The Gut Microbiome in Health and Disease: Focus on the Microbiome-gut-brain Axis

Dr Gerard Clarke

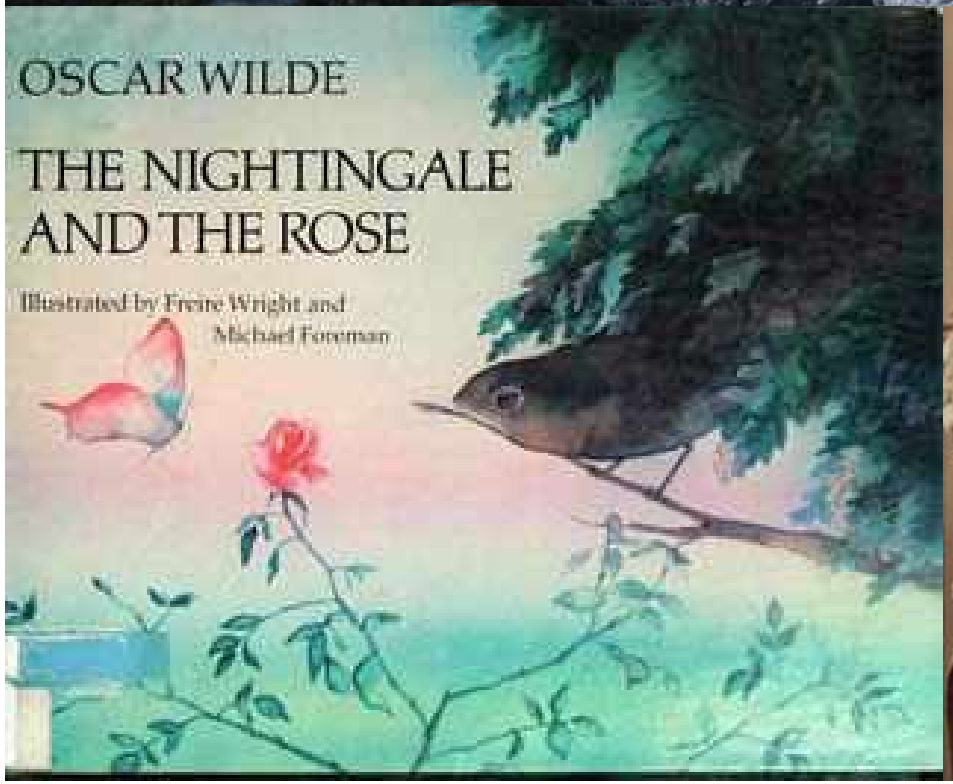
Department of Psychiatry and Neurobehavioural Science &
APC Microbiome Ireland
University College Cork

Metabolic Medical Institute (MMI) Module IV : Gastroenterology: The Cross Roads of Health
October 16th 2020

Disclosures

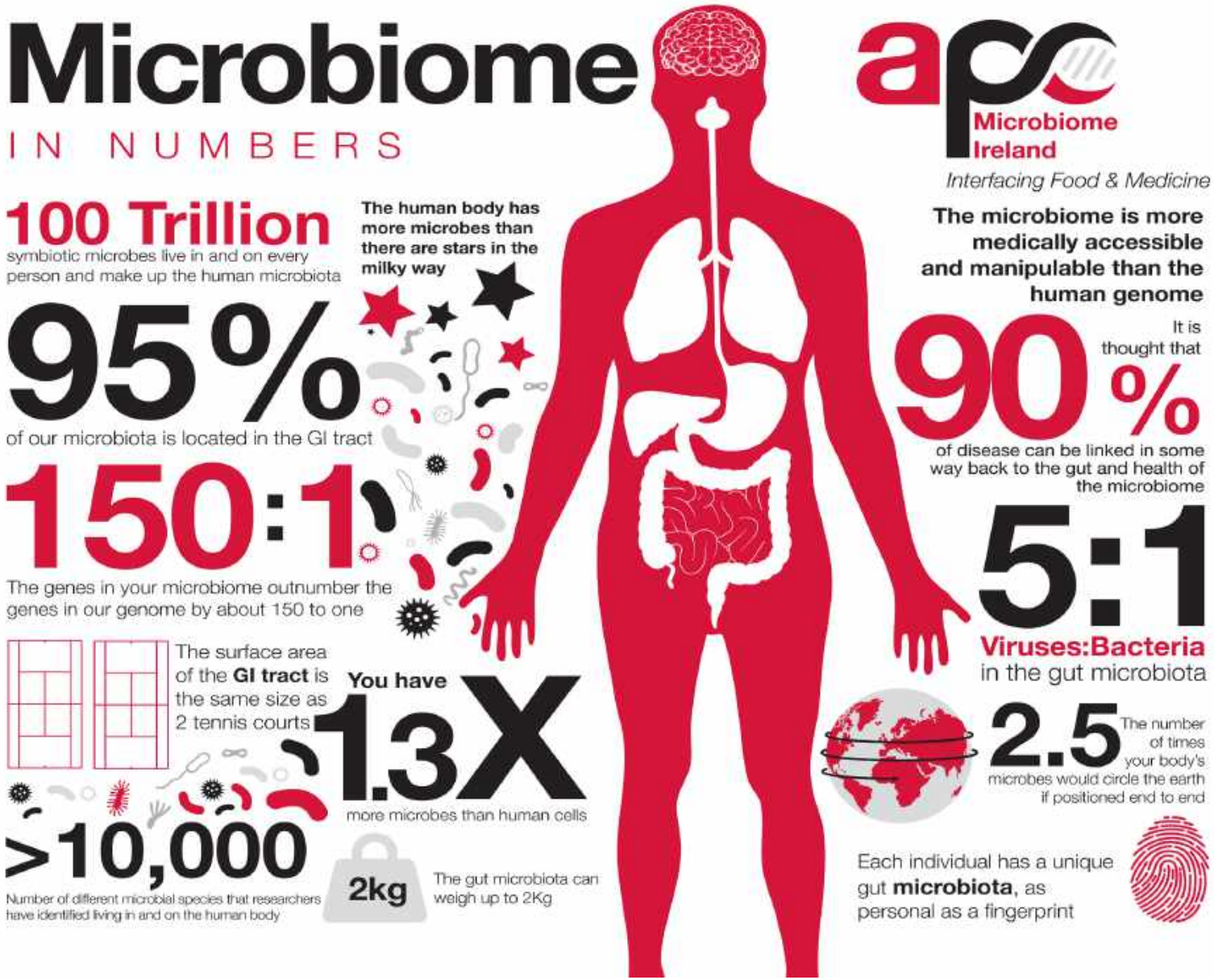
- **Honorarium from Janssen and Probi (Invited Speaker)**
- **Research funding from Pharmavite**
- **Content of presentation neither influenced nor constrained by this support**


Ah, on what little things
does happiness depend.
Oscar Wilde


OSCAR WILDE
THE NIGHTINGALE AND THE ROSE
Illustrated by Freire Wright and Michael Foreman

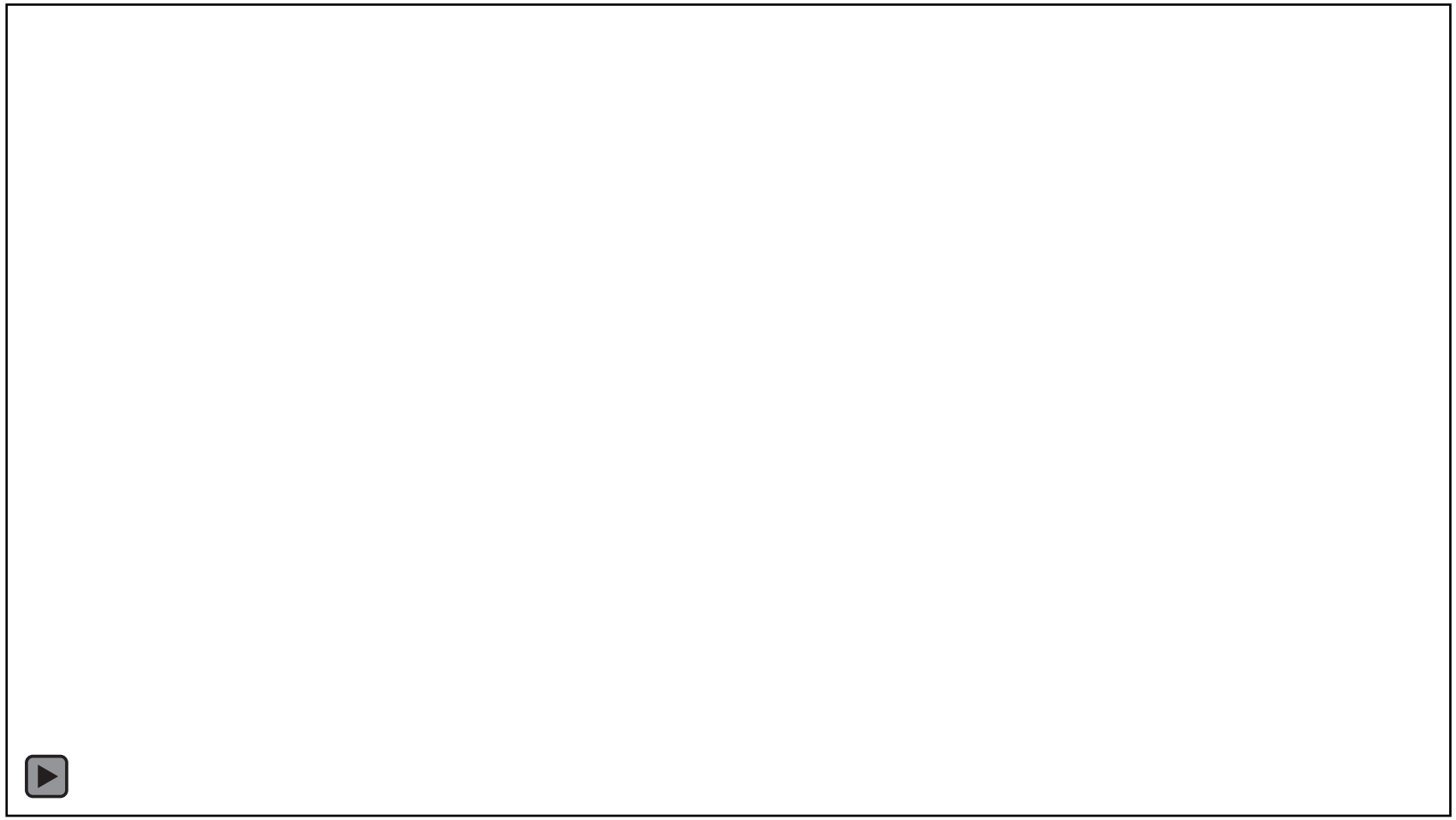
Living in a Microbial World….

http://apc.ucc.ie



The War on Bacteria

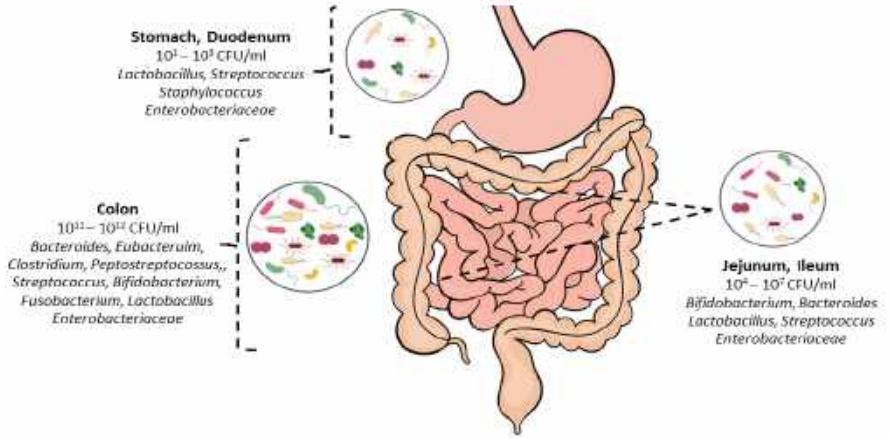
http://apc.ucc.ie



http://www.youtube.com/watch?v=Poxt-D8d0zg&feature=player_detailpage

The Forgotten Organ?

- Bacteria density increases in the jejunum/ileum from the stomach and duodenum
- In the large intestine, colon-residing bacteria achieve the highest cell densities recorded for any ecosystem
- Exert a range of protective, structural and metabolic effects on the intestinal mucosa



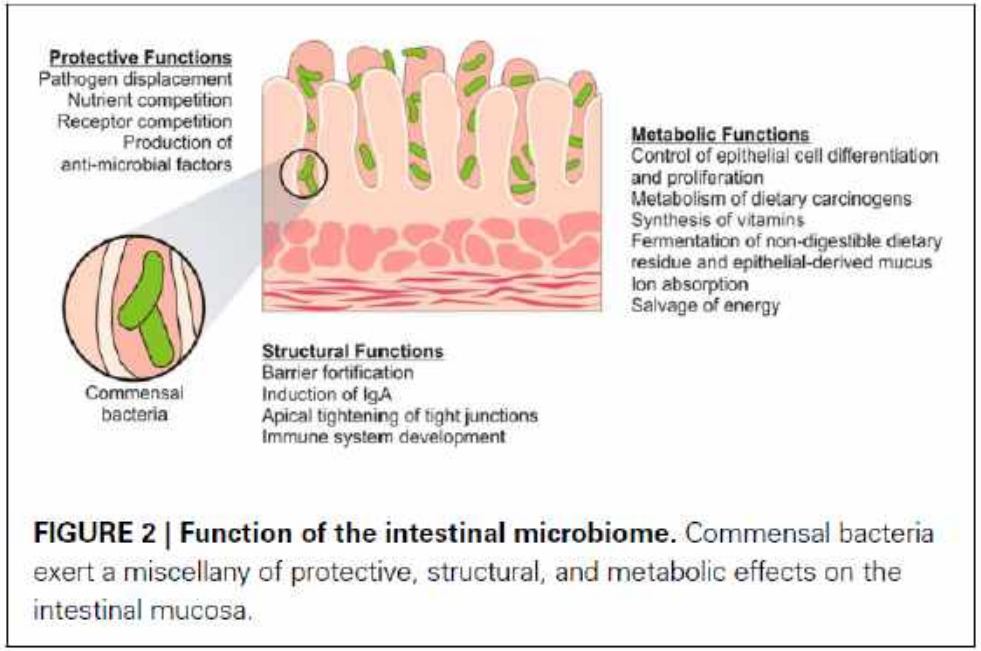
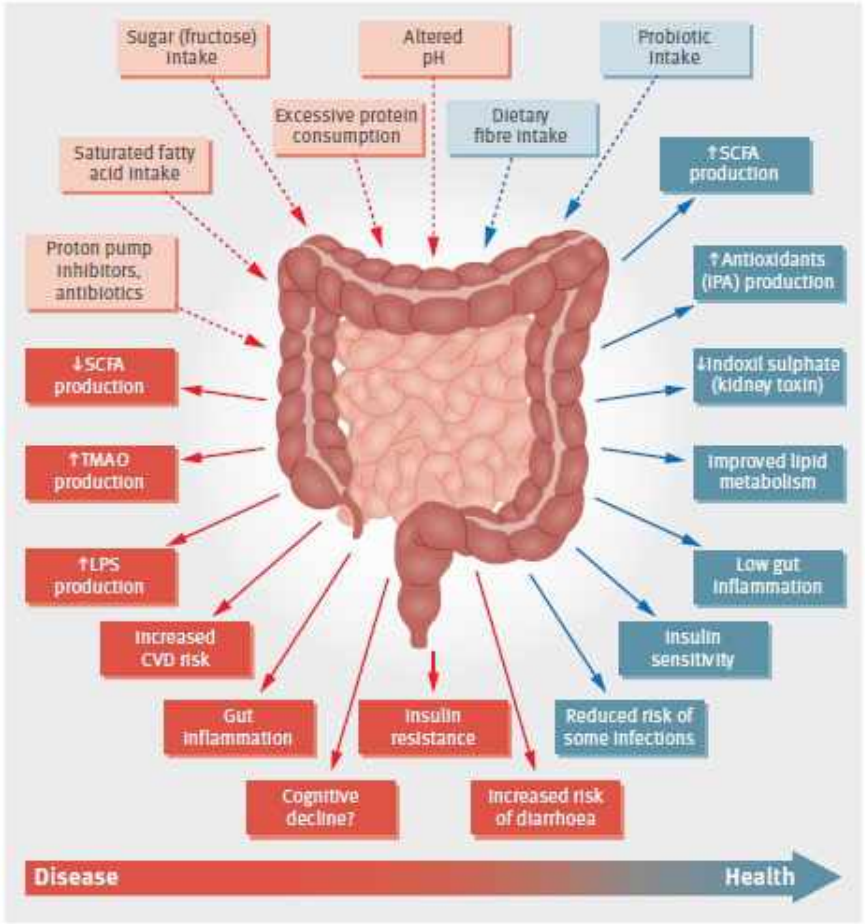


FIGURE 2 | Function of the intestinal microbiome. Commensal bacteria exert a miscellany of protective, structural, and metabolic effects on the intestinal mucosa.

Grenham, Clarke et al., Frontiers in Physiology 2011

Role of the gut microbiota in nutrition and health

Ana M Valdes and colleagues discuss strategies for modulating the gut microbiota through diet and probiotics



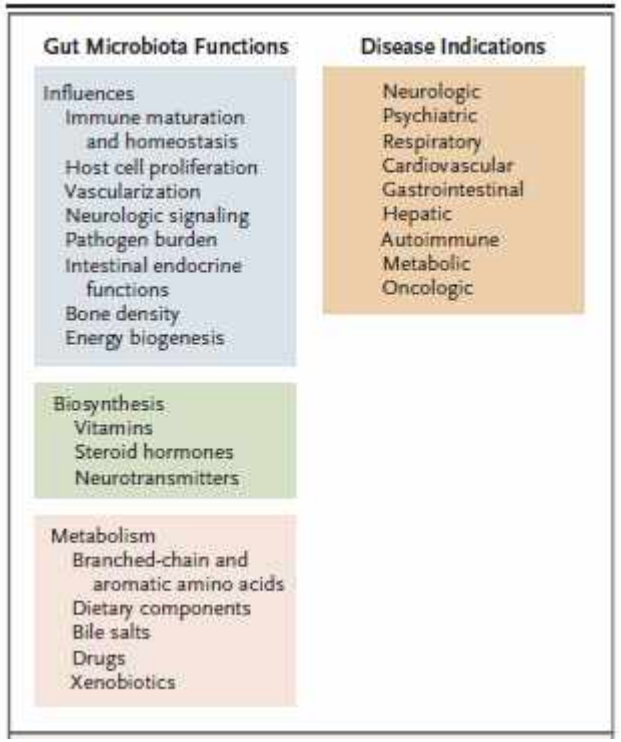
N ENGL J MED 375;24 NEJM.ORG DECEMBER 15, 2016
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Elizabeth G. Phimister, Ph.D., *Editor*

The Human Intestinal Microbiome in Health and Disease

Susan V. Lynch, Ph.D., and Oluf Pedersen, M.D., D.M.Sc.



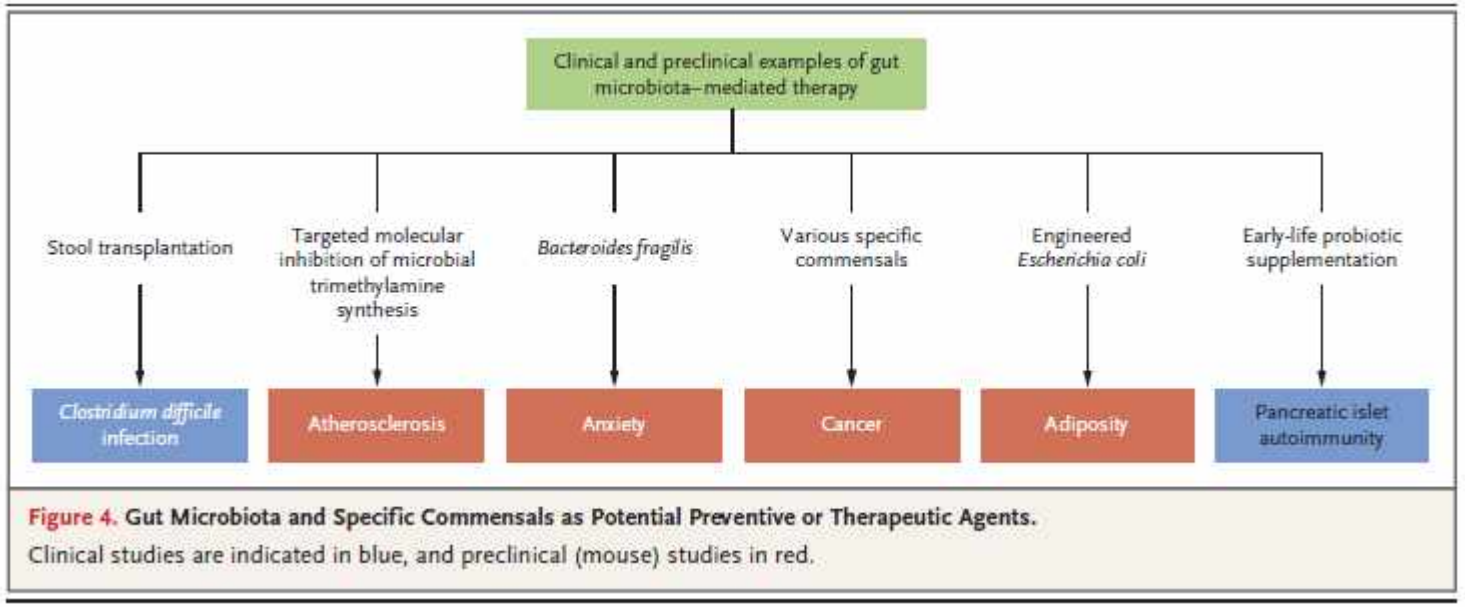


Figure 4. Gut Microbiota and Specific Commensals as Potential Preventive or Therapeutic Agents.
Clinical studies are indicated in blue, and preclinical (mouse) studies in red.

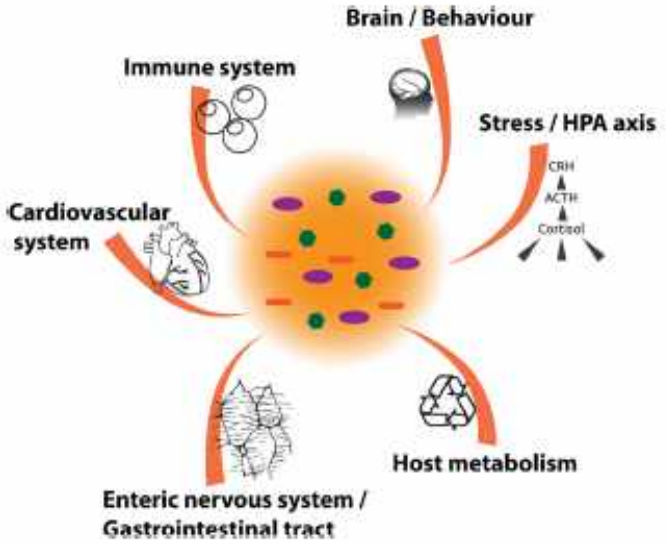
8 JUNE 2012 VOL 336 SCIENCE www.sciencemag.org

The Gut Microbiota

REVIEW

Interactions Between the Microbiota and the Immune System

Lora V. Hooper,[1]* Dan R. Littman,[2] Andrew J. Macpherson[3]



MINIREVIEW

Mol Endocrinol, August 2014, 28(8):1221–1238 mend.endojournals.c

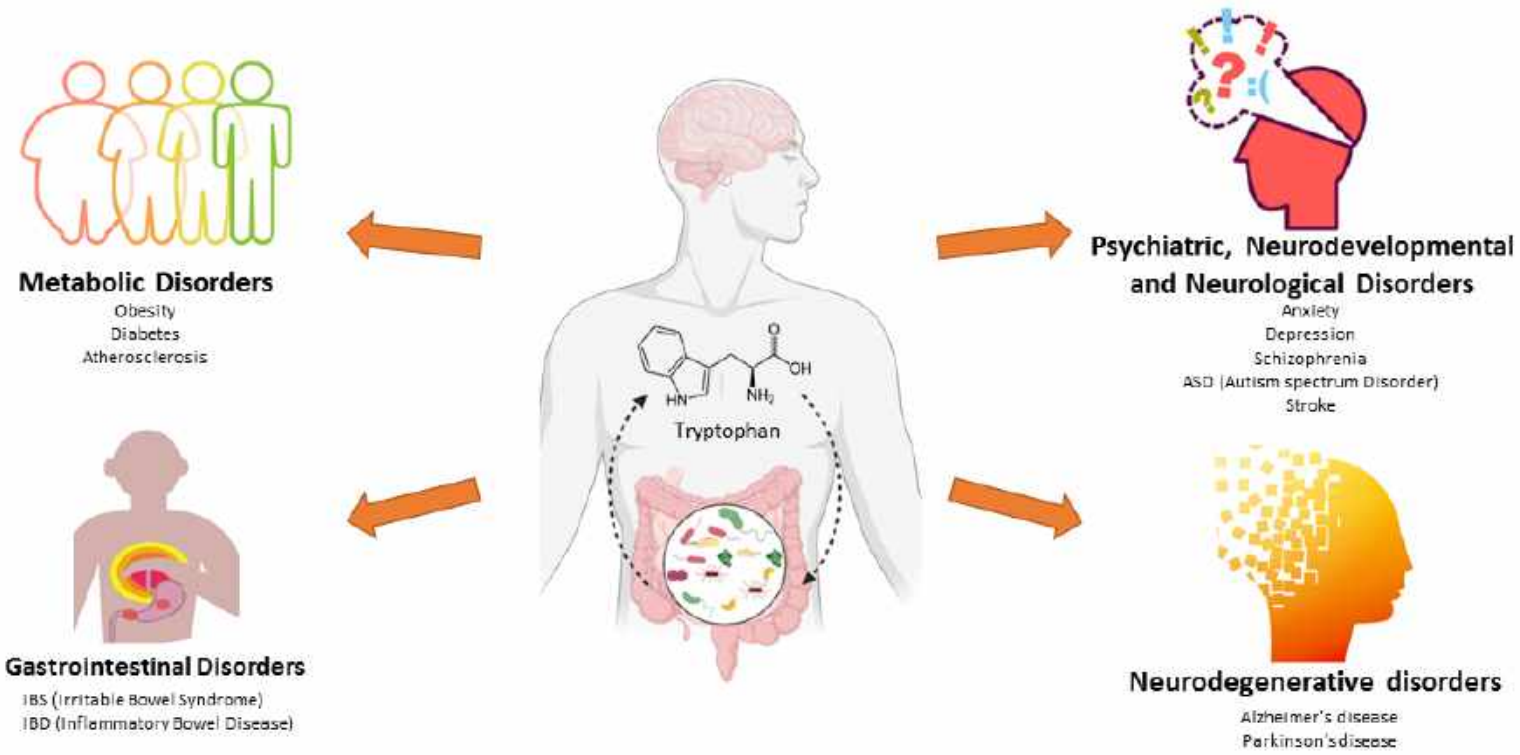
Minireview: Gut Microbiota: The Neglected Endocrine Organ

Gerard Clarke, Roman M. Stilling, Paul J. Kennedy, Catherine Stanton, John F. Cryan, and Timothy G. Dinan

Alimentary Pharmabiotic Centre (G.C., R.M.S., P.J.K., C.S., J.F.C., T.G.D.) and Departments of Psychiatry (G.C., C.S., T.G.D.) and Anatomy and Neuroscience (J.F.C.), University College Cork, Cork, Ireland; and Teagasc (C.S.), Moorepark, Fermoy, Cork, Ireland

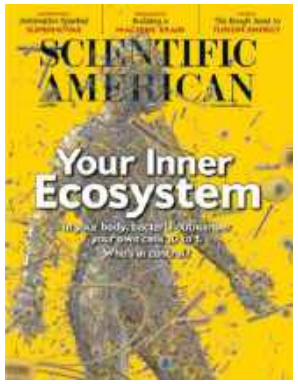
The Gut Microbiome in Disease

http://apc.ucc.ie



Forgotten Organ No More!

http://apc.ucc.ie



MEET THE PSYCHOBIOME

Mounting evidence that gut bacteria influence the nervous system inspires efforts to mine the microbiome for brain drugs

By **Elizabeth Pennisi**, in Cambridge, Massachusetts; Photography by **Ken Richardson**

Katya Gavish is searching for new brain drugs in a seemingly unlikely place: human stool samples. An earnest and focused microbiologist who trained in Russia and loves classical music, she's standing in front of a large anaerobic chamber in a lab at Holobiome, a small startup company here. She reaches into the glass-fronted chamber through Michelin Man–like sleeves to begin to dilute the sample inside. That's the first step toward isolating and culturing bacteria that Gavish and her Holobiome colleagues hope will produce new treatments for depression and other disorders of the brain and nervous system.

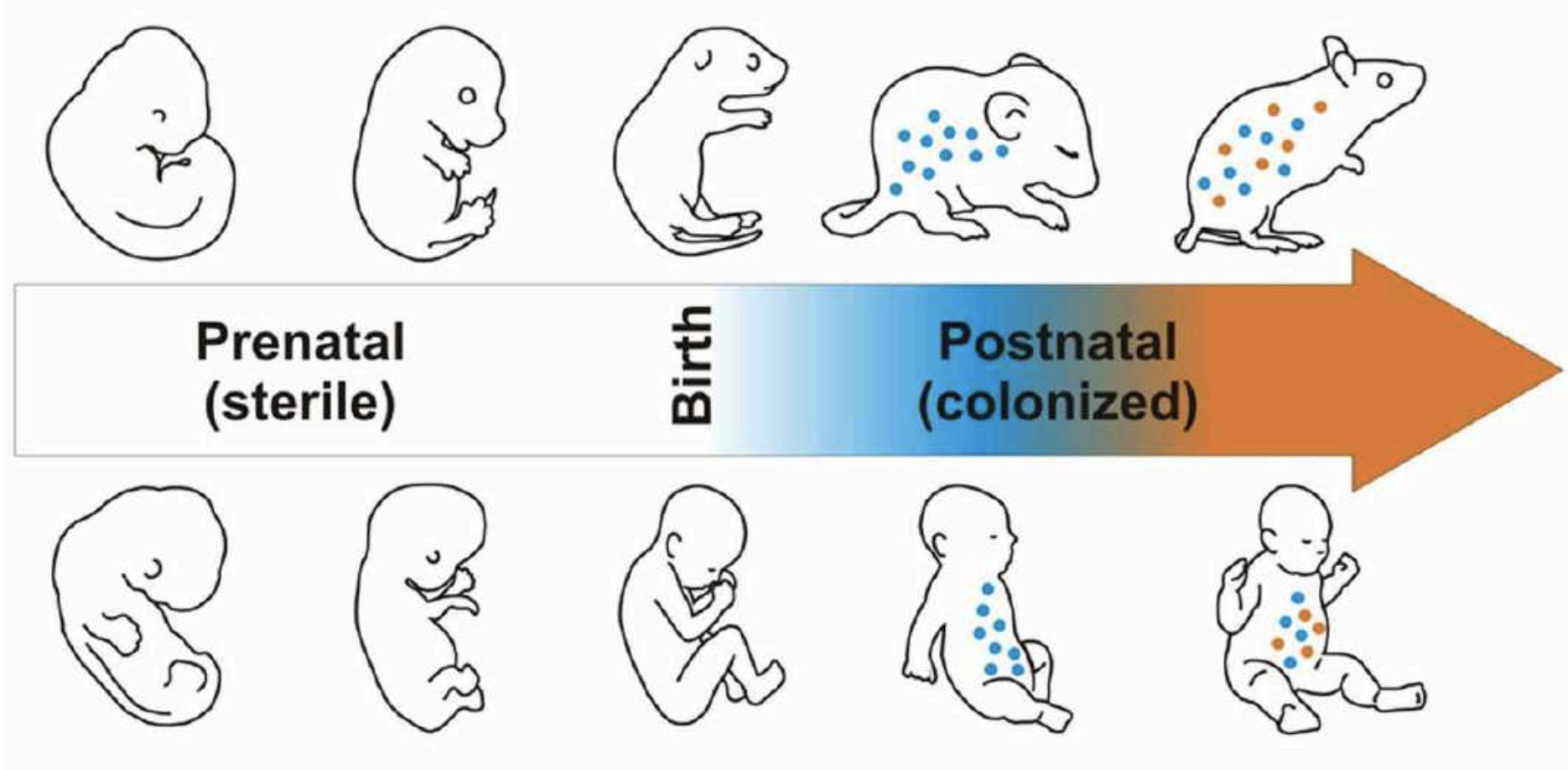
The eight-person company plans to capitalize on growing evidence from epidemiological and animal studies that link gut bacteria in conditions as diverse as autism, anxiety, and Alzheimer's disease. Since its founding a mere 3 years ago, Holobiome has created one of the world's largest collections of human gut microbes. The company's CEO, Phil Strandwitz, cannot yet say exactly what form the new treatments will take. But the targeted ailments include depression and insomnia, as well as constipation, and visceral pain like that typical of irritable bowel syndrome—conditions that may have neurological as well as intestinal components. Strandwitz, a raid-mustached Midwesterner with a Ph.D. in microbiology, isn't prone to visionary statements, but neither is he short on ambition: He predicts the first human trial will start within 3 year.

The allure is simple: Drug development for neuropsychiatric disorders has lagged

570 SCIENCE

Corrected 11 May 2020. See full text.

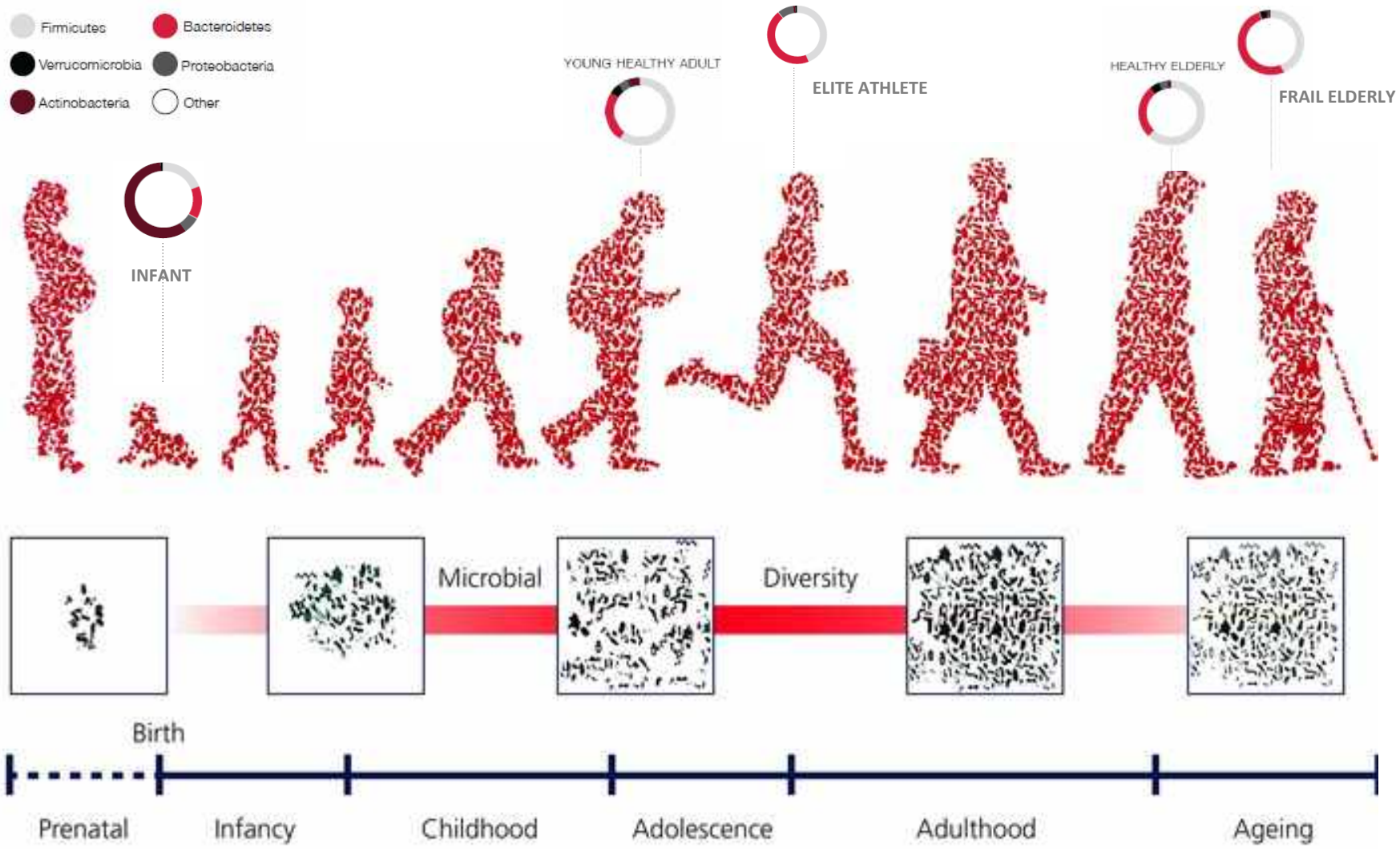
Where do we get our microbiota from?



