



# Masentaako kakka?

Hasse Karlsson, LT, FM,  
Integratiivisen neurotieteen ja psykiatrian professori, Turun  
yliopisto

Ylilääkäri, VSSHP/psykiatria  
Johtaja, Turku Brain and Mind Center



FINNBRAIN - study



Turun yliopisto  
University of Turku

- Jos on pitkään kauhea ummetus, niin kyllä masentaa





# FinnBrain - syntymäkohorttitutkimus

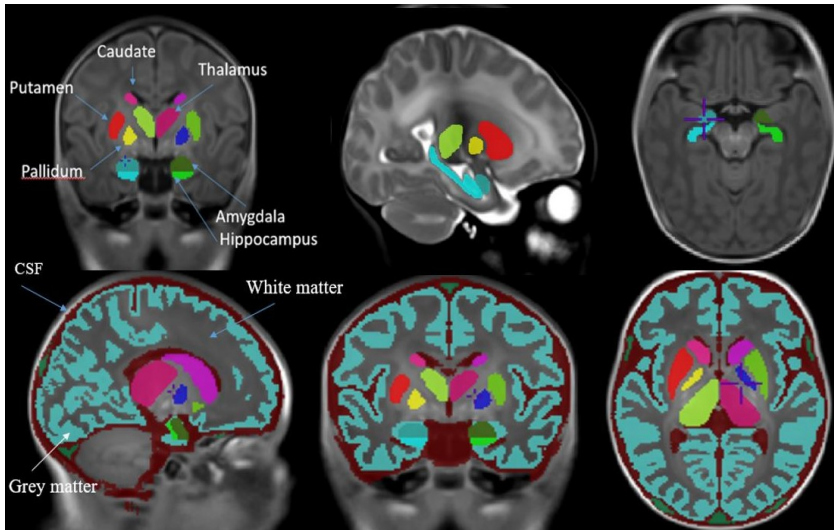
- Yli 4000 perheen (11000 yksilön) prospektiivinen kohortti, jossa selvitetään lapsen aivojen kehitystä, eri sairauksien riskitekijöitä ja niiden mekanismeja
  - Perustettiin 2010
- Lähes 200 tutkijaa, 45 väitöskirjatutkijaa

# EEG-ERP

Prenatal maternal anxiety and depression & auditory ERPs in relation to emotion stimuli in newborn (1-3 days old) infants (repeated at 3 years)



# Brain MRI at age 1 month and repeated later





Later measurement points,  
now 5 years of child age



# Optical imaging (NIRS) using emotion stimuli at 2 months and repeated later at 2 years

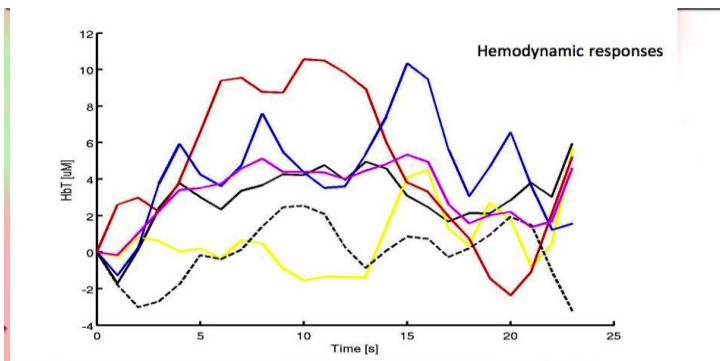


Figure 1: The average of all four auditory conditions (red = angry, blue = sad, yellow = happy, black continuous = neutral; black dashed line = dummy; magenta = average over first four conditions (not including dummy)); HbT is total hemoglobin concentration in micromole.



# Methods

- Brain imaging
  - Brain MRI/DTI/fMRI (child at 1 month and repeatedly after that, currently 5 years)
  - EEG-ERP (child at 1-3 days, and repeatedly after that, currently 3 years)
  - fNIRS (child age 2 months, and repeatedly after that, 2 years done)
- Biological samples
  - Feaces samples (mother, child, several times)
  - Hair cortisol (mother, child, several times)
  - Saliva cortisol during stress test (child at 2,5 months)
  - Blood (DNA, mRNA, cytokines; both parents during pregnancy, child cord blood)
  - Placenta samples
  - Breast milk samples
  - Sperm samples
- Neuropsychological measurements
  - Eye-movement tracking (child at 5 months, 8 months, 12 months, currently 5 years)
  - Neuropsychological assessment using CogState (both parents, child)
  - Child temperament and neurological development (Lab Tab, INTER-NDA)
- Other
  - Speech and language development
  - Mother – child interaction
  - Symptoms (parents, child, several times)
  - Register linkage



Child brain development  
Childhood and adulthood  
illnesses



# Methods

- Brain imaging

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- EEG-ERP (child at 1-3 days, and repeatedly after that, currently 3 years)
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- Neuropsychological measurements

- Eye-movement tracking (child at 5 months, 8 months, 12 months, currently 5 years)
- Neuropsychological assessment using Constate (both parents, child)



temperament and neurological assessment (Lab Tab, INTER-NDA)

