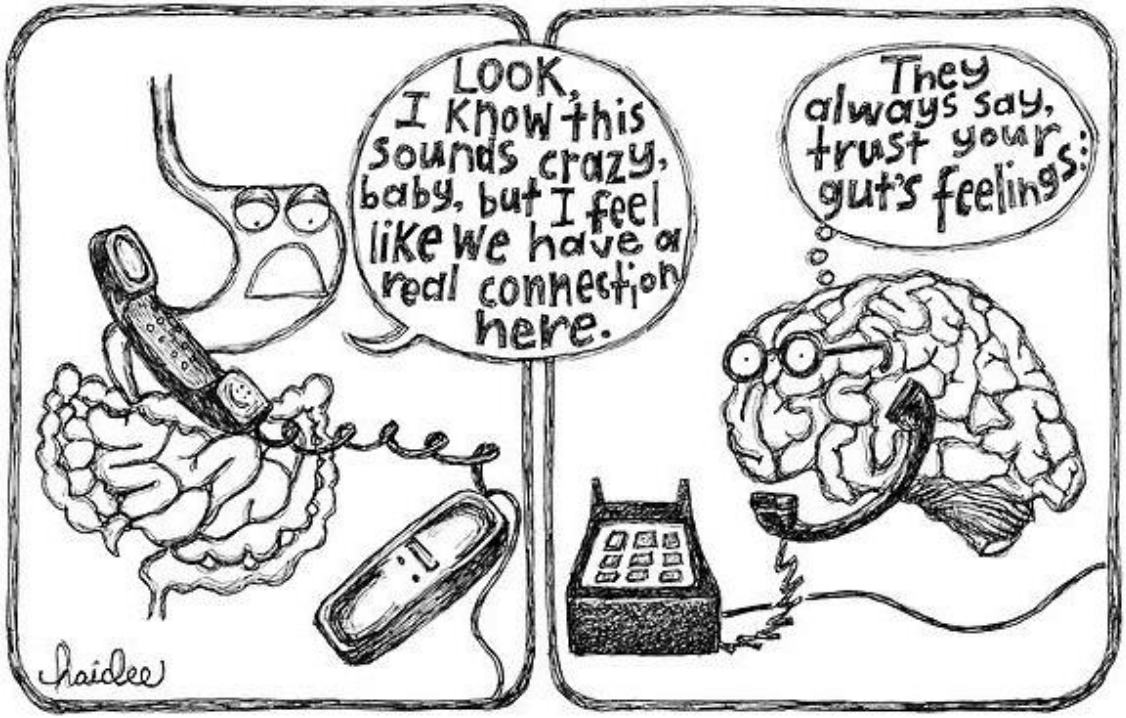
Autisme in de hersenen… én de darmen



Caroline de Theije PhD

Universiteit Utrecht

UMC Utrecht

NVA congres - 11 november 2016

‘onderbuikgevoel’

‘in je broek doen van angst’

‘vlinders in je buik’

100 trillion bacteria
Gut Microbiota

100 million neurons

Surface of approximately
300m²

60 -70% of immune cells

Autisme

genen x omgevingsfactoren

The Rodakis case

"Het is misschien niet wat ons geleerd is"

- John Rodakis- Amerikaanse moleculair bioloog
- Zoon (5 jaar) met autisme

- Dagelijks documenteren van 20 parameters van zijn zoons gedrag → Gedrag afhankelijk van omgevingsfactoren.

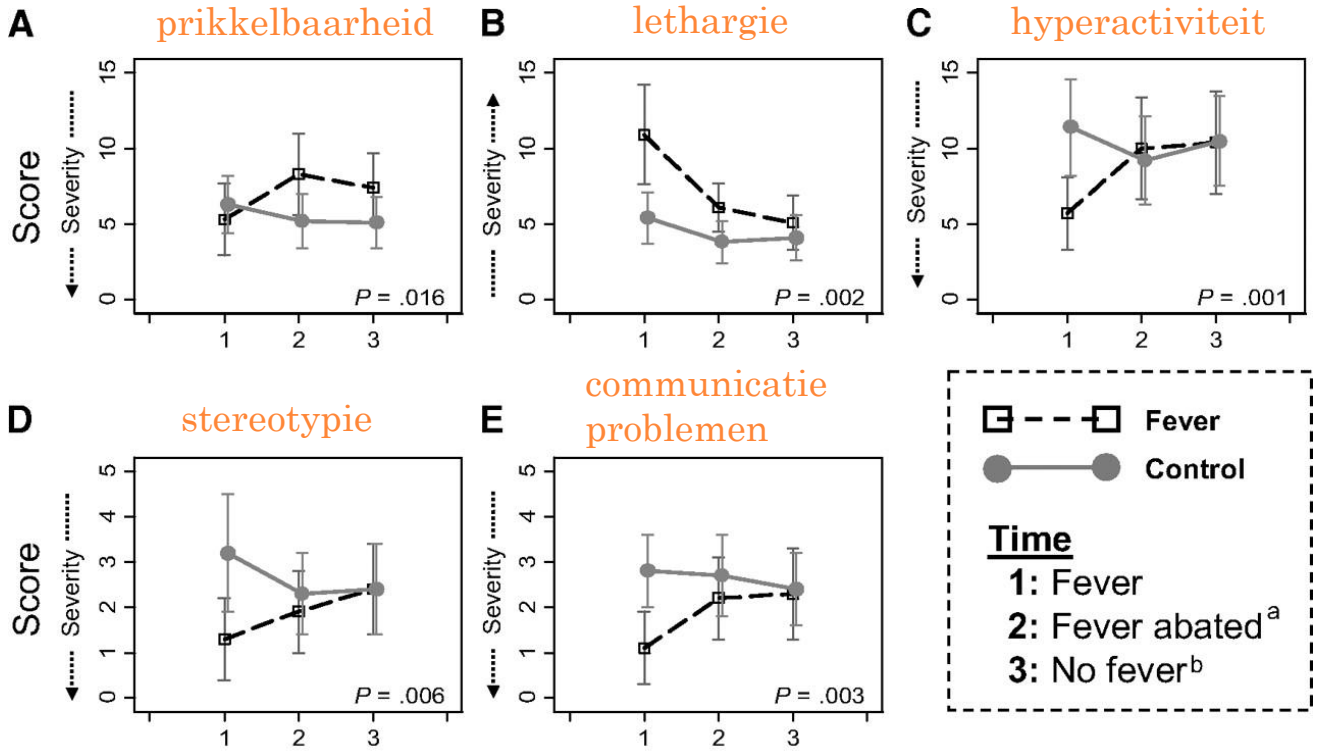
1. **Het koorts-effect**
2. **Het antibiotica-effect**
3. **Het voedings-effect**