Grenham et al., 2011

GI microbiota over lifetime

http://apc.ucc.ie



Cryan and Dinan, J Physiology 2017

Stress response
Immune development

Inflammation
Immunosenesence

Factors Defining the Gut Microbiome

http://apc.ucc.ie

- Chara… …ome
- Stabl…
- Diver…
- Mod…

Clarke et al., Pharmacological Reviews 2019

MILESTONES IN HUMAN MICROBIOTA RESEARCH

A field is born (FOREWORD)

1944 Culturing anaerobes (MILESTONE 1)

1958 Faecal microbiota transplantation for *Clostridioides difficile* infection (MILESTONE 2)

1965 Gut microbiota transfer experiments in germ-free animals (MILESTONE 3)

1972 The microbiota influences metabolism of host-directed drugs (MILESTONE 4)

1981 Microbiota succession in early life (MILESTONE 5)

1996 Sequence-based identification of human associated microbiota (MILESTONE 6)

1998 Stability and individuality of adult microbiota (MILESTONE 7)

2003 Beyond bacteria: studies of other host-associated microorganisms (MILESTONE 8)

2004 Regulation of mucosal immunity by the microbiota (MILESTONE 9)

2005 The importance of adequately feeding your microbiota (MILESTONE 10)

2006 Transfer of host phenotypes through microbiota transplantation (MILESTONE 11)

2006 Impact of diet–microbiota interactions on human metabolism (MILESTONE 12)

2007 Mechanisms of colonization resistance (MILESTONE 13)

2007 Functional human microbiota analyses in vivo using 'omics technologies (MILESTONE 14)

2010 Antibiotic effects on microbiota composition and host health (MILESTONE 15)

2010 Bioinformatics tools enable the analysis of microbiome sequencing data (MILESTONE 16)

2010 Microbiome analyses in large human populations (MILESTONE 17)

2011 The microbiota–gut–brain axis (MILESTONE 18)

2012 Modern culturing efforts expand the culturable microbiota (MILESTONE 19)

2012 Global human microbiome (MILESTONE 20)

2013 Microbially-produced short-chain fatty acids induce regulatory T cell production (MILESTONE 21)

2014 Production of antibiotics by the human microbiota (MILESTONE 22)

2015 Host-targeted drugs affect microbiota populations (MILESTONE 23)

2018 Human microbiota affects response to cancer therapy (MILESTONE 24)

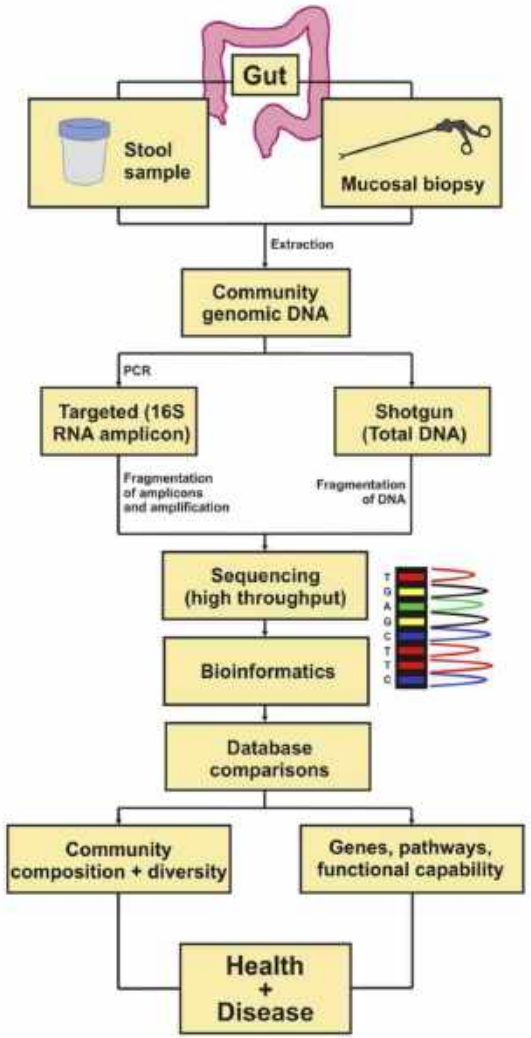
2019 Metagenome-assembled genomes provide unprecedented characterization of human-associated microbiota (MILESTONE 25)

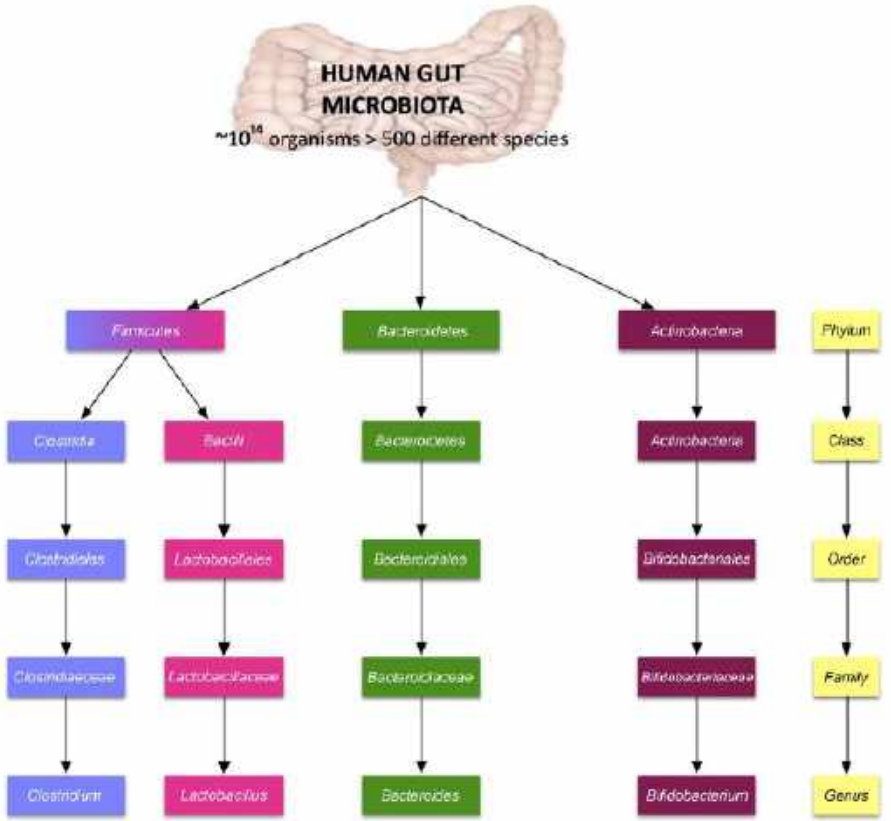
J Physiol 592.14 (2014) pp 2981–2988

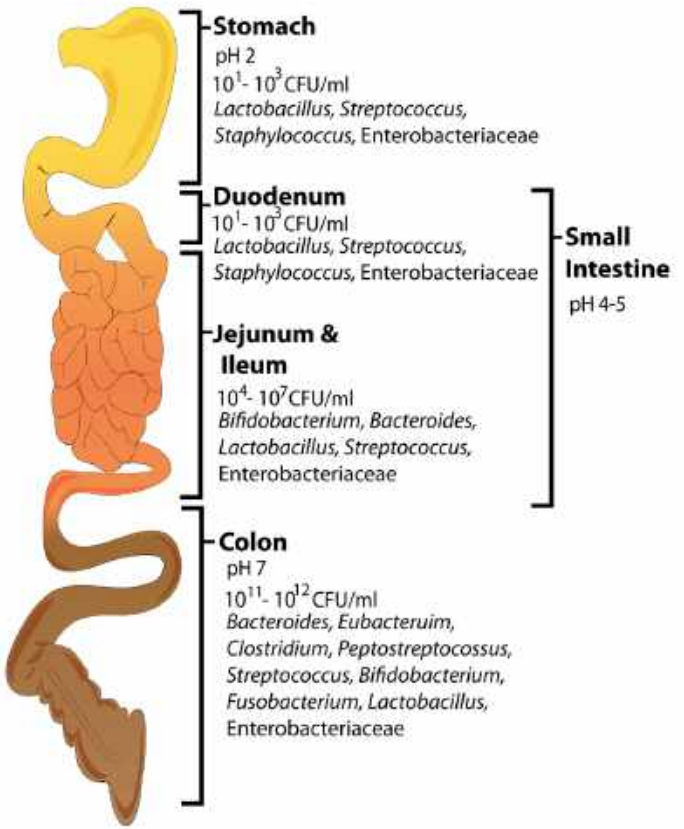
REVIEW ARTICLE

It's a gut feeling: How the gut microbiota affects the state of mind

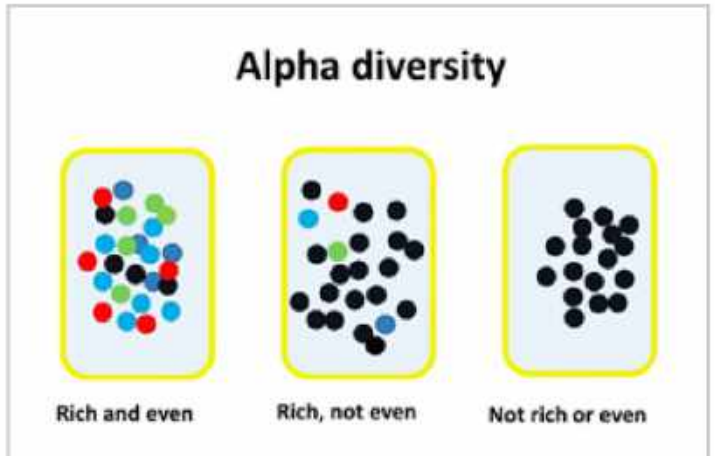
Adam D. Farmer, Holly A. Randall and Qasim Aziz





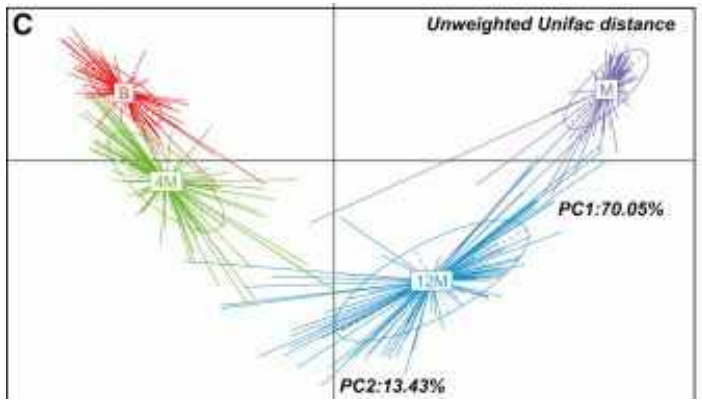


Alpha and Beta Diversity



Stoll et al, The Rheumatologist 2016

Beta diversity

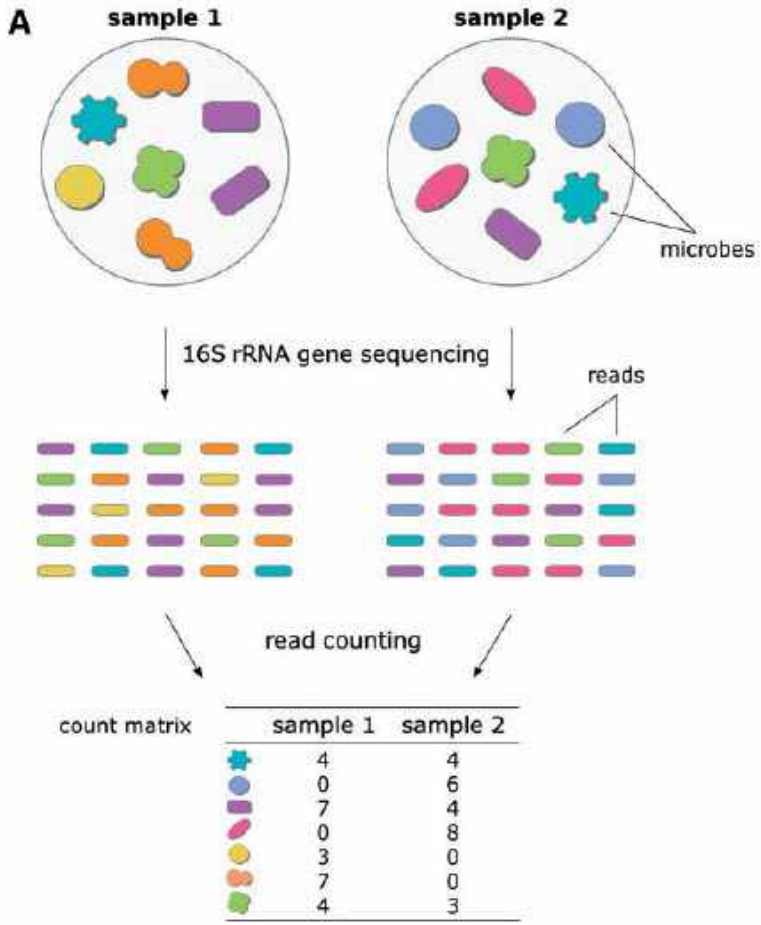


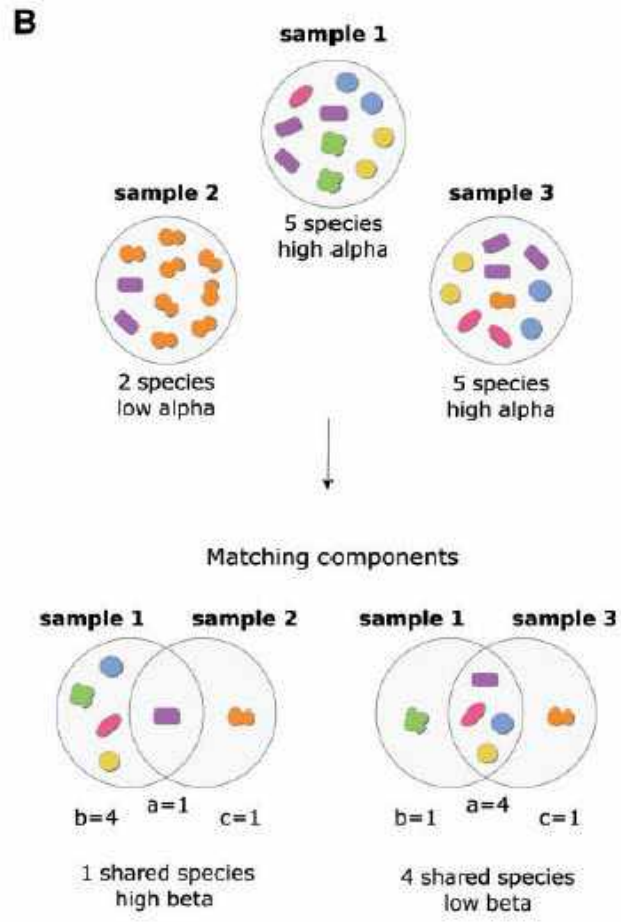
Backhed et al, Cell 2015

- Alpha diversity is a measure of the compositional complexity of a community within a site
- Alpha diversity increases with the number of present species and with the evenness of their relative abundances
- Beta diversity looks at difference in taxonomic abundance profiles from different samples
- Presence–absence data are often used to identify which species are shared by samples and which are not.

Diversity is Key

Briefings in Bioinformatics, 2016, 1–14



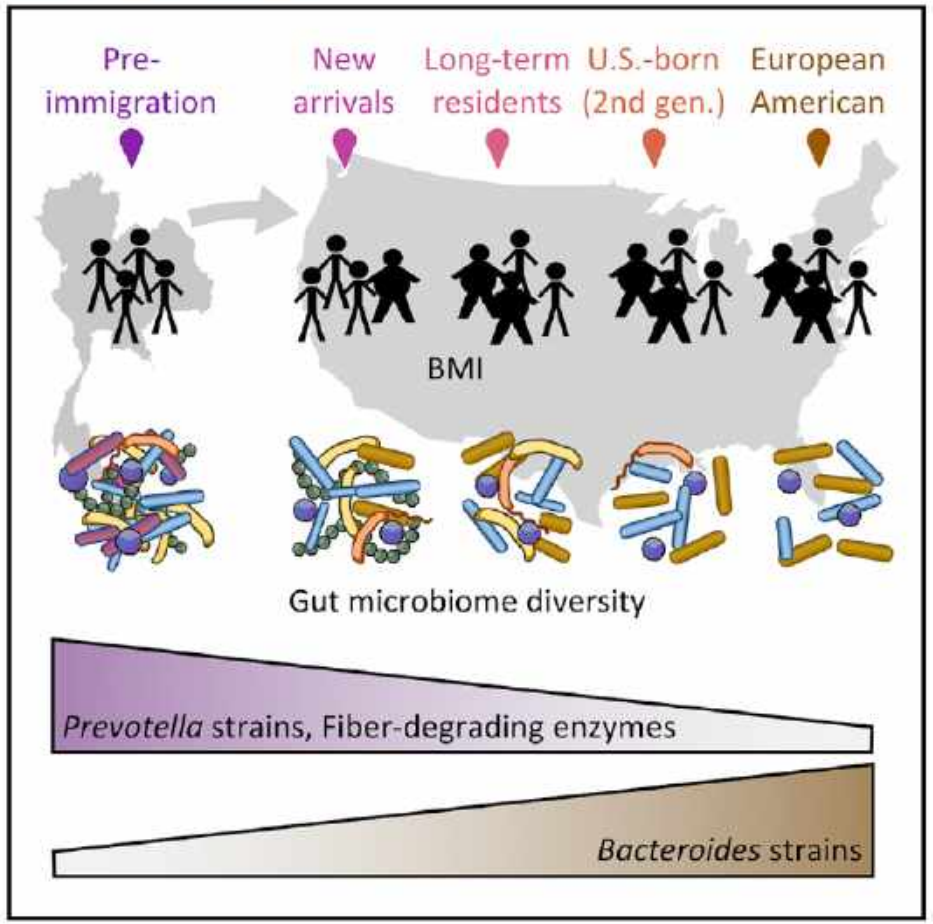


Cell 175, 962–972, November 1, 2018 963 Article

Cell

US Immigration Westernizes the Human Gut Microbiome

Graphical Abstract



Authors

Pajau Vangay, Abigail J. Johnson, Tonya L. Ward, ..., Purna C. Kashyap, Kathleen A. Culhane-Pera, Dan Knights

Correspondence

dknights@umn.edu

In Brief

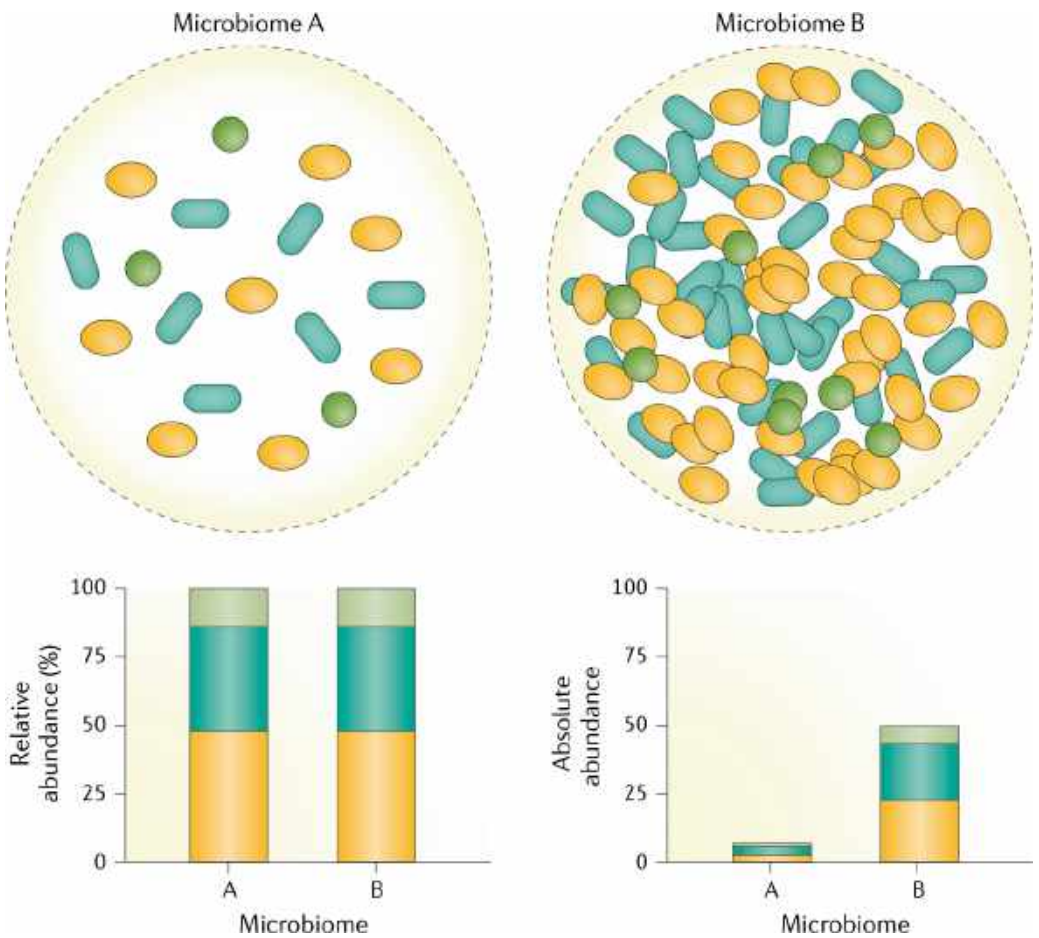
Migration from a non-western nation to the United States is found to be associated with a loss in gut microbiome diversity and function in a manner that may predispose individuals to metabolic disease.

NATURE REVIEWS | GASTROENTEROLOGY & HEPATOLOGY VOLUME 16 | JULY 2019 | 387

COMMENT

Language, numeracy and logic in microbiome science

Fergus Shanahan[1,5]* *and Colin Hill*[2,3]



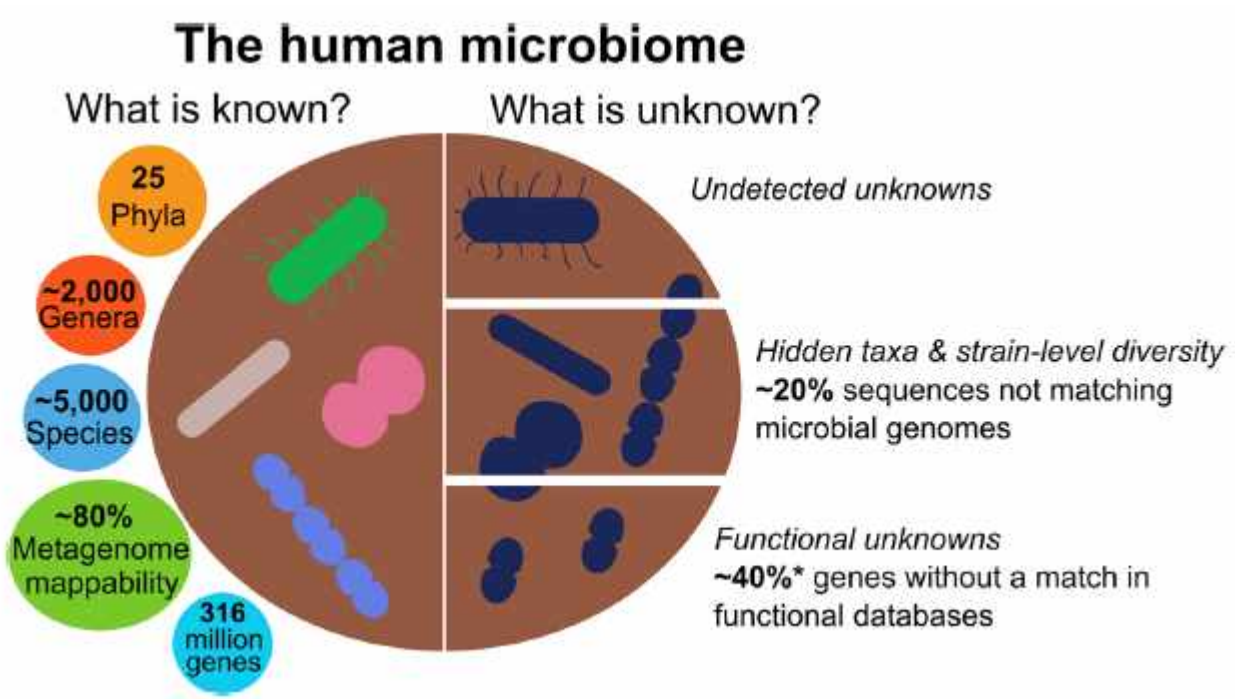
Thomas and Segata *BMC Biology* (2019) 17:48
https://doi.org/10.1186/s12915-019-0667-z

BMC Biology

COMMENT Open Access

Multiple levels of the unknown in microbiome research

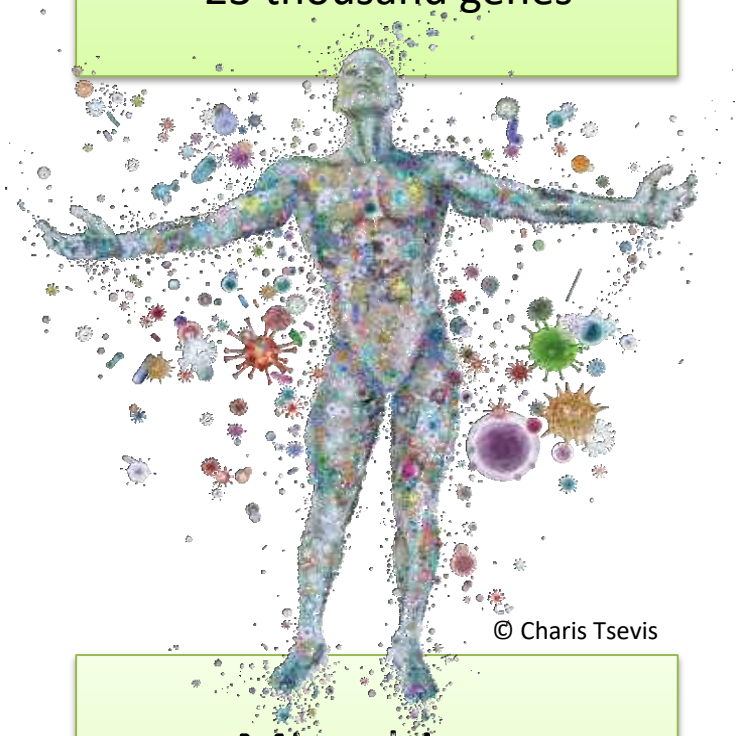
Andrew Maltez Thomas and Nicola Segata*



Microbiome

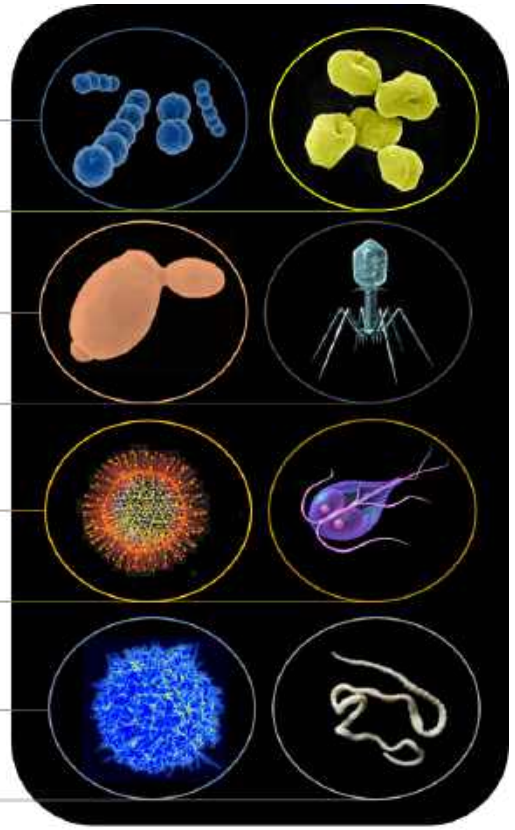
Microbiome Institute
Interfacing Food & Medicine
http://apc.ucc.ie

Human
~10 trillion cells
~23 thousand genes



Microbiota
~100 trillion cells
~3 million genes

- Bacteriome
- Archaeome
- Mycobiome
- Phageome
- Euvirome
- Protozome
- Immunome
- Helminthome



N ENGL J MED 375;24 NEJM.ORG DECEMBER 15, 2016
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REVIEW ARTICLE

Elizabeth G. Phimister, Ph.D., *Editor*

The Human Intestinal Microbiome in Health and Disease

Susan V. Lynch, Ph.D., and Oluf Pedersen, M.D., D.M.Sc.

Table 1. Tools for Analyzing Microbiota.

Approach	Data	Platform	Pros and Cons
Biomarker sequencing (e.g., 16S rRNA gene or internal transcribed spacer region)*	Community composition	Next-generation sequencing	Is cost-effective, is semiquantitative, permits resolution of genus level and in some cases species level; shorts reads may make accurate classification difficult
Metagenomics	Generation of draft genomes, functional capacity, growth dynamics	Next-generation sequencing	Has capacity for strain-level reconstruction, is quantitative, allows for functional annotation with pathway predictions; is currently very costly, has community coverage that may be relatively shallow in more complex assemblages
Metatranscriptomics (RNA sequencing)	Gene expression	Next-generation sequencing	Highly expressed genes are more likely than others to be detected, depletion of human transcripts is possible, requires immediate preservation or processing of fresh or snap-frozen intestinal specimens
Metaproteomics	Protein expression	Liquid or gas chromatography–mass spectrometry	Primarily detects dominant proteins; makes removal of host-derived proteins impossible
Metabolomics	Metabolic productivity	Liquid or gas chromatography–mass spectrometry or magnetic resonance spectroscopy	Is semiquantitative; can be targeted or untargeted; detects metabolites that are platform- and database-dependent; detects metabolites that may originate from microbes, diet, or host

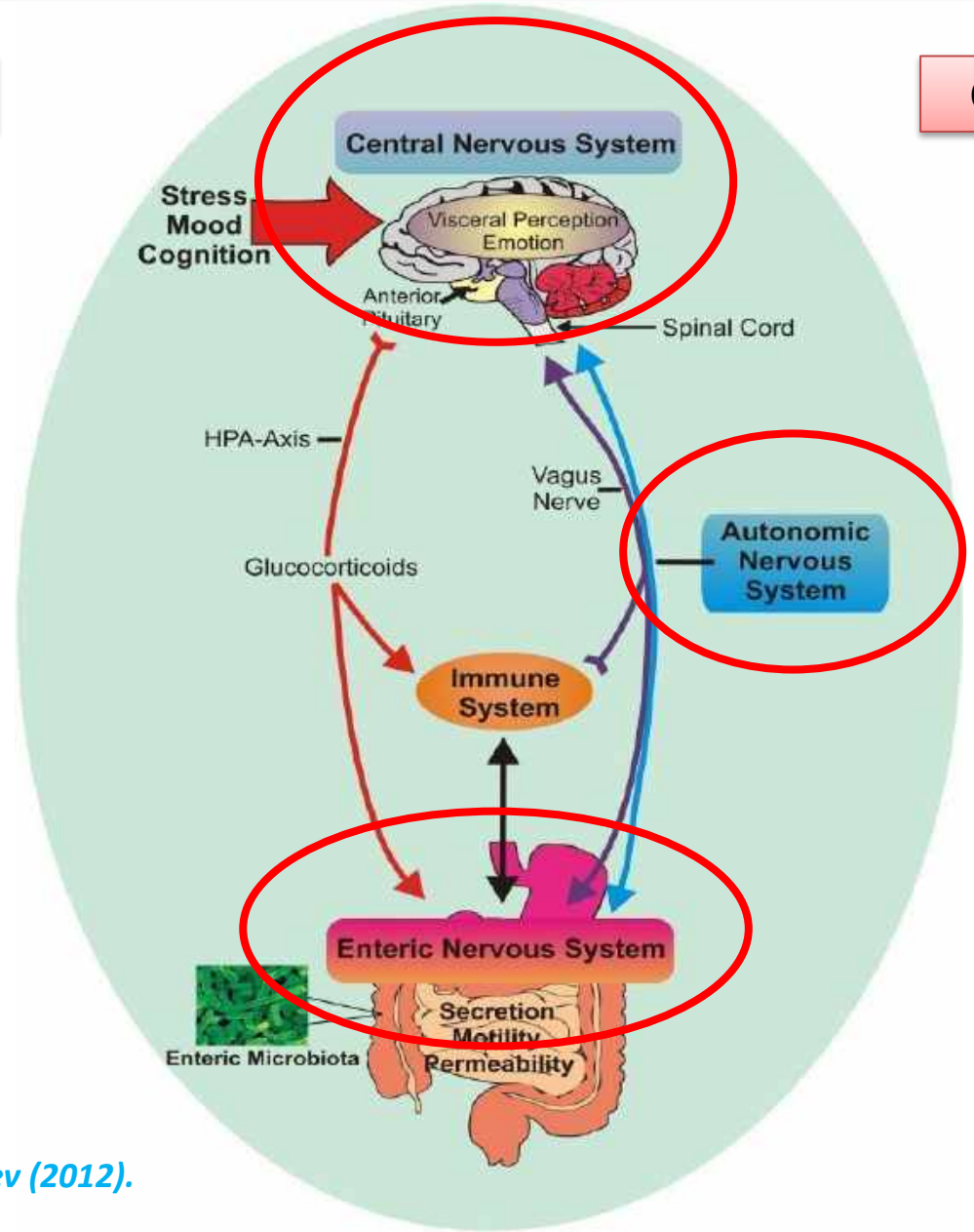
* The term rRNA denotes ribosomal RNA.

The brain-gut –(microbiota) axis

http://apc.ucc.iehttp://apc.ucc.ie

Basic Functions

- Motility
- Secretion
- Permeability
- Mucosal immunity



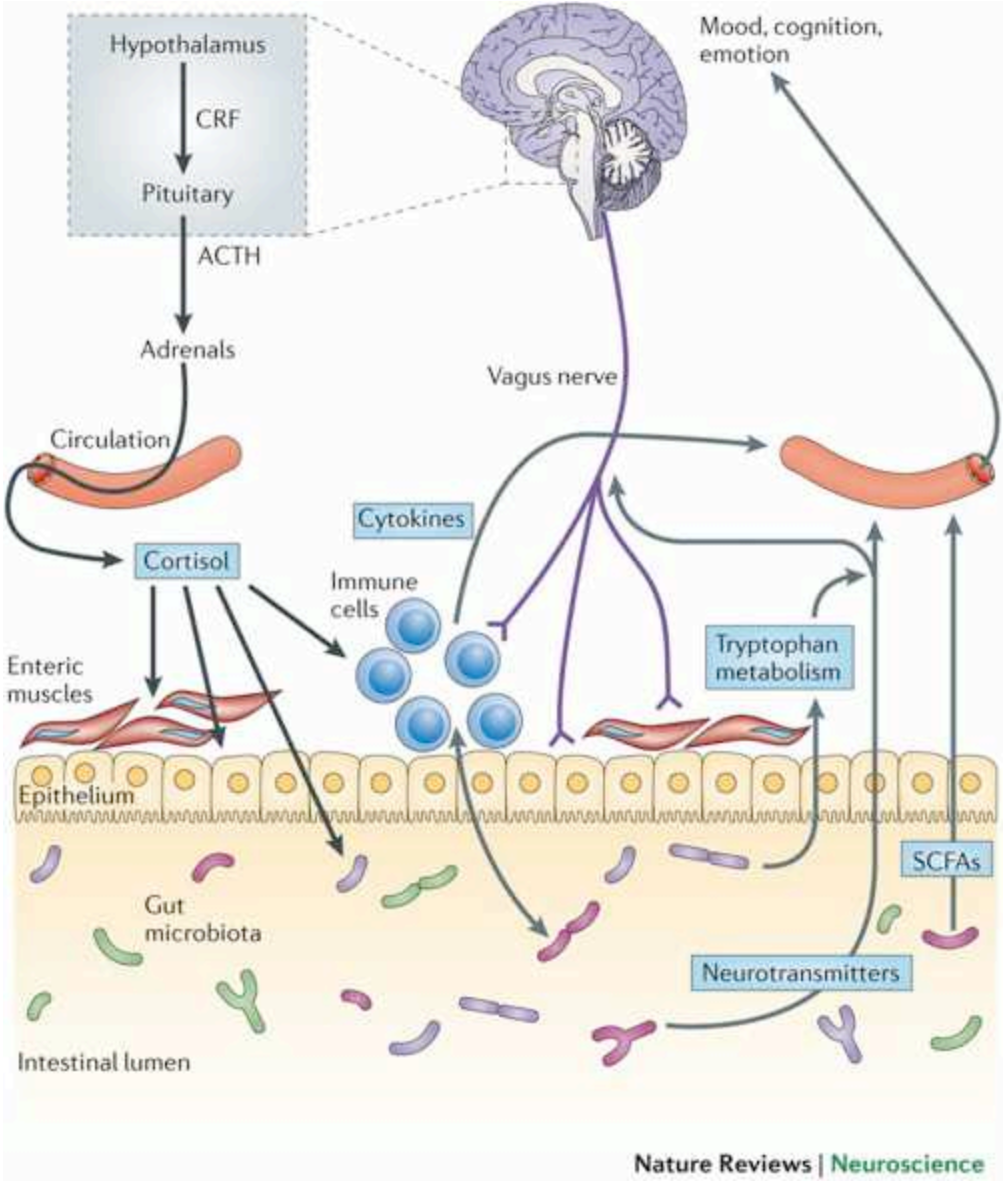
Complex Functions

- Visceral Pain
- Hunger/ satiety
- Mood/ Emotion
- Cognition

Kennedy P.J. et al., Neurosci. Biobehav. Rev (2012).

Signalling Along the Brain-Gut-Microbiota axis

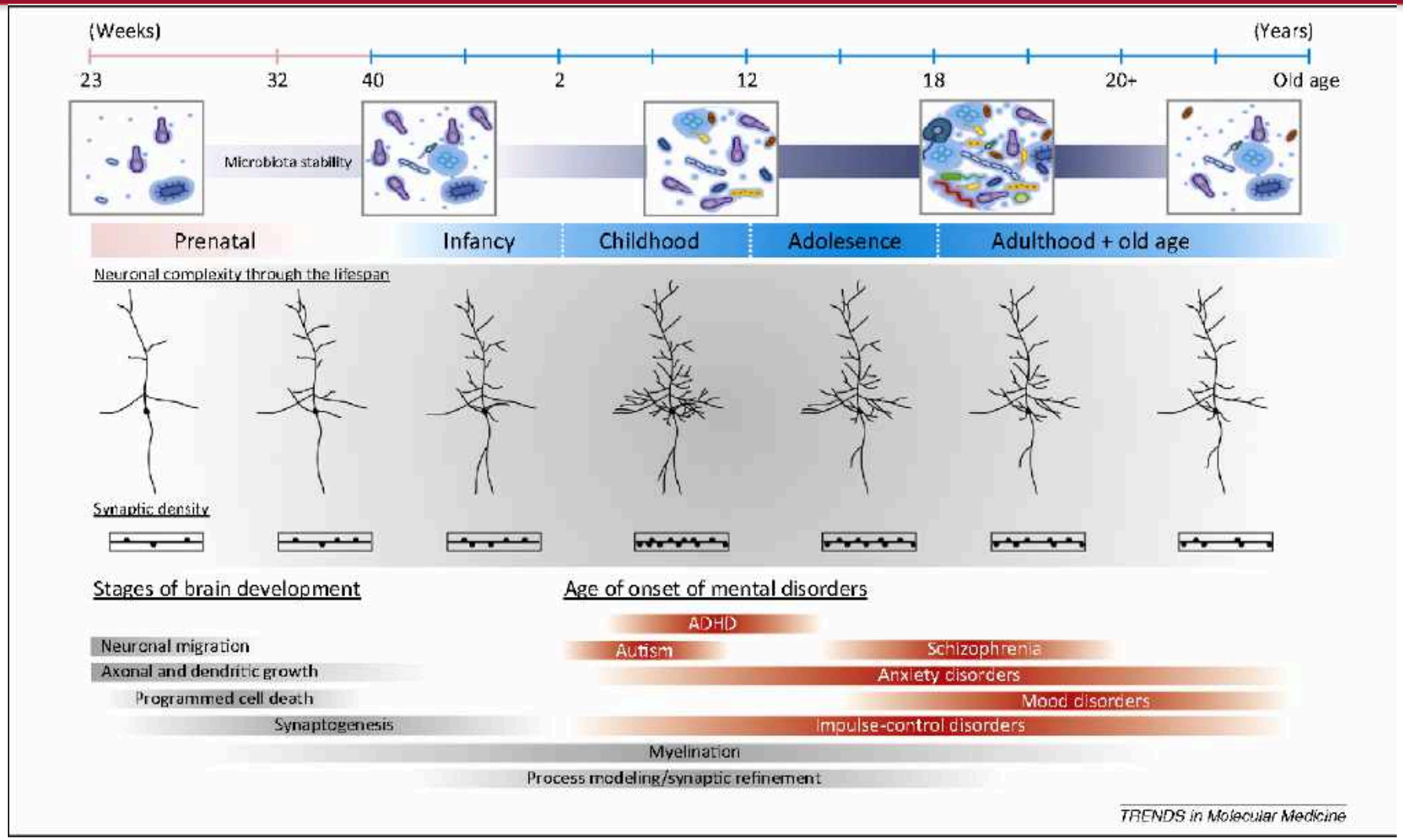
http://apc.ucc.ie



Cryan and Dinan, Nat Rev Neurosci Oct 2012

Microbiota and Neurodevelopment

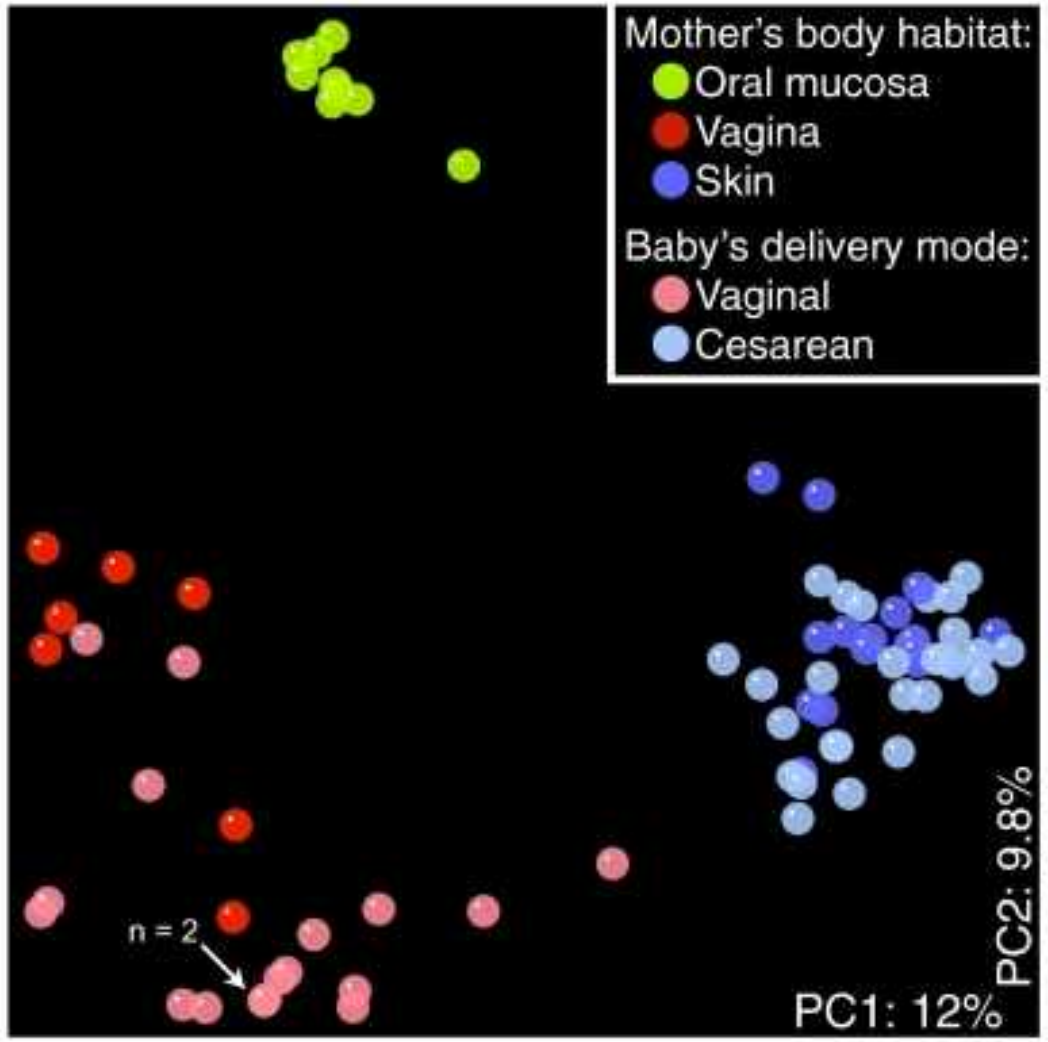
http://apc.ucc.ie



Borre et al., Trends Molecular Medicine 2014

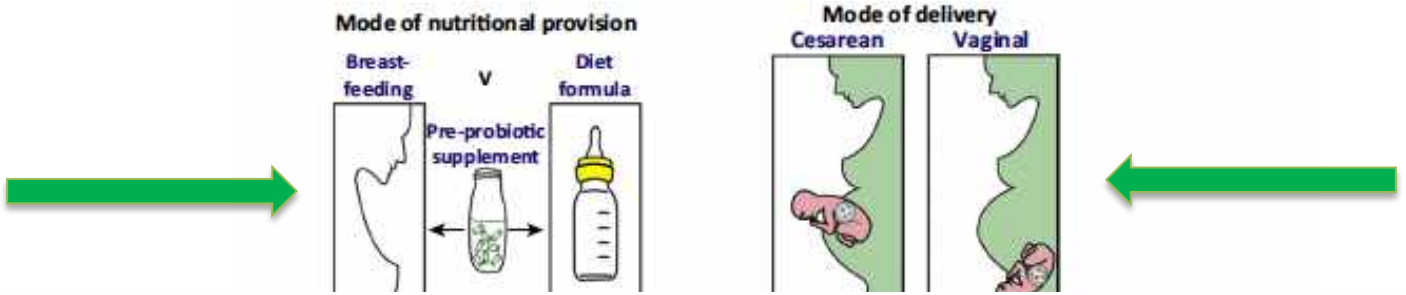
C-section and Infant Microbiome

http://apc.ucc.ie



Dominguez-Bello at al, PNAS 2010

The Gold Standard



Neuroscience 342 (2017) 37–54

REVIEW

EARLY-LIFE ADVERSITY AND BRAIN DEVELOPMENT: IS THE MICROBIOME A MISSING PIECE OF THE PUZZLE?