language development

child interaction

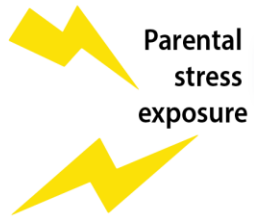
(parents, child, several

package

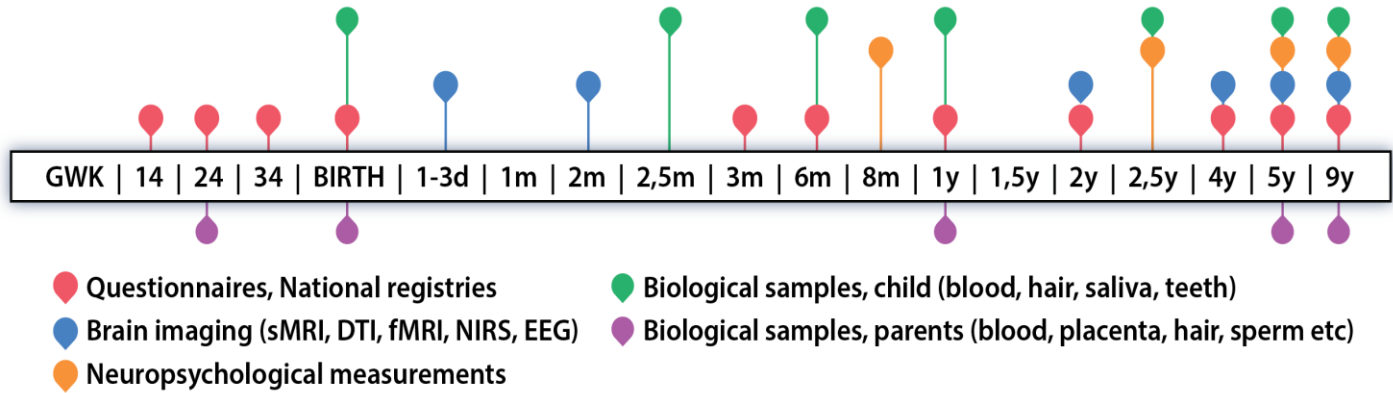


Child brain development  
Childhood and adulthood  
illnesses

Figure 1



Parental stress exposure

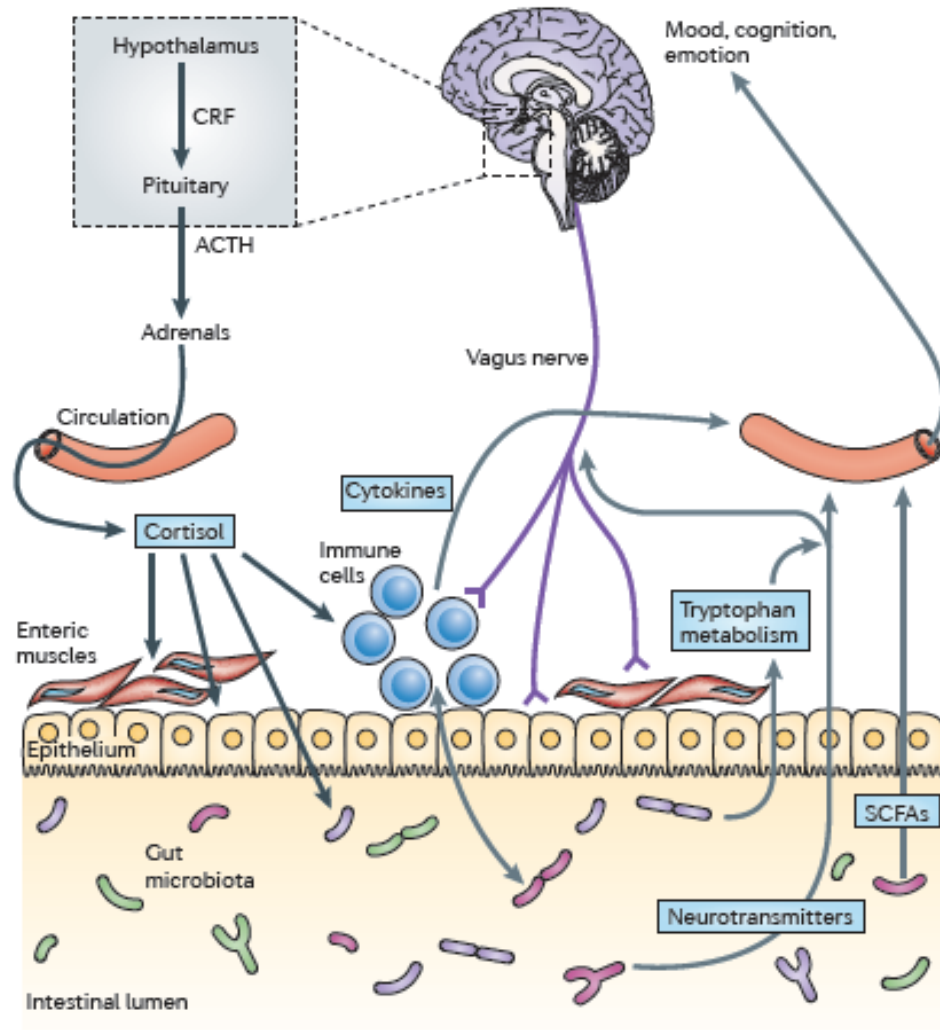


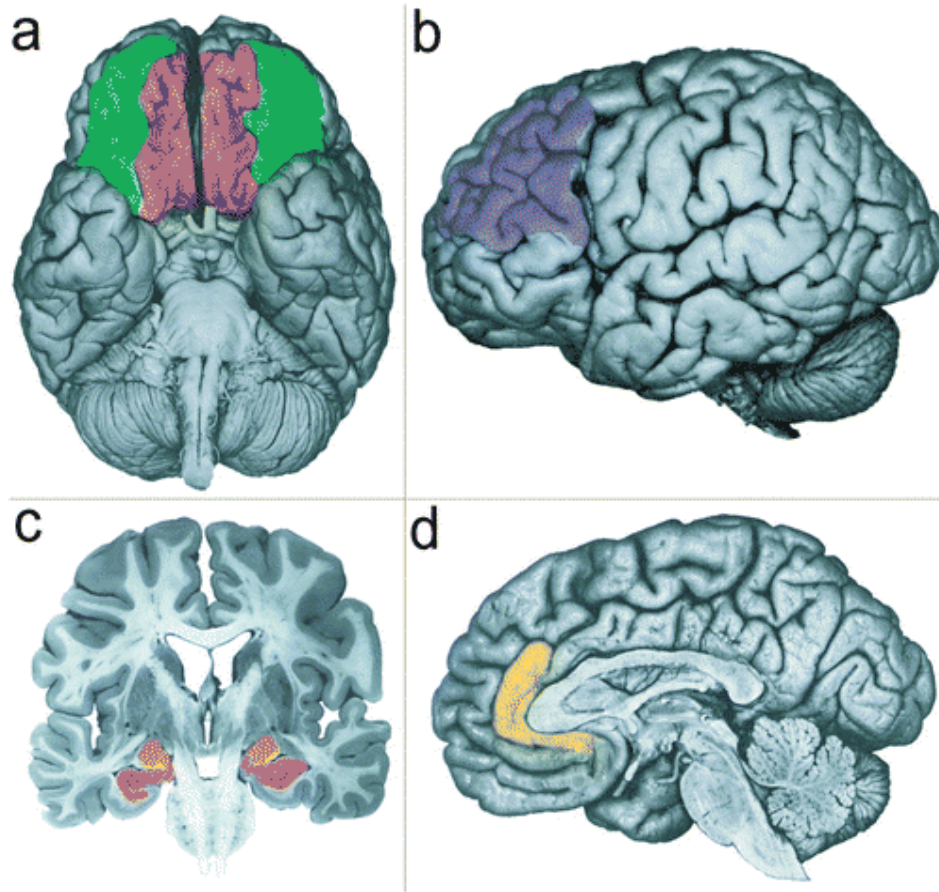


- Ärtyneen paksusuolen ja ahdistuneisuuden sekä masentuneisuuden komorbiditeetti on 50-90%









**Figure 1** Key brain regions involved in affect and mood disorders. (a) Orbital prefrontal cortex (*green*) and the ventromedial prefrontal cortex (*red*). (b) Dorsolateral prefrontal cortex (*blue*). (c) Hippocampus (*purple*) and amygdala (*orange*). (d) Anterior cingulate cortex (*yellow*).

