouwen uitstralen
  - monopoliseren van gesprek

# Dominantie en groeifactoren

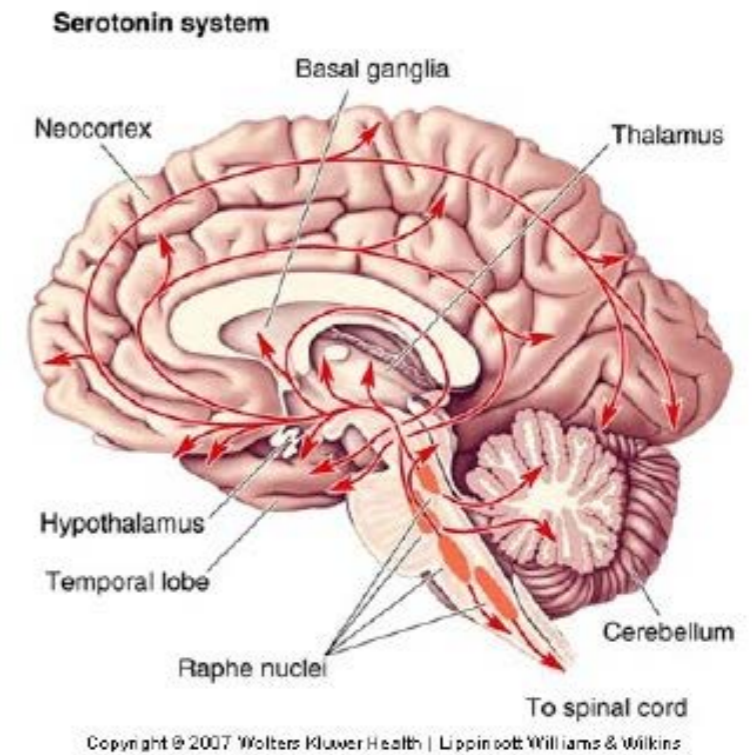


**FIGURE 14.12** ● **A.** Fighting results in an increase in nerve growth factor (NGF). **B.** In the subventricular zone, NGF only increases for the subordinate mouse, whereas brain-derived neurotropic factor (BDNF) increases for the dominant mouse. (Adapted from Fiore M, Amendola T, Triaca V, et al. Fighting in the aged male mouse increases the expression of TrkA and TrkB in the subventricular zone and in the hippocampus. *Behav Brain Res.* 2005;157(2):351-362 and Branchi I, Francia N, Alleva E. Epigenetic control of neurobehavioural plasticity: the role of neurotrophins. *Behav Pharmacol.* 2004;15(5-6):353-362.)