S. M. O'MAHONY,[a,b*] G. CLARKE,[b,c] T. G. DINAN[b,c] AND J. F. CRYAN[a,b*]

Borre et al. Trends Mol Med 2014

Neurobiology of Stress 1 (2015) 81–88

Contents lists available at ScienceDirect

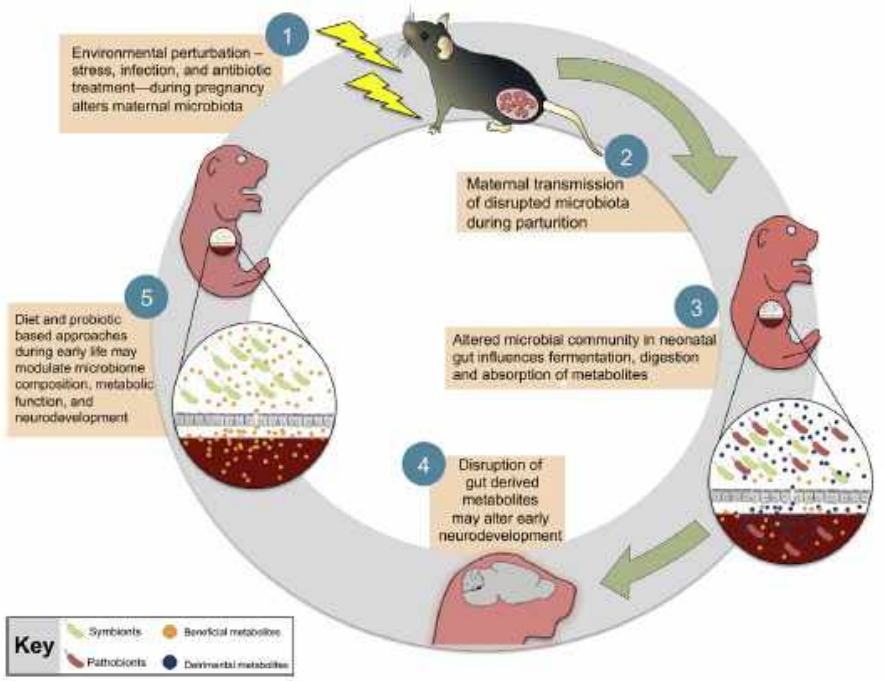
Neurobiology of Stress

journal homepage: http://www.journals.elsevier.com/neurobiology-of-stress/

A novel role for maternal stress and microbial transmission in early life programming and neurodevelopment

Eldin Jašarević, Ali B. Rodgers, Tracy L. Bale*

Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA

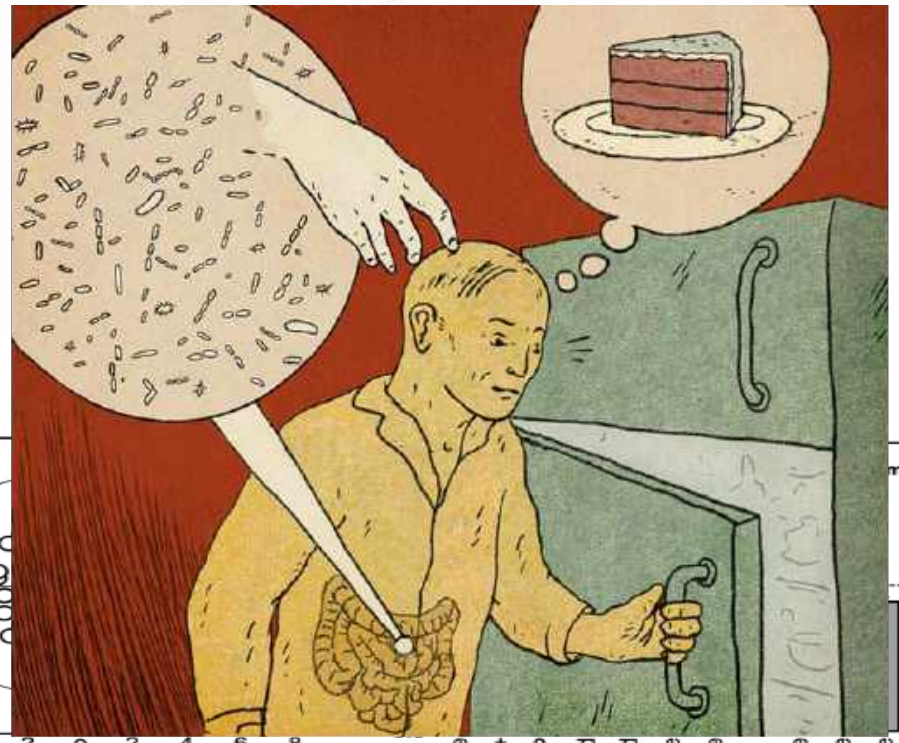


2126 The Journal of Clinical Investigation http://www.jci.org Volume 121 Number 6 June 2011

Gut microbiome, obesity, and metabolic dysfunction

Herbert Tilg[1] and Arthur Kaser[2]

and Tracy L. Bale



http://www.nytimes.com/2014/08/14/science/our-microbiome-may-be-looking-out-for-itself.html?_r=0

http://apc.ucc.ie

Psychoneuroendocrinology (2015) 60, 58–74

Available online at www.sciencedirect.com

ScienceDirect

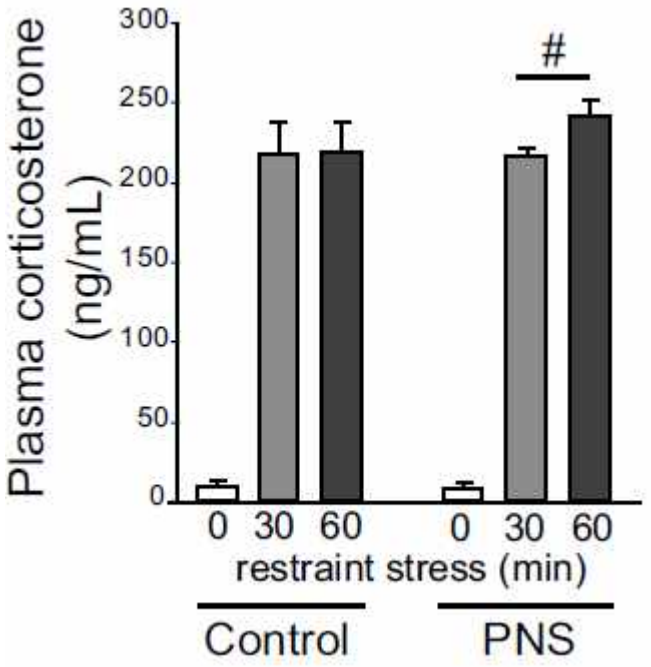
journal homepage: www.elsevier.com/locate/psyneuen

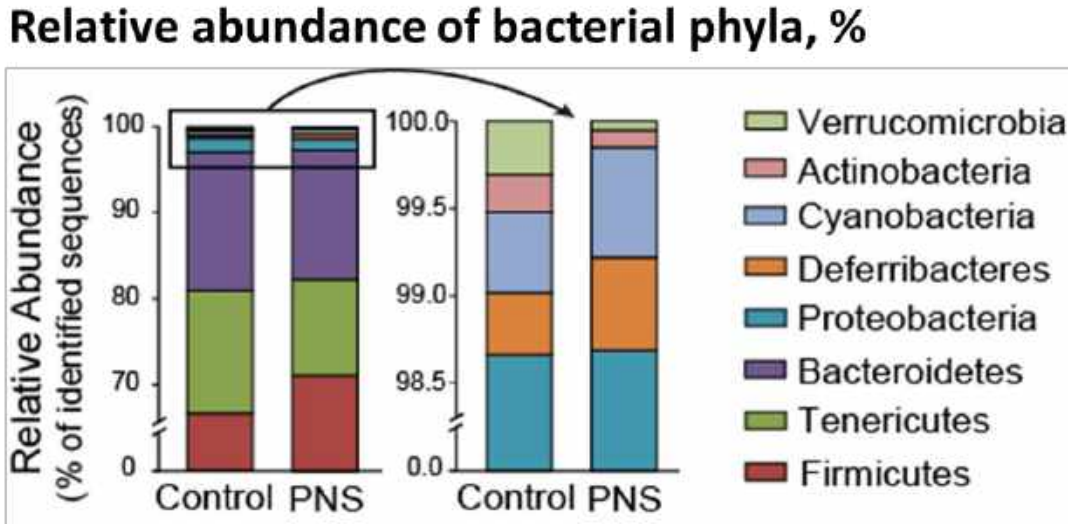
ELSEVIER

Prenatal stress-induced alterations in major physiological systems correlate with gut microbiota composition in adulthood

Anna V. Golubeva[a], Sean Crampton[b], Lieve Desbonnet[a,1], Deirdre Edge[c], Orla O'Sullivan[d], Kevin W. Lomasney[a,e,2], Alexander V. Zhdanov[f], Fiona Crispie[a,d], Rachel D. Moloney[a,3], Yuliya E. Borre[a], Paul D. Cotter[a,d], Niall P. Hyland[a,e], Ken D. O'Halloran[c], Timothy G. Dinan[a,g], Gerard W. O'Keeffe[a,b,h,**], John F. Cryan[a,b,*]

Prenatal stress induced long-lasting alterations in HPA responsivity and in gut microbiota; Abundance of distinct bacteria correlated with stress response





The maternal microbiome modulates fetal neurodevelopment in mice

https://doi.org/10.1038/s41586-020-2745-3
Received: 23 July 2019
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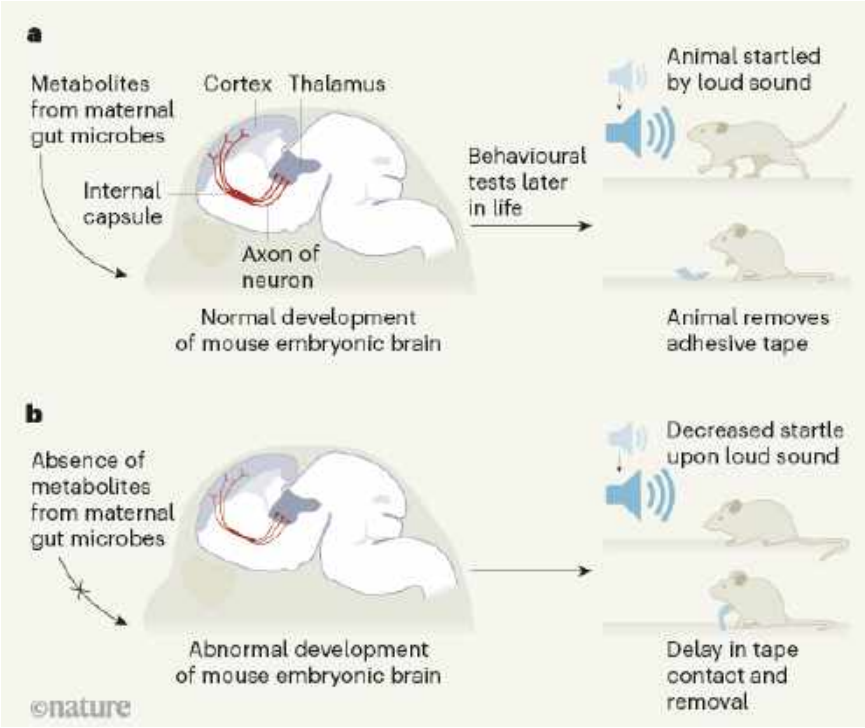
Helen E. Vuong[1], Geoffrey N. Pronovost[1], Drake W. Williams[2], Elena J. L. Coley[1], Emily L. Siegler[1], Austin Qiu[1], Maria Kazantsev[1], Chantel J. Wilson[1], Tomiko Rendon[1] & Elaine Y. Hsiao[1]



Meckel and Kiraly, Nature 2020

http://apc.ucc.ie

Psychoneuroendocrinology (2015) 53, 233–245

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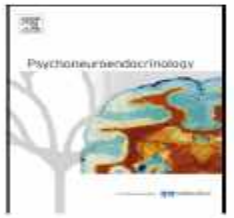
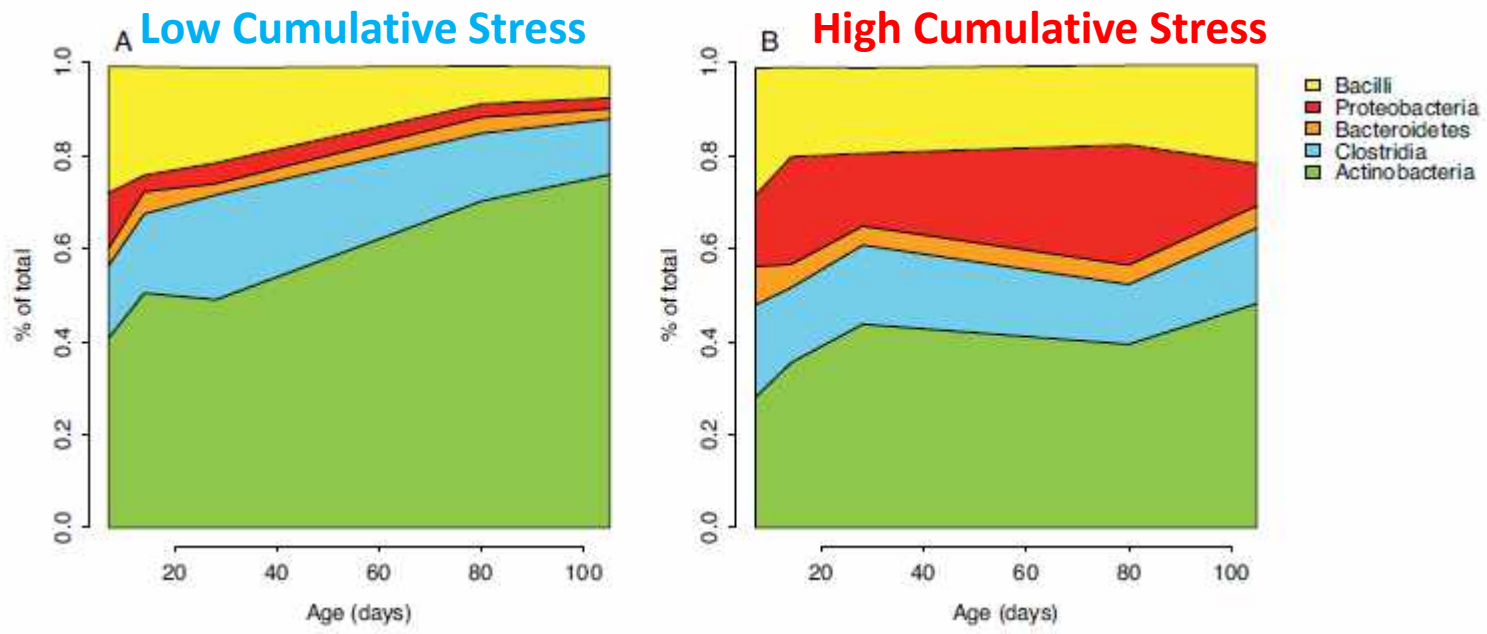
journal homepage: www.elsevier.com/locate/psyneuen



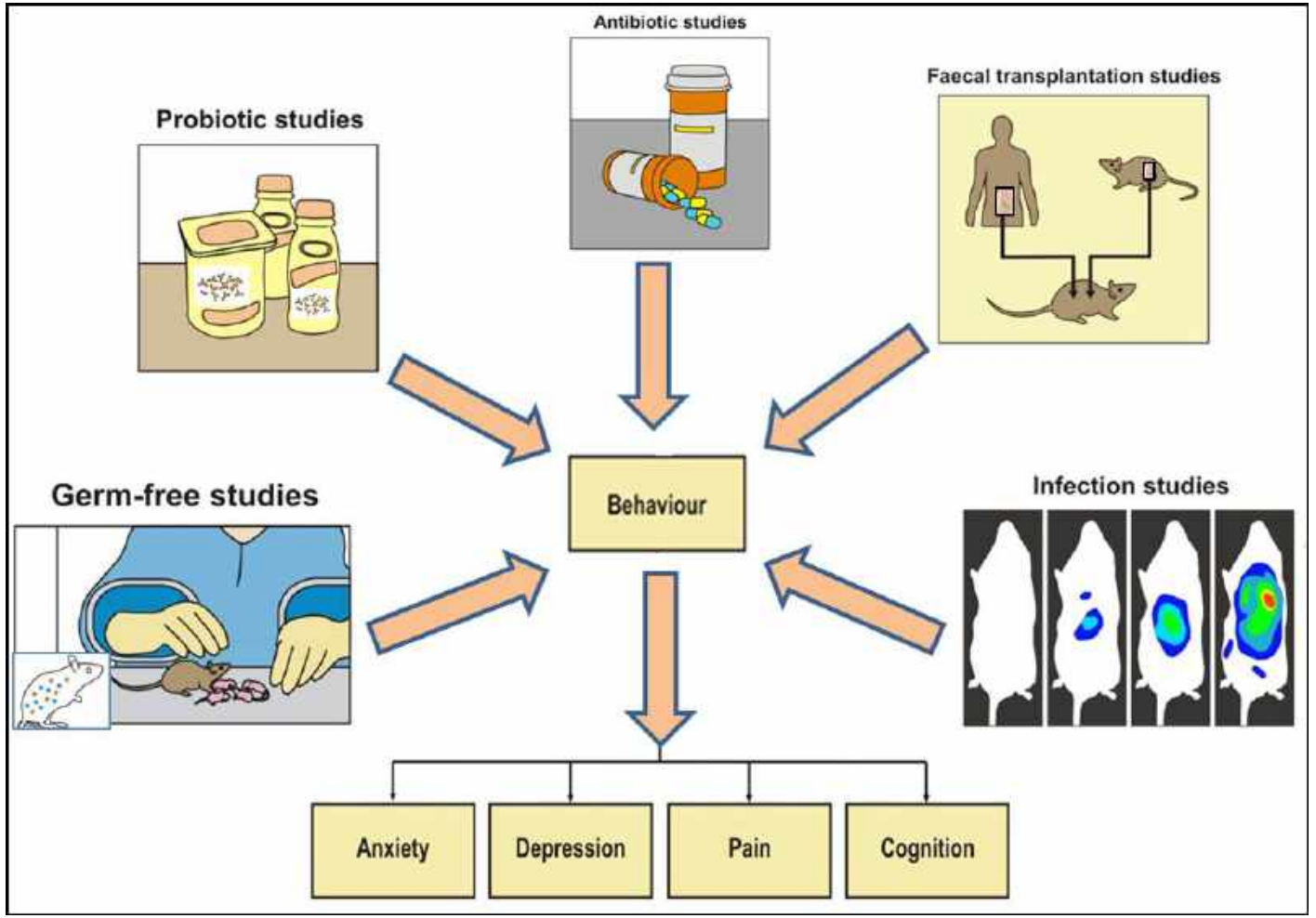
Maternal prenatal stress is associated with the infant intestinal microbiota

Maartje A.C. Zijlmans[a,*,1], Katri Korpela[b,1], J. Marianne Riksen-Walraven[a], Willem M. de Vos[b,c], Carolina de Weerth[a,*]



Microbiota, Brain and Behaviour

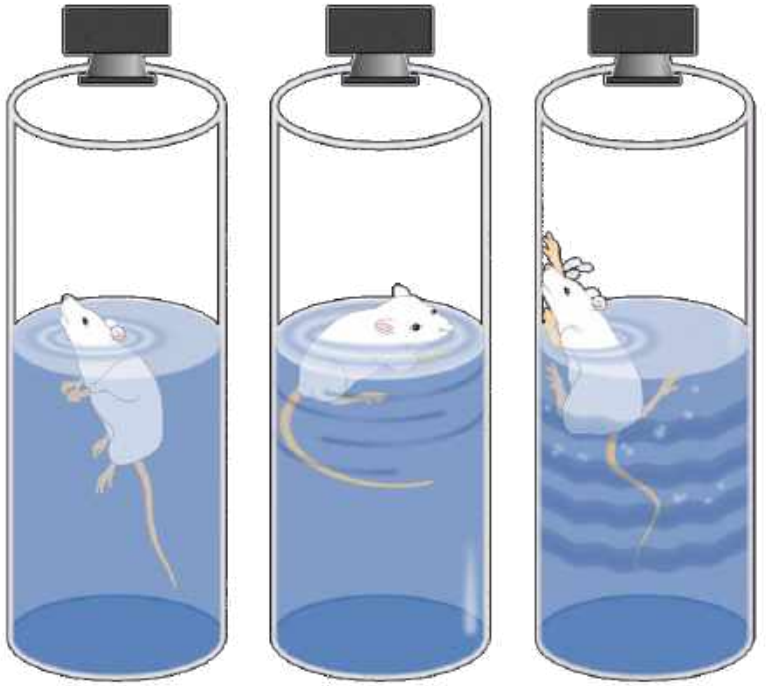
http://apc.ucc.ie



Clarke et al., Encyclopedia Metagenomics 2013

Forced Swim Test (FST)

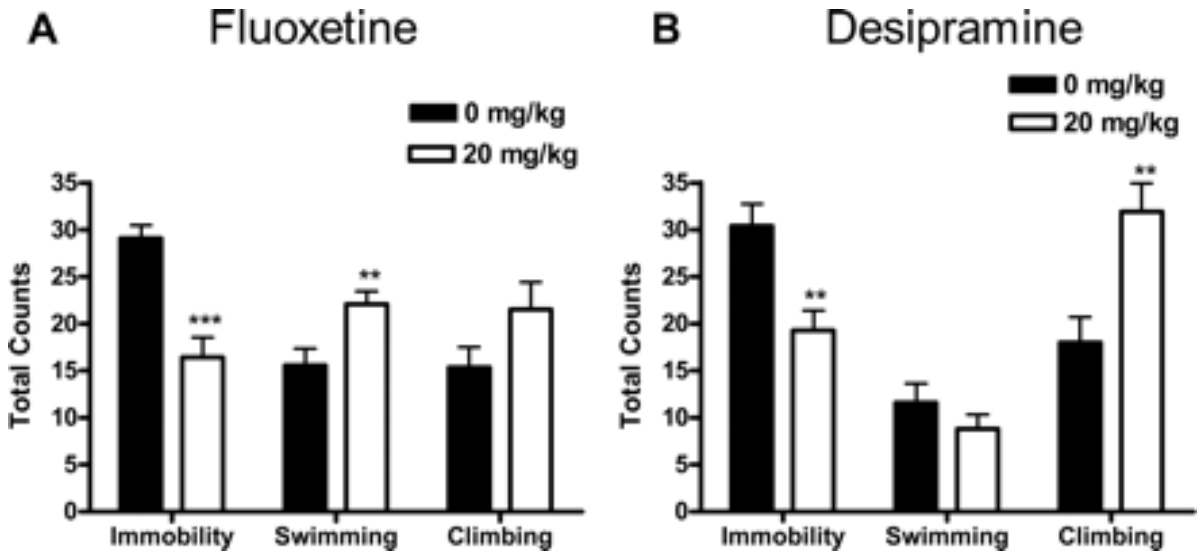
- FST is the most widely-used pharmacological model for assessing antidepressant activity preclinically.
- Animals will develop an immobile posture when placed in an inescapable cylinder of water.
- This immobility is thought to reflect either, a failure of persistence in escape directed behavior i.e. behavioral despair, or the development of passive behavior that disengages the animal from active forms of coping with stressful stimuli.



Cryan et al., Trends Pharmacol Sci, 2002

Forced Swim Test

Forced Swim Test



Slattery et al., J Pharmacology, 2004

- **Effects of Fluoxetine and Desipramine in the modified forced swim test.**
- **(A) Fluoxetine decreased immobility time in the forced swim test and increased swimming behavior**
- **(B) Desipramine decreased immobility time in the forced swim test and increased climbing behavior**

Tests for Assessing Anxiety Response

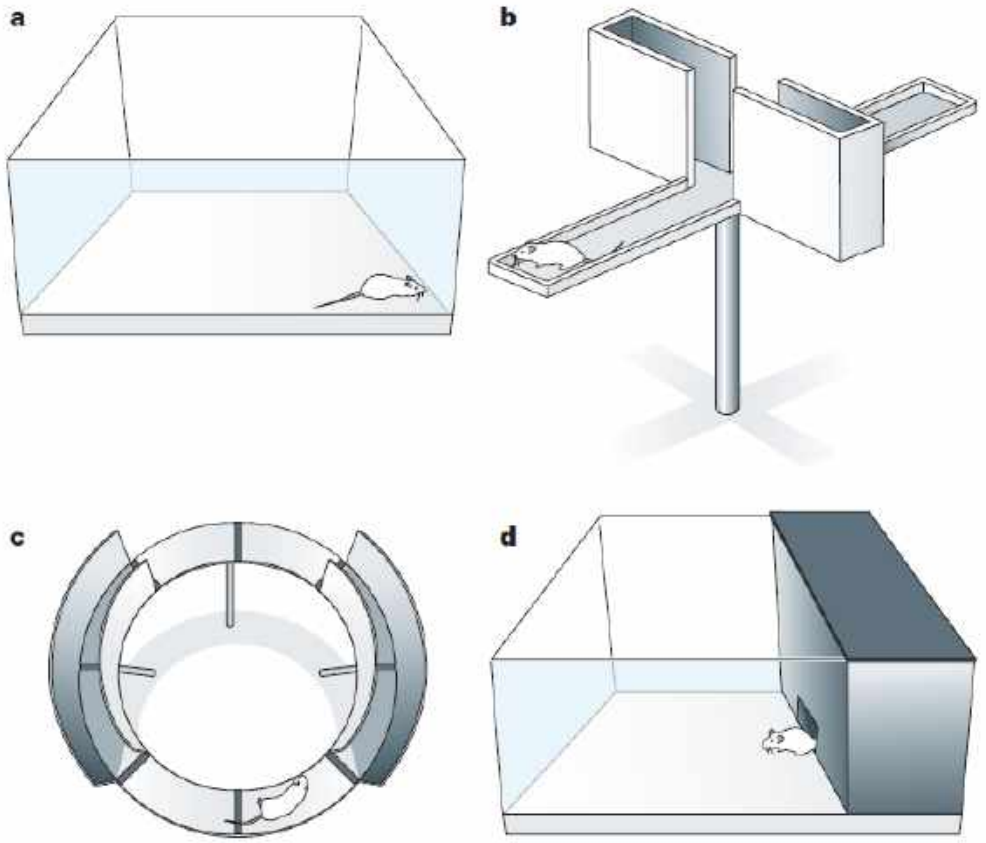
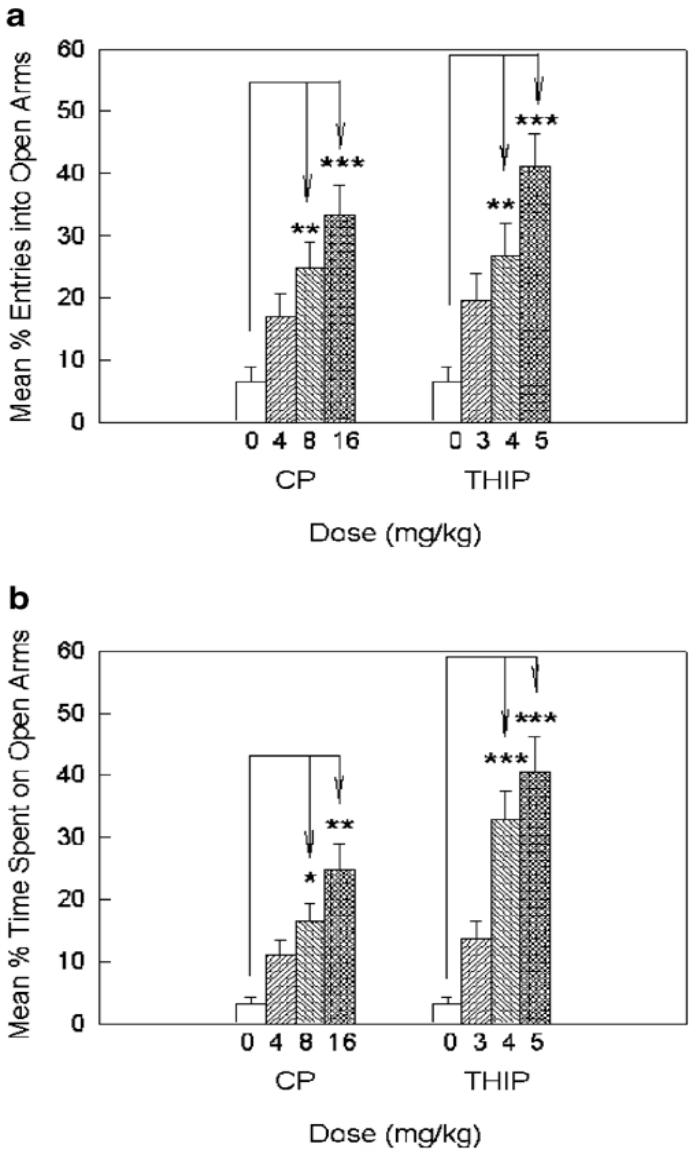
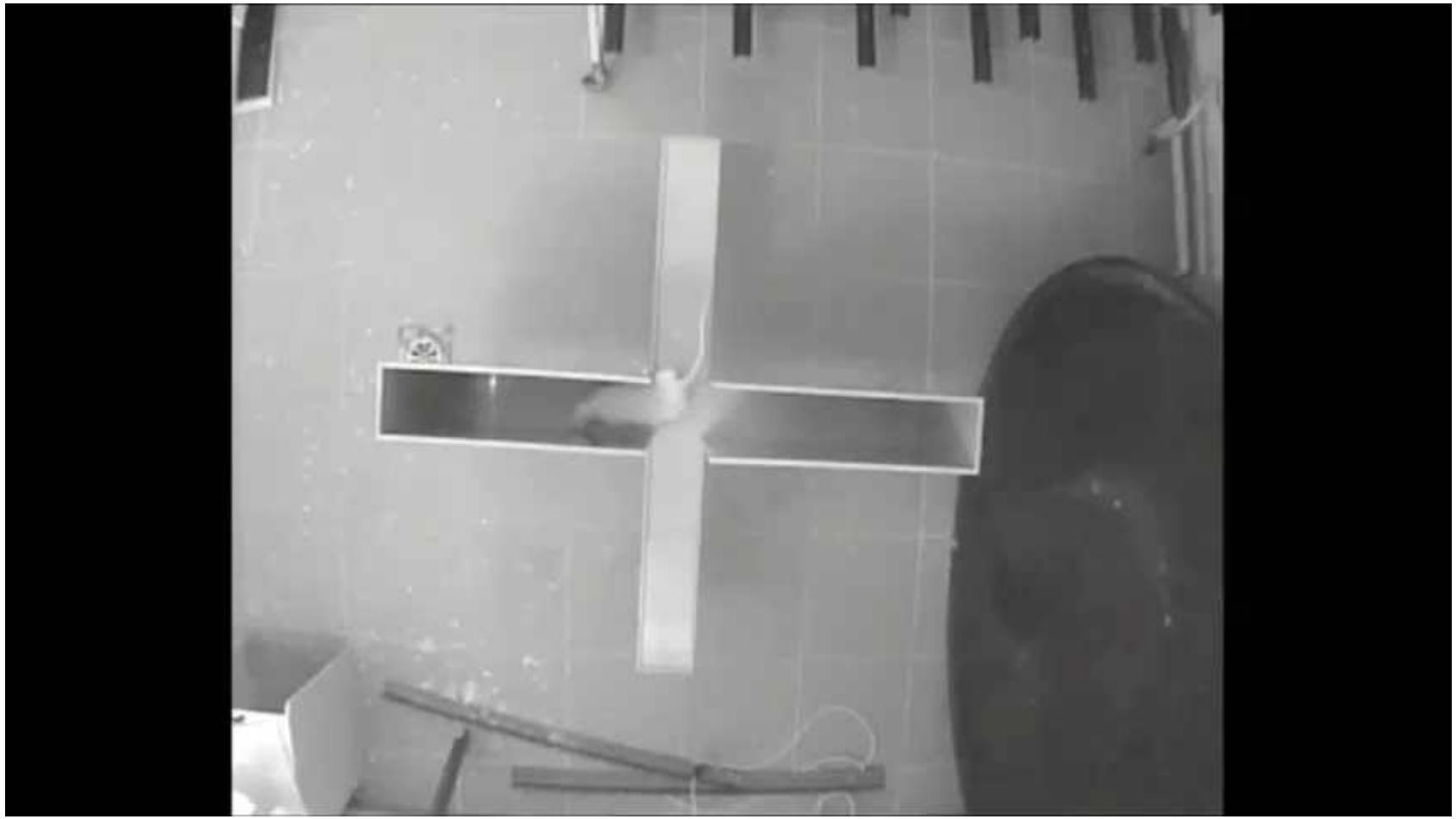


Figure 4 | **Tests for assessing anxiety responses in mice.** Commonly used measures of heightened anxiety-like behaviour include increased avoidance of aversive situations in manipulated mice compared with non-manipulated controls. Tests include the avoidance of the exposed centre of a novel, brightly illuminated open field (**a**), the exposed open arms of the elevated plus-maze (**b**), the exposed areas of elevated zero-maze (**c**) or the brightly illuminated area of the light/dark box (**d**).



Cryan and Holmes, *Nat Rev Drug Discov. Sept 2005*

Elevated Plus Maze



Germ-Free Living?

http://apc.ucc.ie

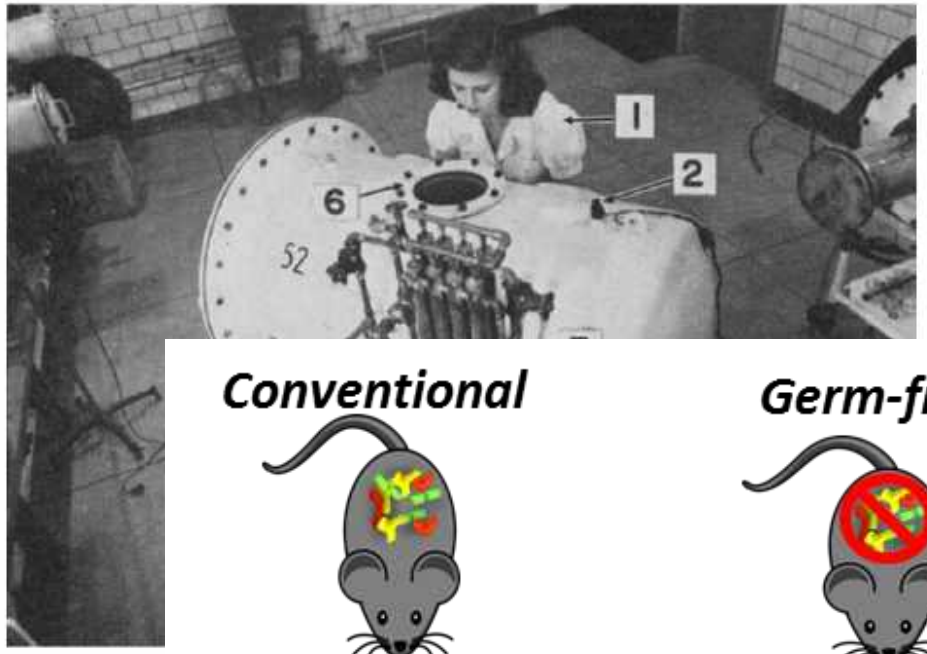
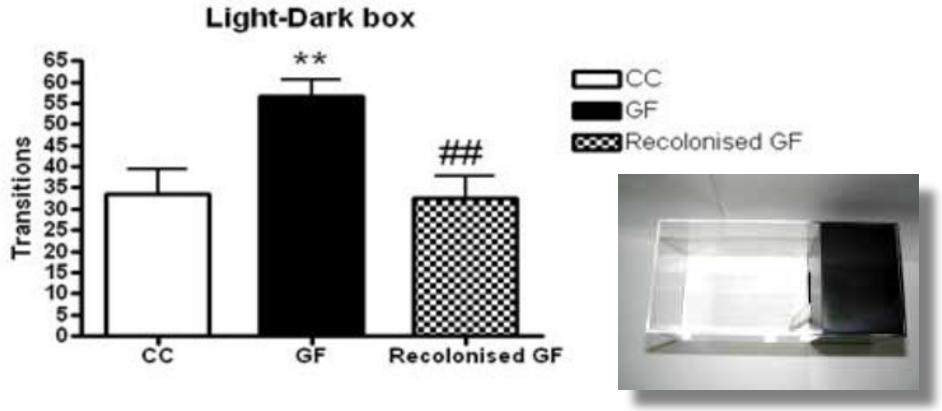


Figure 2. Reyniers's isolator; (1) technician, (2) electrical outlet, (3) air outlet, (4) mobile truck, (5) entrance/exit autoclave, (6) viewing port. *Source:* J. A. Reyniers, P. C. Trexler, and R. F. Ervin, "Rearing Germ-Free Albino Rats," *LOBUND Rep.* 1 (1946): 1–84, 5. © University of Notre Dame. Reprinted with permission.


weeks after the joyous moment when David stepped out of his bubble for the first time, kissed his mother and felt the loving warmth of a human touch.