Literatuur:

- www.NofOne.org
- An n=1 case report of a child with **autism** improving on antibiotics and a father's quest to understand what it may mean. **Rodakis** J. 2015 *Microb Ecol Health Dis.*

1. Het "koorts-effect"

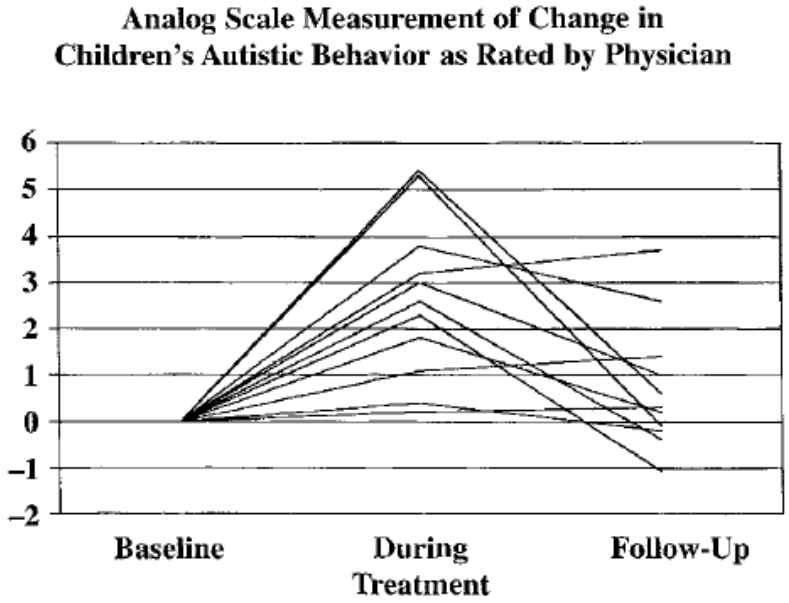
- Tijdelijke verbeteringen in autisme symptomen gedurende koorts



Literatuur:
Behaviors associated with fever in children with autism spectrum disorders. **Curran LK** et al. 2007 *Pediatrics*.

2. Het "antibiotica-effect"

- 10-daagse amoxicillinekuur wegens streptokokken keelinfectie.
- Vanaf dag 4: verbeteringen in autisme symptomen
  - oogcontact
  - meer taalgebruik
  - minder "rigide" denken en handelen
  - meer energie

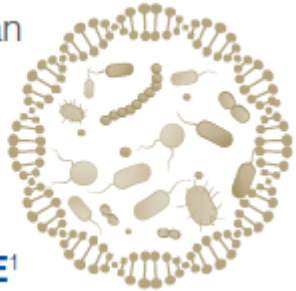


Literatuur:
Short-term benefit from oral vancomycin treatment of regressive-onset autism. **Sandler RH** et al. 2000 *J Child Neurol*

Bacteriën in de darm

There are more than
3 MILLION
MICROBIAL GENES
in our gut microbiota

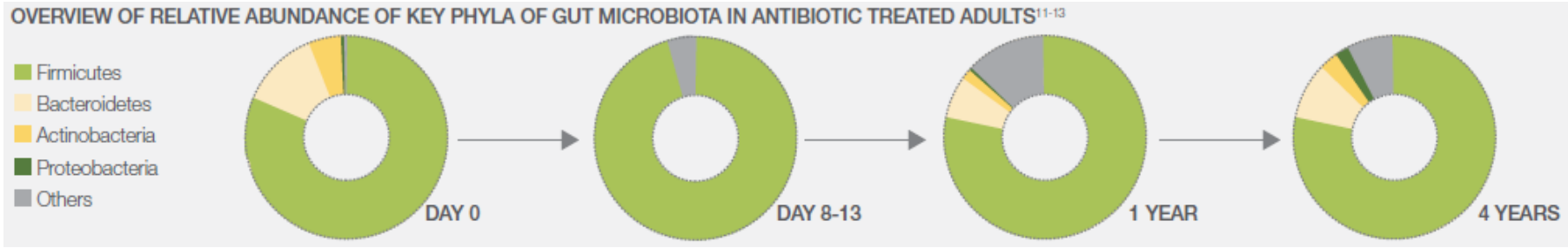
150 TIMES
more genes than in the
HUMAN GENOME[1]



OUR GUT MICROBIOTA EVOLVES THROUGHOUT OUR ENTIRE LIFE
and is the result of a variety of influences:[1-2]

The composition of
GUT MICROBIOTA
IS UNIQUE
to each individual,
just like our
FINGERPRINTS[1]

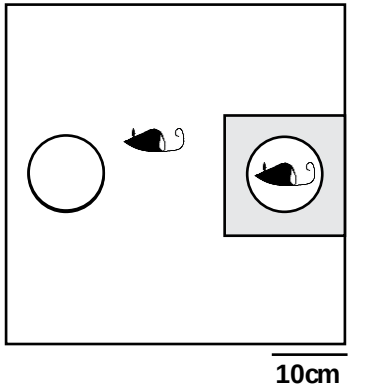
OVERVIEW OF RELATIVE ABUNDANCE OF KEY PHYLA OF GUT MICROBIOTA IN ANTIBIOTIC TREATED ADULTS[11-13]