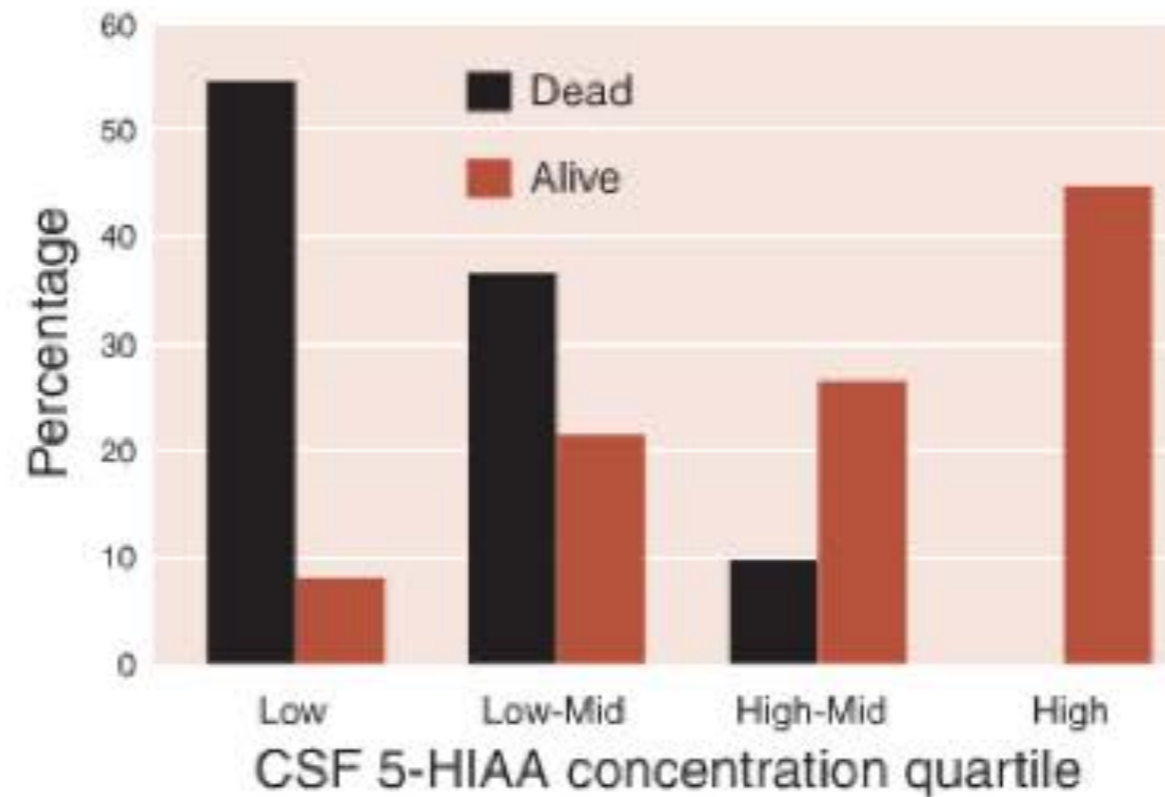
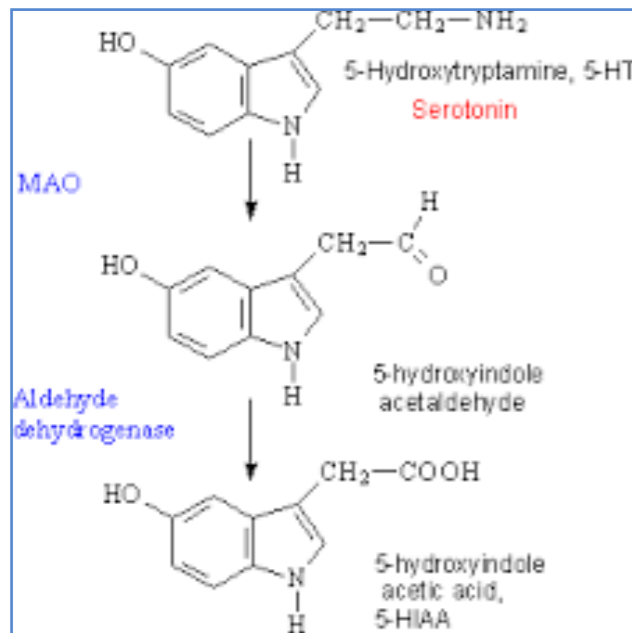
# Serotonine en agressie

- Serotonine raphe neuronen projecteren naar:
  - Hypothalamus
  - Limbische structuren



- Verminderde 5-HT turnover geassocieerd met verhoogde agressie in knaagdieren
- PCPA (blokkeert serotonine synthese) => verhoging agressie

# Serotonine en agressiviteit in apen



**FIGURE 14.13** ● The percentage of 2-year-old monkeys who are still alive after 4 years, separated by the metabolite of serotonin (5-HIAA) in the CSF. (Adapted from Higley JD, Mehlman PT, Higley SB, et al. Excessive mortality in young free-ranging male nonhuman primates with low CSF 5-hydroxyindoleacetic acid concentrations. *Arch Gen Psychiatry*. 1996;53(6):537-543.)