# brain regions & depression

## subcallosal cingulate region

- unconscious and motor responses to emotional stress

## right anterior insula

- self-awareness
- interpersonal experience

### hypothalamus

sleep

appetite

libido

### amygdala

prominent emotions

### hippocampus

memory

### prefrontal cortex

executive functions

self esteem

and Meta-Analysis (PRISMA) guidelines. Nine articles met the eligibility criteria. Disparities in  $\alpha$ -diversity and  $\beta$ -diversity of the microbiota existed in people with depression compared to healthy controls. At the phylum level, there were inconsistencies in the abundance of *Firmicutes*, *Bacteroidetes*, and *Proteobacteria*. However, high abundance in *Actinobacteria* and *Fusobacteria* phyla were observed in people with depression. On the family level, high abundance of *Actinomycineae*, *Coriobacterineae*, *Bifidobacteriaceae*, *Clostridiales incertae sedis XI*, *Porphyromonadaceae*, *Clostridiaceae*, *Lactobacillaceae*, *Streptococcaceae*, *Eubacteriaceae*, *Thermoanaerobacteriaceae*, *Fusobacteriaceae*, *Nocardiaceae*, *Streptomycetaceae*, and low abundance of *Veillonellaceae*, *Prevotellaceae*, *Bacteroidaceae*, *Sutterellaceae*, *Oscillospiraceae*, *Marniabilaceae*, and *Chitinophagaceae* were observed in people with depression. On the genus level, high abundance of *Oscillibacter*, *Blautia*, *Holdemania*, *Clostridium XIX*, *Anaerostipes*, *Anaerofilum*, *Streptococcus*, *Gelria*, *Turicibacter*, *Parabacteroides*, *Eggerthella*, *Klebsiella*, *Paraprevotella*, *Veillonella*, *Clostridium IV*, *Erysipelotrichaceae incertae sedis*, *Eubacterium*, *Parvimonas*, *Desulfovibrio*, *Parasutterella*, *Actinomyces*, *Asaccharobacter*, *Atopobium*, *Olsenella* and low abundance of *Coprococcus*, *Lactobacillus*, *Escherichia/Shigella*, *Clostridium XIVa*, *Dialister*, *Howardella*, *Pyramidobacter*, and *Sutterella* were found in people with depression. Alteration of gut microbiome patterns was evident in people with depression. Further evidence is warranted to allow for the translation of microbiome findings toward innovative clinical strategies that may improve treatment outcomes in people with depression.



*MENTAL HEALTH*

.....  
Thinking  
from  
the Gut

The microbiome may  
yield a new class of  
psychobiotics for the  
treatment of anxiety,  
depression and other  
mood disorders

*By Charles Schmidt*

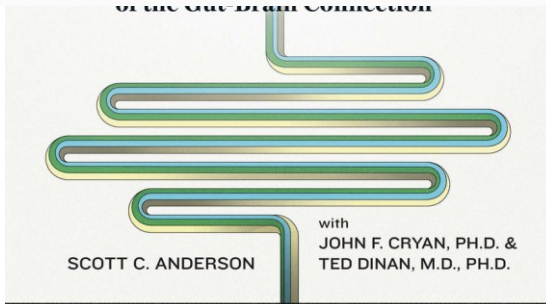
# Psykobiootit?

**\$114.13**



## Composition

300 mg of 5: 1 extract of St. John's wort (0.3% hypericin). 100 mg of lion's mane. 100 mg of L-Tryptophan. 100 mg of N-Acetyl Cysteine NAC. 20,000 million intestinal bacteria (mixture of probiotic strains). 50 mg of dry saffron extract. 1 mg of melatonin. 1.4 mg of vitamin B6.



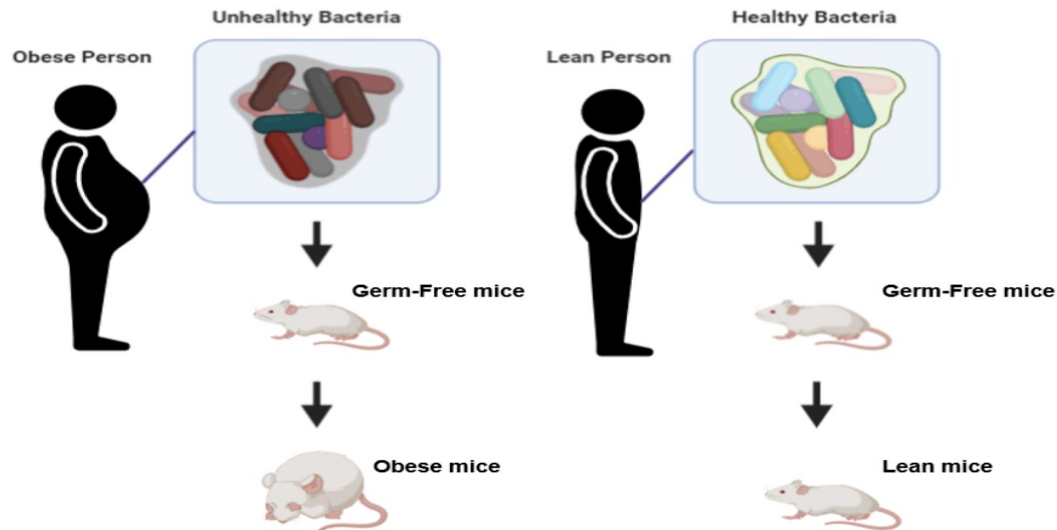
RESEARCH ARTICLE



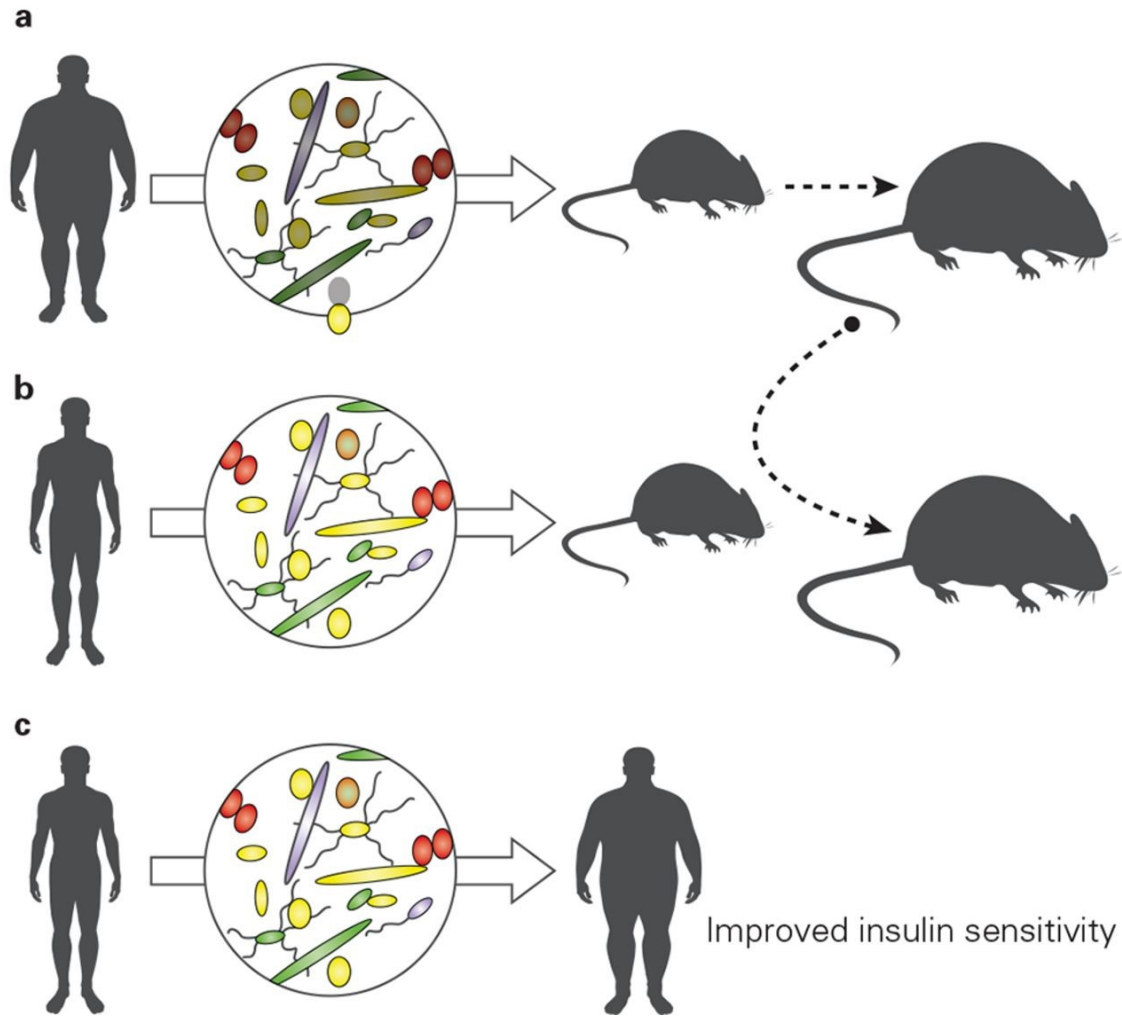
# Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