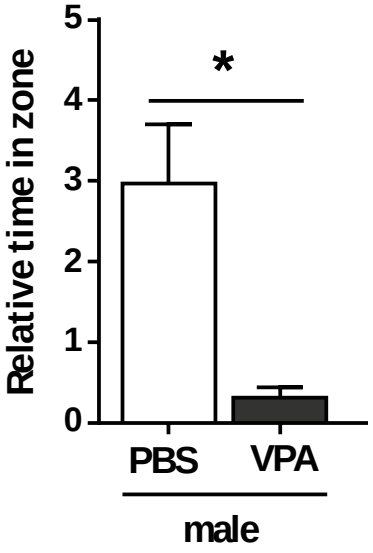


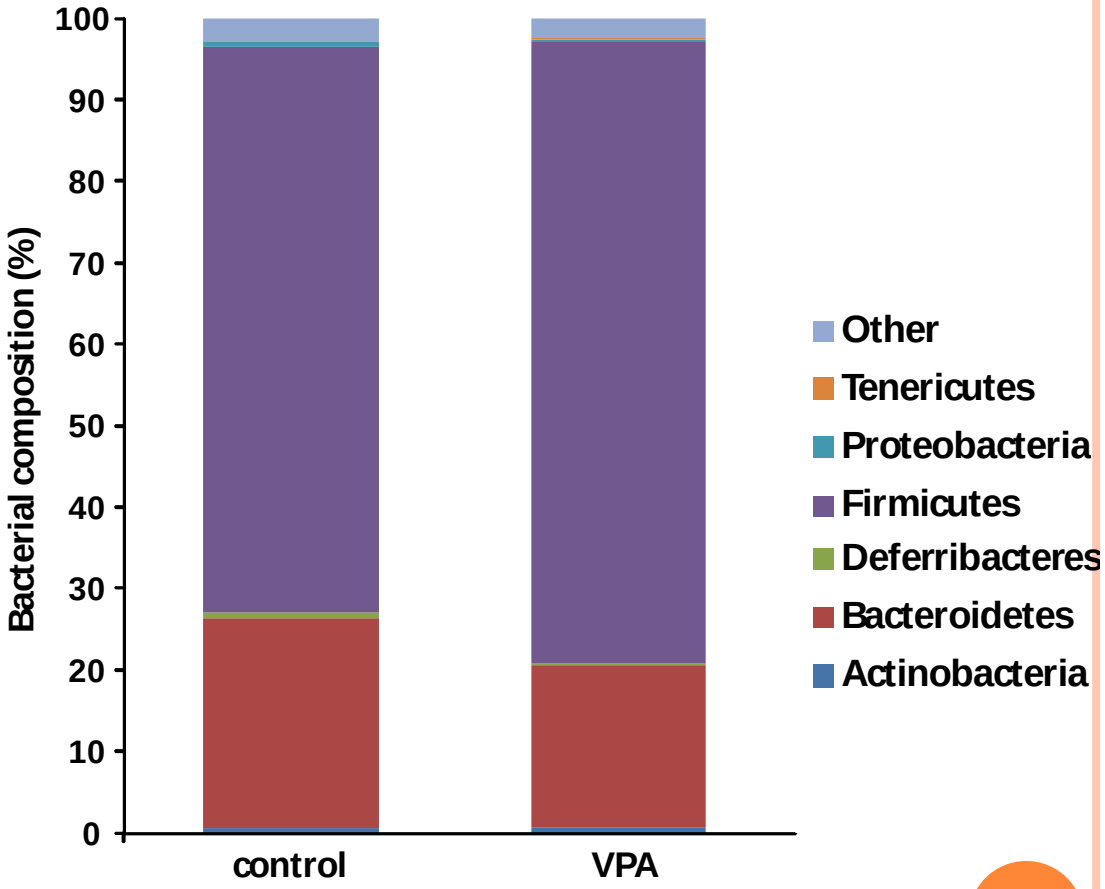
Microbiota samenstelling in ASD

Study (Year)	Country	Study Group: ASD (GI+/GI−)	Study Group: SIB (GI+/GI−)	Study Group: CON (GI+GI−)	Sample Type	Method	Changes in Fecal Microbiome in ASD
Song, Liu, and Finegold (2004)	USA	15	–	8	Stool	16S rRNA gene sequencing	↑ *C. bolteae* and cluster I/IX
Williams et al. (2011), Williams, Hornig, Parekh, and Lipkin (2012)	USA	23 (23/0)	–	9 (9/0)	Intestinal biopsies	16S rRNA gene sequencing	↓ Bacteroidetes ↑ Firmicutes, Proteobacteria, *Sutterella*
Finegold et al. (2010)	USA	33 (33/0)	7 (0/7)	8 (0/8)	Stool	16S rRNA gene sequencing	↑ Bacteroidetes and Proteobacteria: *Desulfovibrio*, *B. Alkaliflexus*, *Acetanaerobacterium*, *Parabacteroides* ↓ Firmicutes and Actinobacteria: *Clostridium*, *Weissella*, *Turicibacter*, *Anaerofilum*, *Pseudoramibacter*, *Ruminococcus*, *Streptococcus*
Kang et al. (2013)	USA	20 (20/0)	–	20 (0/20)	Stool	16S rRNA gene sequencing	↓ *Prevotella*, *Coprocuccus*, *Veillonellaceae*