# Serotonine en agressie in humaan onderzoek



- Laag 5-HIAA correleert met hogere mate van suicidaliteit en hogere letaliteit van suicidepogingen
- 5-HIAA concentratie is omgekeerd gecorreleerd met agressieve incidenten
- Lage conc. 5-HIAA voorspelt herval van daders gekend met geweld
- Tryptofaan-depletie verhoogt agressie en irritatie



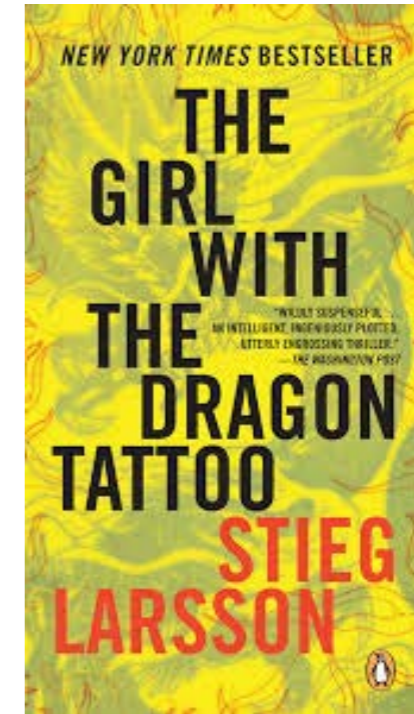
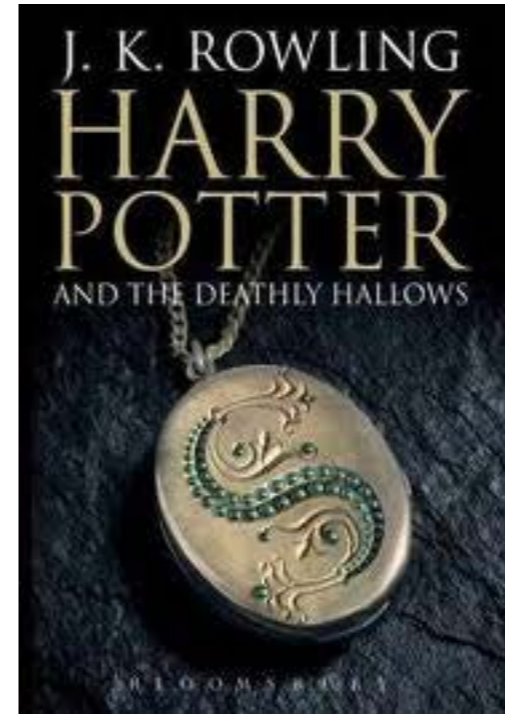
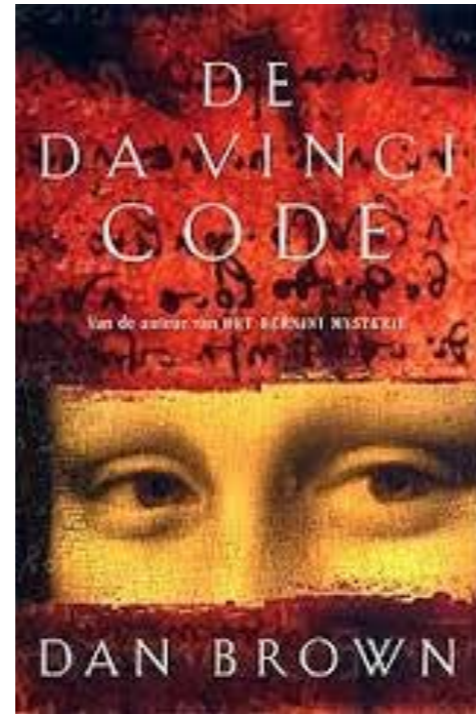
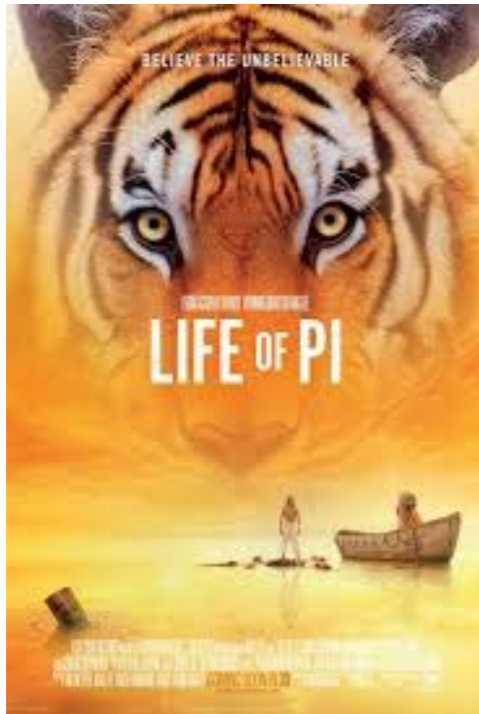
Genieten van geweld