Kirk, R, Bulletin of the History of Medicine, 2012

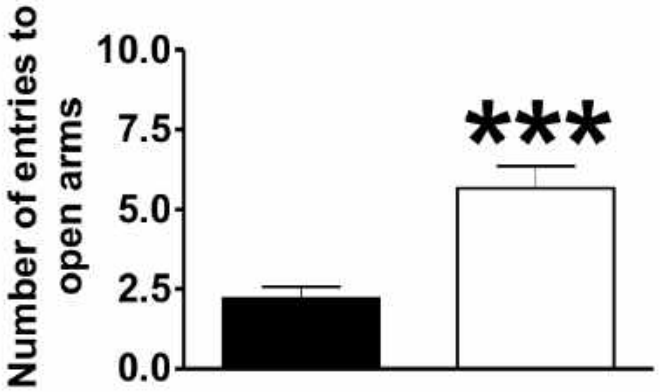
Microbiota Regulates Anxiety



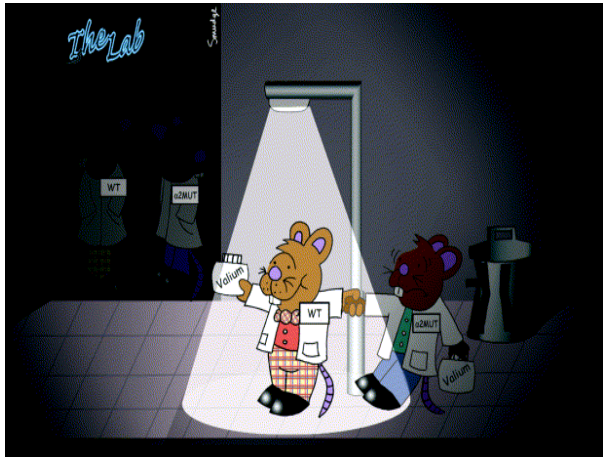
Germ-free animals have lower anxiety-like behaviours

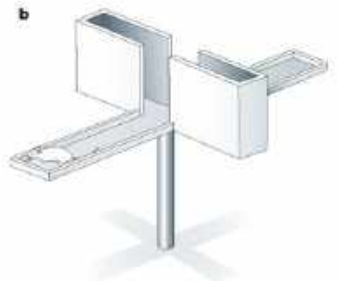
Clarke et al., Mol Psychiatry 2013

Probiotic reduces anxiety-like behaviours



Bravo et al., PNAS Sept 2011





Microbiota Regulates Anxiety

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The Scream (Edvard Munch)

Antibiotics
Infection
Microbiota
Transplantation

Scream adapted, New Scientist, March 12 2013

Probiotics
Microbiota
Transplantation

Early Life Stress and Microbiota

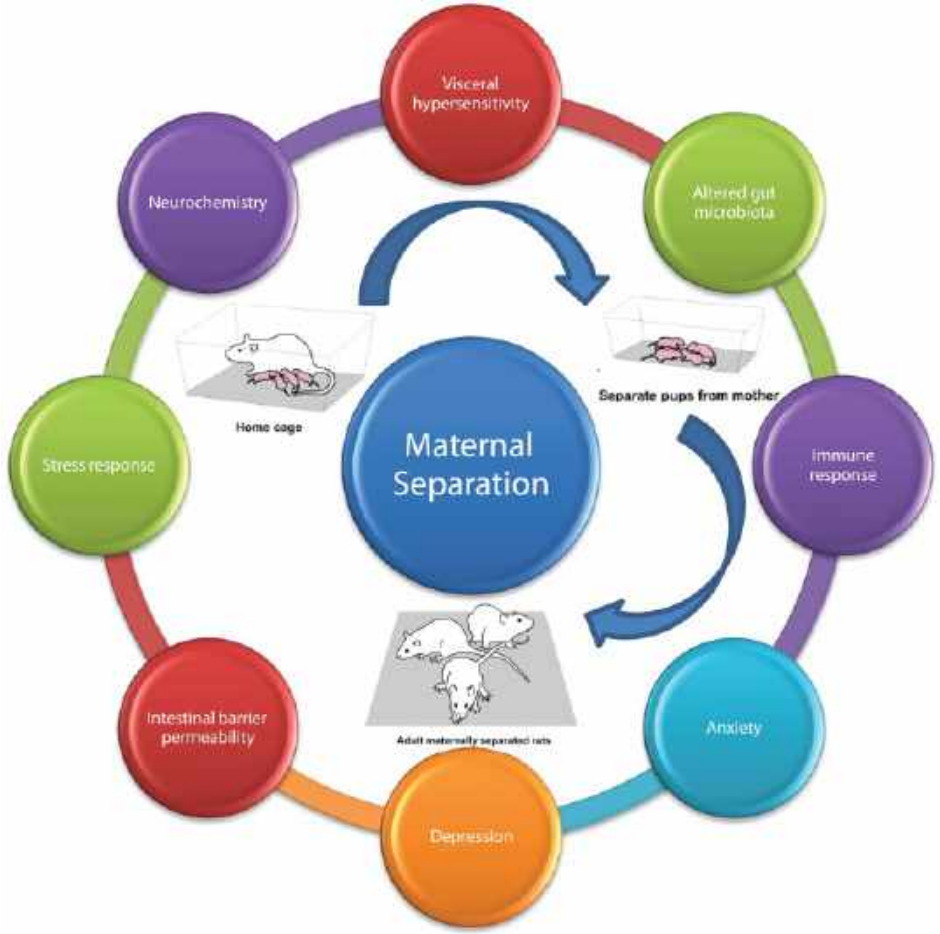
http://apc.ucc.ie

BIOL PSYCHIATRY 2009;65:263–267

Early Life Stress Alters Behavior, Immunity, and Microbiota in Rats: Implications for Irritable Bowel Syndrome and Psychiatric Illnesses

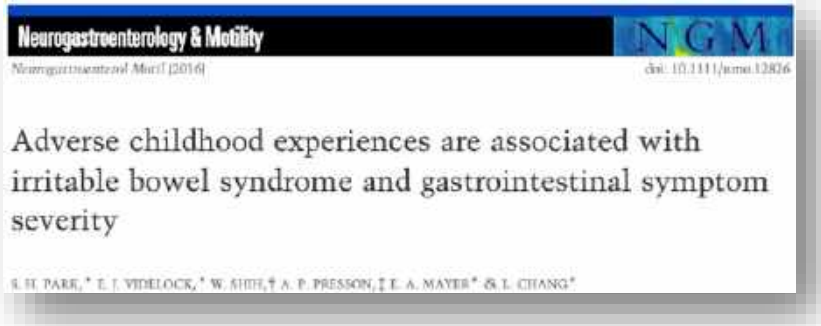
Siobhain M. O'Mahony, Julian R. Marchesi, Paul Scully, Caroline Codling, Anne-Marie Ceolho, Eamonn M.M. Quigley, John F. Cryan, and Timothy G. Dinan

Moloney et al., 2015. Front Psychiatry .16;6:15

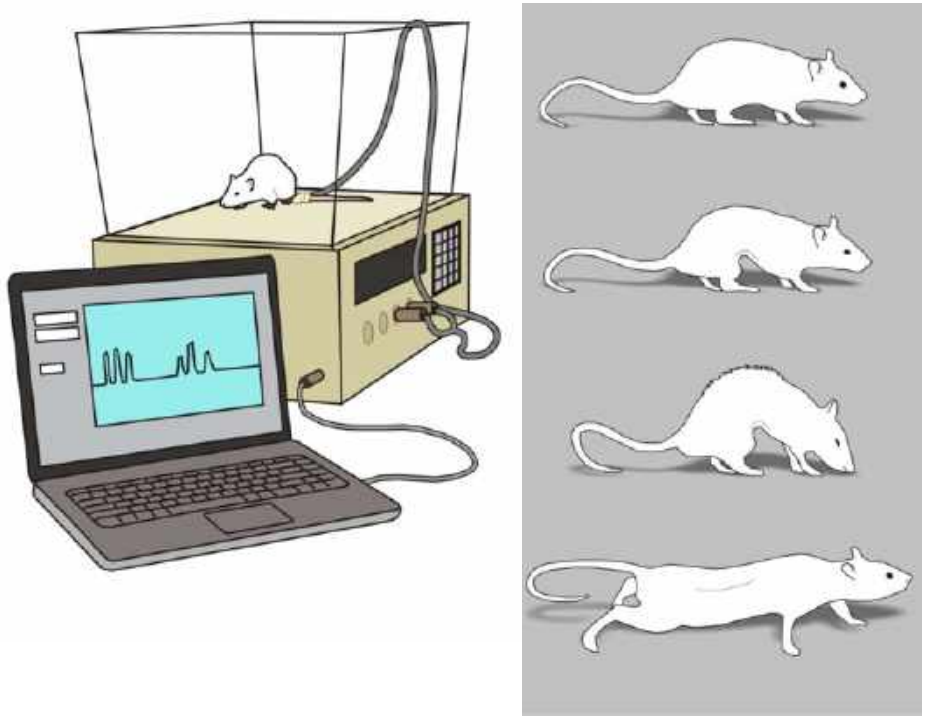


Diversity of Microbiota

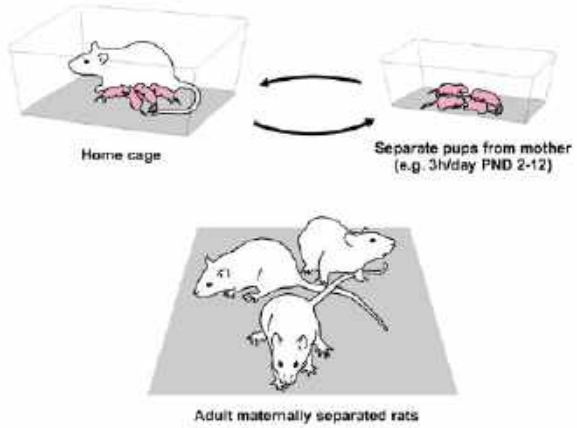
Group	Mean Similarity %	SEM
Non Separated	75.2	16.8
Maternally Separated	59.9 *	21.0



Early Life Stress results in visceral hypersensitivity

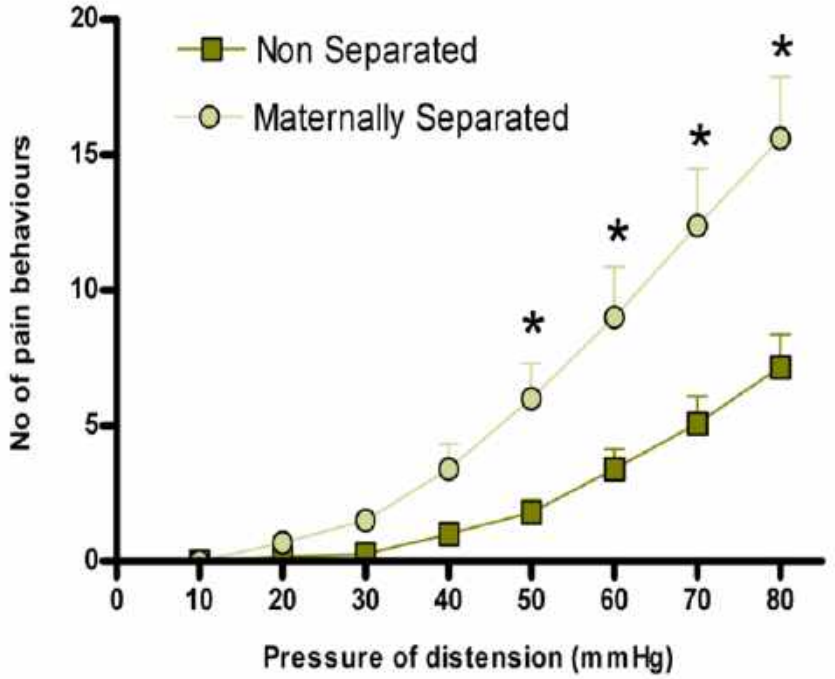


O'Mahony et al., 2009; 2012



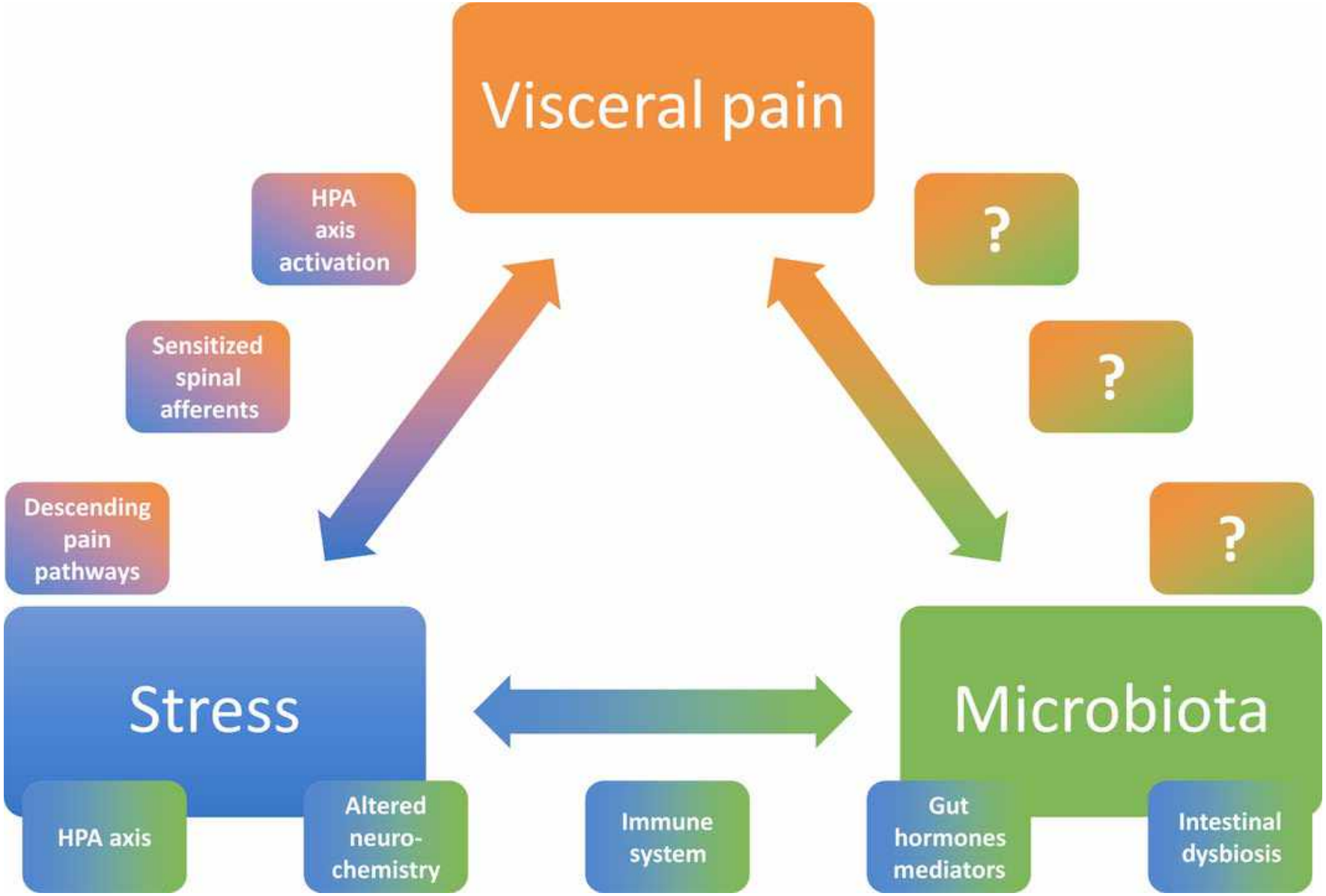
O'Mahony et al. Psychopharmacology (2011)

Pain Behaviours



Stress, Microbiota & Visceral Pain

http://apc.ucc.ie



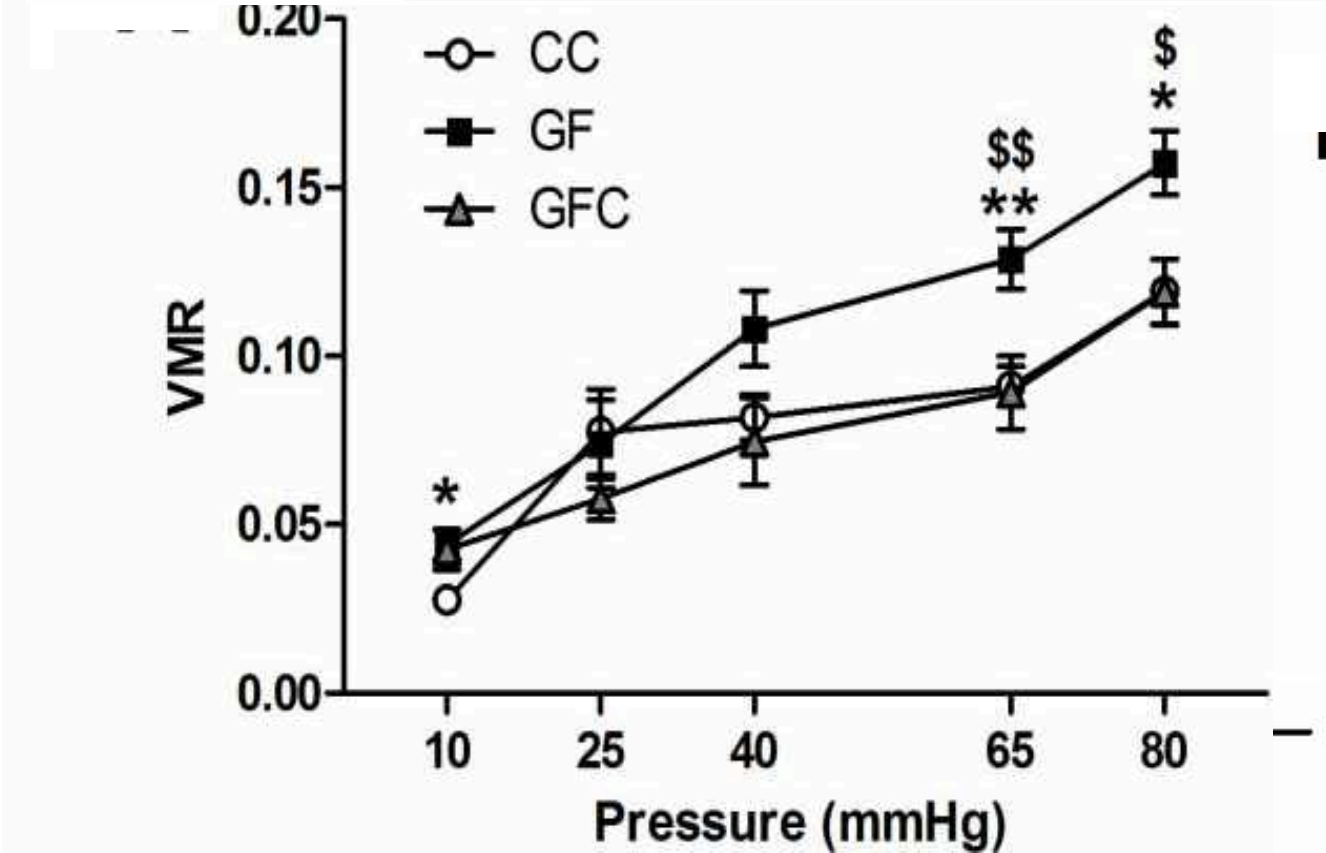
Moloney et al., CNS Neurosci & Ther, 2016

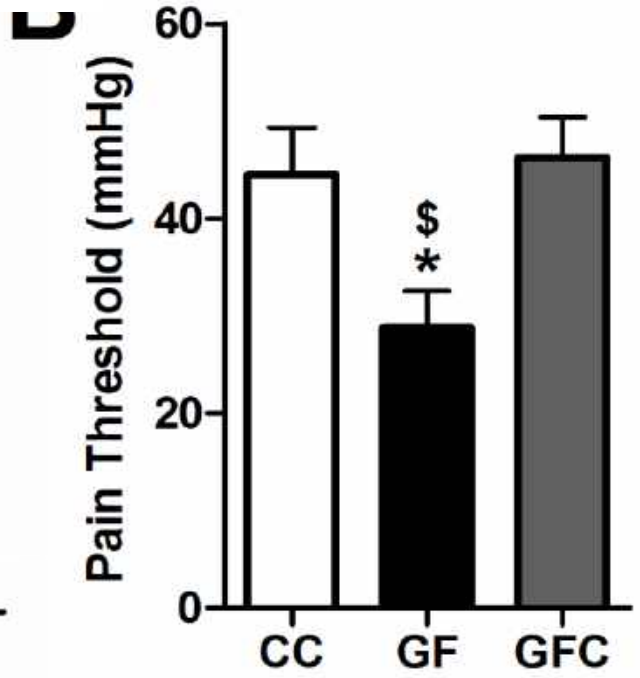
eLIFE elifesciences.org Luczynski et al. eLife 2017;6:e25887. DOI: 10.7554/eLife.25887 RESEARCH ARTICLE

Microbiota regulates visceral pain in the mouse

Pauline Luczynski[1†‡], Monica Tramullas[1†§], Maria Viola[1], Fergus Shanahan[1], Gerard Clarke[1,2], Siobhain O'Mahony[1,3], Timothy G Dinan[1,2], John F Cryan[1,3]*

[1]APC Microbiome Institute, University College Cork, Cork, Ireland; [2]Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland; [3]Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland





Stressors

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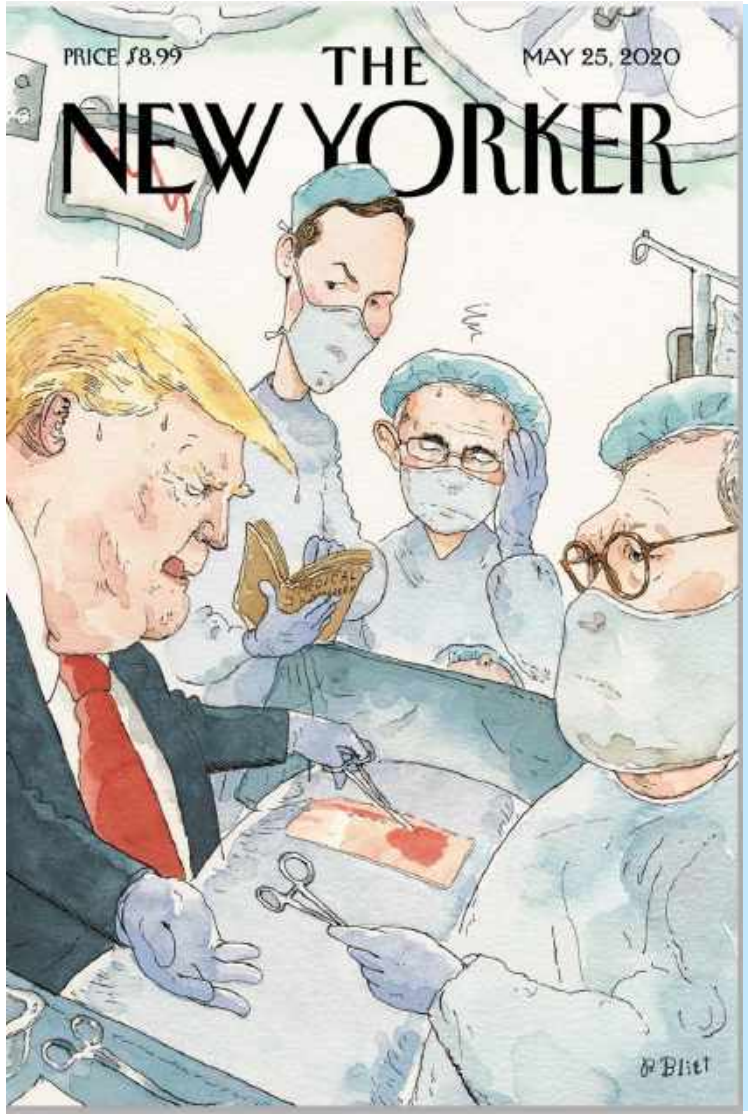
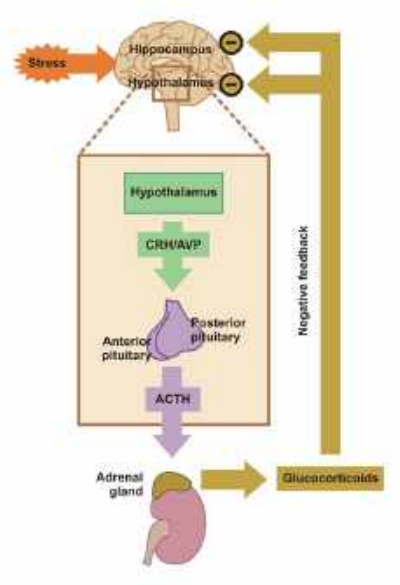
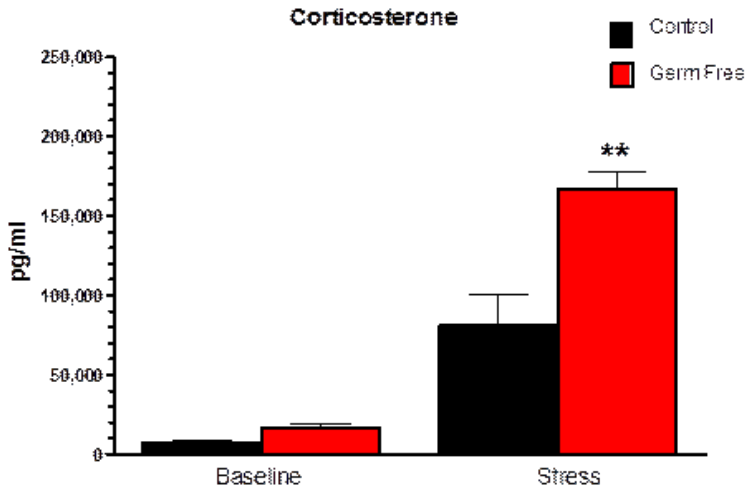
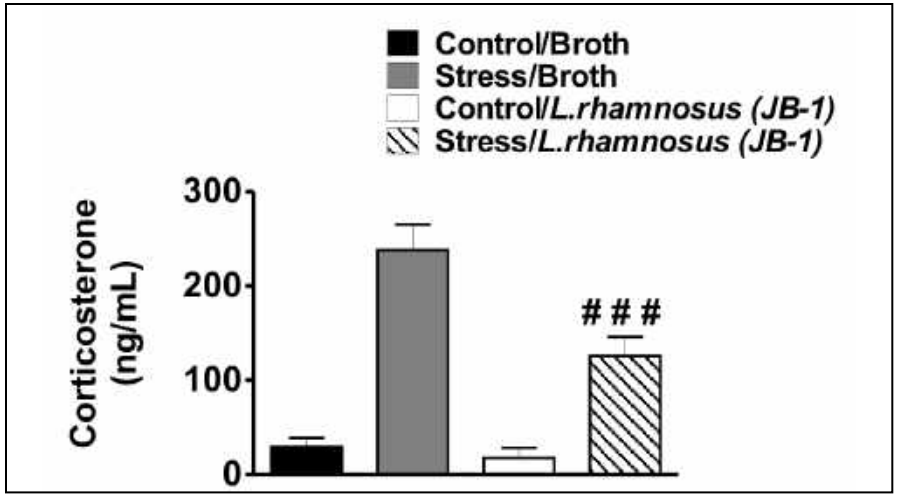


Microbiota Controls Stress Response





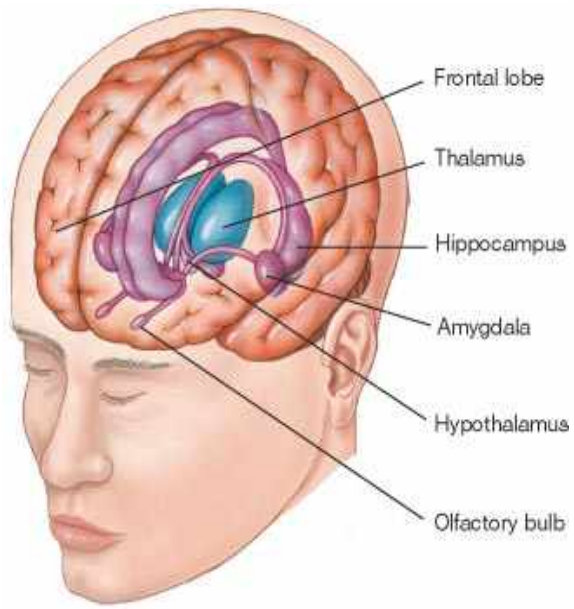
Germ-free animals have an exaggerated stress response

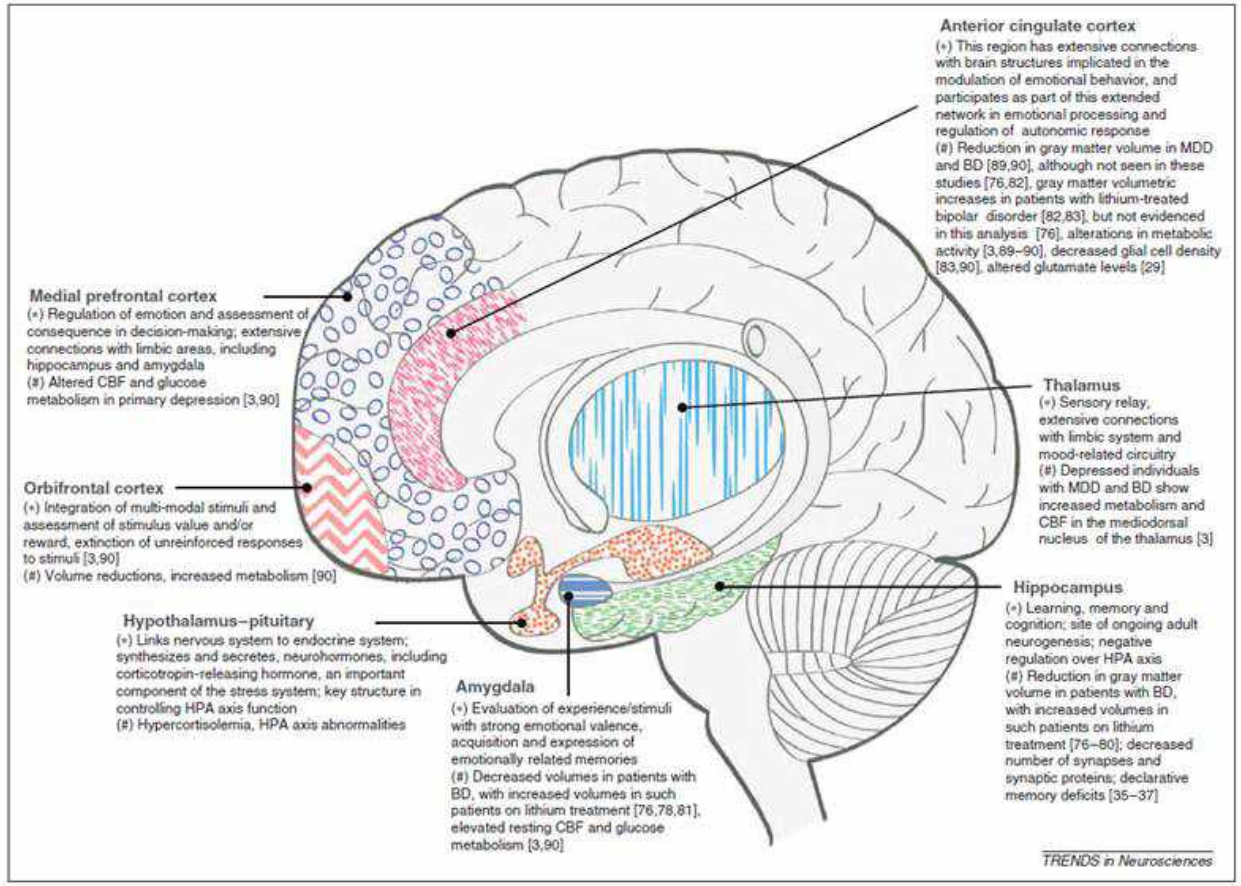


Probiotic Reduces Stress-induced Corticosterone Levels

Bravo et al., PNAS Sept 2011

Functional Annotation of Brain Regions





Schloesser et al., 2012

Microbiota Determines Amygdala Volume & Dendritic Morphology

http://apc.ucc.ie

EJN European Journal of Neuroscience FENS

Research Report

Adult microbiota-deficient mice have distinct dendritic morphological changes: differential effects in the amygdala and hippocampus

Pauline Luczynski[1], Seán O. Whelan[3], Colette O'Sullivan[3], Gerard Clarke[1,2], Fergus Shanahan[1], Timothy G. Dinan[1,2] and John F. Cryan[1,3,*]

DOI: 10.1111/ejn.13291

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Issue

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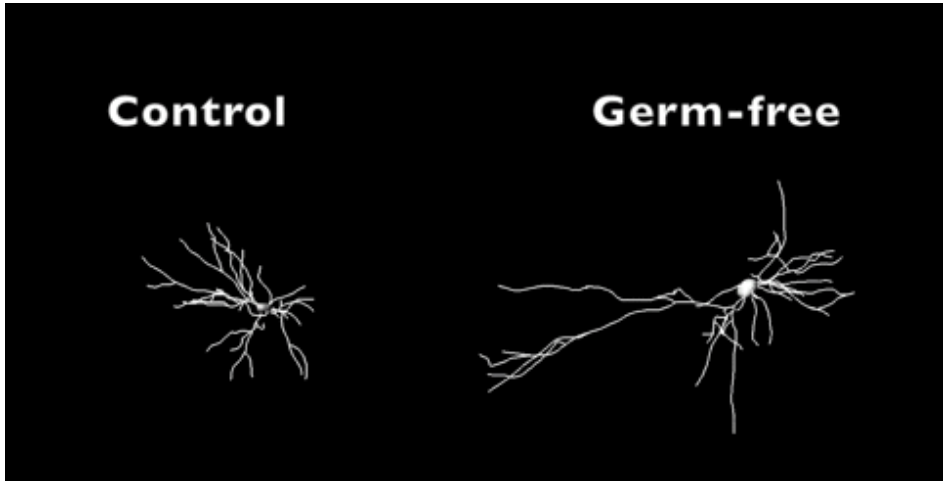
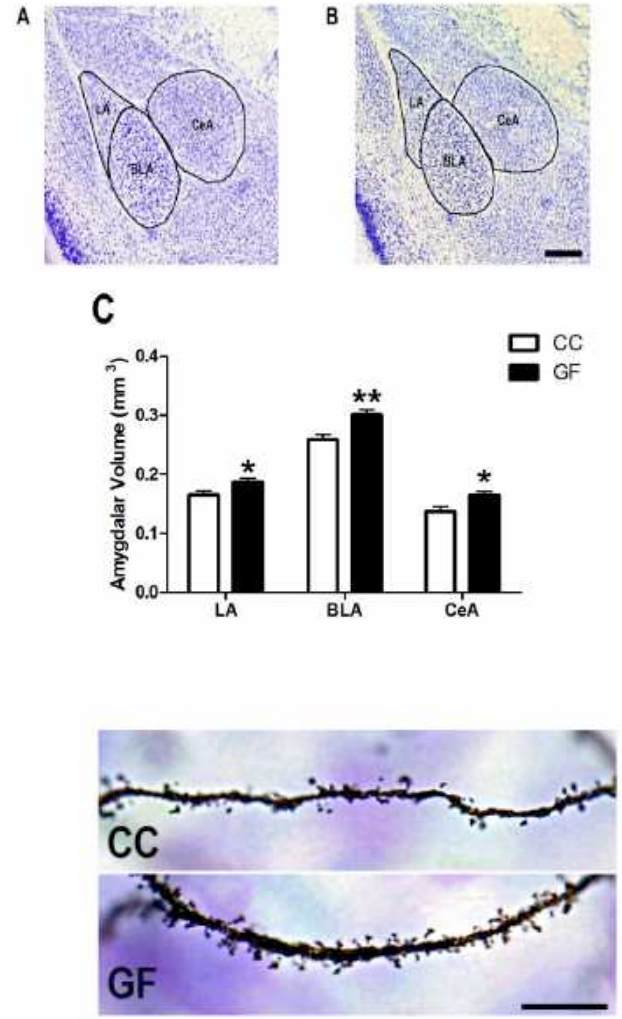
Dendritic Hypertrophy of Basolateral Amygdala Neurons





CC = Conventionally Colonised
GF = Germ Free

OPEN

Molecular Psychiatry (2017) 00, 1–11
www.nature.com/mp

ORIGINAL ARTICLE

The microbion

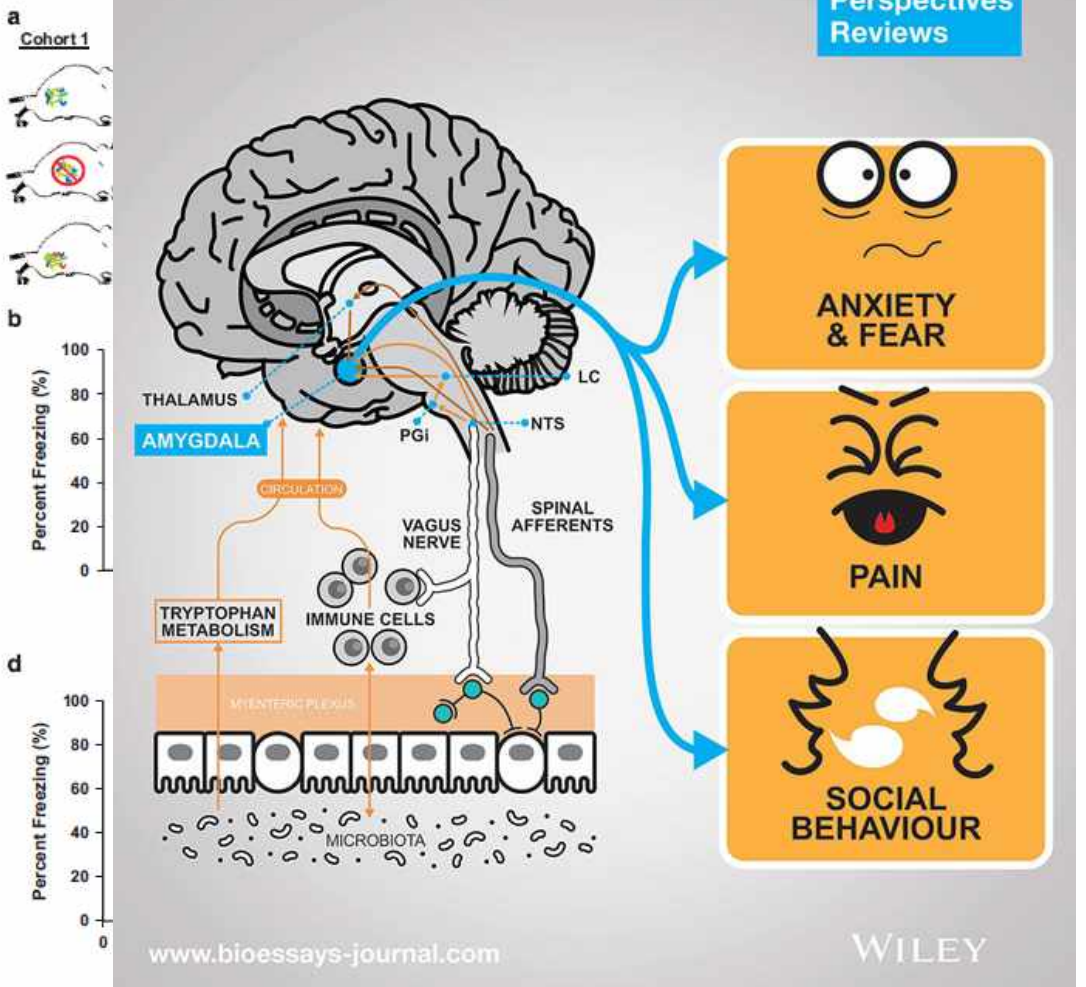
AE Hoban[1,2], RM Stilling[1,2], G M

Volume 40 No. 1 January 2018 · ISSN 0265-9247

BioEssays 1/18

Ideas that Push the Boundaries

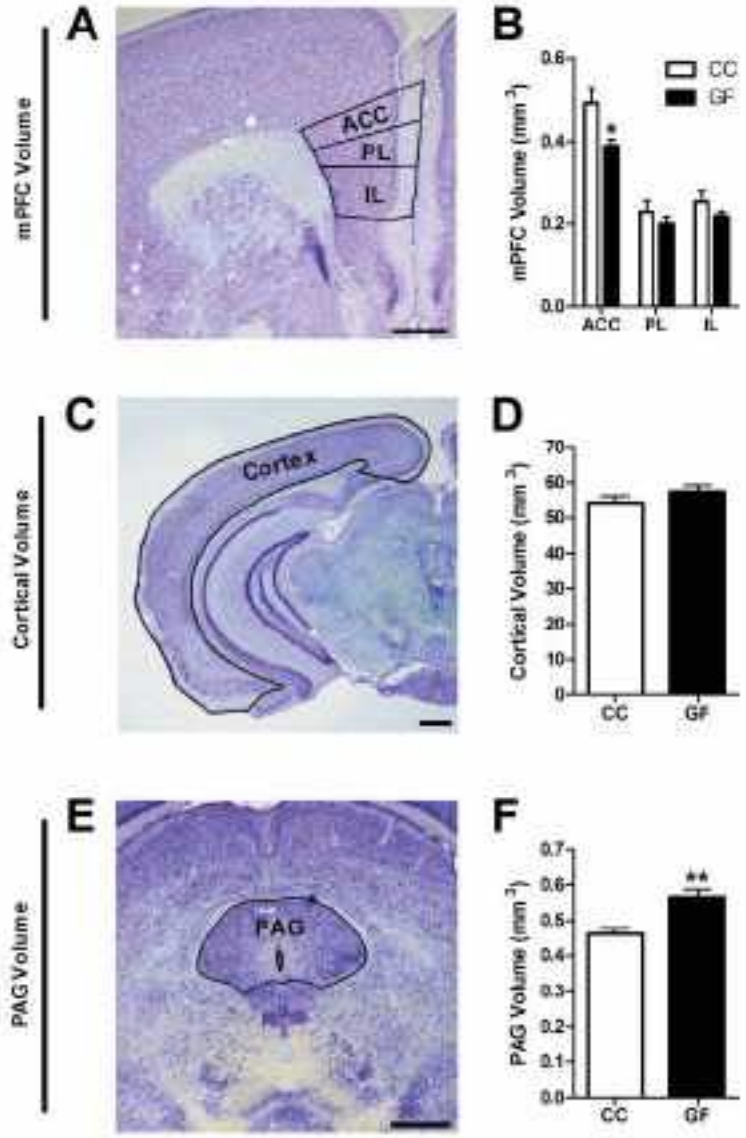
Hypotheses
Perspectives
Reviews



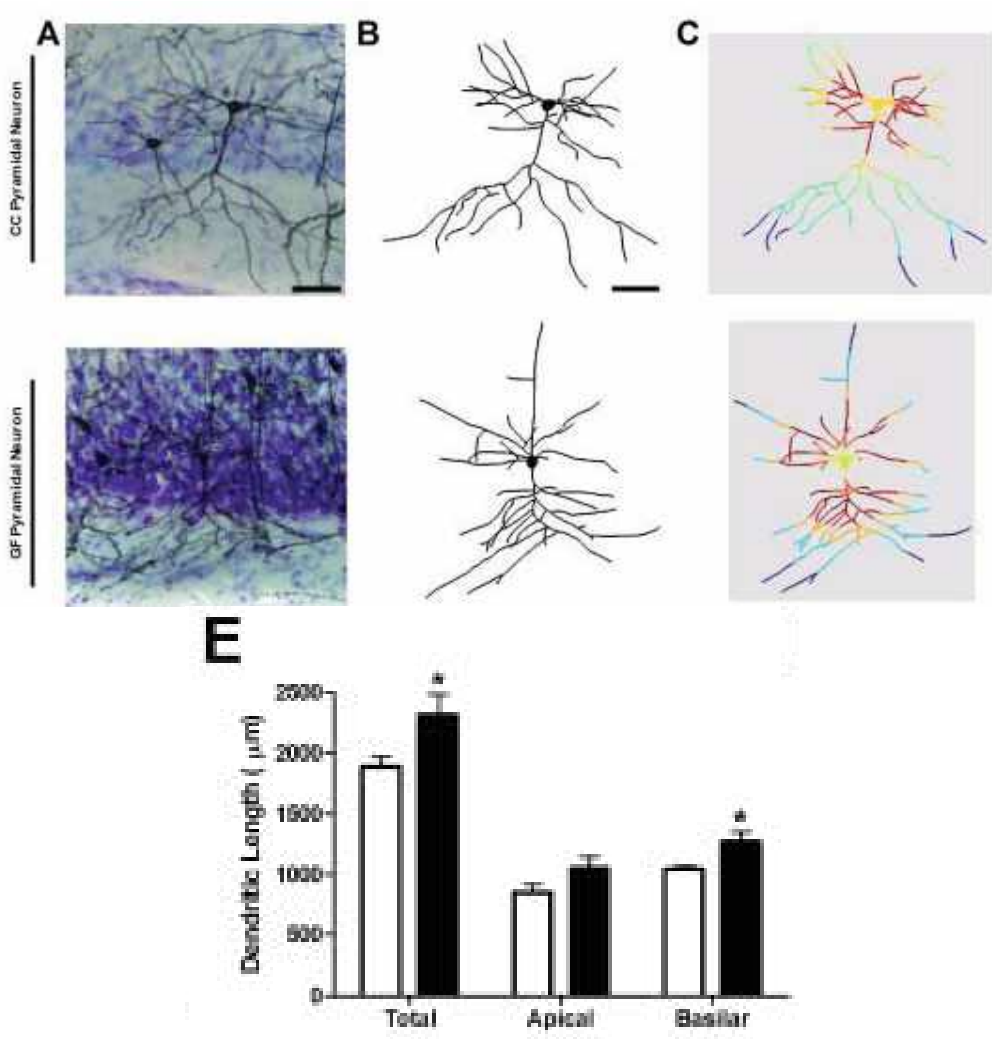
Anatomical correlates of abnormal fear and anxiety can be localised to the amygdala in germ-free animals using cued fear conditioning