Microbiota in muizen met autisme-gerelateerd gedrag

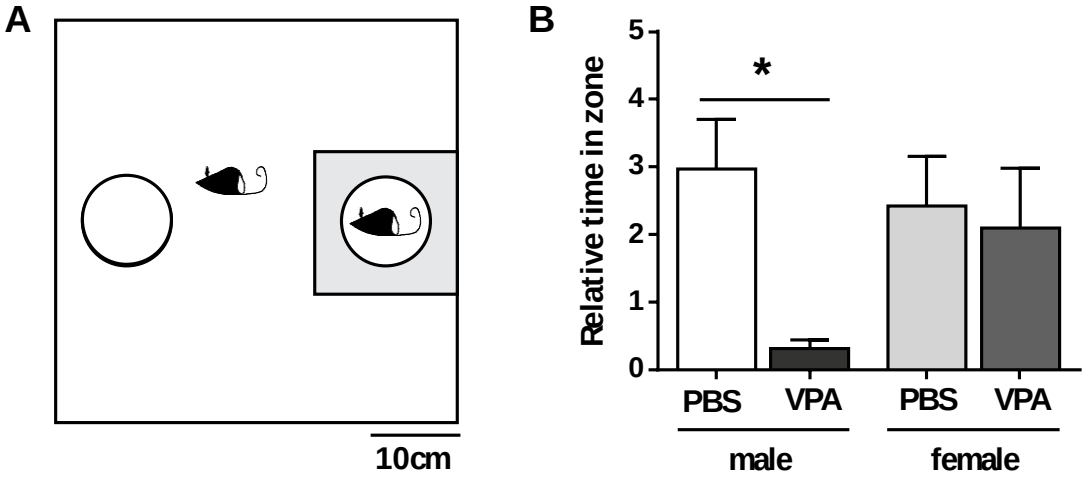


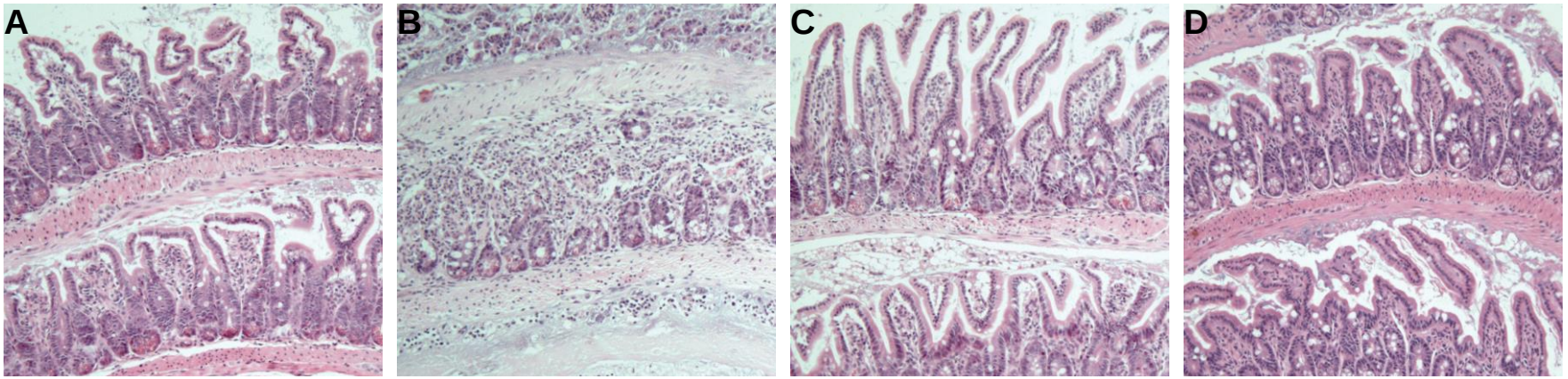




Literatuur:
Altered gut microbiota and activity in a murine model of autism spectrum disorders.
de Theije et al. 2014 *Brain Behavior and Immunity*