VANESSA K. RIDAURA, JEREMIAH J. FAITH, FEDERICO E. REY, JIYE CHENG, ALEXIS E. DUNCAN, ANDREW L. KAU, NICHOLAS W. GRIFFIN, VINCENT LOMBARD, BERNARD HENRISSAT, [...] JEFFREY I. GORDON [+16 authors](#) [Authors Info & Affiliations](#)

SCIENCE • 6 Sep 2013 • Vol 341, Issue 6150 • DOI: 10.1126/science.1241214



# Microbiota in overnutrition.



Fergus Shanahan et al. Gut 2017;66:1709-1717



# Ulosteen siirroistako apu depressioon ja.....?

- Kun siirretään kakkaa, niin mitä kaikkea siirretään?

# Weight Gain After Fecal Microbiota Transplantation

**Neha Alang<sup>1</sup> and Colleen R. Kelly<sup>2</sup>**

<sup>1</sup>Department of Internal Medicine, Newport Hospital, and <sup>2</sup>Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island



# Probiotics alleviate depressive behavior in chronic unpredictable mild stress rat models by remodeling intestinal flora

Qiufeng Li<sup>a</sup>, Li Li<sup>b</sup>, Xueqin Niu<sup>a</sup>, Chunling Tang<sup>a</sup>, Huaizhi Wang<sup>a</sup>, Jing Gao<sup>a</sup> and Jian Hu<sup>a</sup>



Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: [www.elsevier.com/locate/bbr](http://www.elsevier.com/locate/bbr)



Research report

## Probiotic treatment (*Bifidobacterium longum subsp. longum* 35624™) affects stress responsivity in male rats after chronic corticosterone exposure

Gabriel S. Haas, Wan Wang, Malak Saffar, Sean M. Mooney-Leber<sup>1</sup>, Susanne Brummelte\*

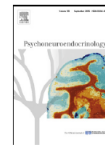
Department of Psychology, Wayne State University, 5057 Woodward Ave, 7th Floor, Detroit, MI, USA



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Psychoneuroendocrinology

journal homepage: [www.elsevier.com/locate/psyneuen](http://www.elsevier.com/locate/psyneuen)



frontiers  
in Behavioral Neuroscience

ORIGINAL RESEARCH  
published: 12 November 2020  
doi: 10.3389/fnbeh.2020.581296



## Probiotic treatment reduces depressive-like behaviour in rats independently of diet

Anders Abildgaard<sup>a,b,\*</sup>, Betina Elfving<sup>a</sup>, Marianne Hokland<sup>c</sup>, Gregers Wegener<sup>a,d</sup>, Sten Lund<sup>e</sup>



## A Probiotic Mixture Induces Anxiolytic- and Antidepressive-Like Effects in Fischer and Maternally Deprived Long Evans Rats

Valérie Daugé<sup>1\*</sup>, Catherine Philippe<sup>2</sup>, Mahendra Mariadassou<sup>3</sup>, Olivier Rué<sup>4</sup>, Jean-Charles Martin<sup>4</sup>, Marie-Noëlle Rossignol<sup>3</sup>, Nathalie Dourmap<sup>6</sup>, Ljubica Svljar<sup>7</sup>, Franck Tourmiaire<sup>2</sup>, Magali Monnoye<sup>2</sup>, Deborah Jardet<sup>8</sup>, Marie Bangratz<sup>8</sup>, Sophie Holowacz<sup>9</sup>, Sylvie Rabot<sup>2</sup> and Laurent Naudon<sup>1</sup>

## Transferring the blues: Depression-associated gut microbiota induces neurobehavioural changes in the rat

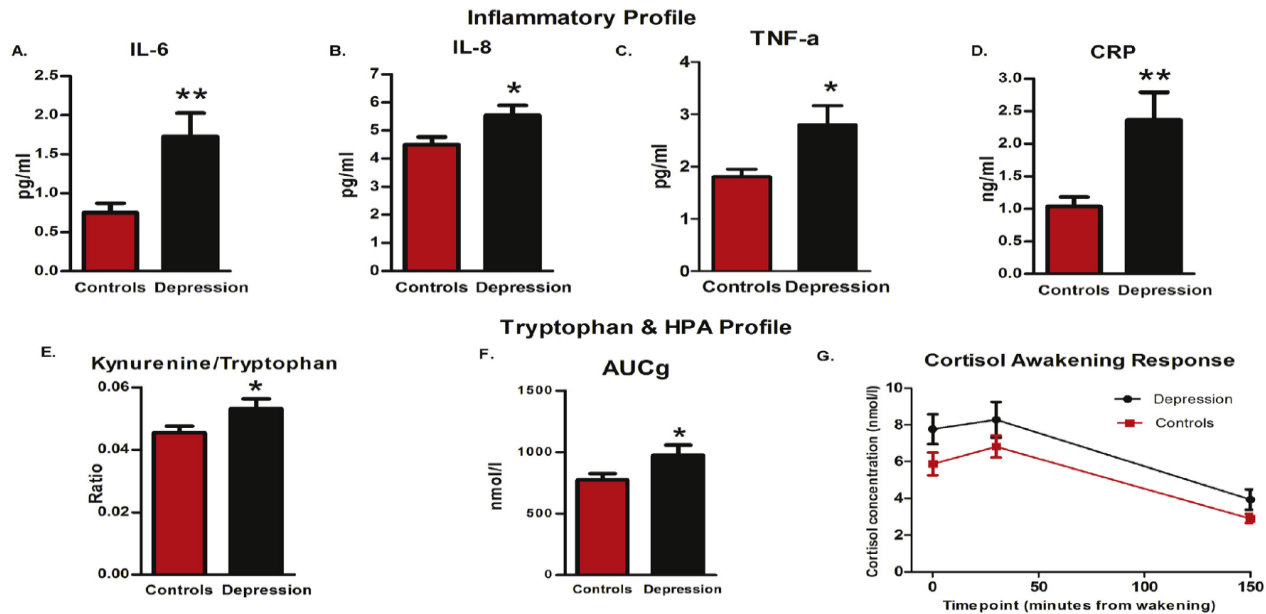
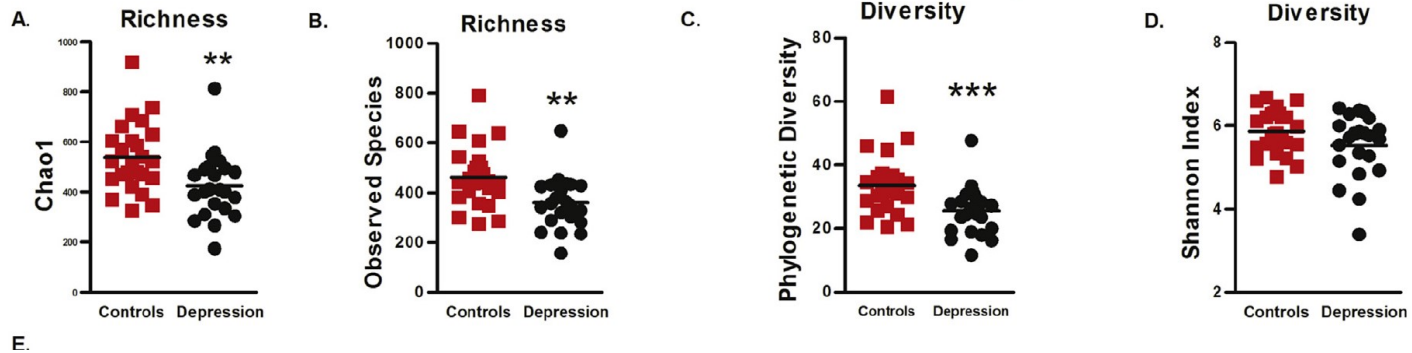