Morphological changes in pain-related brain areas of germ free mice

Reduction in ACC and increase in PAG volume in GF mice



Basilar dendritic elongation in ACC pyramidal neurons of GF mice



Luczinski, Tramullas et al., eLIFE 2017

Regulation of Prefrontal Cortex Myelination by the Microbiota

OPEN

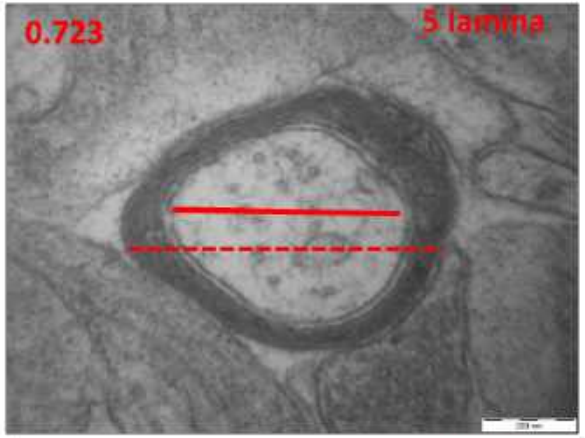
Citation: Transl Psychiatry (2016) 6, e774; doi:10.1038/tp.2016.42
www.nature.com/tp

ORIGINAL ARTICLE

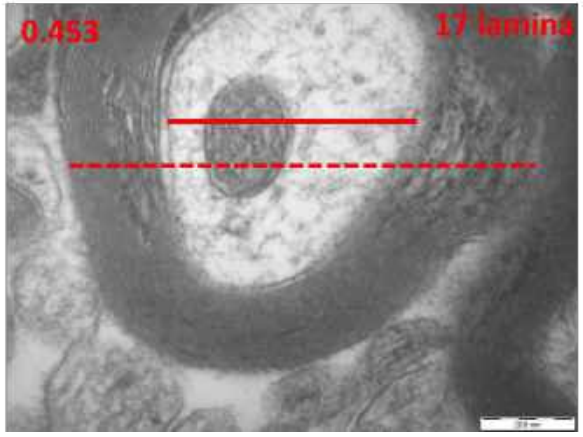
Regulation of prefrontal cortex myelination by the microbiota

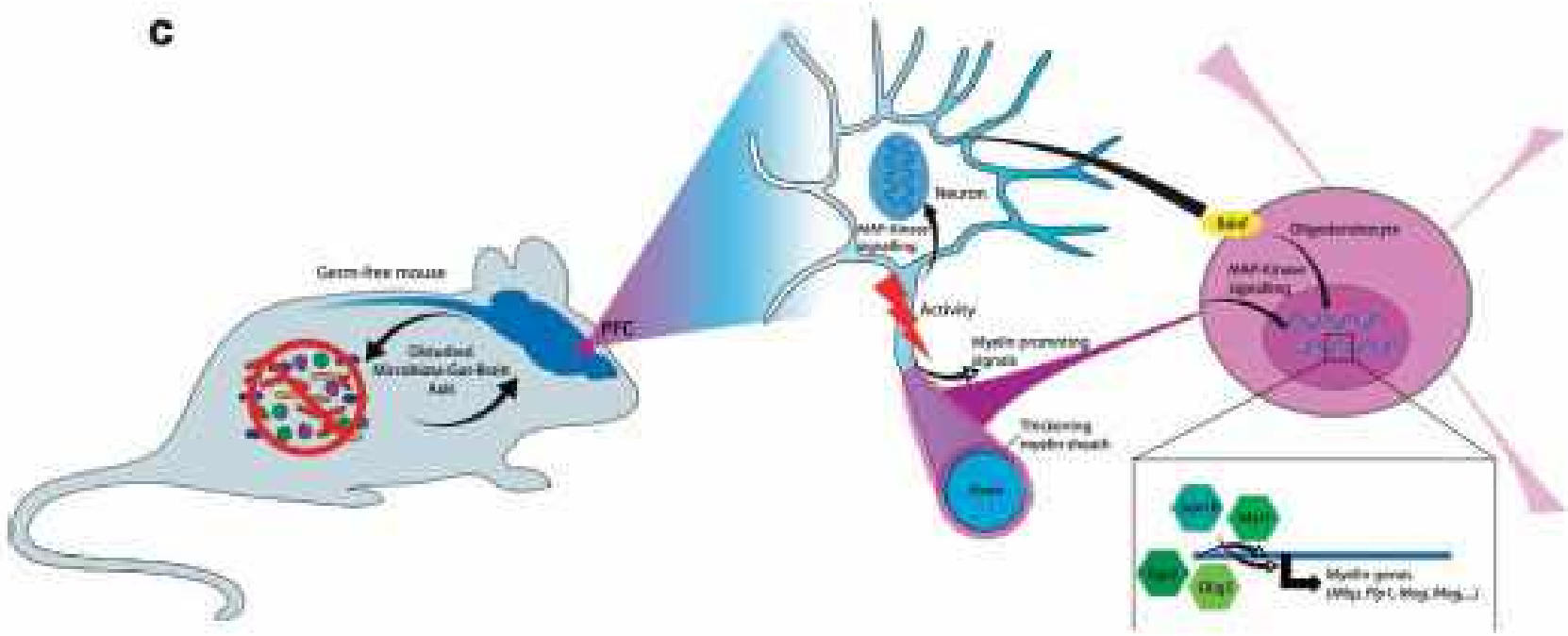
AE Hoban[1,2], RM Stilling[1,2], FJ Ryan[1,3], F Shanahan[1], TG Dinan[1,4], MJ Claesson[1,3], G Clarke[1,4,5,6] and JF Cryan[1,2,5,6]

Control

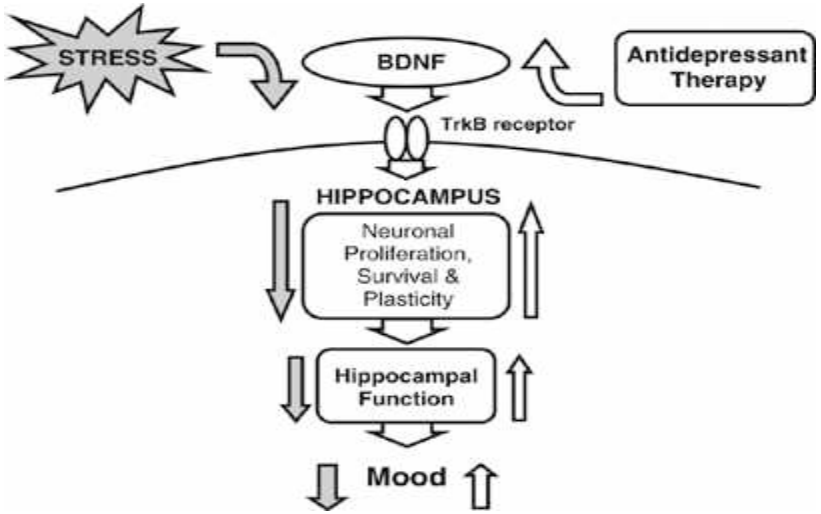


Germ-free

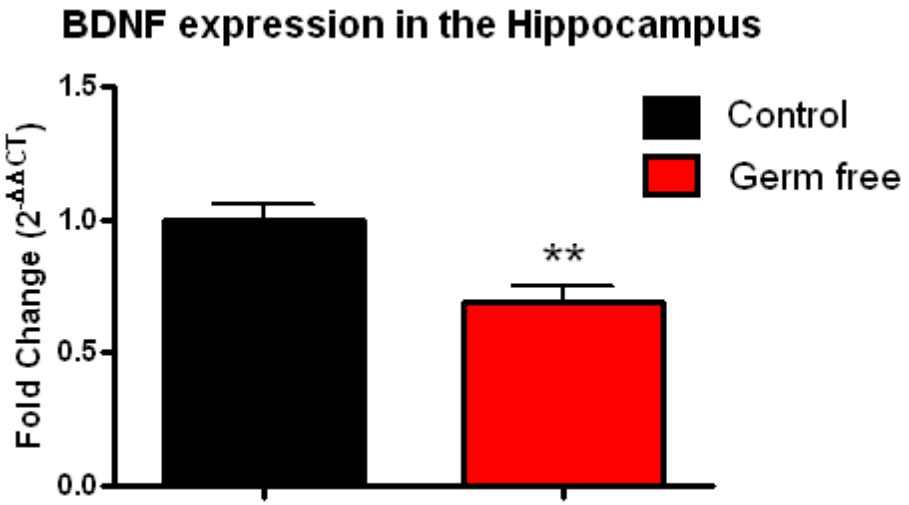




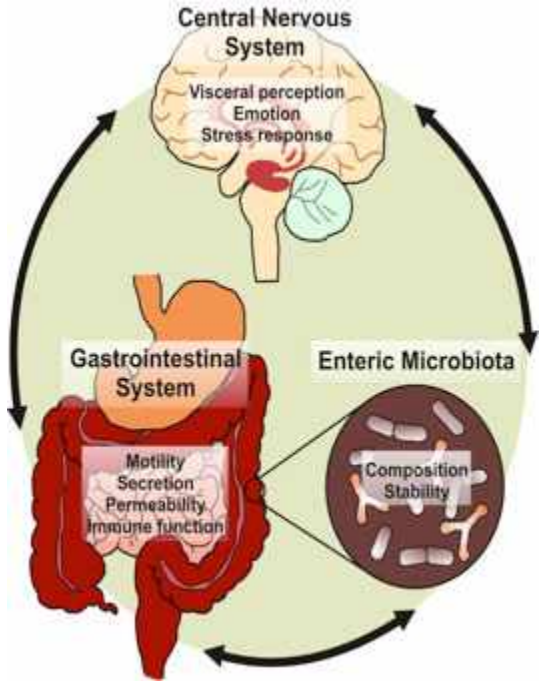
Abnormal Brain Development in Microbiota Deficient Mice: Hippocampus

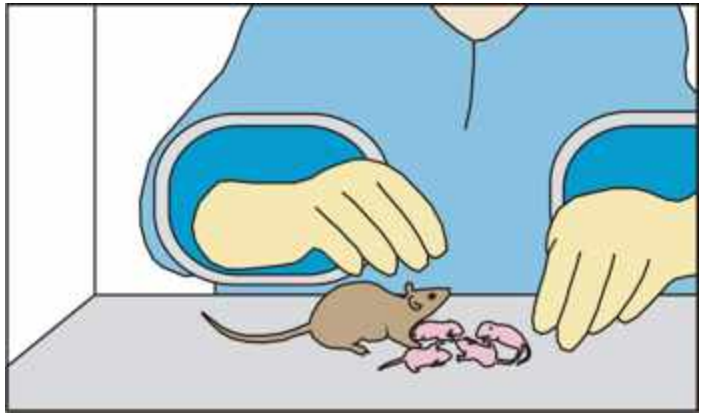


Groves et al., Mol Psych 2007

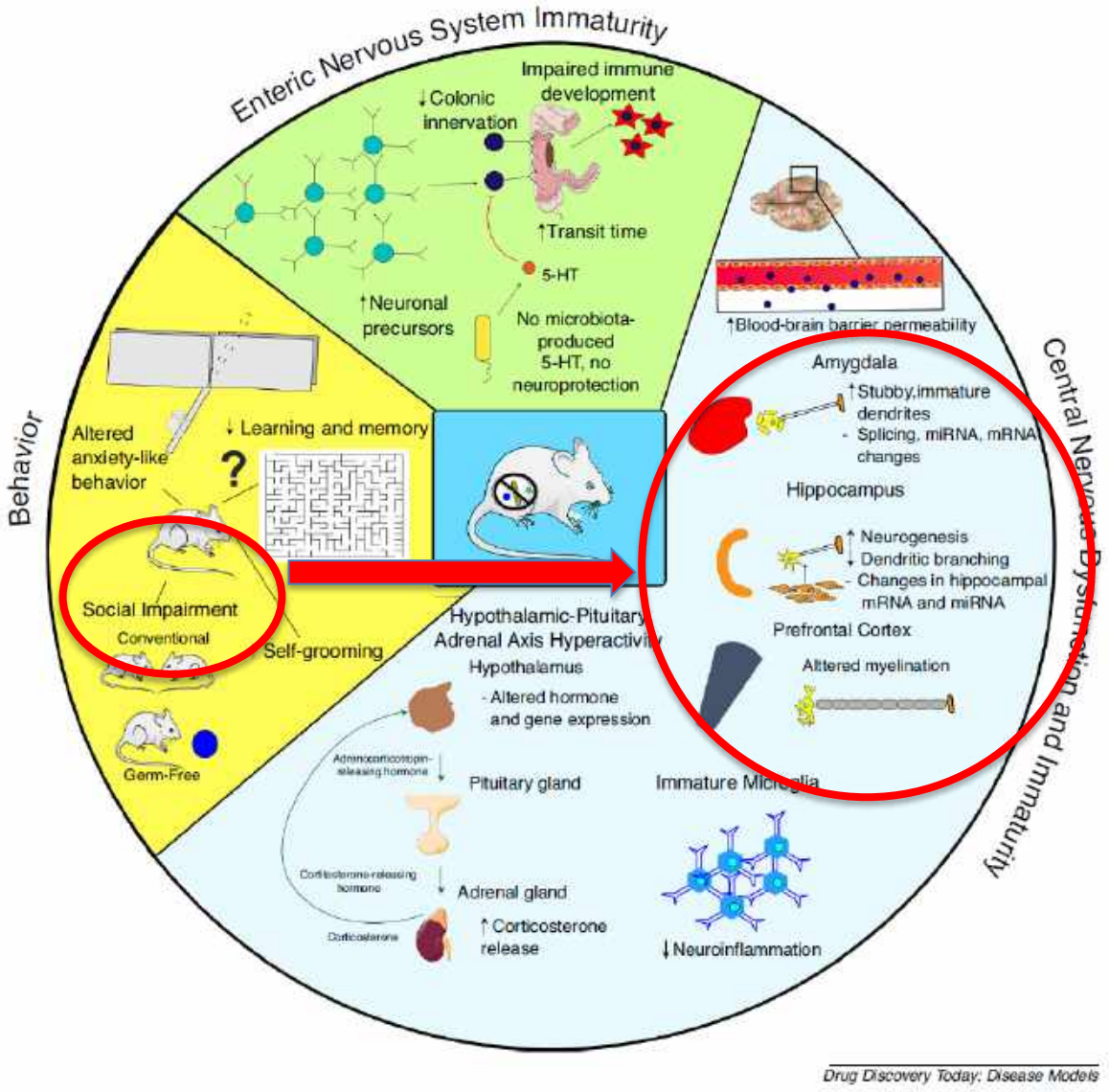


Clarke et al., Mol Psychiatry 2013





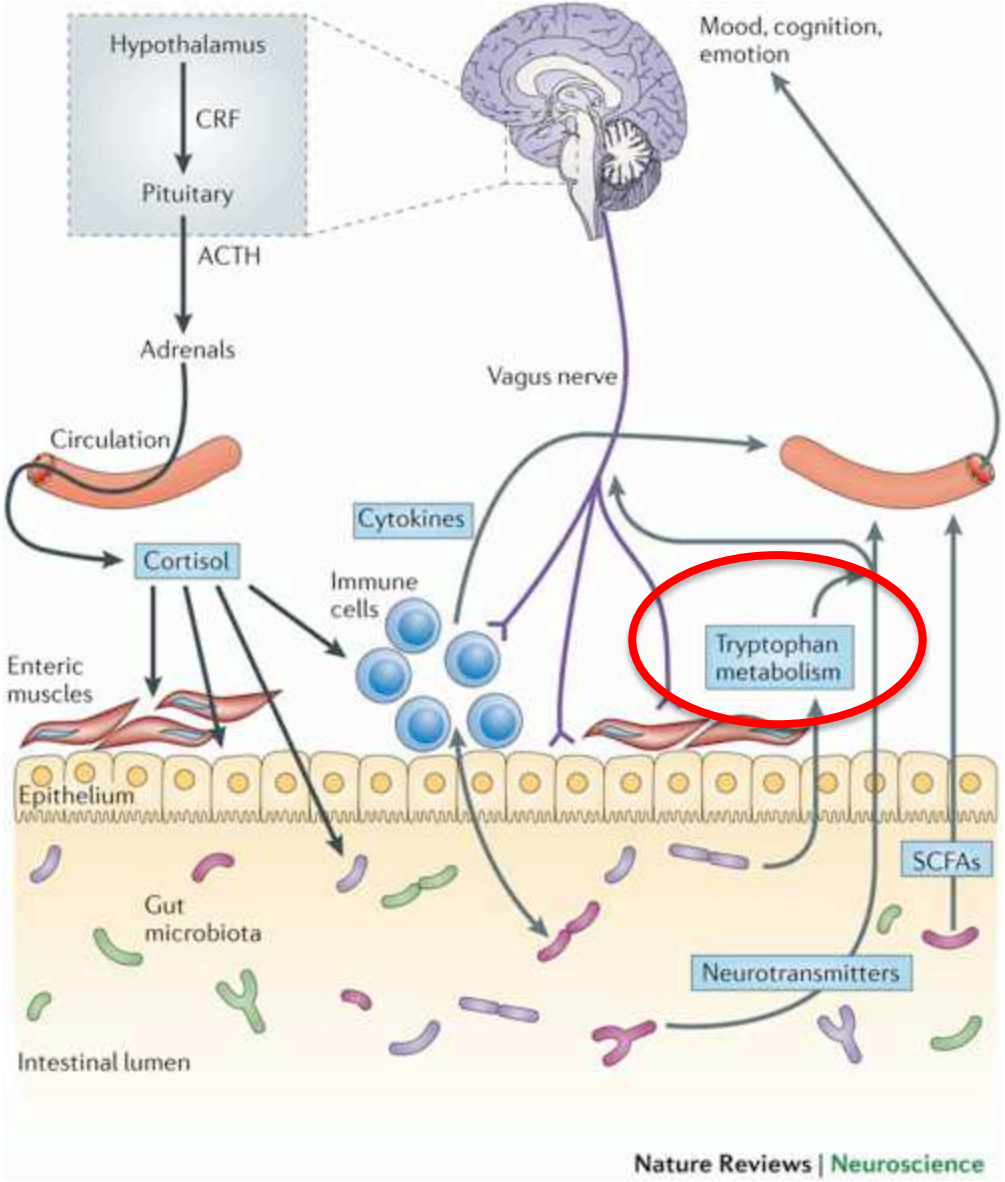
The Germ-free Phenotype



Drug Discovery Today: Disease Models

Spichak et al., Drug Dis Today 2019

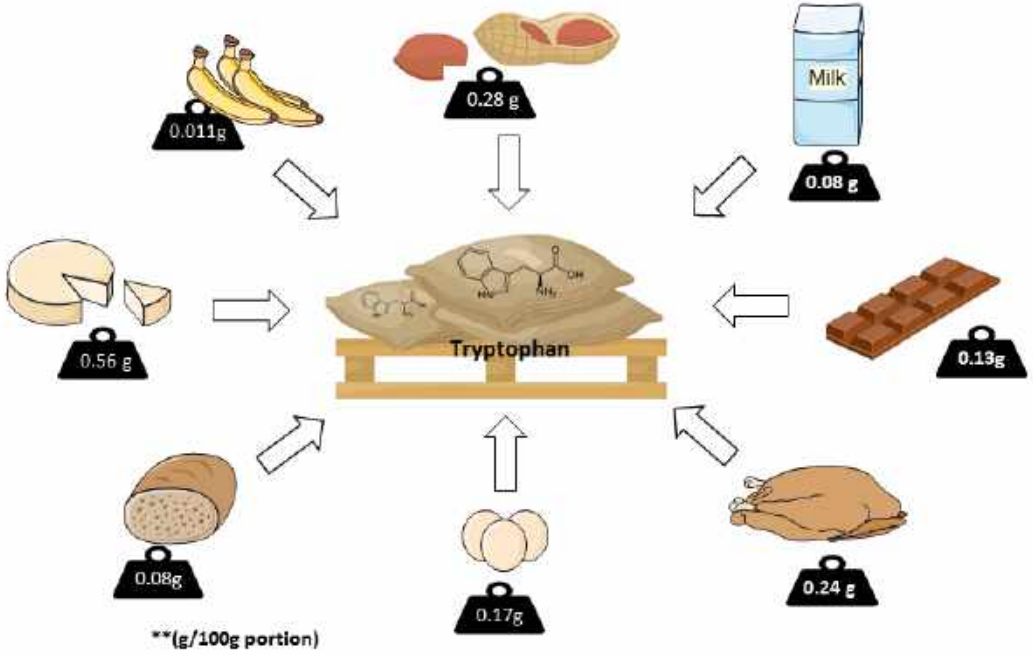
Signalling Along the Brain-Gut-Microbiota axis

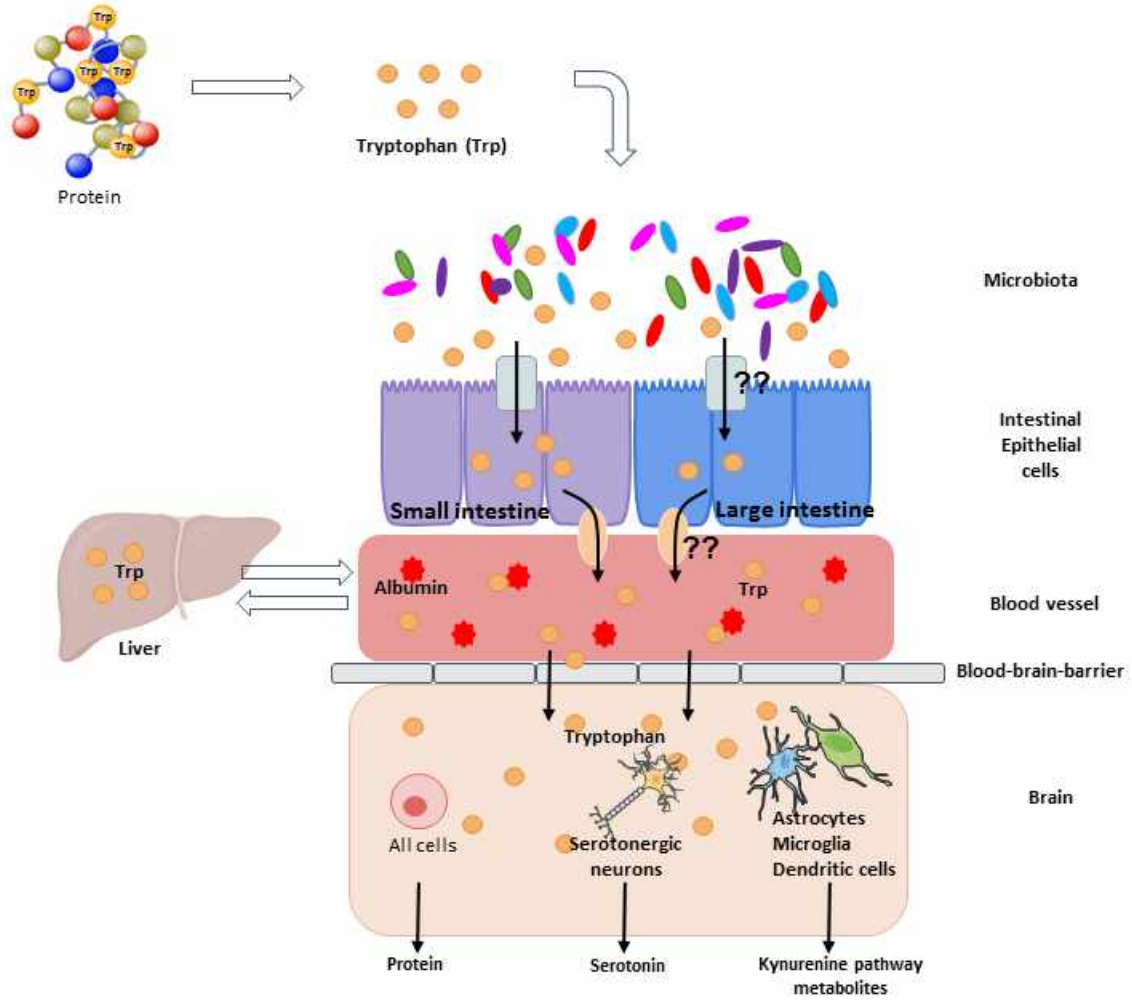


Cryan and Dinan, Nat Rev Neurosci Oct 2012

Tryptophan – A (microbial) Building Block

http://apc.ucc.ie





Behavioural Brain Research 277 (2015) 32–48

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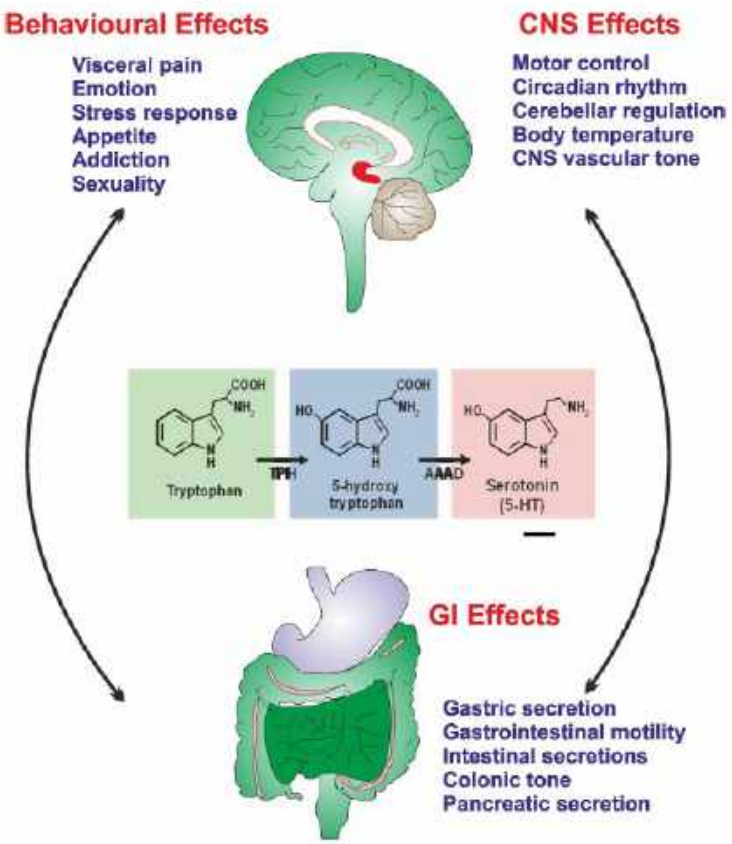
Review

Serotonin, tryptophan metabolism and the brain-gut-microbiome axis

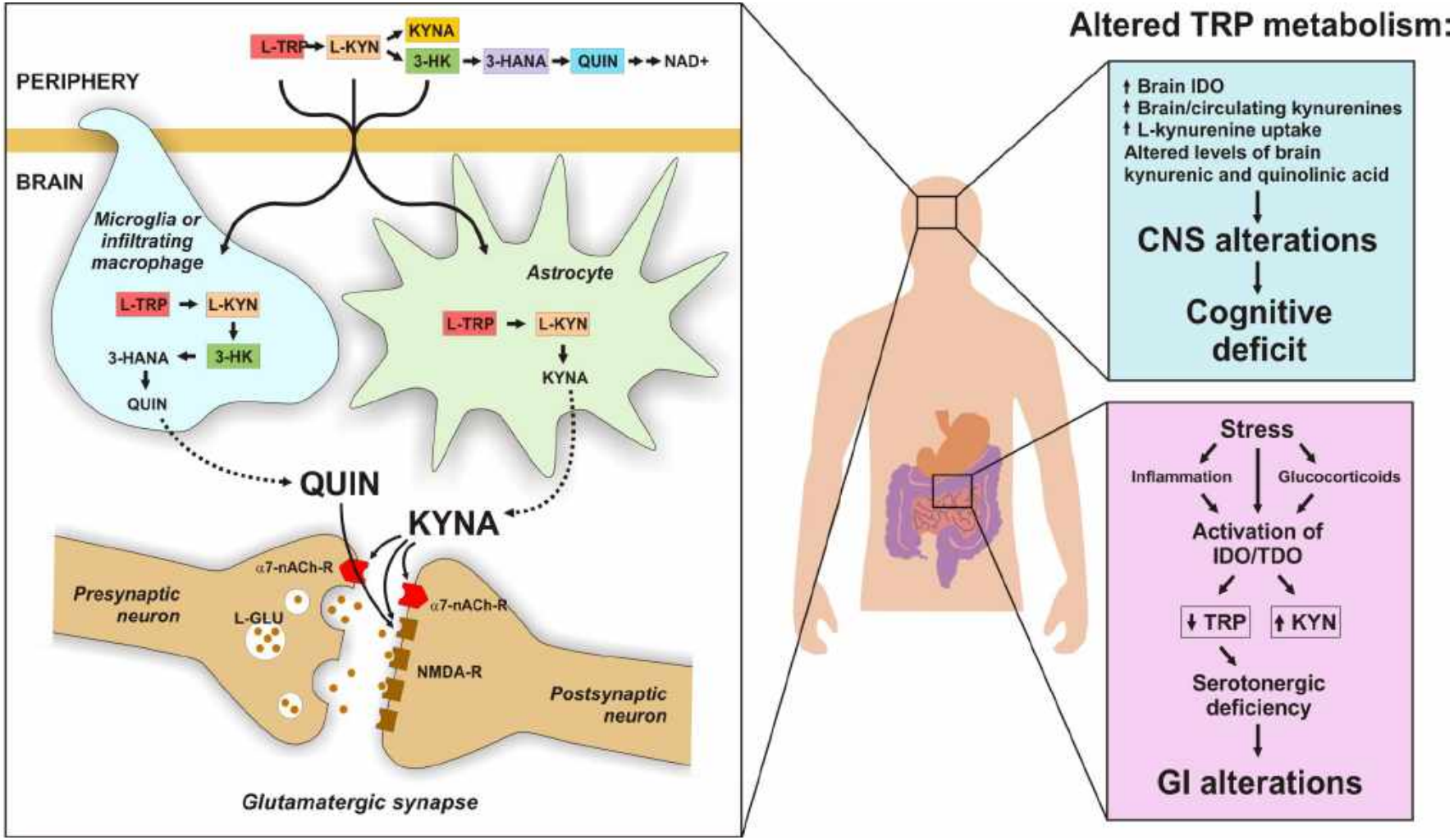
S.M. O'Mahony[a,b,1], G. Clarke[a,c,*,1], Y.E. Borre[a], T.G. Dinan[a,c], J.F. Cryan[a,b]



"Of course you feel great. These things are loaded with antidepressants."

The Kynurenine Pathway

http://apc.ucc.ie



O'Mahony et al, Behavioural Brain Research 2015

Microbiota Regulates Tryptophan Metabolism

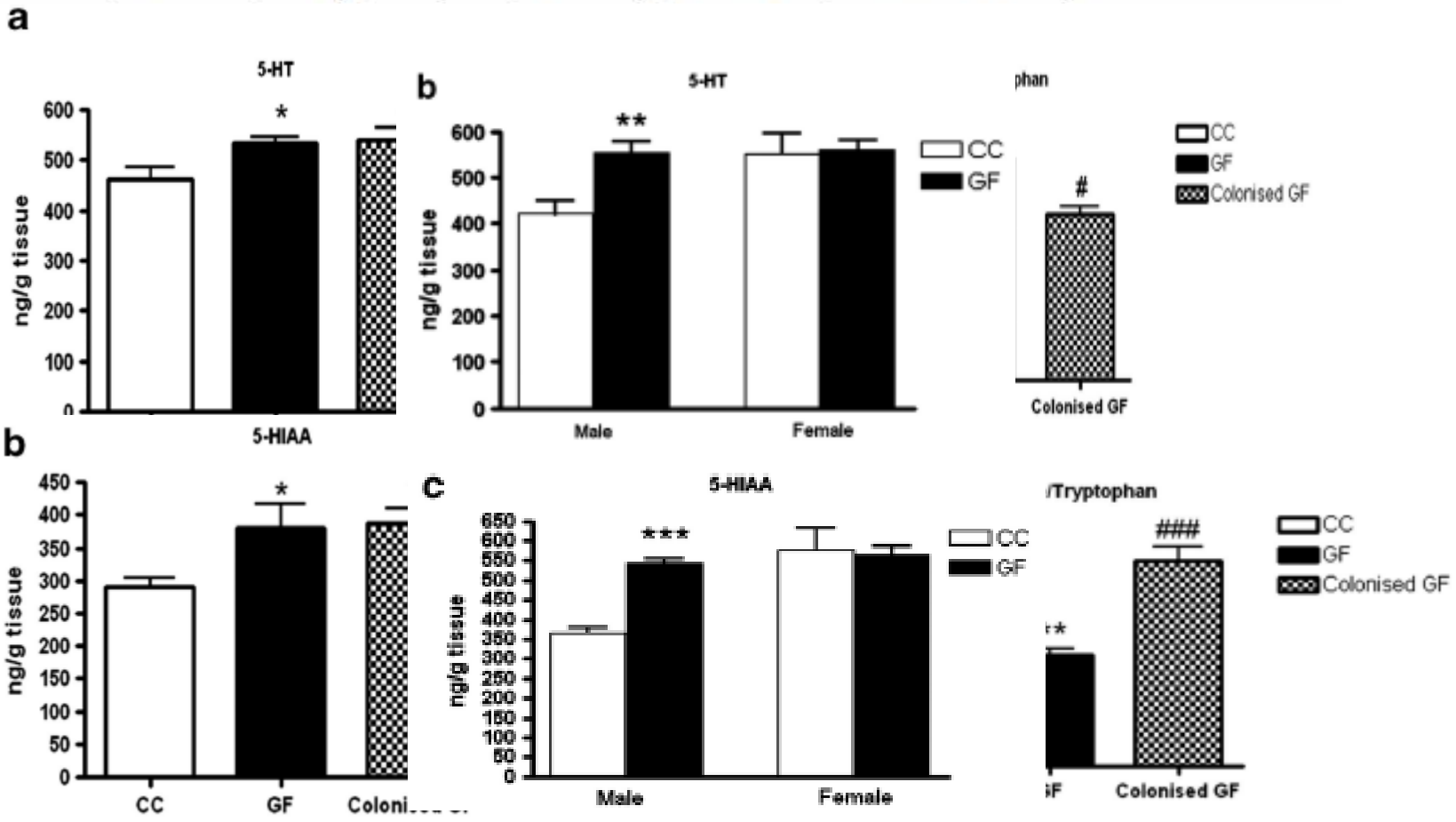
Molecular Psychiatry (2013) 18, 666–673

www.nature.com/mp

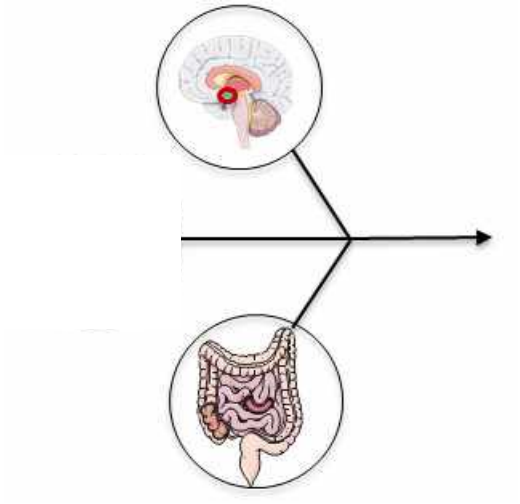
ORIGINAL ARTICLE

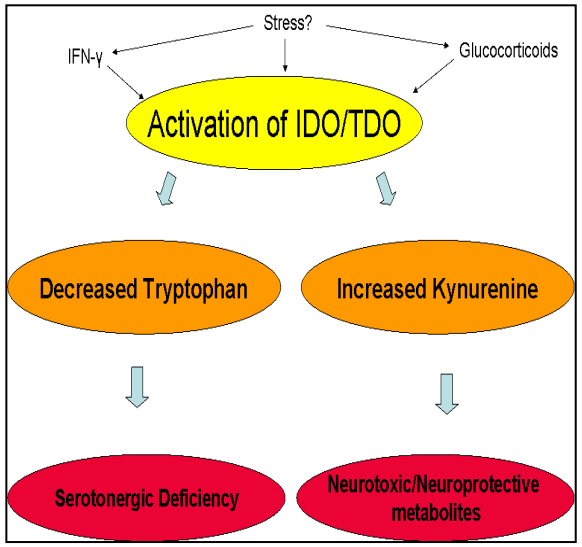
The microbiome-gut-brain axis during early life regulates the hippocampal serotonergic system in a sex-dependent manner

G Clarke[1,2], S Grenham[1], P Scully[1], P Fitzgerald[1], RD Moloney[1], F Shanahan[1,3], TG Dinan[1,2] and JF Cryan[1,4]