Darmproblemen in muizen met autisme-gerelateerd gedrag

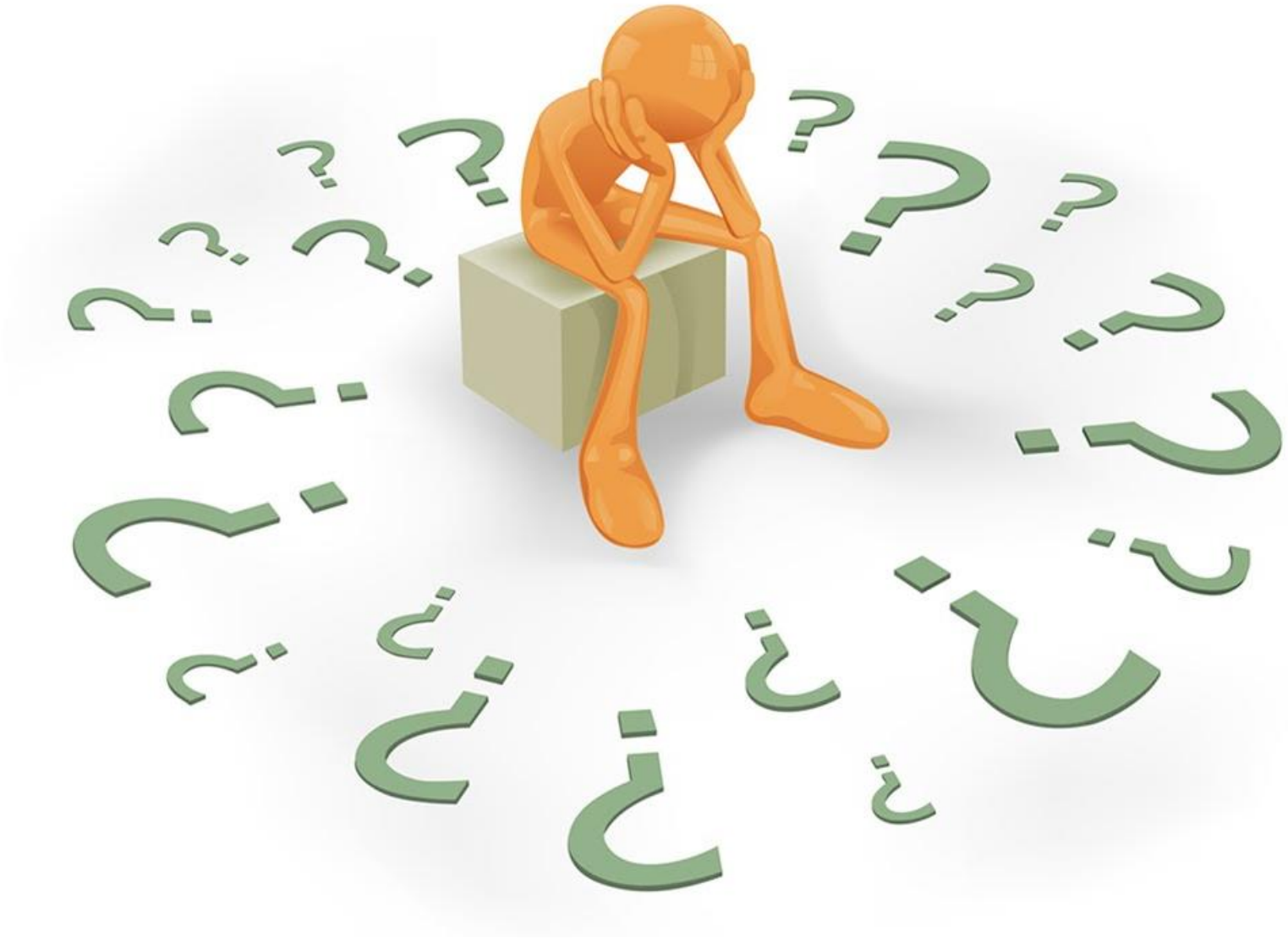




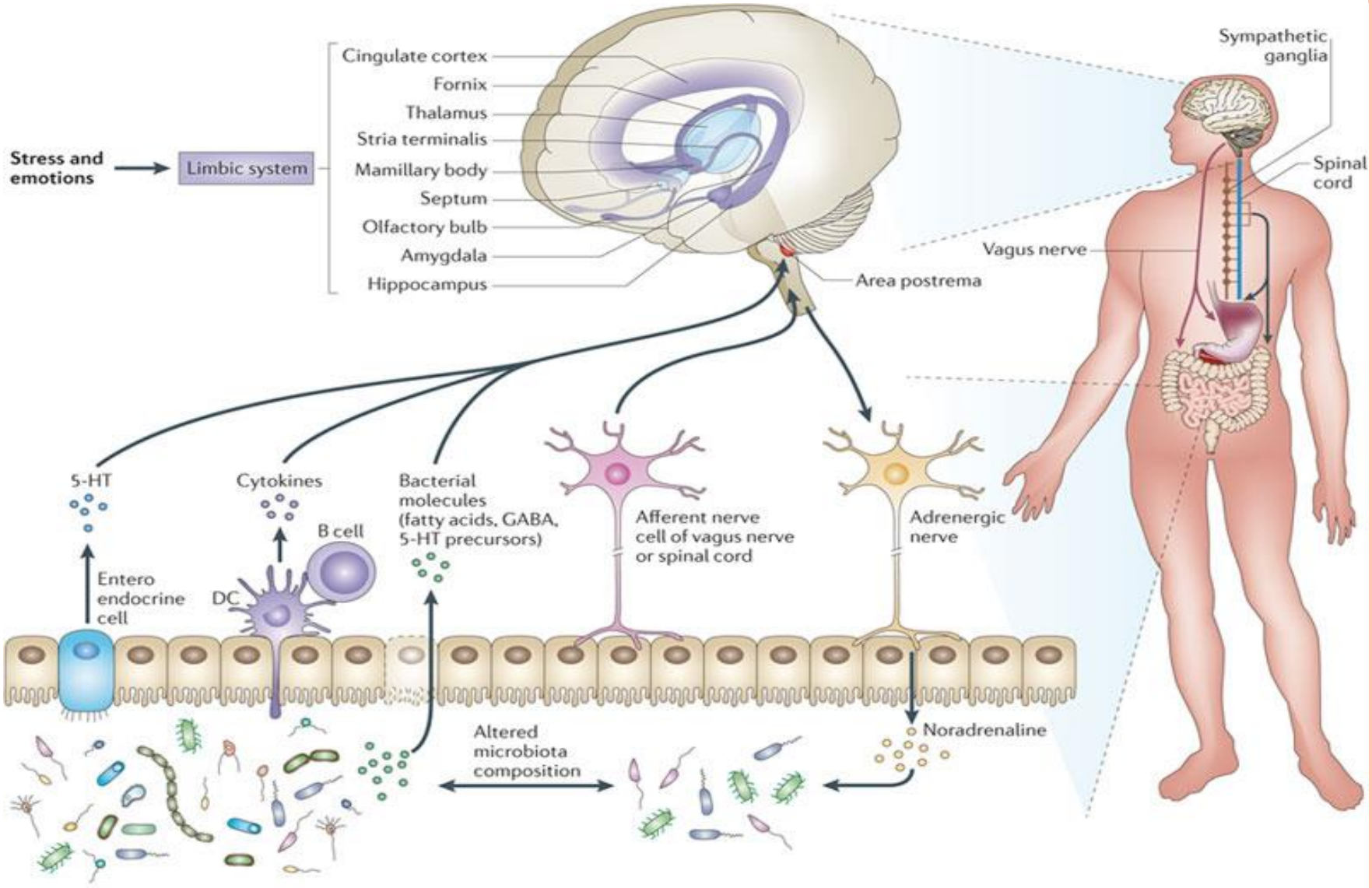
PBS male **VPA male** **PBS female** **VPA female**

Literatuur:
Intestinal inflammation in a murine model of autism spectrum disorders.
de Theije et al. 2014 *Brain Behavior and Immunity*