John R. Kelly <sup>a, b</sup>, Yuliya Borre <sup>a</sup>, Ciaran O' Brien <sup>a, c</sup>, Elaine Patterson <sup>a, c</sup>, Sahar El Aidy <sup>a, d</sup>, Jennifer Deane <sup>c</sup>, Paul J. Kennedy <sup>a</sup>, Sasja Beers <sup>a</sup>, Karen Scott <sup>a</sup>, Gerard Moloney <sup>a</sup>, Alan E. Hoban <sup>a</sup>, Lucinda Scott <sup>b</sup>, Patrick Fitzgerald <sup>a</sup>, Paul Ross <sup>c</sup>, Catherine Stanton <sup>c</sup>, Gerard Clarke <sup>a, b</sup>, John F. Cryan <sup>a, e</sup>, Timothy G. Dinan <sup>a, b, \*</sup>



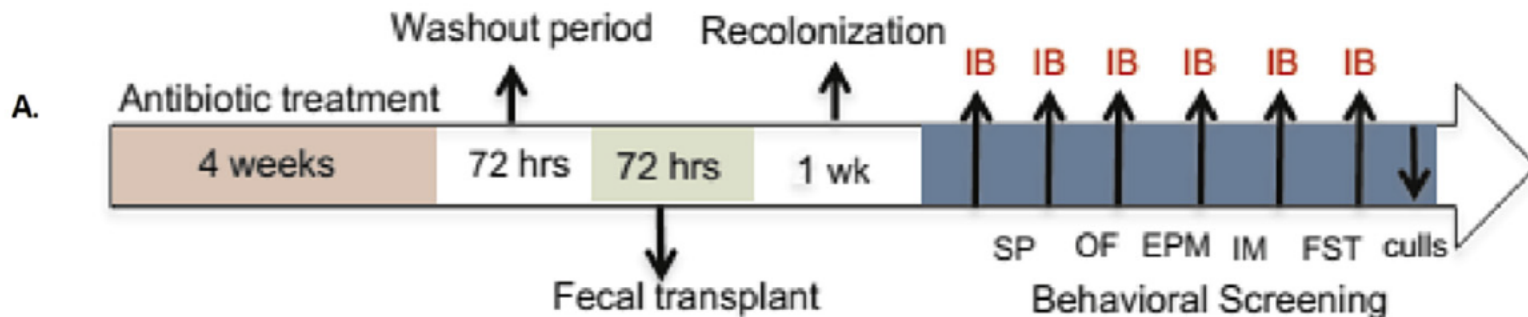


## Altered Microbiota Richness & Diversity in Depression

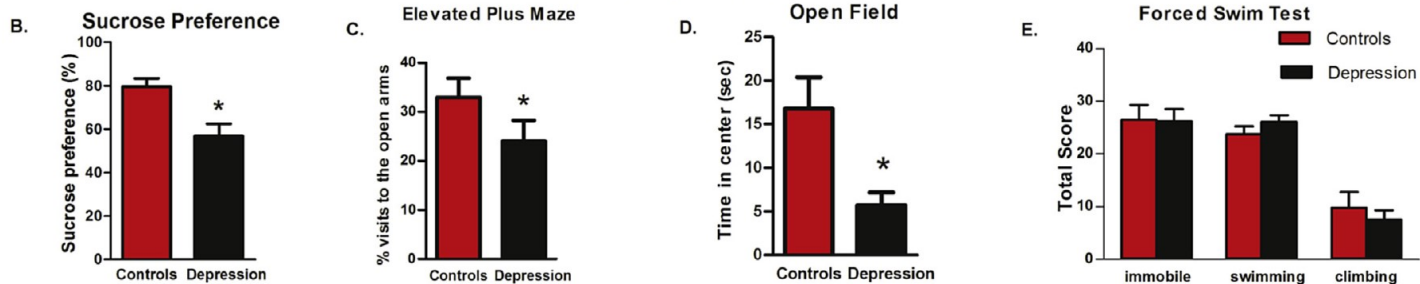


**Fig. 1.** Altered Inflammatory, Tryptophan, and HPA profile in depressed patients. The depressed patients had significantly increased levels of (A) IL-6, ( $p = 0.009$ ), (B) IL-8, ( $p = 0.021$ ) (C) TNF- $\alpha$  ( $p = 0.022$ ) and (D) CRP ( $p = 0.001$ ) compared to the healthy controls. The depressed group had a significantly increased (E) Kynurenine/tryptophan ratio ( $p = 0.049$ ) and a greater cortisol output as measured by the (F) Area under the Curve with respect to ground (AUCg) ( $p = 0.045$ ), though no significant difference in the (G) Cortisol Awakening Response (CAR) ( $p = 0.21$ ).