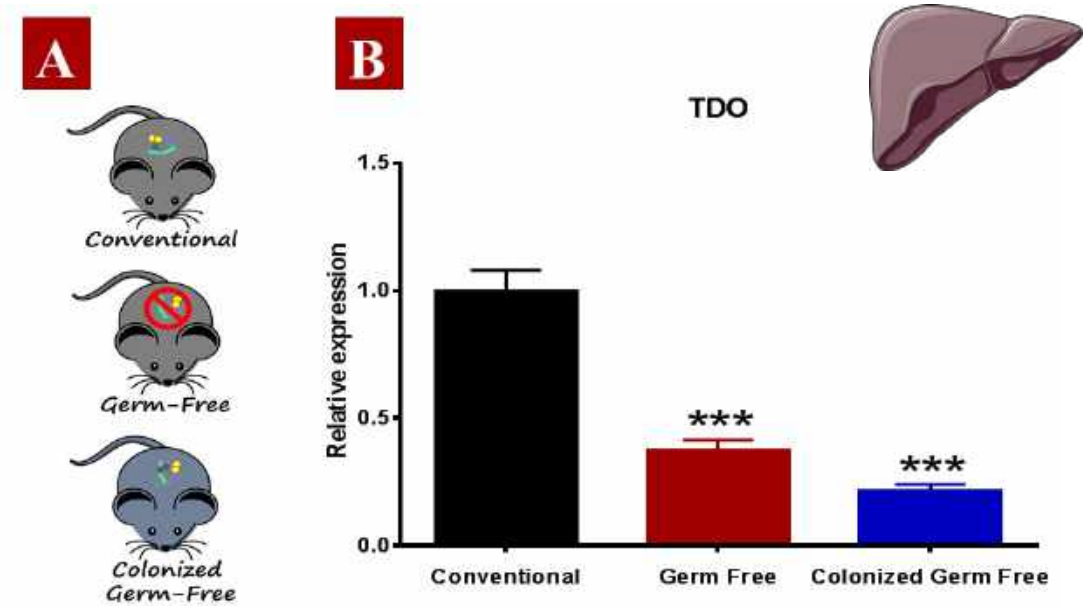


Microbial Regulation of Hepatic Gene Expression





Kennedy et al., World J Gastro 2014



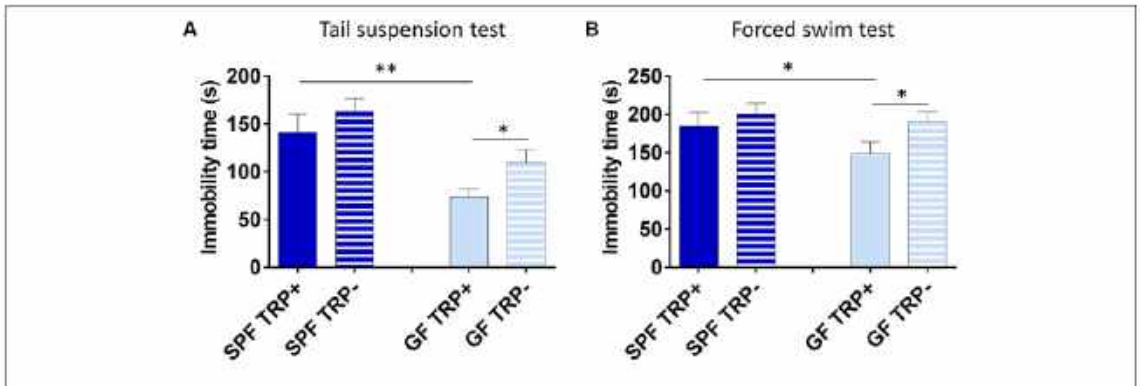
Gheorghe et al, Unpublished data

frontiers in Behavioral Neuroscience

ORIGINAL RESEARCH
published: 04 June 2019
doi: 10.3389/fnbeh.2019.00123

Role of Tryptophan in Microbiota-Induced Depressive-Like Behavior: Evidence From Tryptophan Depletion Study

*Iva Lukić[1], Dmitriy Getselter[1], Omry Koren[2] and Evan Elliott[1]**



Tryptophan depletion normalizes depression-like behavior of germ-free animals

SCIENTIFIC REPORTS

OPEN

Microbiota alteration is associated with the development of stress-induced despair behavior

Received: 11 October 2016
Accepted: 31 January 2017
Published: 07 March 2017

Ioana A. Marin[1,2,3], Jennifer E. Goertz[1,2], Tiantian Ren[4], Stephen S. Rich[5], Suna Onengut-Gumuscu[5], Emily Farber[5], Martin Wu[4], Christopher C. Overall[1,2], Jonathan Kipnis[1,2,3,*] & Alban Gaultier[1,2,3,*]

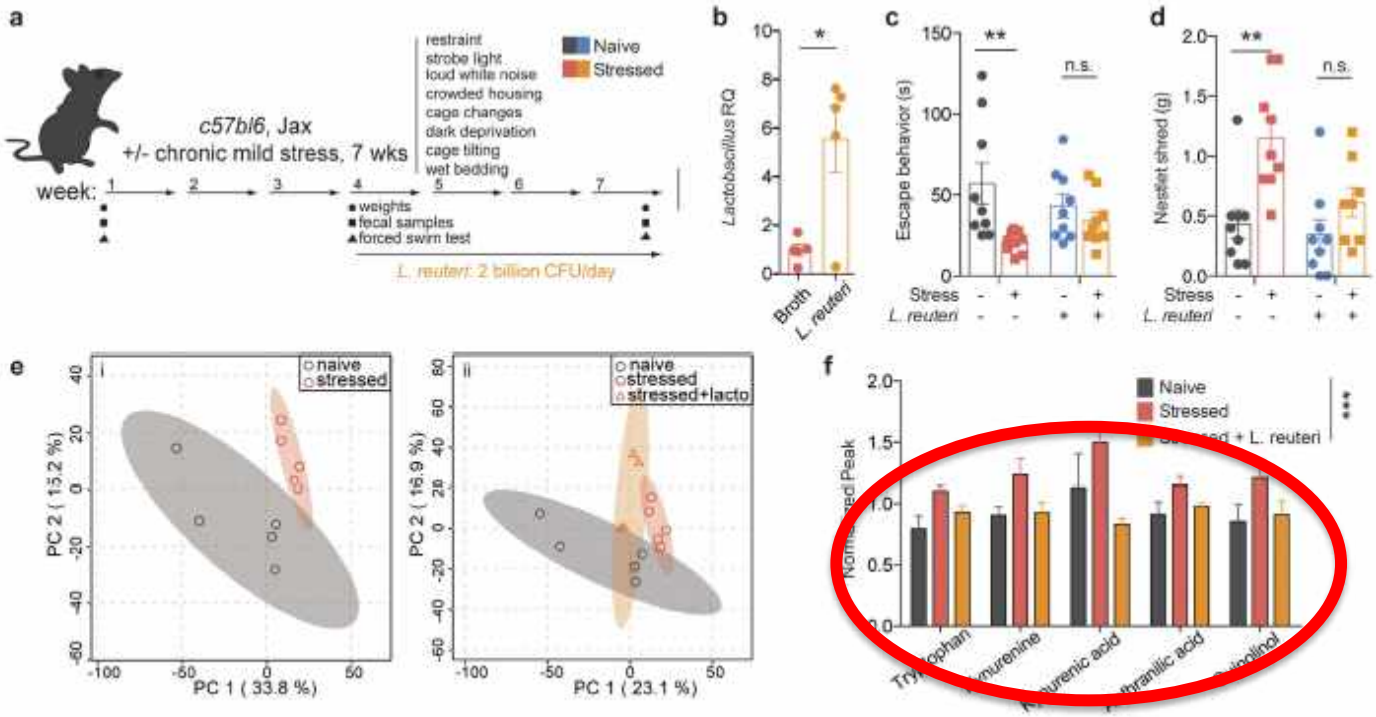


Figure 3. Treatment with probiotic *L. reuteri* ameliorates the escape behavior induced by chronic stress.

Restoring intestinal *Lactobacillus* levels normalized stress-induced behavior and suppressed kynurenine production

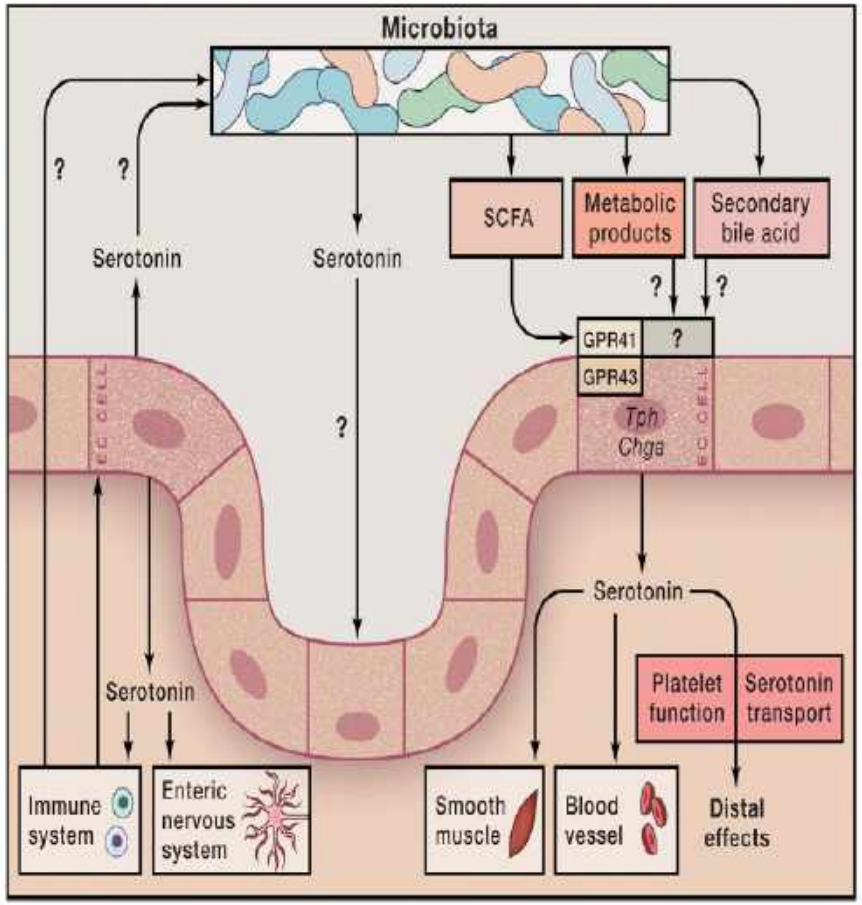
Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis

Jessica M. Yano,[1] Kristie Yu,[1] Gregory P. Donaldson,[1] Gauri G. Shastri,[1] Phoebe Ann,[1] Liang Ma,[2] Cathryn R. Nagler,[3] Rustem F. Ismagilov,[2] Sarkis K. Mazmanian,[1] and Elaine Y. Hsiao[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA
[2]Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA
[3]Department of Pathology and Department of Medicine, I
*Correspondence: ehsiao@caltech.edu
http://dx.doi.org/10.1016/j.cell.2015.02.047

Leading Edge
Previews

Gut Microbiota: The Link to Your Second Brain

Vanessa Ridaura[1,2] and Yasmine Belkaid[1,2,*]



Stress alters Serotonergic Signalling in the Gut-Brain axis

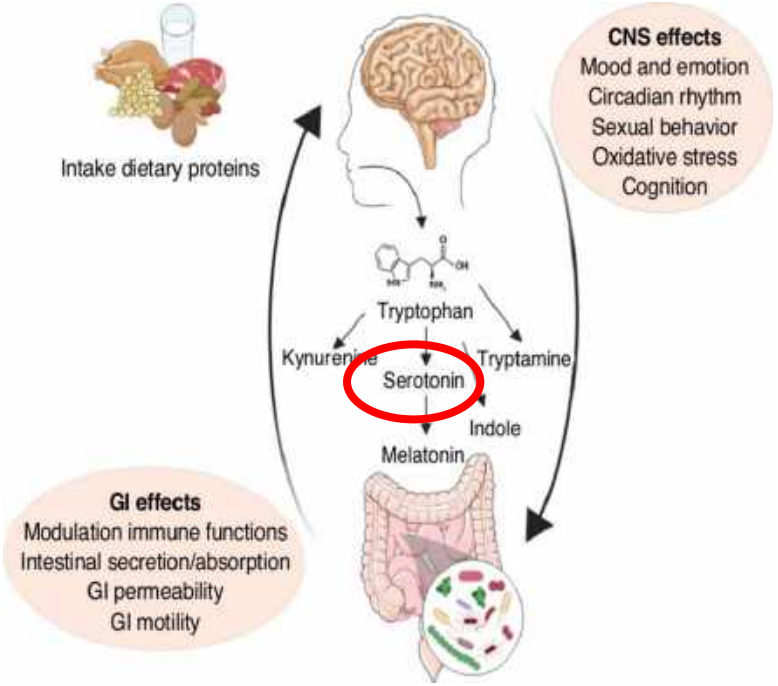
Received: 24 January 2020 | Revised: 6 April 2020 | Accepted: 17 April 2020
DOI: 10.1111/mmi.13881

ORIGINAL ARTICLE

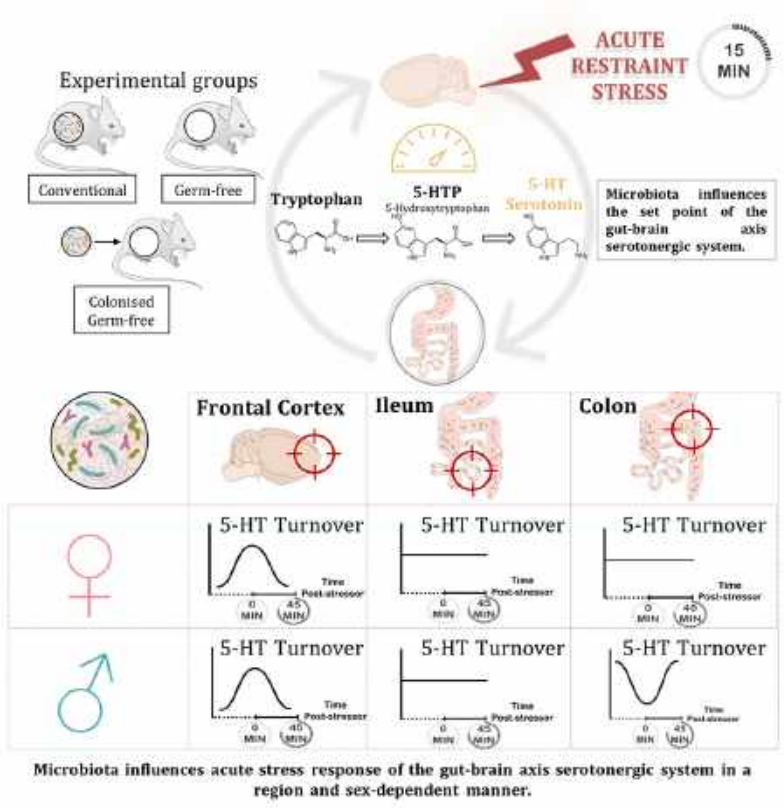
WILEY

Gut-brain axis serotonergic responses to acute stress exposure are microbiome-dependent

Joshua M. Lyte[1] | Cassandra E. Gheorghe[1] | Michael S. Goodson[2] | Nancy Kelley-Loughnane[2] | Timothy G. Dinan[1,3] | John F. Cryan[1,4] | Gerard Clarke[1,3]



Gheorghe et al., Curr Opin Pharm 2019



Microbiota influences acute stress response of the gut-brain axis serotonergic system in a region and sex-dependent manner.

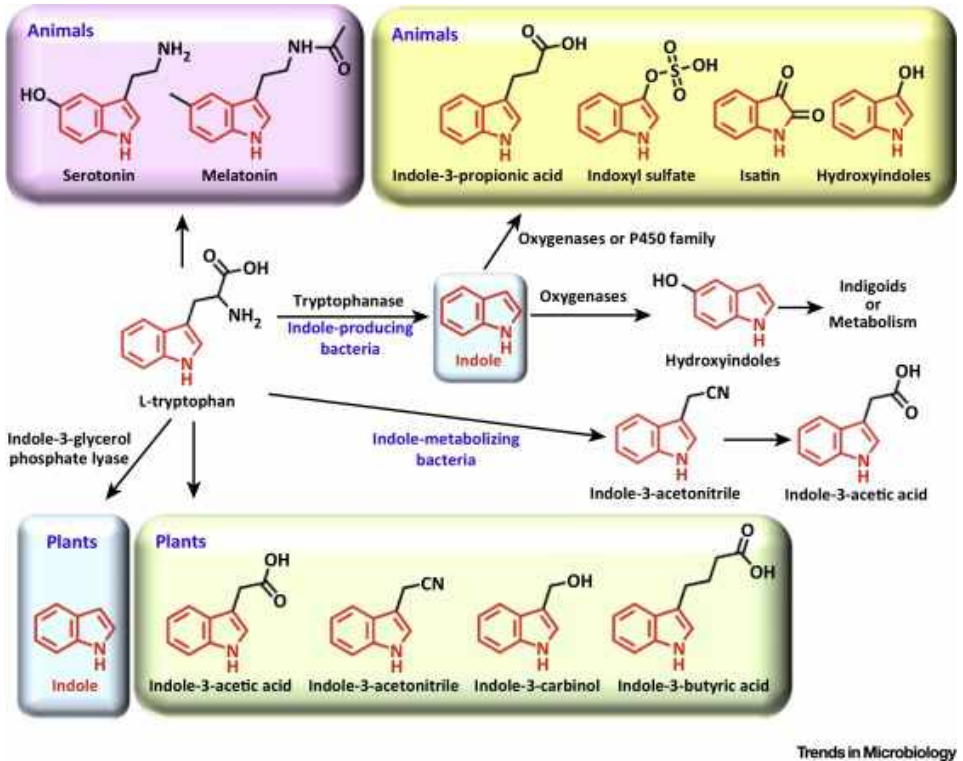
Trends in Microbiology

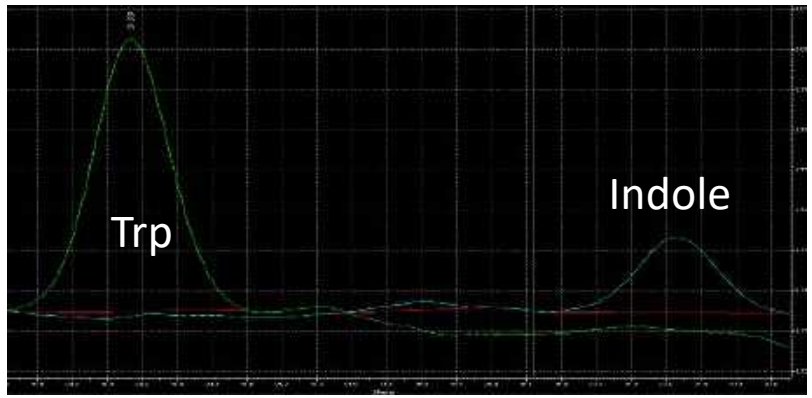
CellPress

Review

Roles of Indole as an Interspecies and Interkingdom Signaling Molecule

Jin-Hyung Lee,[1] Thomas K. Wood,[2] and Jintae Lee[1,*]





Lyte et al., Unpublished data

LETTER

NATURE | www.nature.com/nature

https://doi.org/10.1038/s41586-018-0119-x

Microglial control of astrocytes in response to microbial metabolites

Veit Rothhammer[1], Davis M. Borucki[1], Emily C. Tjon[1], Maisa C. Takenaka[1], Chun-Cheih Chao[1], Alberto Ardura-Fabregat[2], Kalil Alves de Lima[1], Cristina Gutiérrez-Vázquez[1], Patrick Hewson[1], Ori Staszewski[2], Manon Blain[3], Luke Healy[3], Tradite Neziraj[1], Matilde Borio[1], Michael Wheeler[1], Loic Lionel Dragin[4], David A. Laplaud[5], Jack Antel[3], Jorge Ivan Alvarez[4], Marco Prinz[2,6] & Francisco J. Quintana[1,7]*

NEWS & VIEWS | NATURE | 1

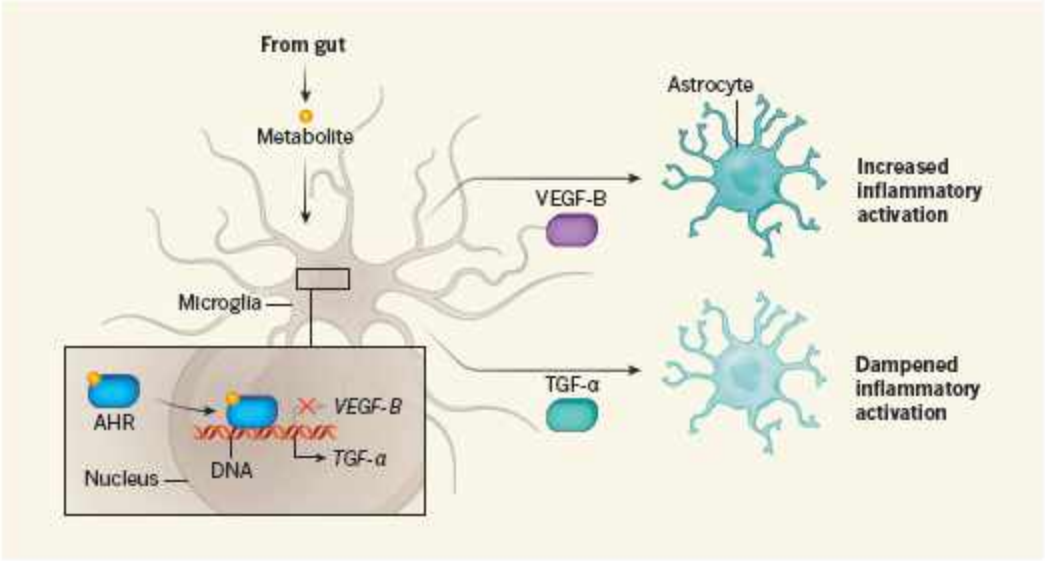
https://doi.org/10.1038/d41586-018-05113-0

IMMUNOLOGY

Gut molecules control brain inflammation

Metabolite molecules produced by the gut's microbes activate immune cells in the brain called microglia, which signal to astrocyte cells to mediate responses to inflammation in the central nervous system.

HARTMUT WEKERLE



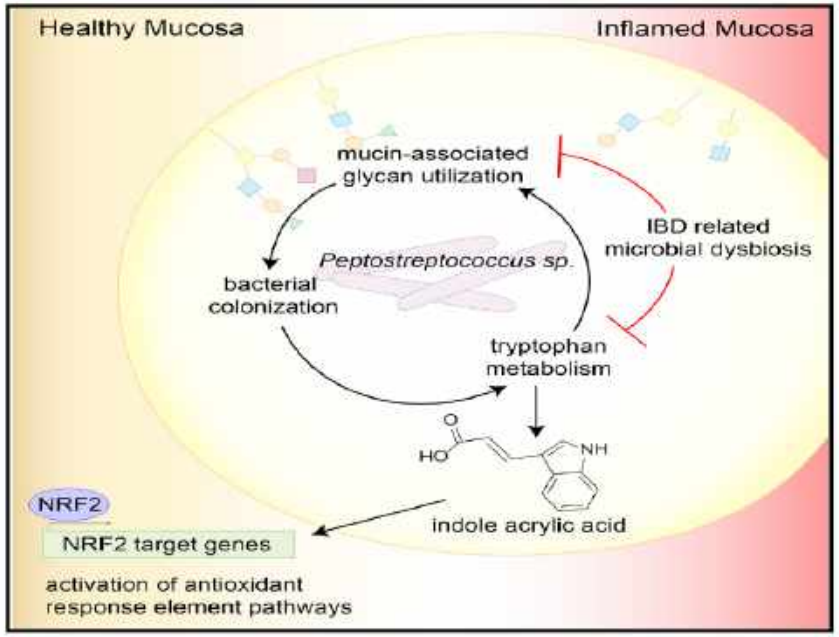
microglia inhibits inflammation in the CNS.

Cell Host & Microbe 22, 25–37, July 12, 2017

Cell Host & Microbe

Indoleacrylic Acid Produced by Commensal *Peptostreptococcus* Species Suppresses Inflammation

Graphical Abstract



Authors

Marta Wlodarska, Chengwei Luo, Raivo Kolde, ..., Hera Vlamakis, Jeffrey A. Porter, Ramnik J. Xavier

Correspondence

xavier@molbio.mgh.harvard.edu

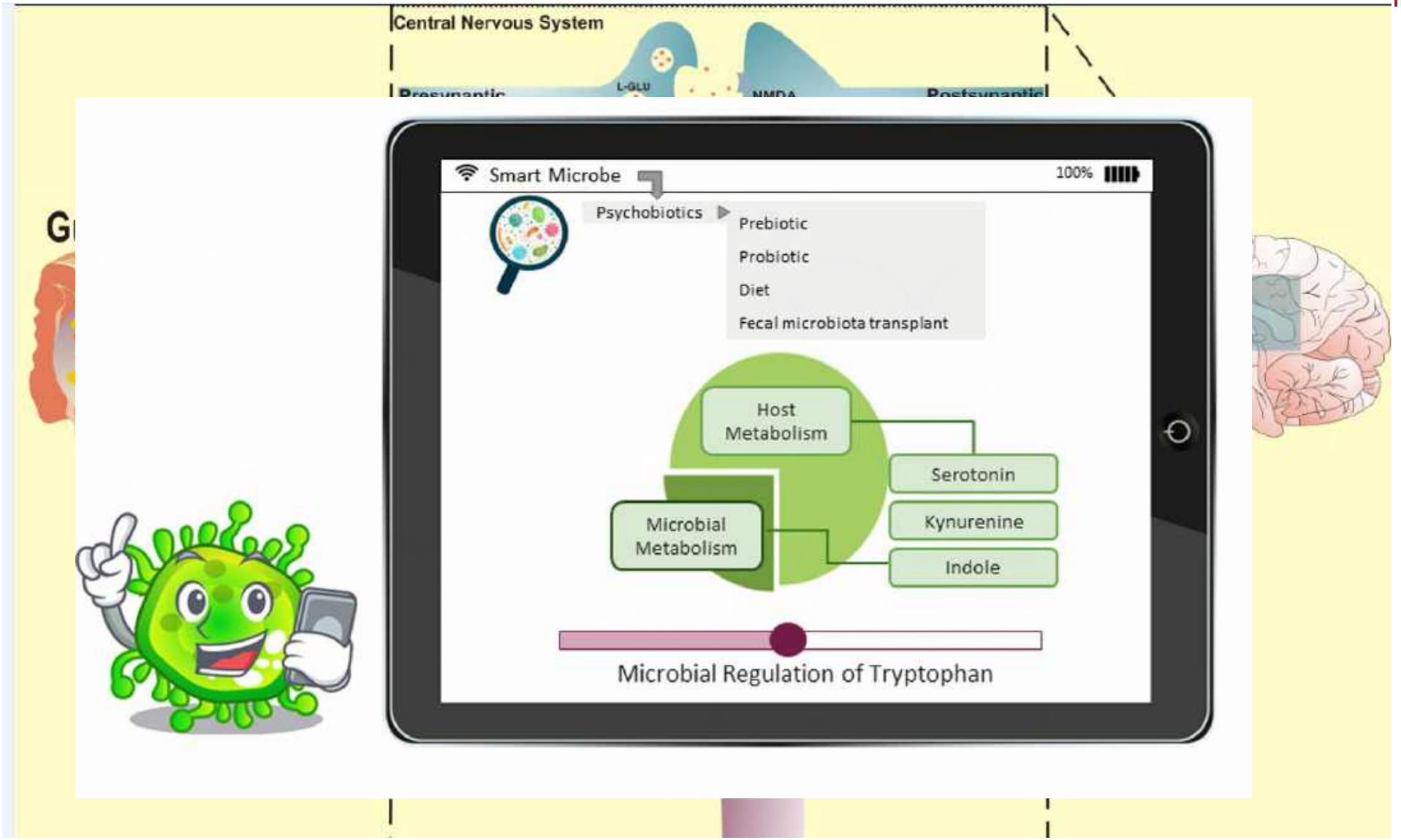
In Brief

Wlodarska et al. provide insight into intestinal mucin as an exemplar of a critical host-derived colonization factor that attracts bacteria that may promote intestinal health. One such mucin utilizer, *Peptostreptococcus russellii*, produces the tryptophan metabolite indoleacrylic acid, which has beneficial effects on intestinal epithelial barrier function and mitigates inflammatory responses.

Highlights

- Computational analysis identifies *Peptostreptococcus russellii* as a mucin utilizer
- *Peptostreptococcus* species produce the tryptophan metabolite indoleacrylic acid (IA)
- IA promotes intestinal epithelial barrier function and mitigates inflammatory responses
- Microbes of IBD patients have reduced ability to cleave mucins and metabolize tryptophan

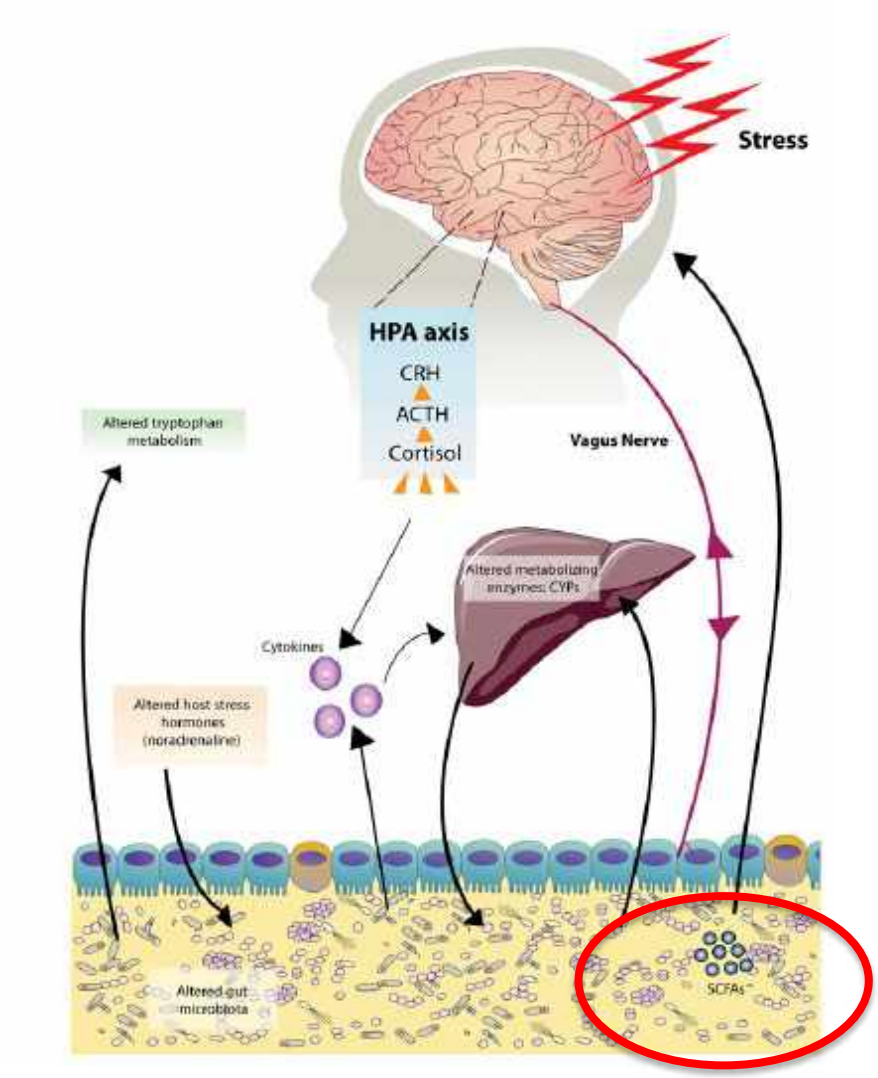
Summary

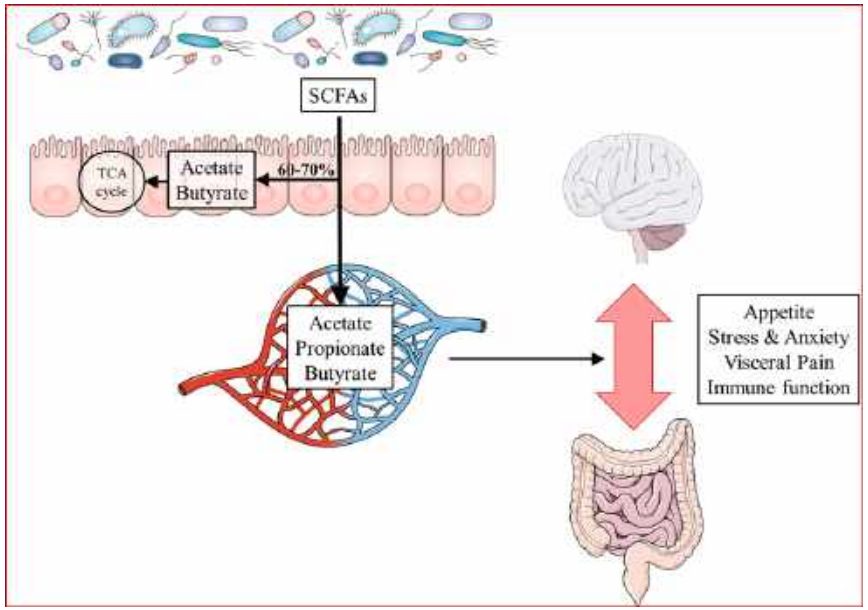


Kennedy et al., Neuropharmacology 2017

Signalling Along the Brain-Gut-Microbiota axis

http://apc.ucc.ie



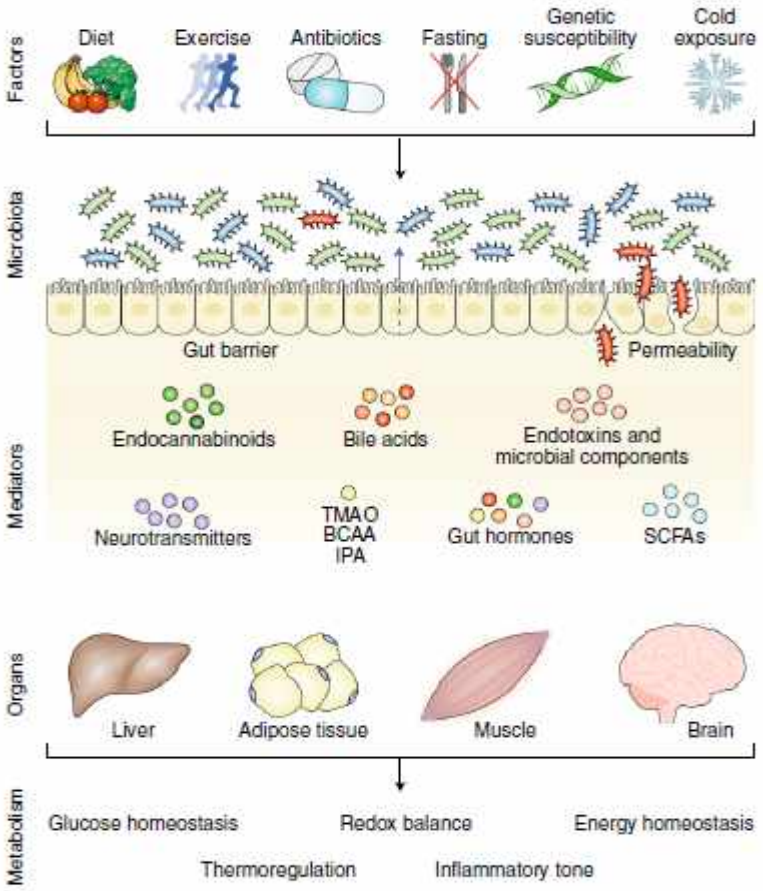


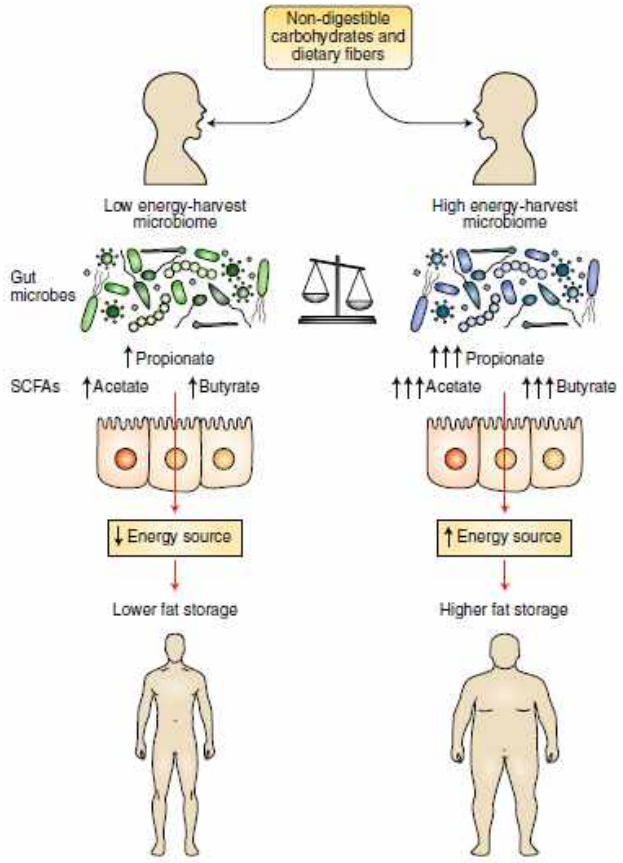
Clarke et al., Pharmacological Reviews 2019

REVIEW ARTICLE
https://doi.org/10.1038/s42255-018-0017-4
nature metabolism

Microbial regulation of organismal energy homeostasis

Patrice D. Cani[1,2]*, Matthias Van Hul[1,2], Charlotte Lefort[1,2], Clara Depommier[1,2], Marialetizia Rastelli[1,2] and Amandine Everard[1,2]



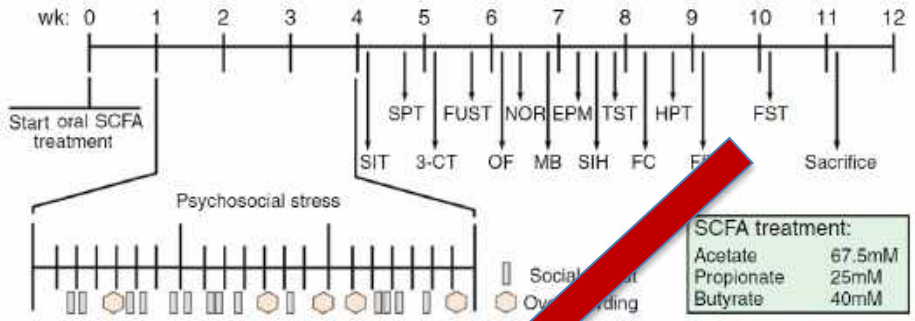


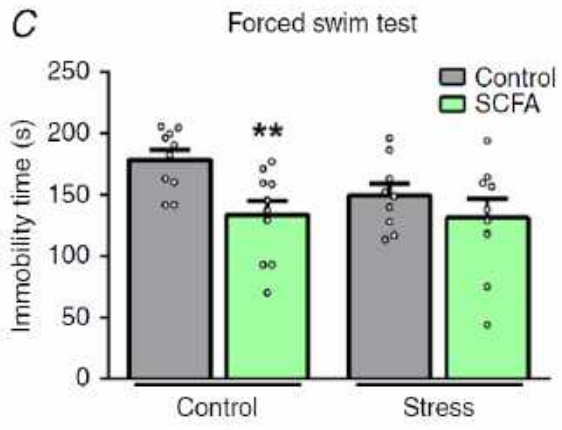
J Physiol 596.20 (2018) pp 4923–4944

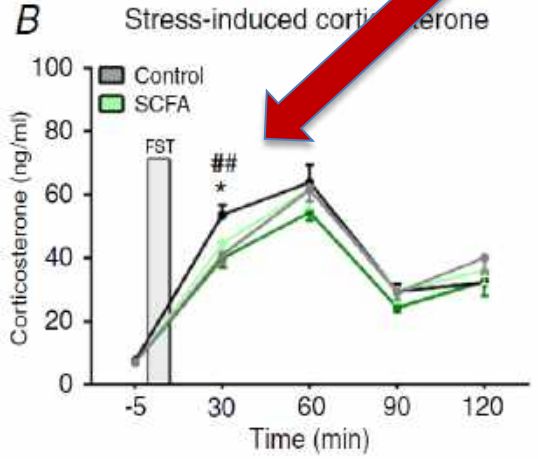
Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain–gut axis alterations