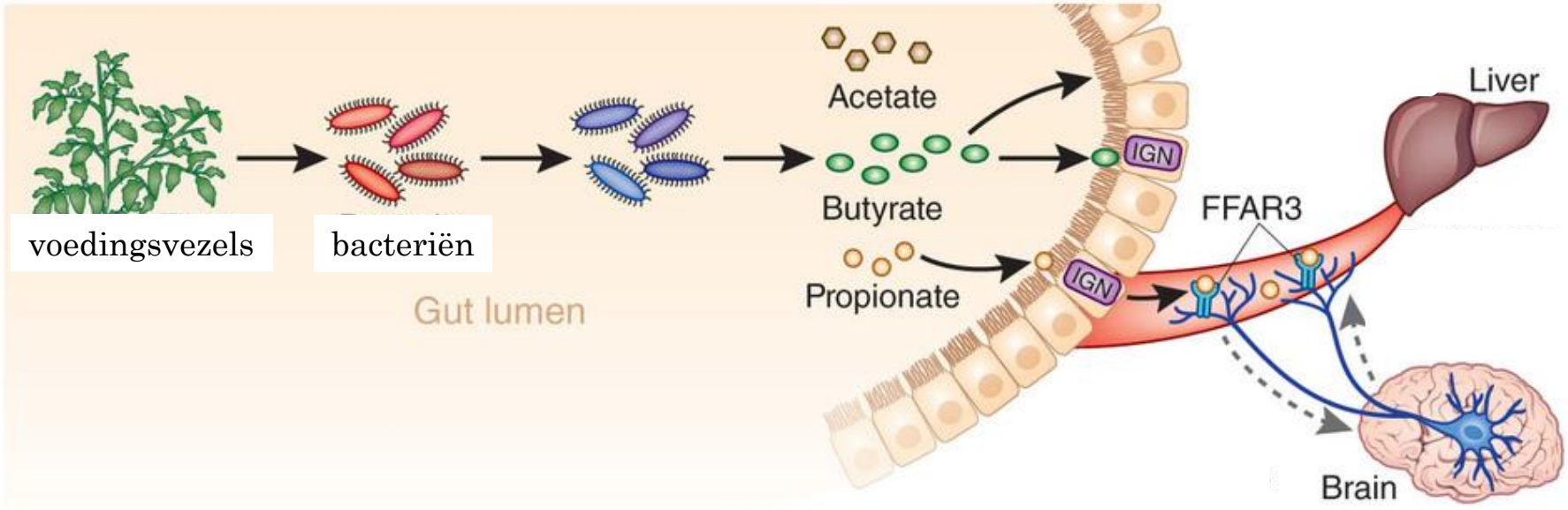
Hoe beïnvloeden darmbacteriën gedrag?



Routes van darm naar brein

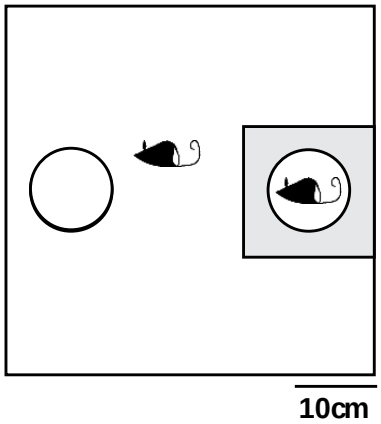


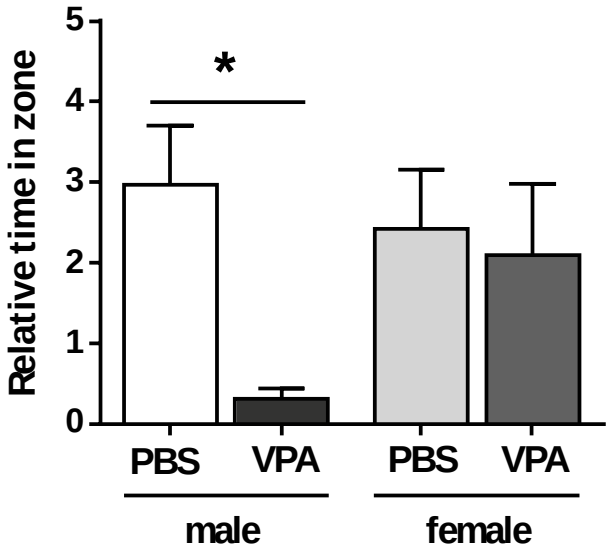
Korte-keten vetzuren

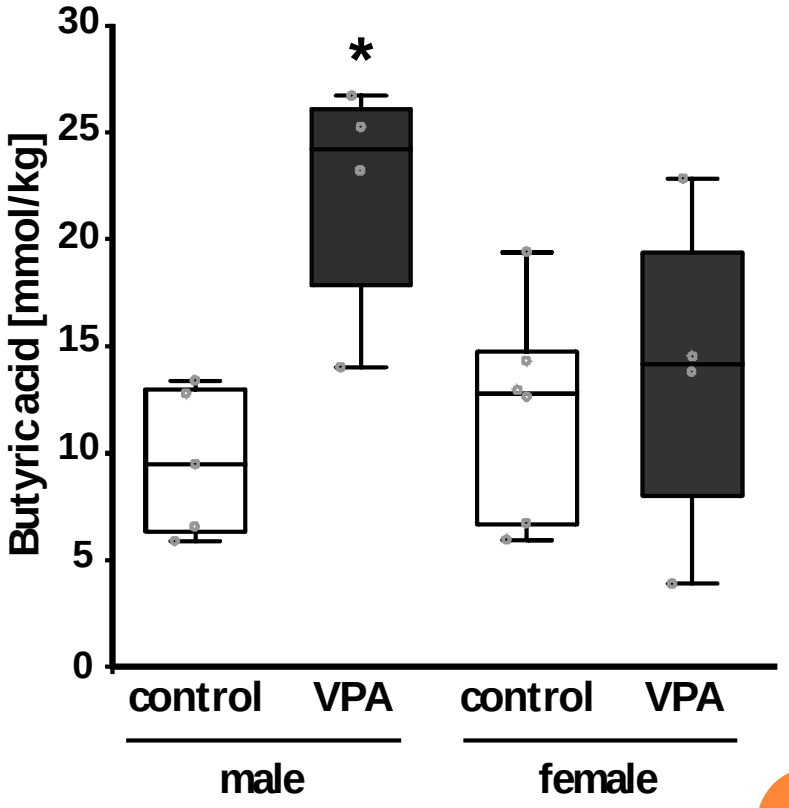


- Orale antibiotica: verlagen de aanwezigheid van butyraat-producerende bacteriën