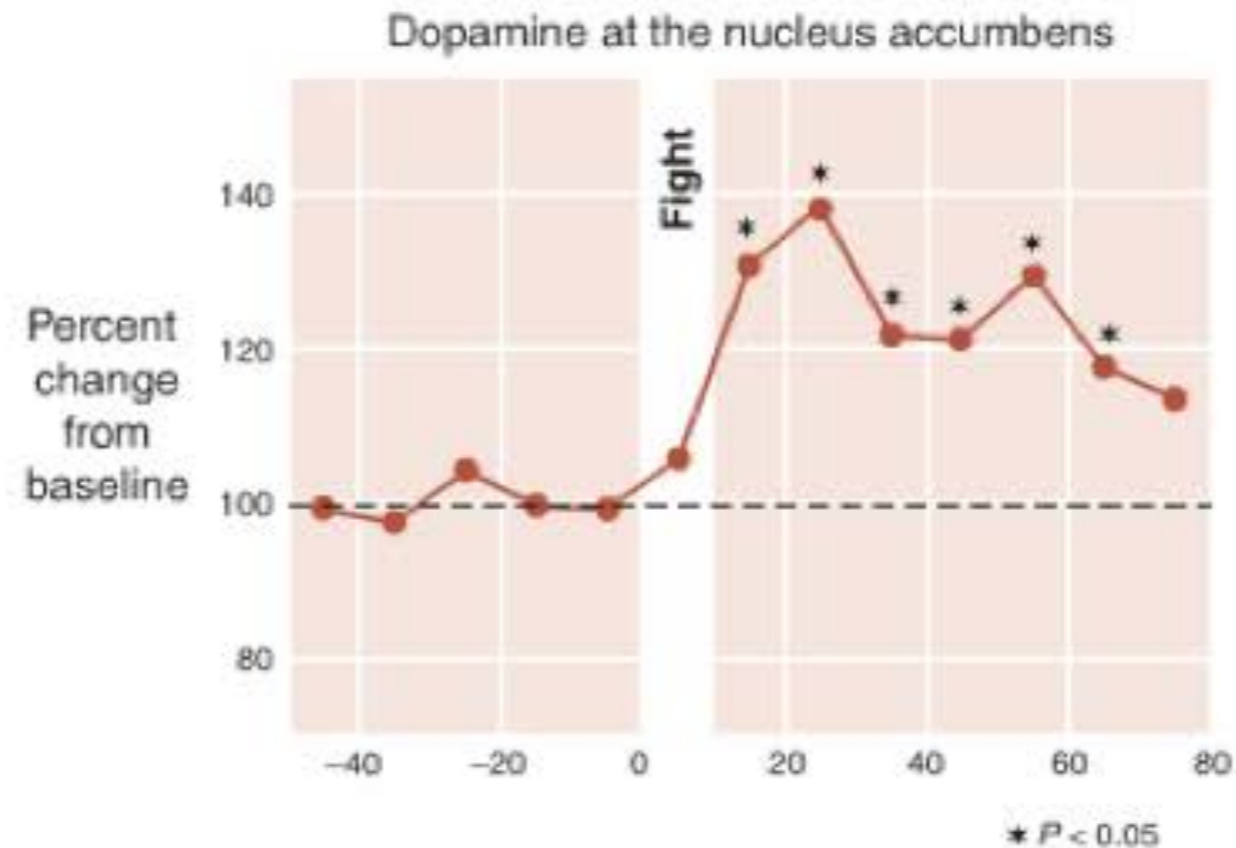
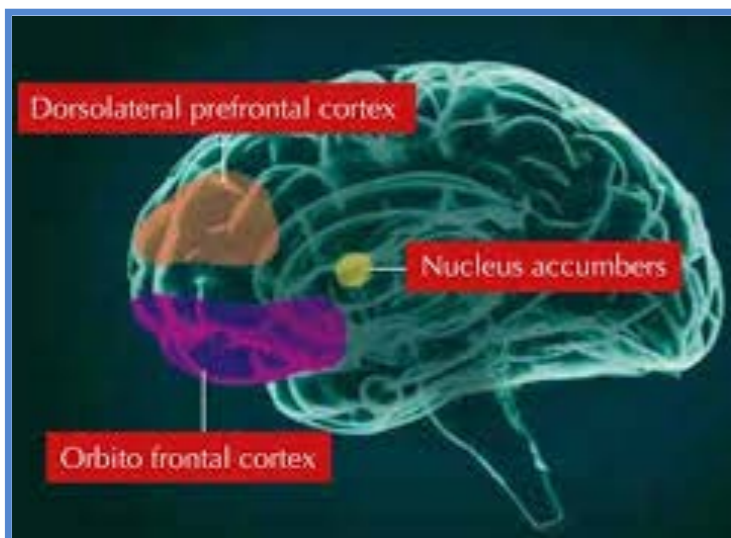
# Boxoffice Top 10 movies