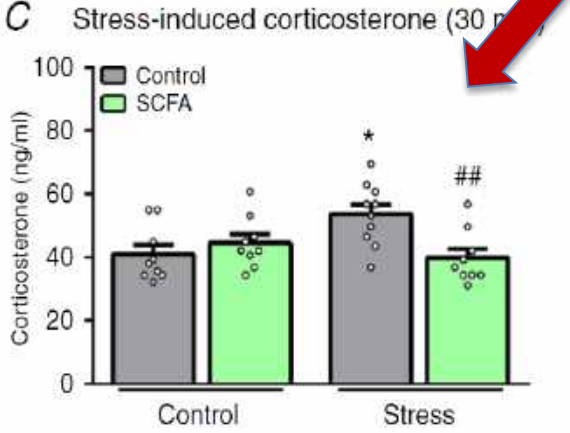
Marcel van de Wouw[1,2], Marcus Boehme[2], Joshua M. Lyte[2], Niamh Wiley[2,4], Conall Strain[2,4], Orla O'Sullivan[2,4], Gerard Clarke[2,3], Catherine Stanton[2,4], Timothy G. Dinan[2,3] and John F. Cryan[1,2,3]

[1]*Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland*
[2]*APC Microbiome Ireland, University College Cork, Cork, Ireland*
[3]*Department of Psychiatry and Neurobehavioral Science, University College Cork, Cork, Ireland*
[4]*Teagasc Food Research Centre, Moorepark, Fermoy, Cork, Ireland*









Cryan et al., Trends Pharmacol Sci, 2002

Physiology & Behavior 223 (2020) 113004

Contents lists available at ScienceDirect

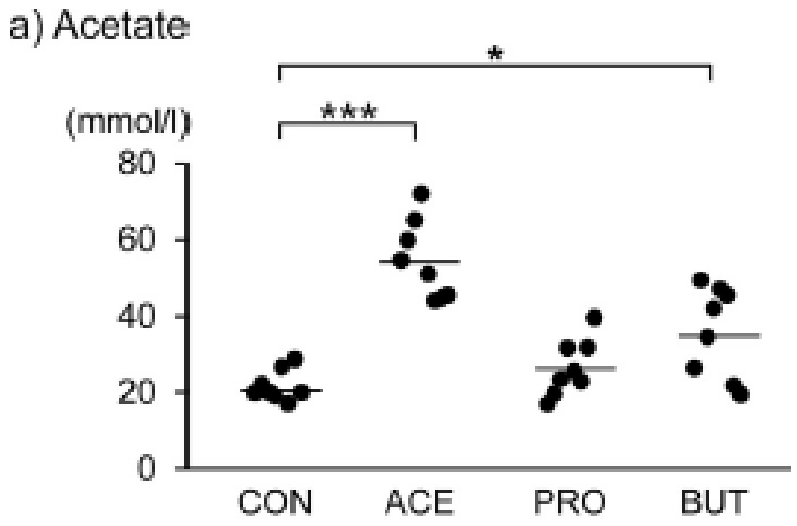
Physiology & Behavior

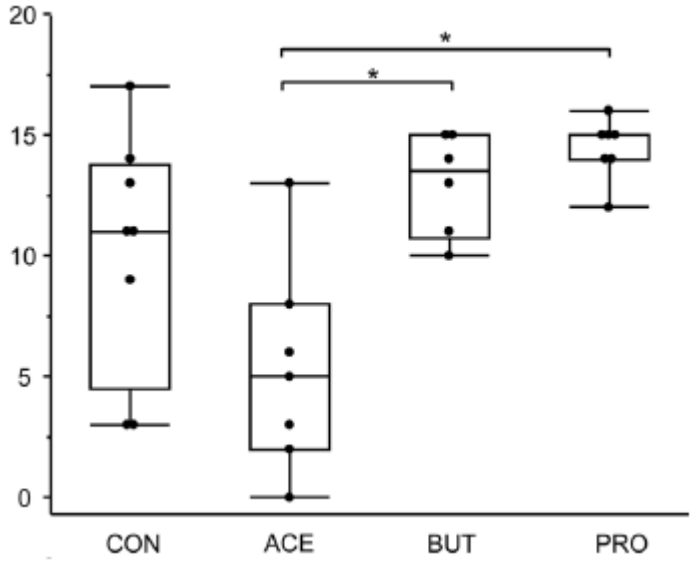
journal homepage: www.elsevier.com/locate/physbeh

Dietary delivery of acetate to the colon using acylated starches as a carrier exerts anxiolytic effects in mice

Tae Kimura-Todani[a], Tomokazu Hata[a], Noriyuki Miyata[a], Shu Takakura[a], Kazufumi Yoshihara[a], Xue-Ting Zhang[a], Yasunari Asano[a], Altanzul Altaisaikhan[a], Takamitsu Tsukahara[b], Nobuyuki Sudo[a,*]

[a] Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[b] Kyoto Institute of Nutrition & Pathology, Kyoto, Japan





Anxiety-like behaviours reduced by targeted increase of acetate in colon using aceylated starch

Neuropsychopharmacology

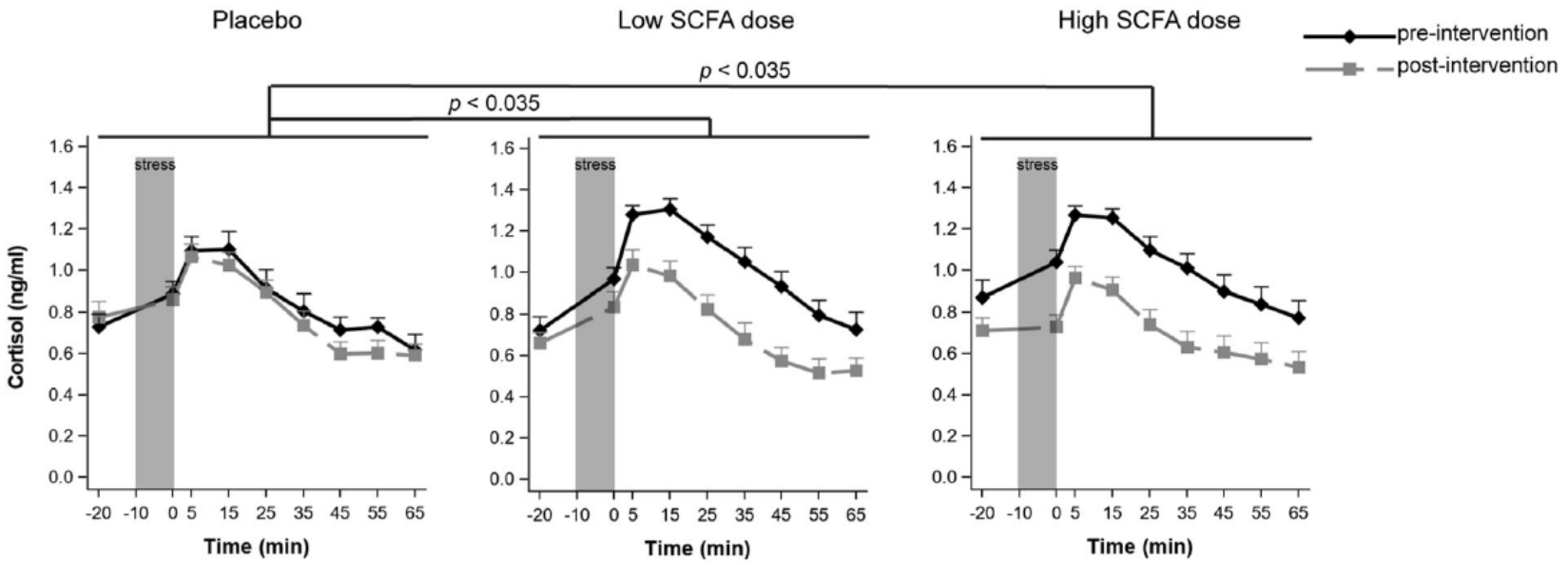
Neuropsychopharmacology (2020) 0:1 – 10

www.nature.com/npp

ARTICLE

Colon-delivered short-chain fatty acids attenuate the cortisol response to psychosocial stress in healthy men: a randomized, placebo-controlled trial

Boushra Dalile[1], Bram Vervliet[2], Gabriela Bergonzelli[3], Kristin Verbeke[1] and Lukas Van Oudenhove[1]

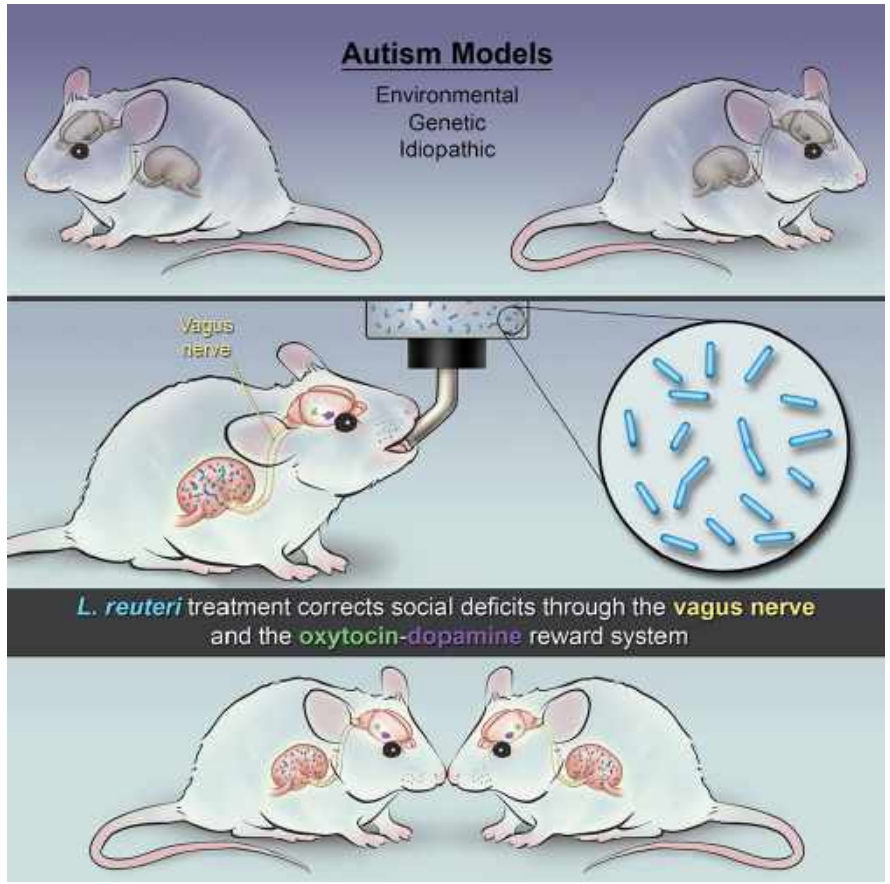


Neuron 101, 246–259, January 16, 2019

Neuron
Article

Mechanisms Underlying Microbial-Mediated Changes in Social Behavior in Mouse Models of Autism Spectrum Disorder

Martina Sgritta,[1,2] Sean W. Dooling,[1,2,3] Shelly A. Buffington,[1,2] Eric N. Momin,[4] Michael B. Francis,[1,2] Robert A. Britton,[5] and Mauro Costa-Mattioli[1,2,3,6,*]



Treatment with *L. reuteri* rescues social deficits in several ASD mouse models and in germ-free mice via the vagus nerve.

Translational Research

http://apc.ucc.ie

Gary Larson

ARTICLE IN PRESS

Annals of Epidemiology xxx (2016) 1–7

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Review article

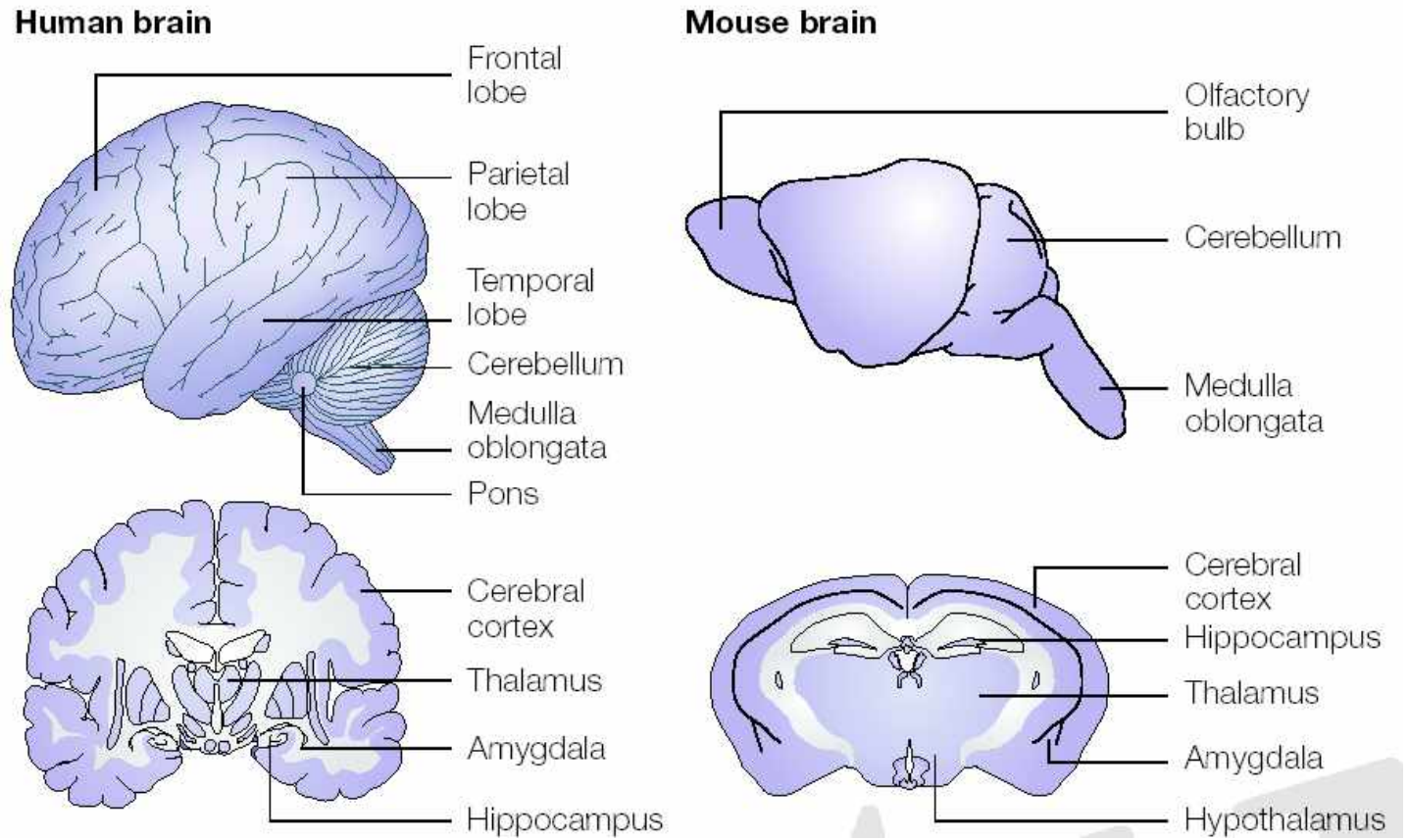
Brain-gut-microbiota axis: challenges for translation in psychiatry

John R. Kelly MD [a,b], Gerard Clarke PhD [a,b], John F. Cryan PhD [a,c], Timothy G. Dinan MD, PhD [a,b,*]

[a] Alimentary Pharmabiotic Centre, APC Microbiome Institute, University College Cork, Cork, Ireland
[b] Department of Psychiatry and Neurobehavioural Science, University College Cork, Cork, Ireland
[c] Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

Cryan et al., Trends in Pharmacol. Sci. 2002

Human vs Mouse Brain



Cryan and Holmes, *Nature Rev Drug Discov. Sept 2005*

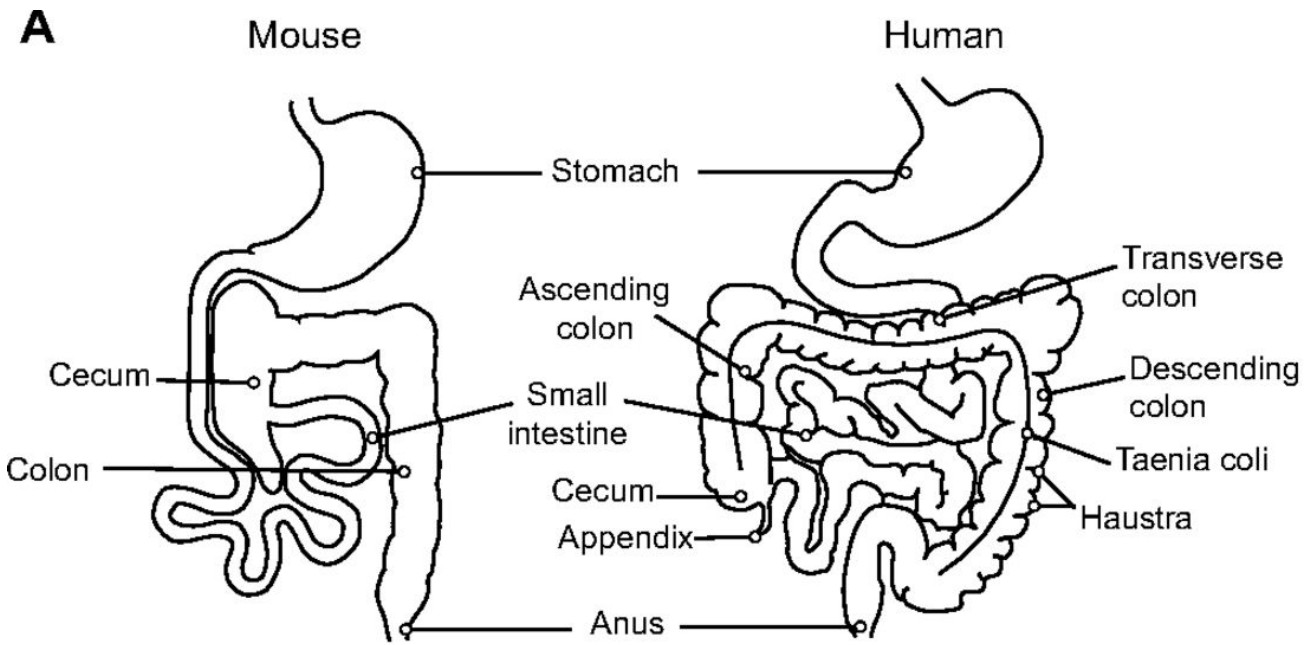
Human vs Mouse GI Tract

© 2015. Published by The Company of Biologists Ltd | Disease Models & Mechanisms (2015) 8, 1-16 doi:10.1242/dmm.017400

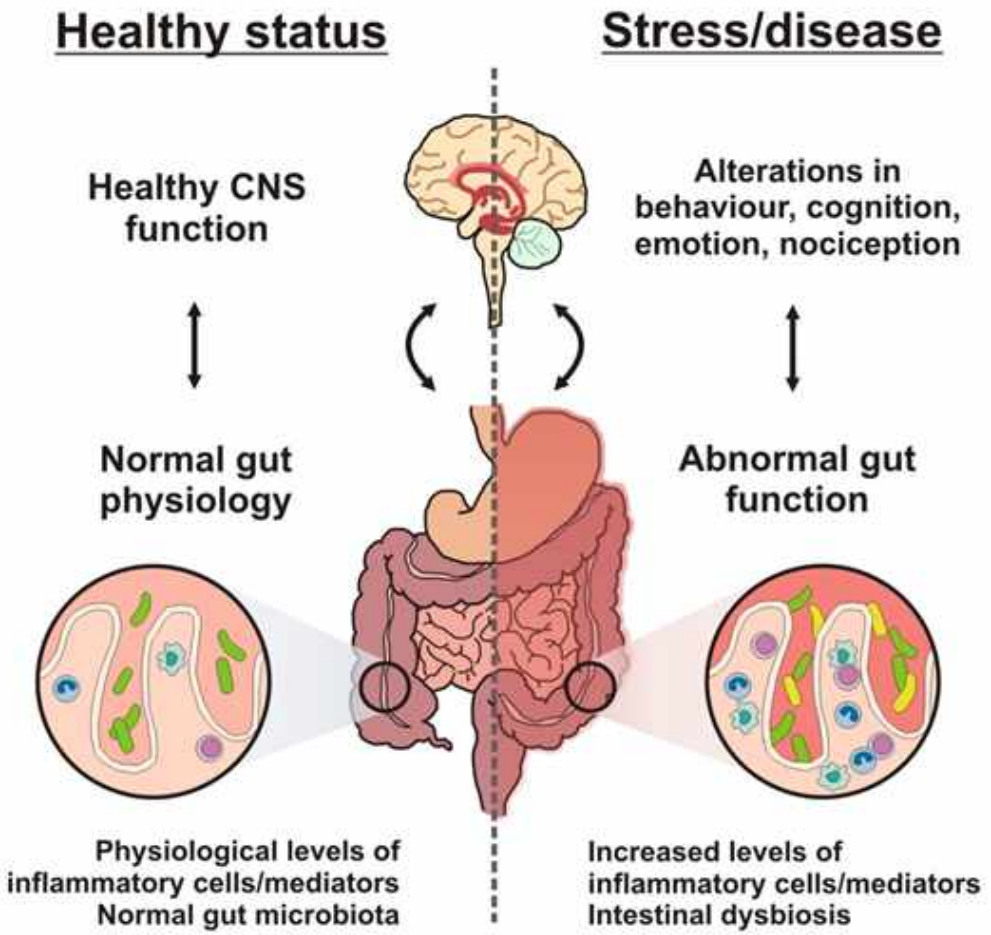
SPECIAL ARTICLE

How informative is the mouse for human gut microbiota research?

Thi Loan Anh Nguyen[1,2,3,*], Sara Vieira-Silva[1,2,3,*], Adrian Liston[1,2] and Jeroen Raes[1,2,3,‡]



Microbiota-Gut-Brain Axis

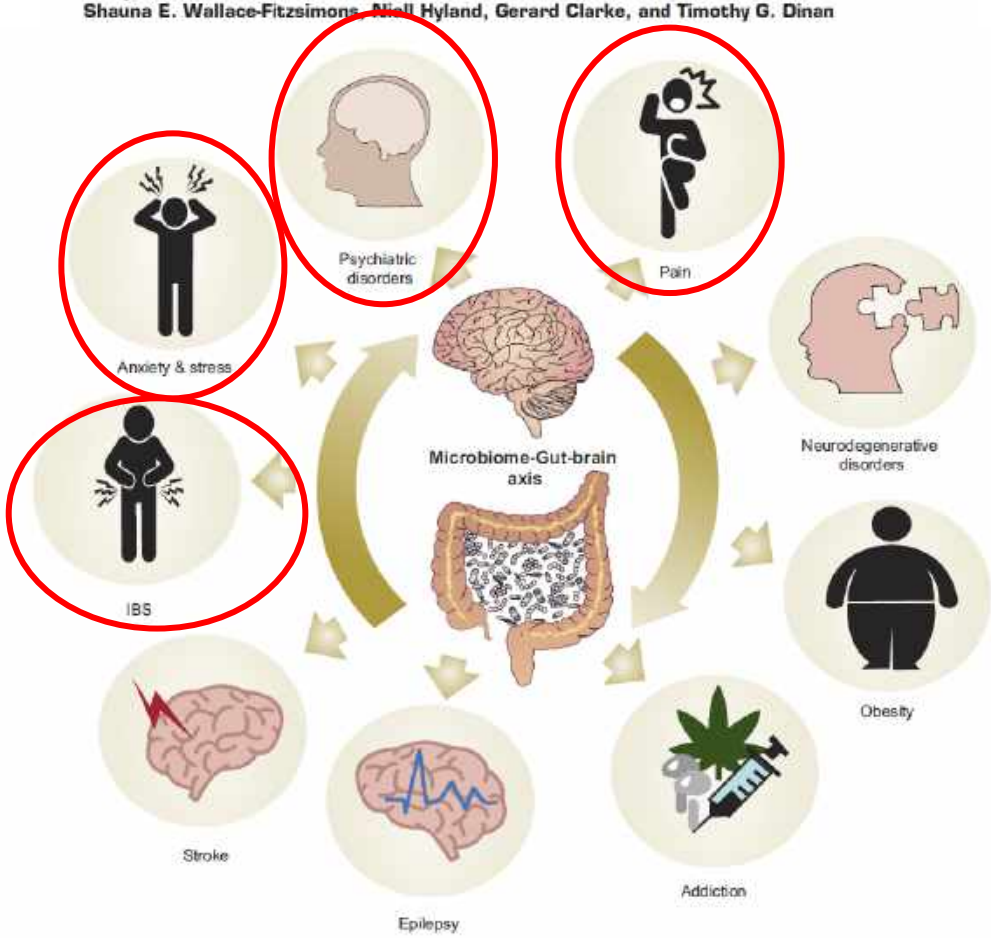


Grenham, Clarke et al., Frontiers in Physiology 2011

Physiol Rev 99: 1877–2013, 2019
Published August 28, 2019; doi:10.1152/physrev.00018.2018

THE MICROBIOTA-GUT-BRAIN AXIS

John F. Cryan, Kenneth J. O'Riordan, Caitlin S. M. Cowan, Kiran V. Sandhu, Thomaz F. S. Bastiaanssen, Marcus Boehme, Martin G. Codagnone, Sofia Cussotto, Christine Fulling, Anna V. Golubeva, Katherine E. Guzzetta, Minal Jaggar, Caitriona M. Long-Smith, Joshua M. Lyte, Jason A. Martin, Alicia Molinero-Perez, Gerard Moloney, Emanuela Morelli, Enrique Morillas, Rory O'Connor, Joana S. Cruz-Pereira, Veronica L. Peterson, Kieran Rea, Nathaniel L. Ritz, Eoin Sherwin, Simon Spichak, Emily M. Teichman, Marcel van de Wouw, Ana Paula Ventura-Silva, Shauna E. Wallace-Fitzsimons, Niall Hyland, Gerard Clarke, and Timothy G. Dinan



PRIMEVIEW

MAJOR DEPRESSIVE DISORDER

nature REVIEWS DISEASE PRIMERS

For the Primer, visit doi:10.1038/nrdp.2016.65

Major depressive disorder (MDD) is a psychiatric condition that is characterized by persistent depressed mood, diminished interests, impaired cognitive function and vegetative symptoms, such as disturbed sleep or appetite.

MECHANISMS

No mechanism can explain all aspects of MDD, although several models are available that explain aspects of the disease and implicated pathways. For example, one explanation for MDD is that — against a backdrop of genetic vulnerability — stress, particularly in early life, results in persistent increases in the activity of the hypothalamic–pituitary–adrenal (HPA) axis, which produces cortisol and other hormones. Coupled with inflammation, overactivity of the HPA axis might alter brain structure and function; reduced neurogenesis and neuroplasticity are thought to precipitate depression-like symptoms by impairing the stress response. Other factors that might have a role in the development and pathophysiology of MDD include reduced synaptic neurotransmission (for example, of serotonin), reduced volumes of certain brain regions (such as the hippocampus, which is involved in emotional regulation), increased connectivity and activation of the amygdala (which amplifies negative thoughts) and hyperconnectivity of the default mode network (which contributes to self-focus and rumination).

Designed by Neil Smith and Laura Marshall

DIAGNOSIS

MDD diagnosis requires the presence of at least five of the following symptoms in the same 2-week period

MDD is diagnosed when the symptoms cause considerable distress or impairment, cannot be attributed to another condition or substance use, and the individual has not had manic or hypomanic episodes

Specifiers can also be applied to further characterize the type of MDD, for example, MDD with melancholic or psychotic features

Depressed mood and/or diminished interest or pleasure must be evident for a diagnosis

EPIDEMIOLOGY

The 12-month prevalence of MDD has been estimated to be similar between high-income (5.5%) and low-income and middle-income (5.9%) countries, showing that MDD is a global health condition.

Women are more affected than men, with a median age of onset of approximately 25 years in both sexes. Individuals who experience childhood trauma not only have a more than twofold increased risk of MDD later in life but also have higher symptom severity, a poorer disease course and a greater likelihood of treatment non-responsiveness than those without early-life trauma.

MANAGEMENT

The treatment options for MDD centre on psychotherapy and pharmacotherapy. Psychotherapies available include cognitive, behavioural, psychodynamic, problem-solving, interpersonal and mindfulness-based approaches. All have been shown to be effective, although no differences between types are evident. Available pharmacotherapies largely target neurotransmitter receptors, reuptake transporters and oxidases that breakdown neurotransmitters once reabsorbed. Patients who are unresponsive to a given treatment can be given a different one or combinations of treatments (psychotherapies and pharmacotherapies).

QUALITY OF LIFE

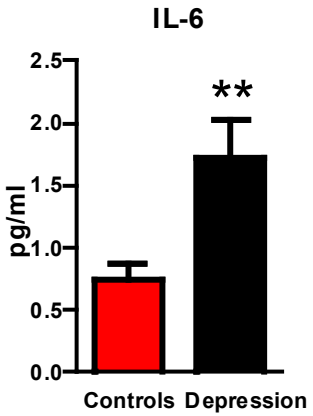
Although MDD negatively influences many domains of life, the most important concern for patients with MDD is suicide, the risk of which has been reported to be almost 20-fold higher than in the general population. Behavioural and psychosocial interventions to prevent suicide and suicide attempts have been shown to be effective. Furthermore, restricting access to and encouraging help-seeking at areas known to be 'suicide hotspots' (often used for suicides) might also be effective.

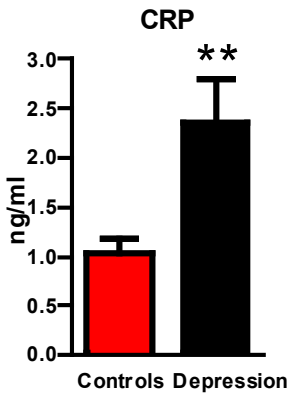
One in six individuals will experience MDD in their lifetime

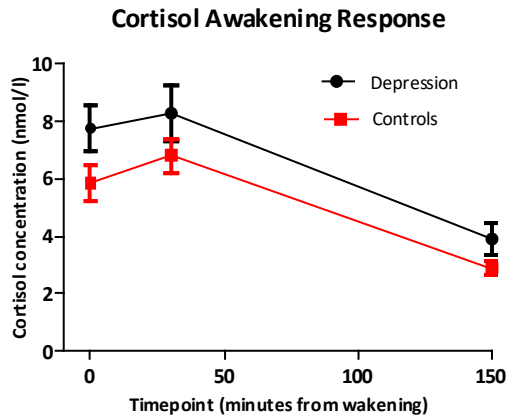
Article number: 16065; doi:10.1038/nrdp.2016.65; published online 15 Sep 2016

Neurobiology of Depression

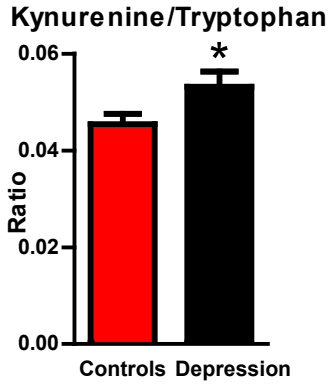
http://apc.ucc.ie

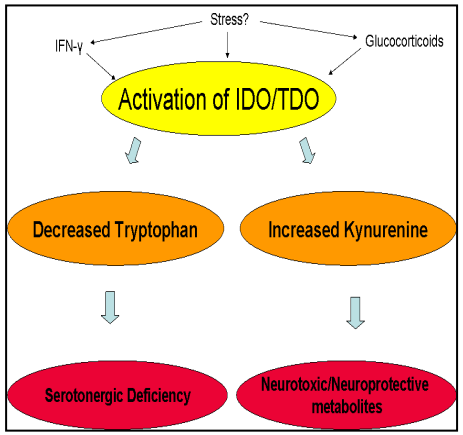






Immune activation and hyperactive HPA Axis





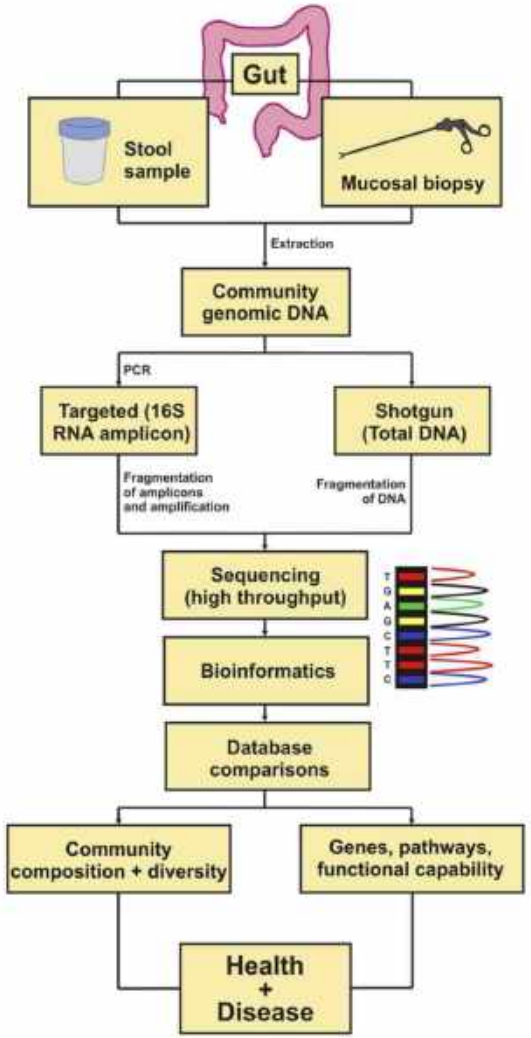
Alterations in tryptophan metabolism

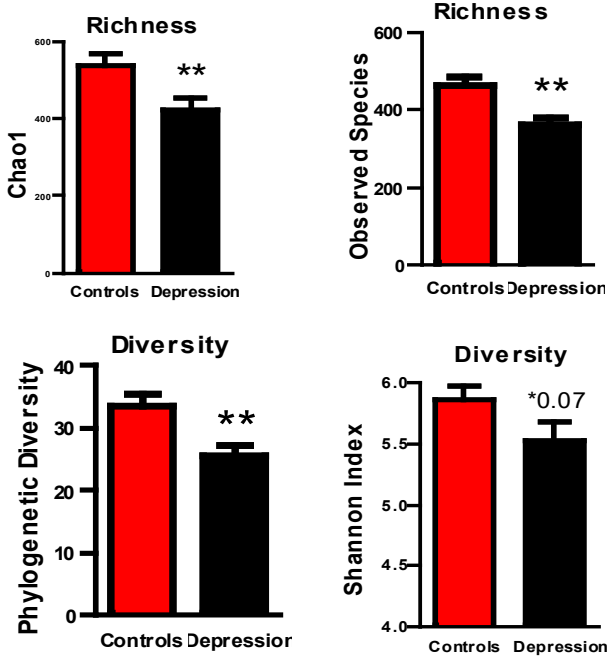
Kennedy et al., World J Gastro 2014

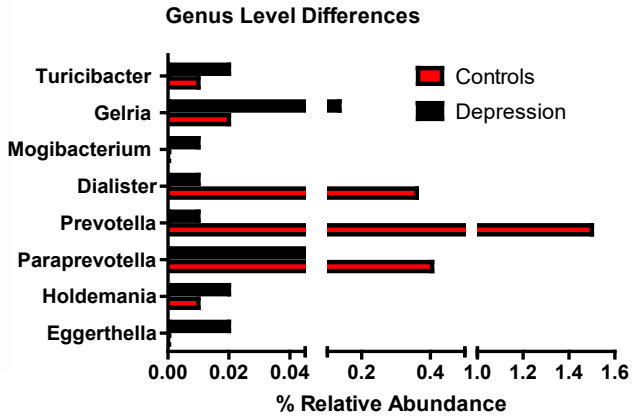
Kelly et al., J Psych Res 2016

Altered Microbiota in Depression

http://apc.ucc.ie





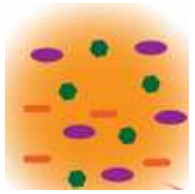


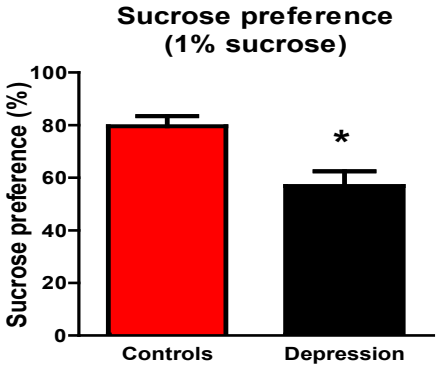
Reduced microbial diversity in depression

Prevotella, a genus of Gram-negative bacteria, is reduced in depression

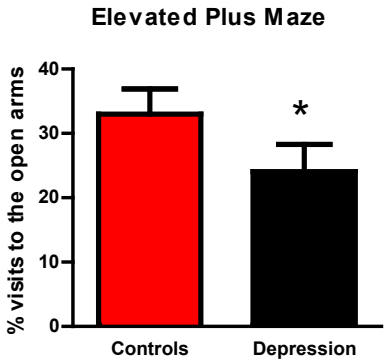
Kelly et al., J Psych Res 2016

Transfer of Depressive Phenotype

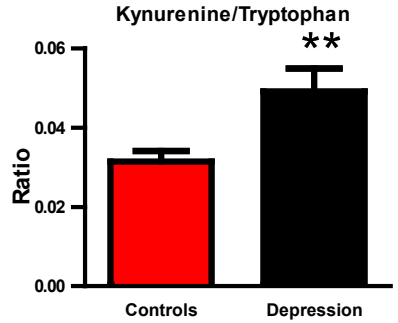


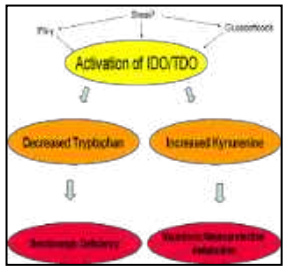


Anhedonia-like behaviours transferred via gut microbiota



Anxiety-like behaviours transferred via gut microbiota





Tryptophan metabolism Profile transferred via gut microbiota

Kelly et al., J Psych Res 2016

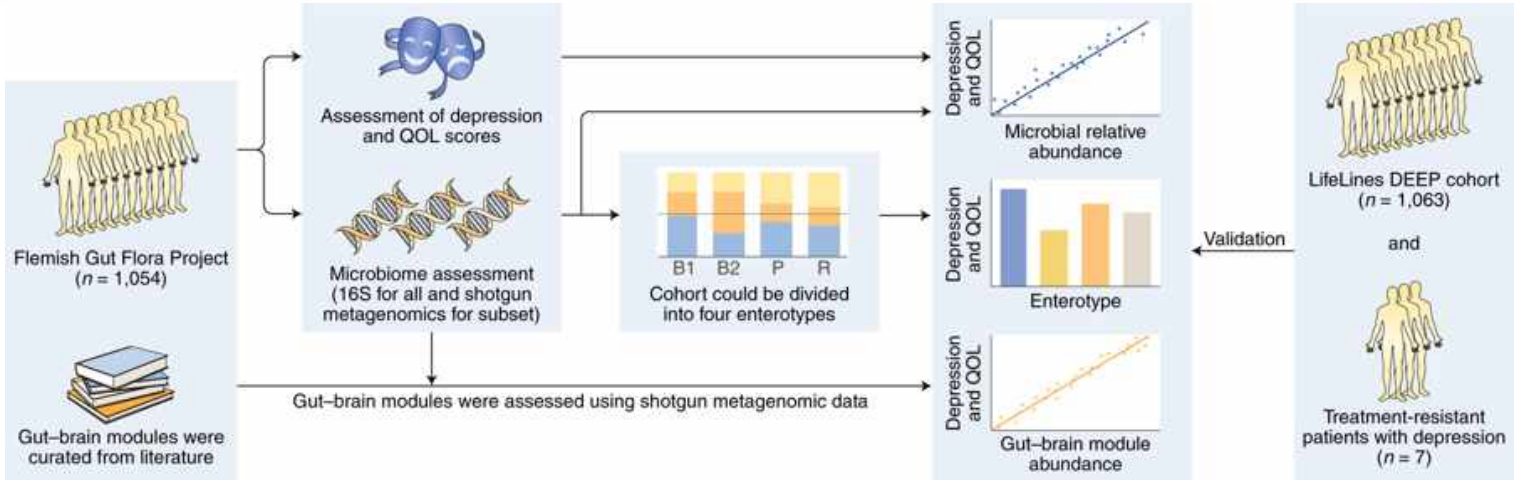
nature microbiology

ARTICLES

https://doi.org/10.1038/s41564-018-0337-x

The neuroactive potential of the human gut microbiota in quality of life and depression