KORTE-KETEN VETZUREN IN MUIZEN MET AUTISME-GERELATEERD GEDRAG







Literatuur:
Altered gut microbiota and activity in a murine model of autism spectrum disorders.
de Theije et al. 2014 *Brain Behavior and Immunity*

Mogelijke behandelstrategieën

- Antibiotica
  - lange termijn behandeling gevaarlijk voor zowel individu als samenleving
- Microbiota transplantatie van gezonde donors
  - veiligheid en lange termijn effect op gezondheid nog niet vastgesteld
- Voedingspatronen aanpassen
  - minder risicovol
  - verandert microbiota samenstelling
  - effectiviteit op gedrag in de mens onbekend

1. Elimineren van “schadelijke” voedingsstoffen
2. Toevoegen van “gunstige” voedingsstoffen

1. Het "voedings-effect"

- Eliminatie van gluten leidde niet tot gedragsveranderingen

- Eliminatie van zuivel leidde vanaf dag 3 tot verbeteringen in autisme symptomen:
  - Meer oogcontact
  - Verbetering in verbale communicatie

Klinisch bewijs voor eliminatie van gluten of zuivel

- Te weinig studies met een juiste opzet en grootte van de studie

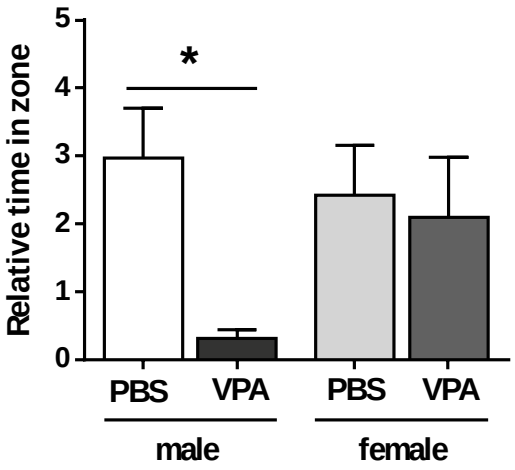
  →In patiënten met autisme is er geen bewijs voor de effectiviteit van gluten of zuivel eliminatie

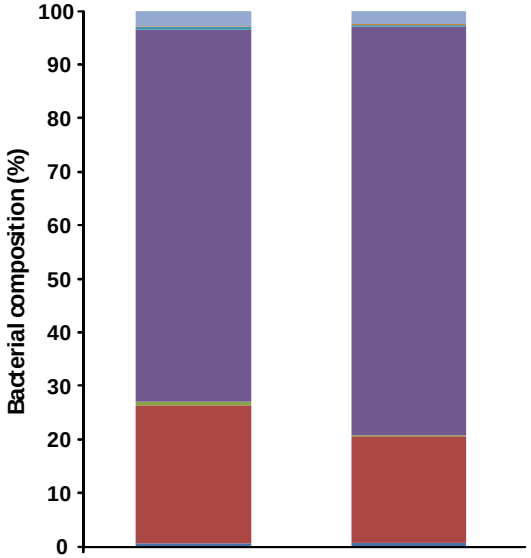
  → Alleen geadviseerd wanneer er tevens sprake is van een allergie of intolerantie

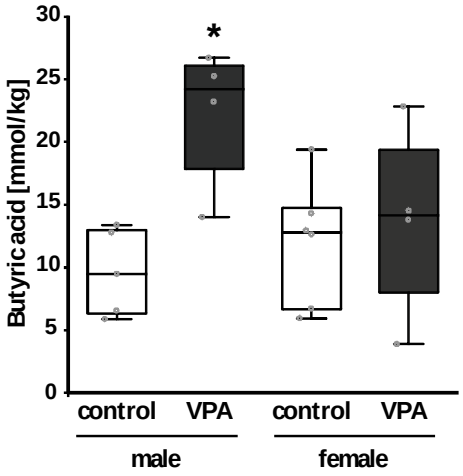
Literatuur:
Evidence of the gluten-free and casein-free diet in autism spectrum disorders: a systematic review. **Marí-Bauset S** 2014 *J Child Neurol.*

Voedingsinterventie in muizen met autisme-gerelateerd gedrag

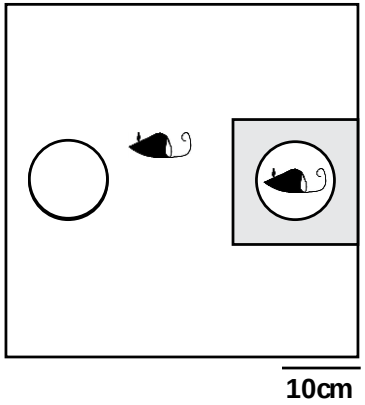
- Toevoeging van “gunstige” voedingscomponenten
  - Prebiotische vezels
  - Omega-3 vetzuren
  - 200% vitamines