# Andere media



# The thrill of fighting: rol van dopamine



**FIGURE 14.15** ● Increase in dopamine at the nucleus accumbens following an aggressive encounter with another rat. (Adapted from van Erp AM, Miczek KA. Aggressive behavior, increased accumbal dopamine, and decreased cortical serotonin in rats. *J Neurosci*. 2000;20:9320-9325.)

# Biologie van agressie: conclusie

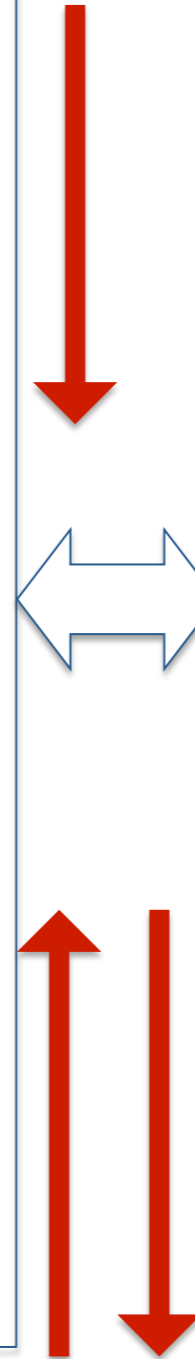
- Corticale structuren
  - Orbitofrontale regio
  - Anterior cingulate cortex



- Subcorticale structuren
  - Hypothalamus
  - Amygdala
  - Limbisch systeem

## Biomarkers:

- Neurotransmitters
  - DA, serotonine
- Hormonen
- Groeifactoren



Aanleg mede bepaald door psychosociale factoren

# Vragen?