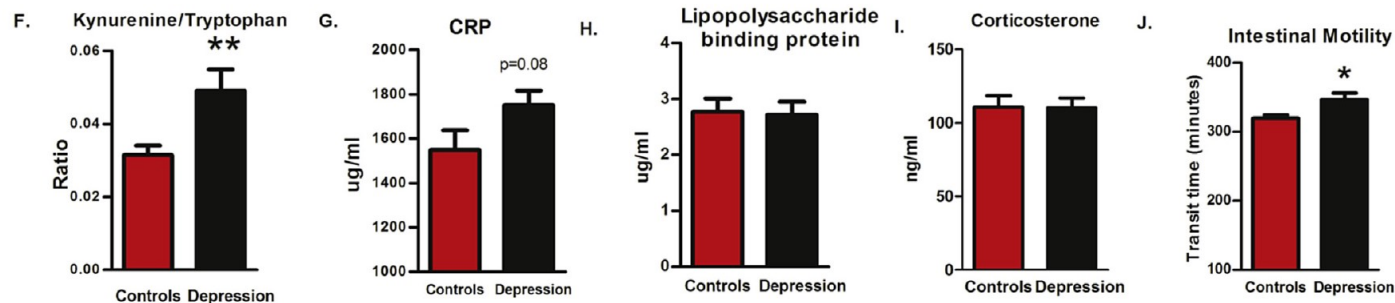
# Experimental Design



## Behavioural Profile

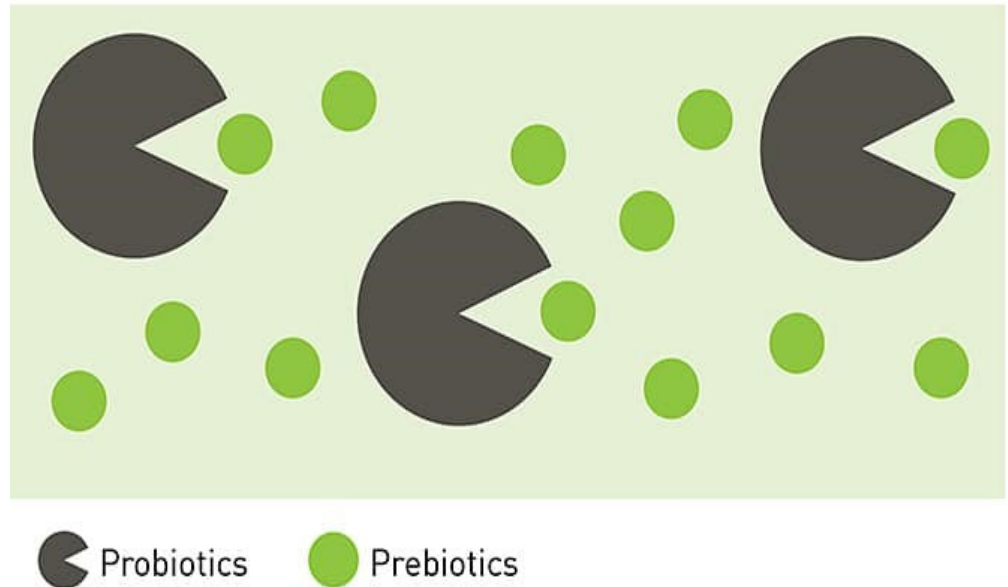


## Physiological Profile



# Miten suoliston flooraa voi ihmisellä manipuloida?

- Ravinto
- Probiotit
- Ulosteen siirrot



# Interventiot ihmisillä

Brain, Behavior, and Immunity 48 (2015) 258–264



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Brain, Behavior, and Immunity

journal homepage: [www.elsevier.com/locate/ybrbi](http://www.elsevier.com/locate/ybrbi)



A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood<sup>☆</sup>



Laura Steenbergen<sup>a,b,\*</sup>, Roberta Sellaro<sup>a,b</sup>, Saskia van Hemert<sup>c</sup>, Jos A. Bosch<sup>d</sup>, Lorenza S. Colzato<sup>a,b</sup>

<sup>a</sup>Leiden University, Institute for Psychological Research, Cognitive Psychology, Wassenaarseweg 52, 2333 AK Leiden, The Netherlands

<sup>b</sup>Leiden Institute for Brain and Cognition, P.O. Box 9600, 2300 RC Leiden, The Netherlands

<sup>c</sup>Winclove Probiotics, Hulstweg 11, 1032 LB Amsterdam, The Netherlands

<sup>d</sup>University of Amsterdam, Psychology Department, Clinical Psychology, Weesperplein 4, 1018 XA Amsterdam, The Netherlands

interventions. The present study aimed to test if a multispecies probiotic containing *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, and *Lactococcus lactis* (W19 and W58) may reduce cognitive

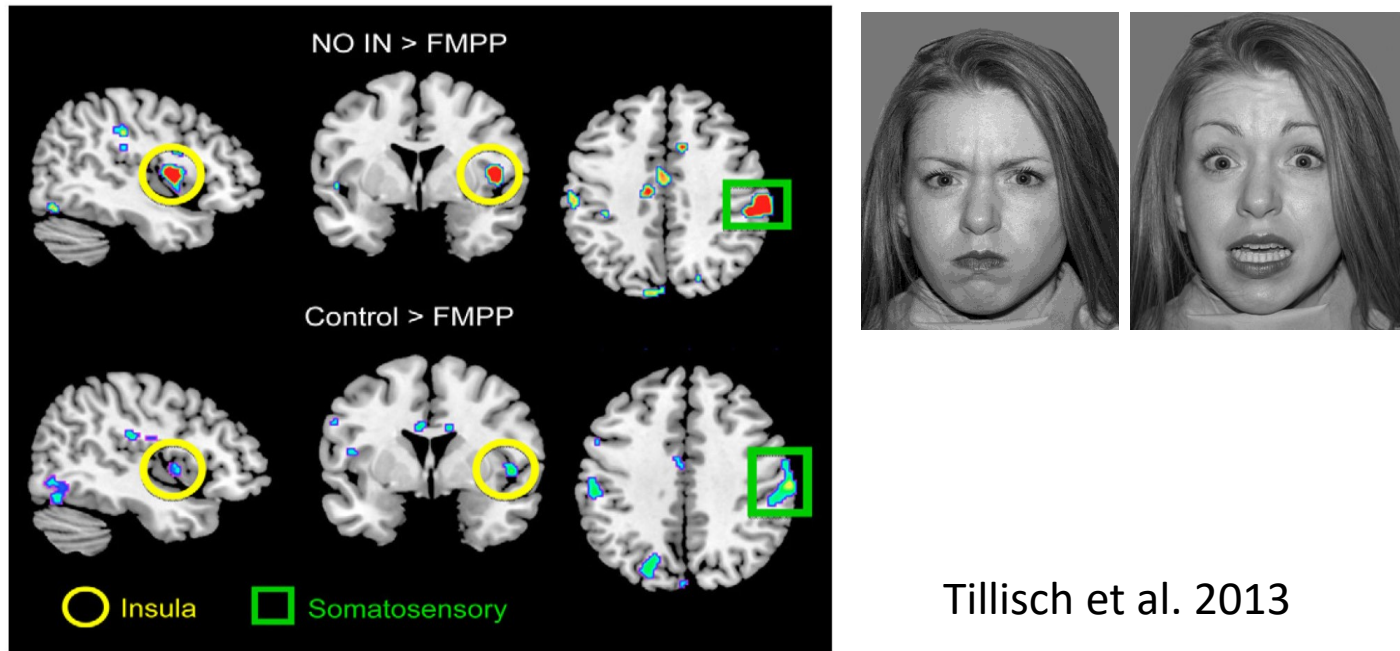
thoughts. **Conclusion:** These results provide the first evidence that the intake of probiotics may help  
Probiotics supplementation warrants further research as a potential preventive strategy for depression.