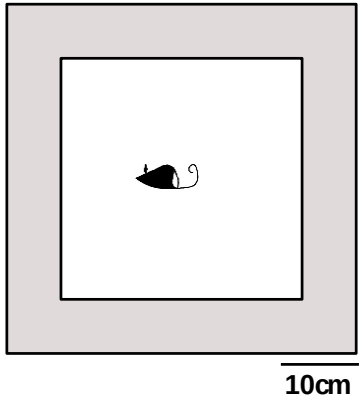


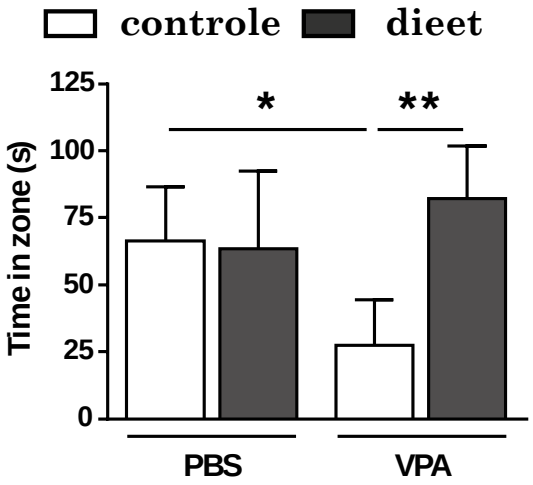


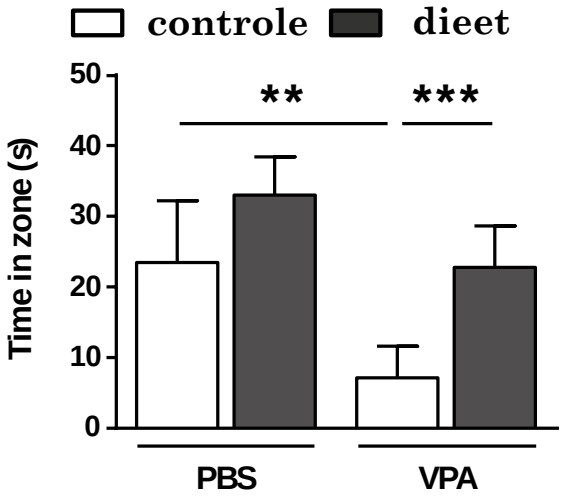


VOEDING HERSTELT HET GEDRAG IN MUIZEN



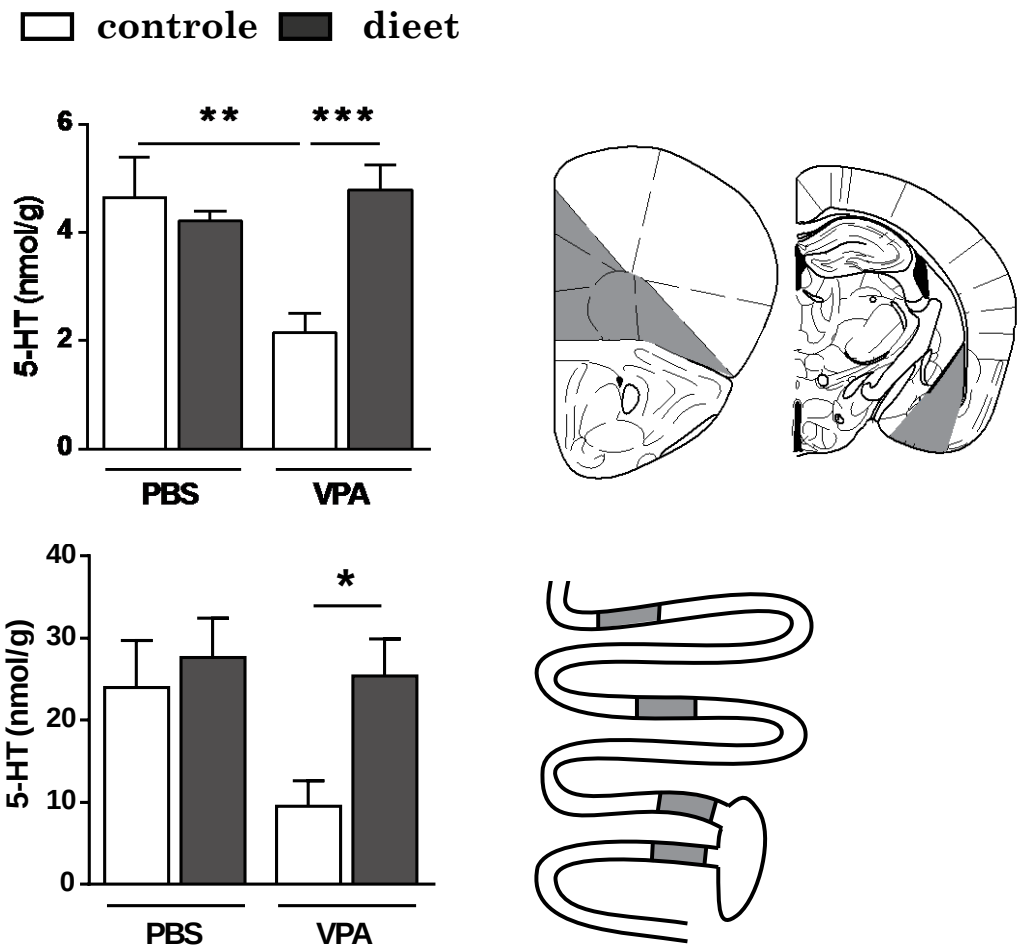






Literatuur:
de Theije et al. 2016 *Submitted*

Voeding herstelt neurotransmitter serotonine in muizen



Literatuur:
de Theije et al. 2016 *Submitted*

Conclusies


+

≠


Darmproblemen en andere samenstelling darmbacteriën

Verandering in microbiota leidt tot verandering in gedrag

?

Voeding verbetert het gedrag

?

Dankwoord

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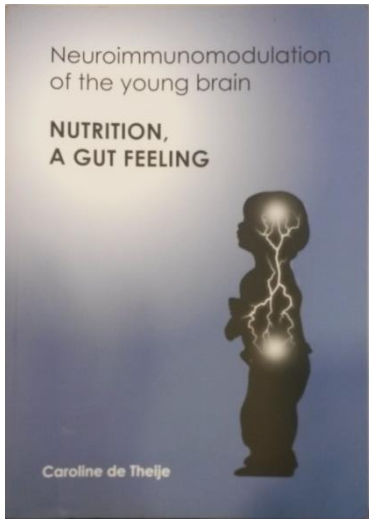

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