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# Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity

KIRSTEN TILLISCH<sup>1</sup>, JENNIFER LABUS<sup>1</sup>, LISA KILPATRICK<sup>1</sup>, ZHIGUO JIANG<sup>1</sup>, JEAN STAINS<sup>1</sup>, BAHAR EBRAT<sup>1</sup>, DENIS GUYONNET<sup>2</sup>, SOPHIE LEGRAIN-RASPAUD<sup>2</sup>, BEATRICE TROTIN<sup>2</sup>, BRUCE NALIBOFF<sup>1</sup>, and EMERAN A. MAYER<sup>1</sup>

The FMPP contained *Bifidobacterium animalis* subsp *Lactis*, *Streptococcus thermophiles*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp *Lactis*.



Tillisch et al. 2013

**Figure 2.**

Regions showing reduced activity in response to an emotional faces attention task after FMPP intervention are shown, with significant regions demarcated.

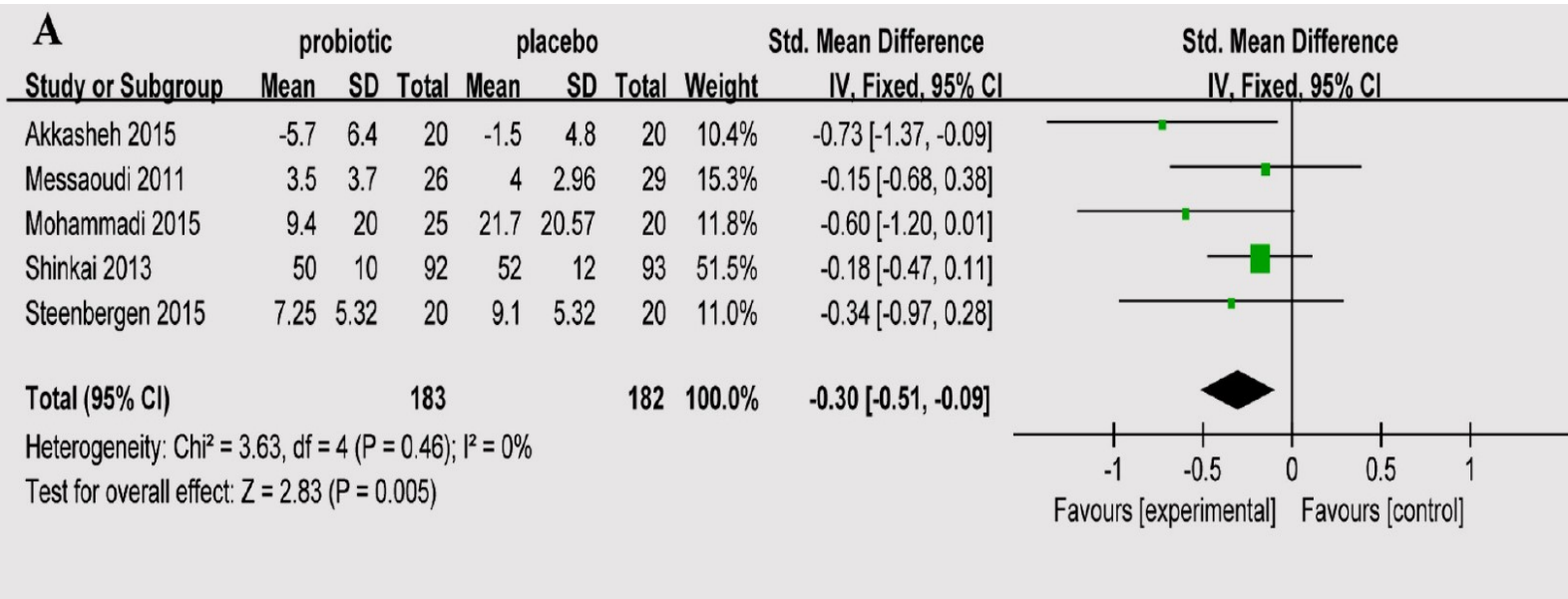




Review

# Effect of Probiotics on Depression: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Ruixue Huang, Ke Wang and Jianan Hu \*



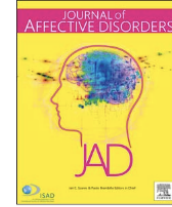


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# Journal of Affective Disorders

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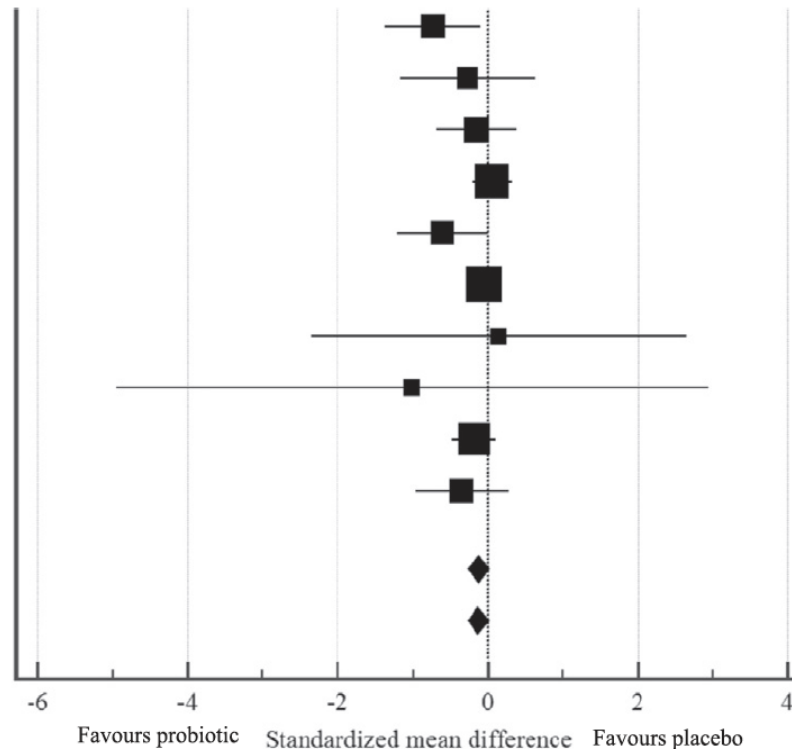
Review article

## A meta-analysis of the use of probiotics to alleviate depressive symptoms


Qin Xiang Ng<sup>a,\*</sup>, Christina Peters<sup>b</sup>, Collin Yih Xian Ho<sup>c</sup>, Donovan Yutong Lim<sup>d</sup>, Wee-Song Yeo<sup>c,e</sup>



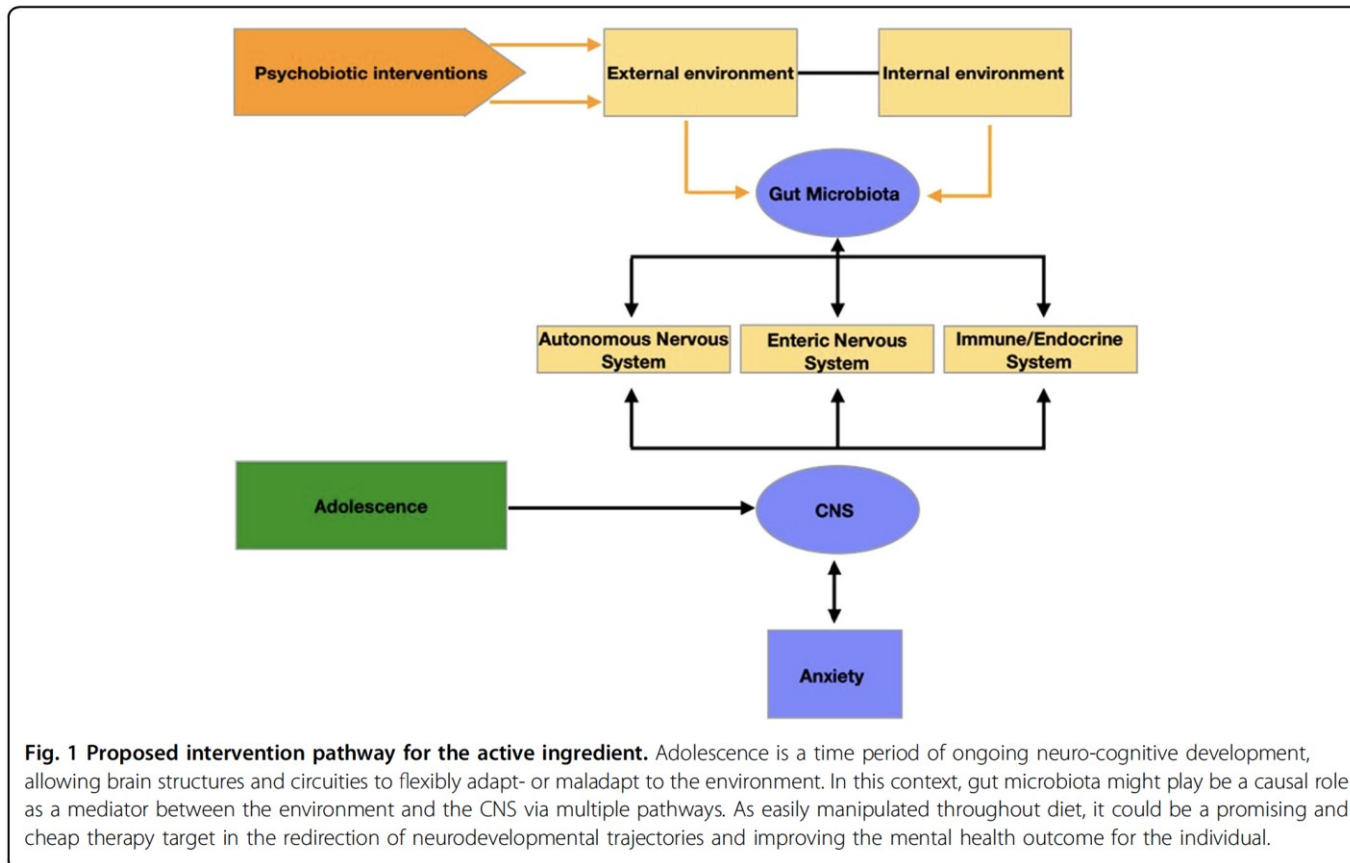
Akkasheh, 2016  
Chung, 2014  
Messaoudi, 2011  
Nishihara, 2014  
Mohammadi, 2016  
Östlund-Lagerström, 2016  
Pinto-Sanchez, 2017  
Romijn, 2017  
Shinkai, 2013  
Steenbergen, 2015  
Total (fixed effects)  
Total (random effects)



# Psychobiotic interventions for anxiety in young people: a systematic review and meta-analysis, with youth consultation

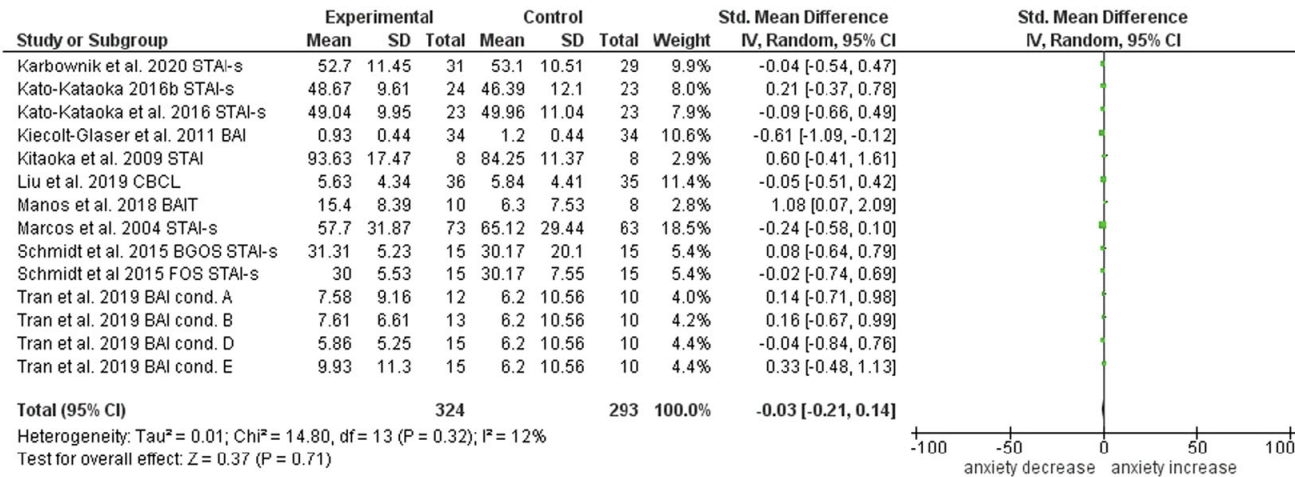
[Kathrin Cohen Kadosh](#) , [Melissa Basso](#), [Paul Knytl](#), [Nicola Johnstone](#), [Jennifer Y. F. Lau](#) & [Glenn R. Gibson](#)

*Translational Psychiatry* **11**, Article number: 352 (2021) | [Cite this article](#)



**Fig. 1 Proposed intervention pathway for the active ingredient.** Adolescence is a time period of ongoing neuro-cognitive development, allowing brain structures and circuitries to flexibly adapt- or maladapt to the environment. In this context, gut microbiota might play a causal role as a mediator between the environment and the CNS via multiple pathways. As easily manipulated throughout diet, it could be a promising and cheap therapy target in the redirection of neurodevelopmental trajectories and improving the mental health outcome for the individual.

# Tulos = 0



**Fig. 3** Forest plot of the studies investigating the effect of psychobiotics on anxiety measures.

# Psychobiotics and the gut–brain axis: in the pursuit of happiness

This article was published in the following Dove Press journal:  
Neuropsychiatric Disease and Treatment  
16 March 2015  
[Number of times this article has been viewed](#)

**Conclusions:** Clinicians are encouraged to consider patients' gut health when evaluating and treating psychiatric conditions, such as anxiety and depression. Optimization and diversification of gut flora through the use of psychobiotics—probiotics that confer mental health benefits—may soon become standard practice in conjunction with traditional psychiatric treatment modalities such as pharmacotherapy and psychotherapy.