Mireia Valles-Colomer[1,2], Gwen Falony[1,2], Youssef Darzi[1,2], Ettje F. Tigchelaar[3], Jun Wang[1,2], Raul Y. Tito[1,2,4], Carmen Schiweck[5], Alexander Kurilshikov[3], Marie Joossens[1,2], Cisca Wijmenga[3,6], Stephan Claes[5,7], Lukas Van Oudenhove[7,8], Alexandra Zhernakova[3], Sara Vieira-Silva[1,2,9] and Jeroen Raes[1,2,9*]



Dinan and Cryan, Nature Microbiology 2019

Irritable Bowel Syndrome

http://apc.ucc.ie

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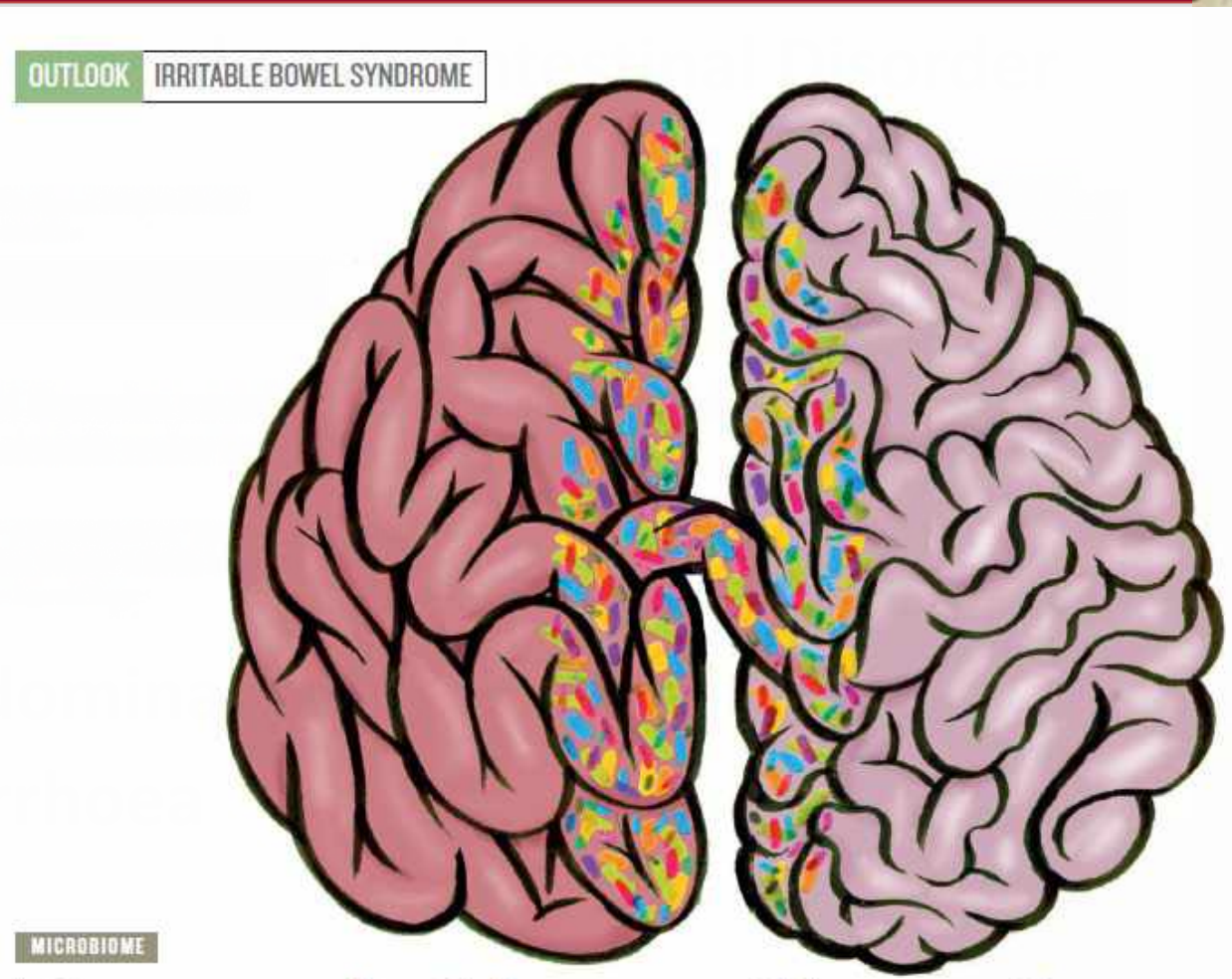
DOI 10.100

ORIGIN

Anxiet
(IBS):

Guillaum
Aroldo D
Marion L



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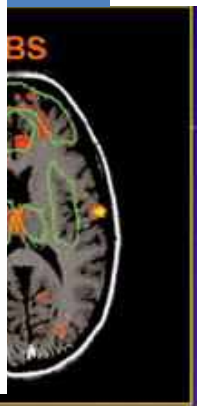


Mertz et al., Gastroenterology 2000

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

GUT MICROBIOTA

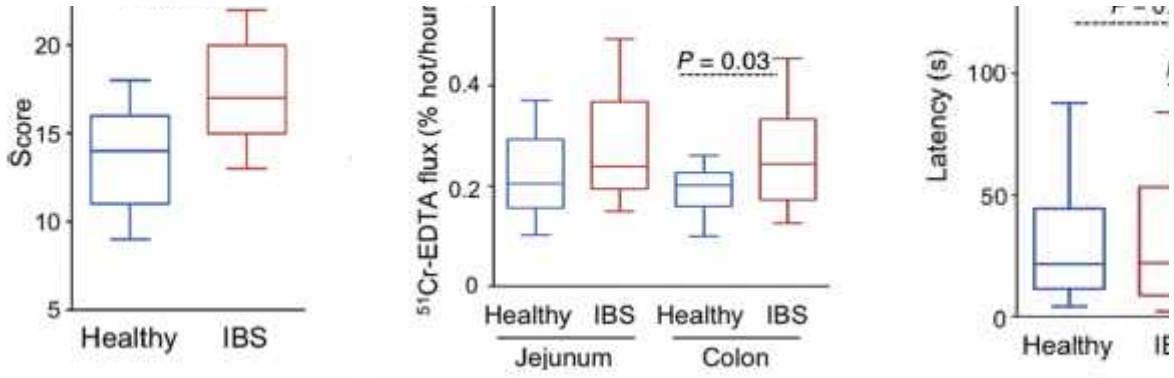
Transplantation of fecal microbiota from patie irritable bowel syndrome alters gut function a behavior in recipient mice

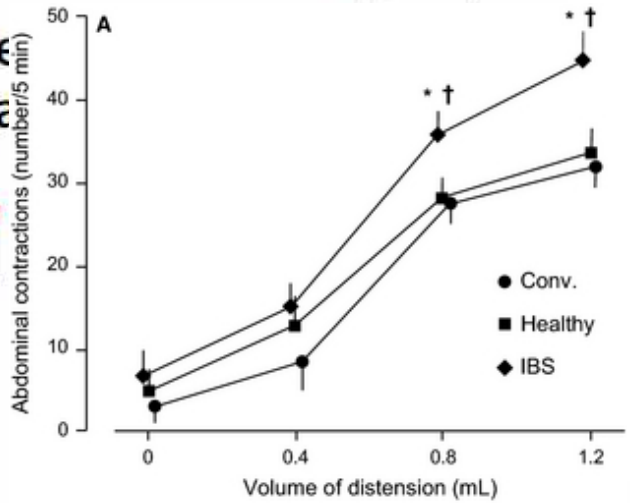
Neurogastroenterology & Motility

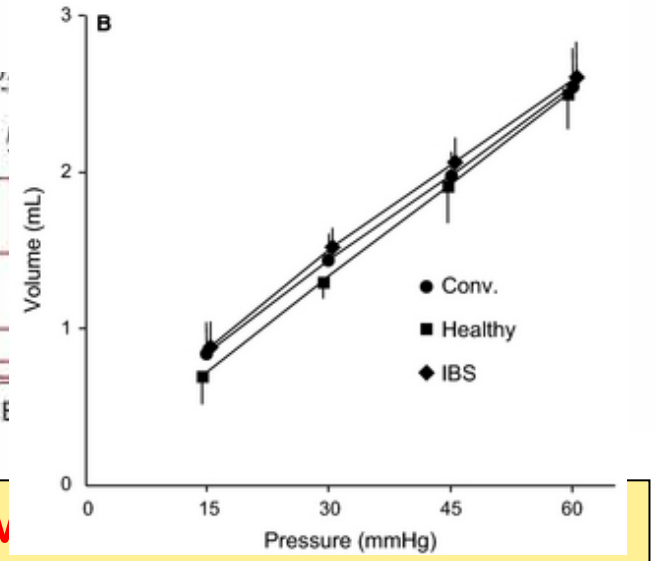
Neurogastroenterol Motil (2013) **25**, e272–e282 doi: 10.1111/nmo.12103

The hypersensitivity to colonic distension of IBS patients can be transferred to rats through their fecal microbiota

L. CROUZET,* E. GAULTIER,† C. DEL'HOMME,* C. CARTIER,† E. DELMAS,* M. DAPOIGNY,‡ J. FIORAMONTI† & A. BERNALIER-DONADILLE*







Only the microbiota from IBS subjects v induced anxiety-like behaviours in the recipient animals

Acute Stress Challenges - TSST

A) Key Procedural Stages:

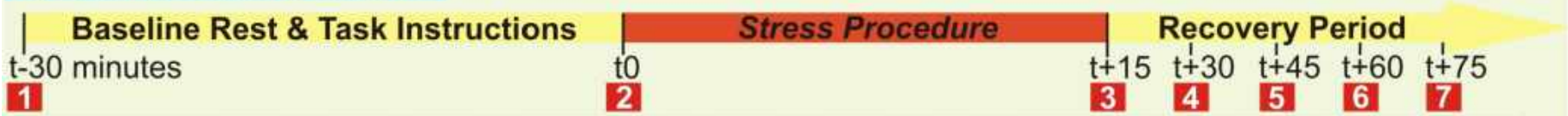
1. Baseline Rest
Following baseline sample collections participant rests quietly alone in **Room A**

2. Task Instructions
"Imagine you have applied for your ideal job for which you must convince the committee members why you are the perfect candidate"

3. Stress Procedure
In Room B:
- 3 Minute Preparation
- 5 Minute Speech
- 5 Minute Mental Arithmetic

4. Recovery Period
Participant returns to **Room A** for recovery and further measures are collected

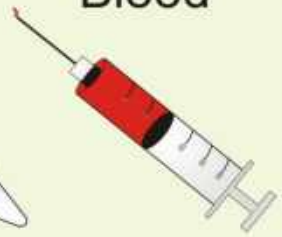
B) Example Sampling Schedule:



C) Measures:

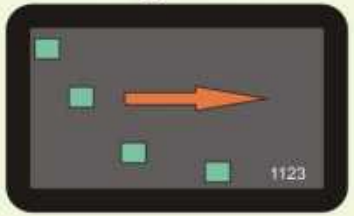
Saliva

Blood



Psychophysiological

Cognitive



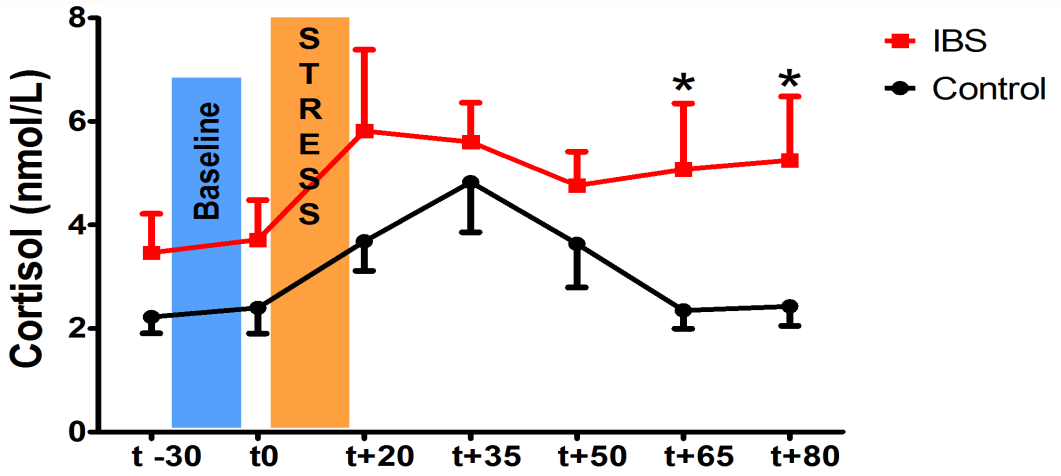
Psychometric

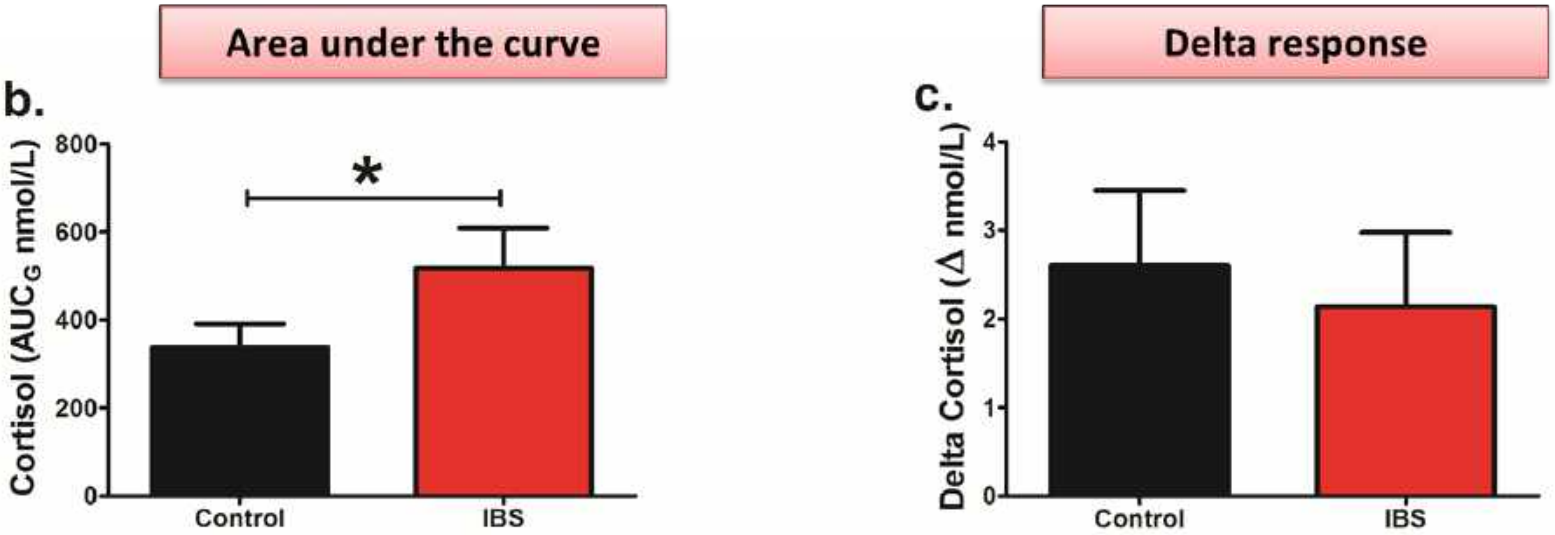
Psychological Medicine, Page 1 of 12. © Cambridge University Press 2014
doi:10.1017/S0033291714000552X

ORIGINAL ARTICLE

A sustained hypothalamic–pituitary–adrenal axis response to acute psychosocial stress in irritable bowel syndrome

P. J. Kennedy[1,2], J. F. Cryan[1,3], E. M. M. Quigley[1,4], T. G. Dinan[1,2] and G. Clarke[1,2]*





Cognitive Neurobiology of IBS

Neuroscience and Biobehavioral Reviews 36 (2012) 310–340

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

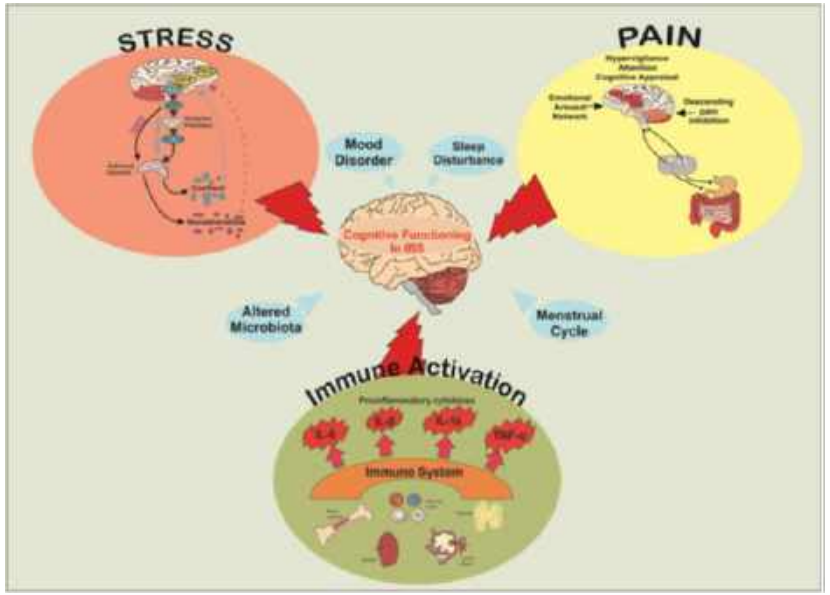
journal homepage: www.elsevier.com/locate/neubiorev

Review

Gut memories: Towards a cognitive neurobiology of irritable bowel syndrome

Paul J. Kennedy[a,c], Gerard Clarke[a,c], Eamonn M.M. Quigley[a,d], John A. Groeger[e], Timothy G. Dinan[a,c], John F. Cryan[a,b,*]

Can modulation of the gut microbiota affect cognitive performance in humans?



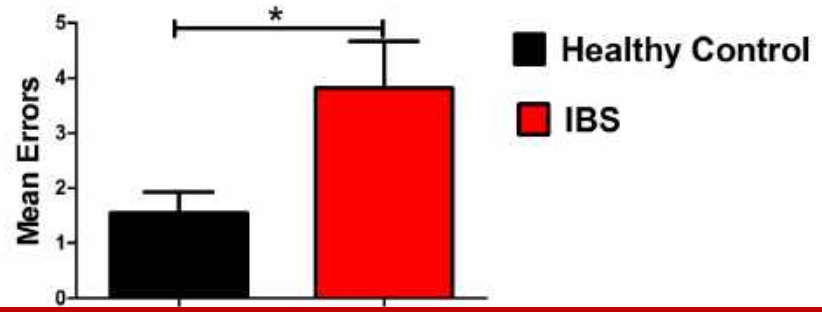
Psychological Medicine, Page 1 of 14. © Cambridge University Press 2013
doi:10.1017/S0033291713002171

ORIGINAL ARTICLE

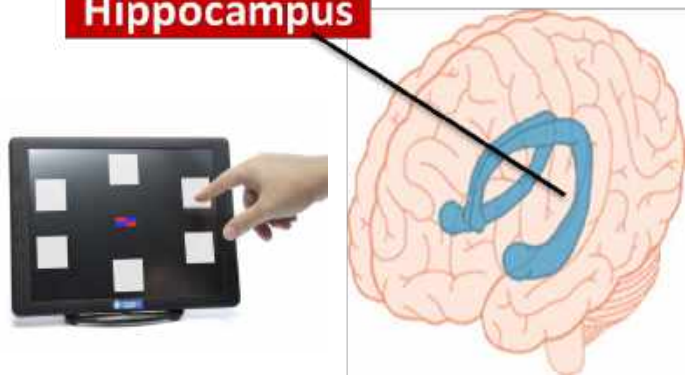
Cognitive performance in irritable bowel syndrome: evidence of a stress-related impairment in visuospatial memory

P. J. Kennedy[1,2], G. Clarke[1,2], A. O'Neill[1], J. A. Groeger[3], E. M. M. Quigley[1,4], F. Shanahan[1,4], J. F. Cryan[1,5] and T. G. Dinan[1,2]*

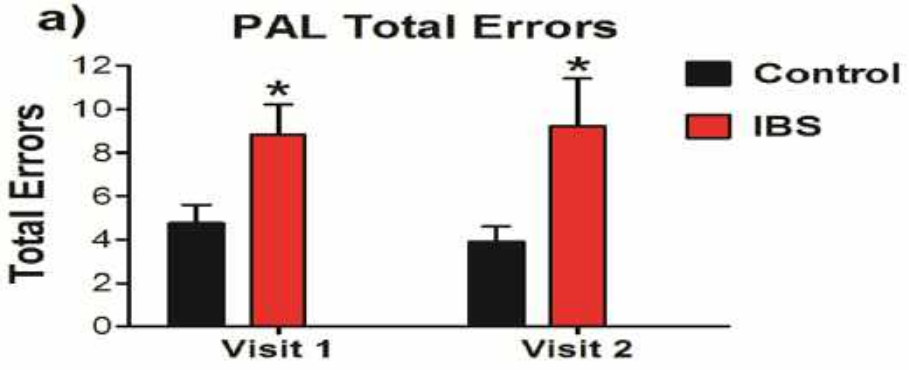
Baseline: Visuospatial memory deficit



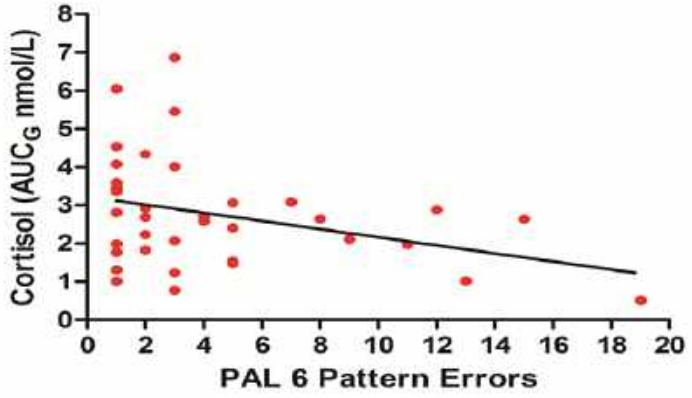
Hippocampus



6 & 12 months: Consistent memory deficit



Cortisol levels related to cognition



frontiers in PHARMACOLOGY

ORIGINAL RESEARCH ARTICLE
published: 21 May 2012
doi: 10.3389/fphar.2012.00090

A distinct profile of tryptophan metabolism along the kynurenine pathway downstream of toll-like receptor activation in irritable bowel syndrome

Gerard Clarke[1,2], Declan P. McKernan[4], Gabor Gaszner[3], Eamonn M. Quigley[1,5], John F. Cryan[1,7] and Timothy G. Dinan[1,5]*

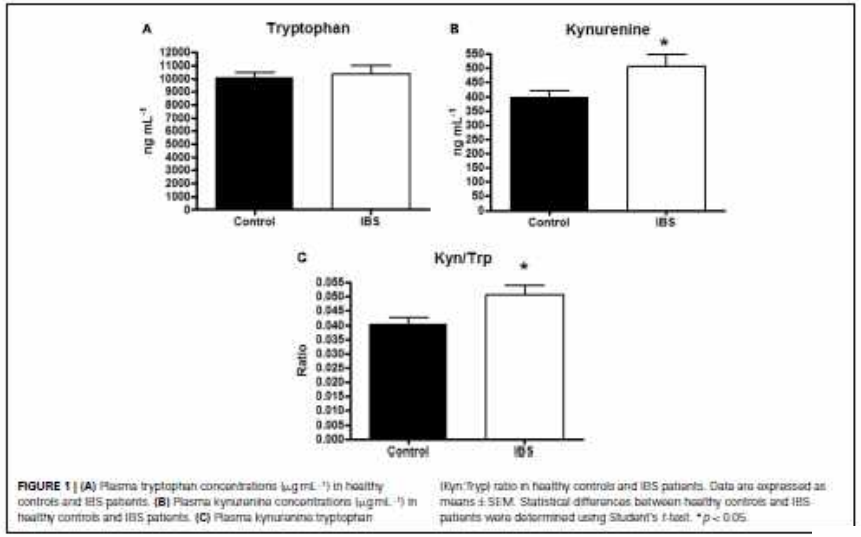


FIGURE 1 | (A) Plasma tryptophan concentrations (μg mL⁻¹) in healthy controls and IBS patients. (B) Plasma kynurenine concentrations (μg mL⁻¹) in healthy controls and IBS patients. (C) Plasma kynurenine:tryptophan (Kyn:Trypl ratio in healthy controls and IBS patients. Data are expressed as means ± SEM. Statistical differences between healthy controls and IBS patients were determined using Student's *t*-test. *$p < 0.05$

BMC Gastroenterology

BioMed Central

Research article

Open Access

Tryptophan degradation in irritable bowel syndrome: evidence of indoleamine 2,3-dioxygenase activation in a male cohort

Gerard Clarke*[1,2], Peter Fitzgerald†[1,2], John F Cryan†[2,3], Eugene M Cassidy†[1], Eamonn M Quigley†[2,4] and Timothy G Dinan†[1,2]

Address: [1]Department of Psychiatry, University College Cork, Cork, Ireland, [2]Alimentary Pharmabiotic Centre, University College Cork, Cork, Ireland, [3]Department of Pharmacology & Therapeutics, University College Cork, Cork, Ireland and [4]Department of Medicine, University College Cork, Cork, Ireland

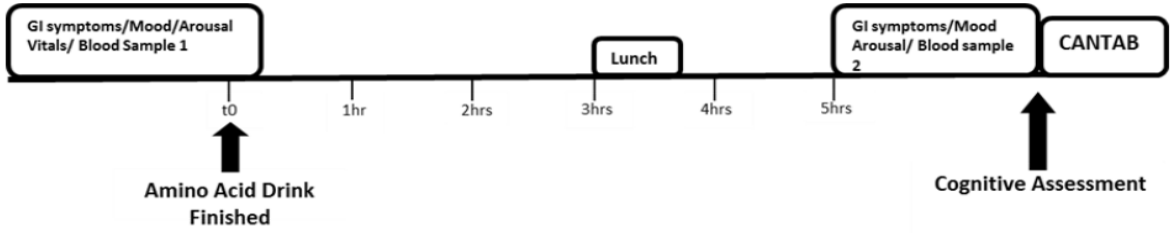
Neurogastroenterol Motil (2008) **20**, 1291–1297 doi: 10.1111/j.1365-2982.2008.01195.x

Tryptophan catabolism in females with irritable bowel syndrome: relationship to interferon-gamma, severity of symptoms and psychiatric co-morbidity

P. FITZGERALD,* M. CASSIDY EUGENE,* G. CLARKE,†,* P. SCULLY,†,* S. BARRY,* M. M. QUIGLEY EAMONN,† F. SHANAHAN,† J. CRYAN† & G. DINAN TIMOTHY†,*

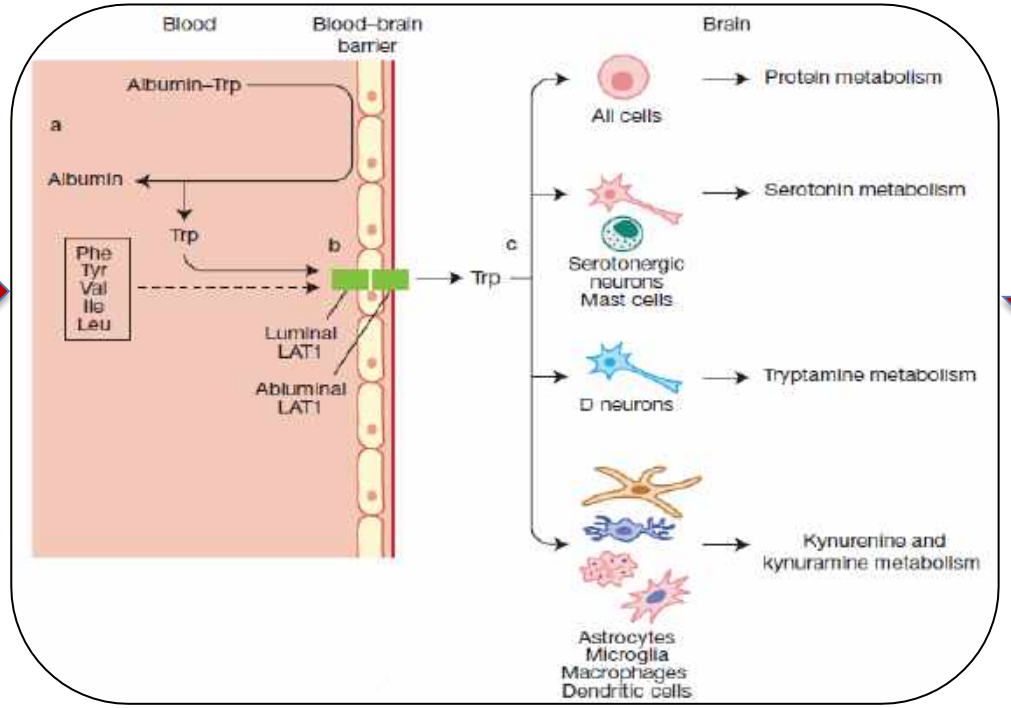
Acute tryptophan depletion (ATD)

http://apc.ucc.ie



Amino Acid Drink (no TRP)

L-Alanine
L-Argine
L-Cysteine
Glycine
L-Histidine
L-Isoleucine
L-Leucine
L Lysine
L-Methionine
L-Phenylalanine
L-Proline
L-Serine
L-Threonine
L-Thyrosine
L-Valine



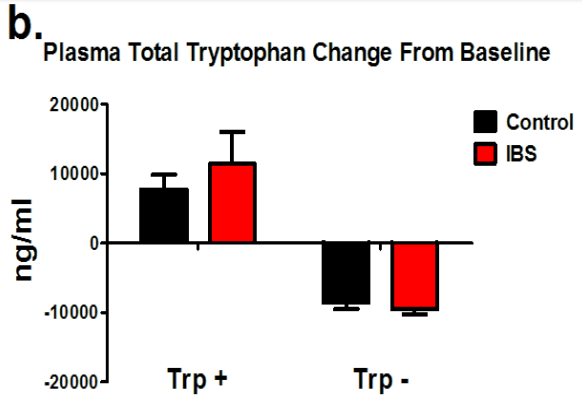
Brain levels: Kynurenine?

Tryptophan competes with other LNAAs to cross blood brain barrier

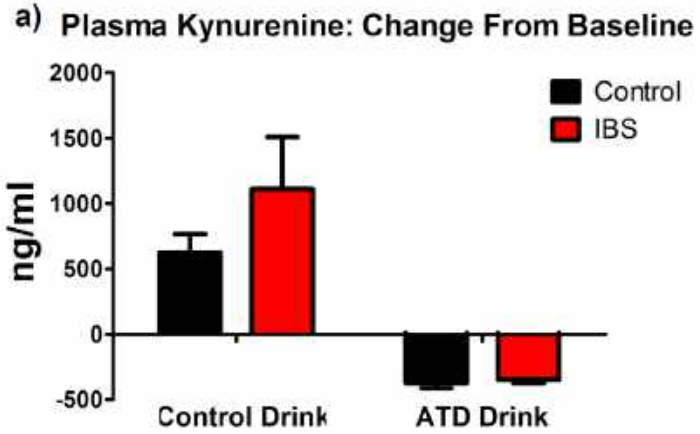
Ruddick et al., Expert Rev Mol Med (2006)

Reducing Kynurenine Improves Performance?

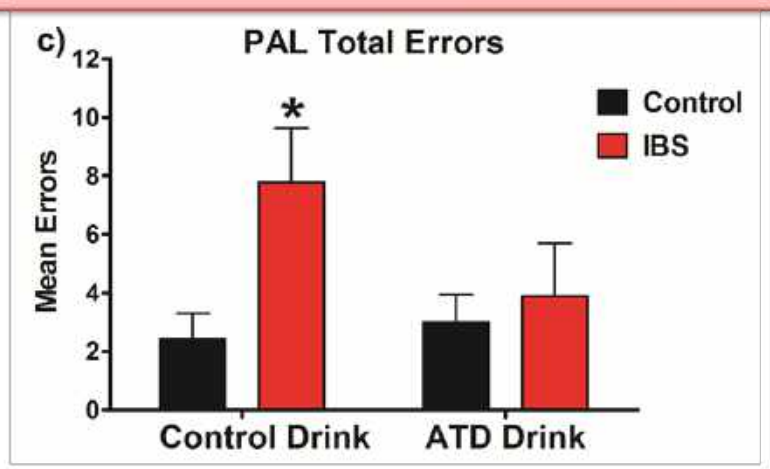
Acute tryptophan depletion significantly depletes plasma tryptophan levels



Acute tryptophan depletion significantly depletes plasma kynurenine levels



Acute tryptophan depletion *improves* visuospatial memory performance in irritable bowel syndrome (IBS)



Psychopharmacology
DOI 10.1007/s00213-014-3767-z

ORIGINAL INVESTIGATION

Acute tryptophan depletion reduces kynurenine levels: implications for treatment of impaired visuospatial memory performance in irritable bowel syndrome

Paul J. Kennedy · Andrew P. Allen · Ann O'Neill · Eamonn M. M. Quigley · John F. Cryan · Timothy G. Dinan · Gerard Clarke

AP&T Alimentary Pharmacology and Therapeutics

Review article: probiotics for the treatment of irritable bowel syndrome – focus on lactic acid bacteria

G. Clarke*,†, J. F. Cryan*,‡, T. G. Dinan*,† & E. M. Quigley*,§

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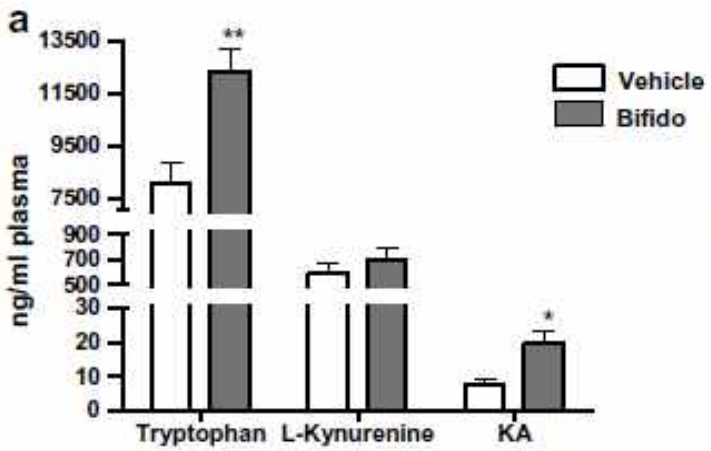
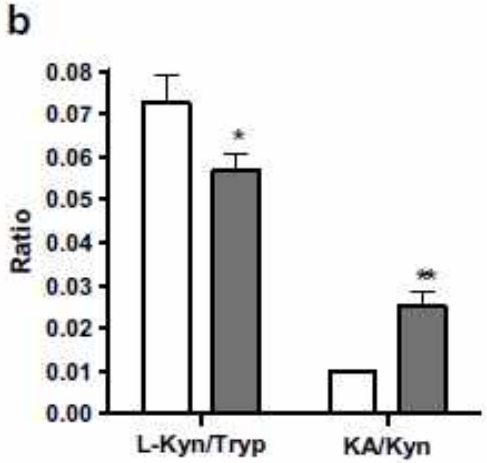
Available online at www.sciencedirect.com
ScienceDirect
Journal of Psychiatric Research 43 (2009) 164–174

JOURNAL OF PSYCHIATRIC RESEARCH
www.elsevier.com/locate/jpsychires

The probiotic *Bifidobacteria infantis*: An assessment of potential antidepressant properties in the rat

Lieve Desbonnet [a,*], Lillian Garrett [a], Gerard Clarke [a], John Bienenstock [b]
Timothy G. Dinan [a]





Camilleri M, Boeckxstaens G. *Gut* 2017;**66**:966–974. doi:10.1136/gutjnl-2016-313425

Dietary and pharmacological treatment of abdominal pain in IBS

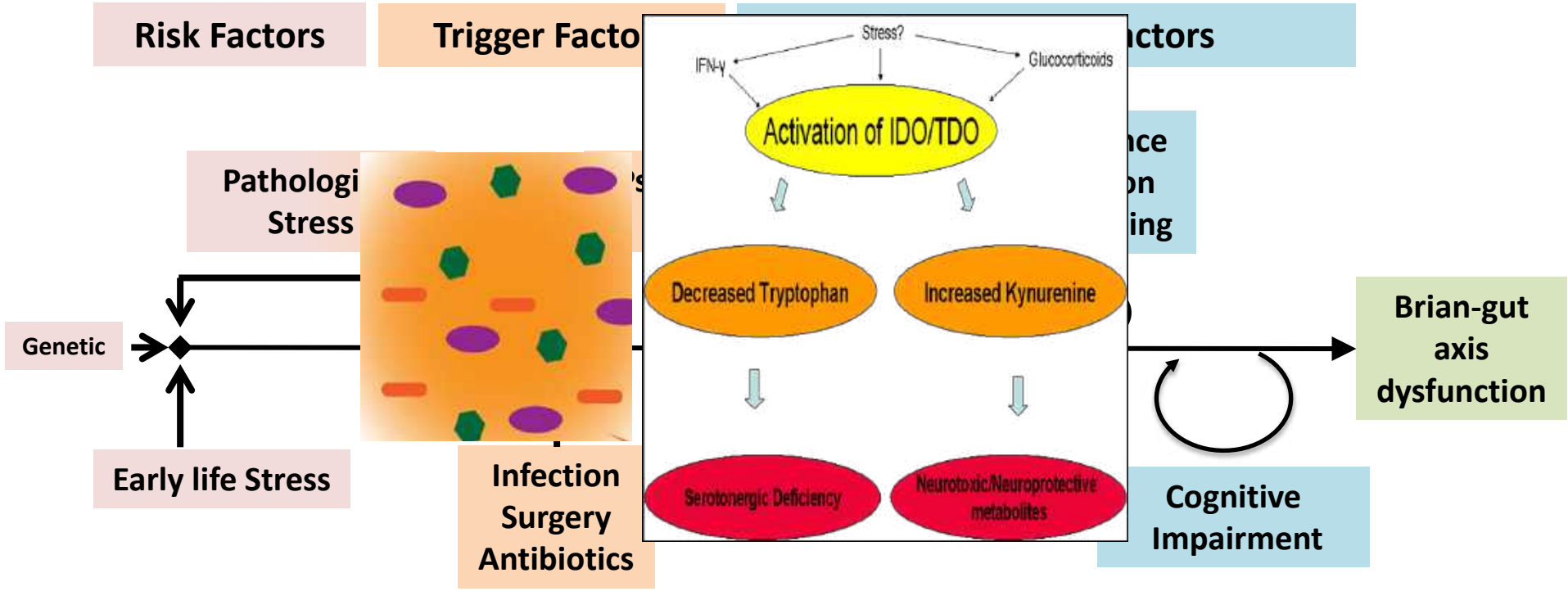
Michael Camilleri,[1] Guy Boeckxstaens[2]

Table 1 Efficacy of interventions on the relief of symptoms in IBS: relative risk (RR) or OR and CI based on systematic reviews and meta-analyses

Intervention	Parameter	RR or OR	Ref. #
Dietary or probiotics or antibiotics			
Bran, ispaghula and unspecified fibre	Abdominal pain	RR 0.87 (0.76 to 1.00)	21
Low FODMAP diet	Abdominal pain	OR 1.81 (1.13 to 2.88)	24
Probiotics	Global improvement	SEM: −0.25 (−0.36 to −0.14)	40
Probiotics: combination of *Escherichia coli* and *Enterococcus faecalis* or *E. coli* alone	Abdominal pain	RR 1.96 (1.14 to 3.36)	42 43
Rifaximin	Global improvement	OR 1.57 (1.22 to 2.01)	48
Rifaximin	Bloating	OR 1.55 (1.23 to 1.96)	48
Antispasmodics			
Peppermint oil	Global improvement	RR 2.23 (1.78 to 2.81)	70
Antidepressants			
Antidepressant therapy	Global improvement	RR 0.66 (0.57 to 0.78)	72
	Abdominal pain	RR 0.62 (0.43 to 0.88)	72
Antidepressant therapy	Global improvement	RR 0.67 (0.58 to 0.77)	73 74
Antidepressant therapy	Abdominal pain	RR 0.62 (0.43 to 0.88)	73 74
Drugs targeting specific GI receptors			
Alosetron	Abdominal pain and discomfort	RR 1.30 (1.22 to 1.39)	81
	Overall risk difference	0.13 (0.1 to 0.16)	81
Alosetron	Abdominal pain and discomfort	RR 1.23 (1.15 to 1.32)	82
	Global improvement	RR 1.5 (1.40 to 1.72)	82
Ondansetron	Adequate relief response	RR 4.7 (2.6 to 8.5)	86
Linaclotide	Adequate relief response	RR 1.95 (1.3 to 2.9)	94
	Abdominal pain	RR 1.58 (1.02 to 2.46)	94

FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyol.

An Updated Model of Brain-Gut Axis Dysfunction

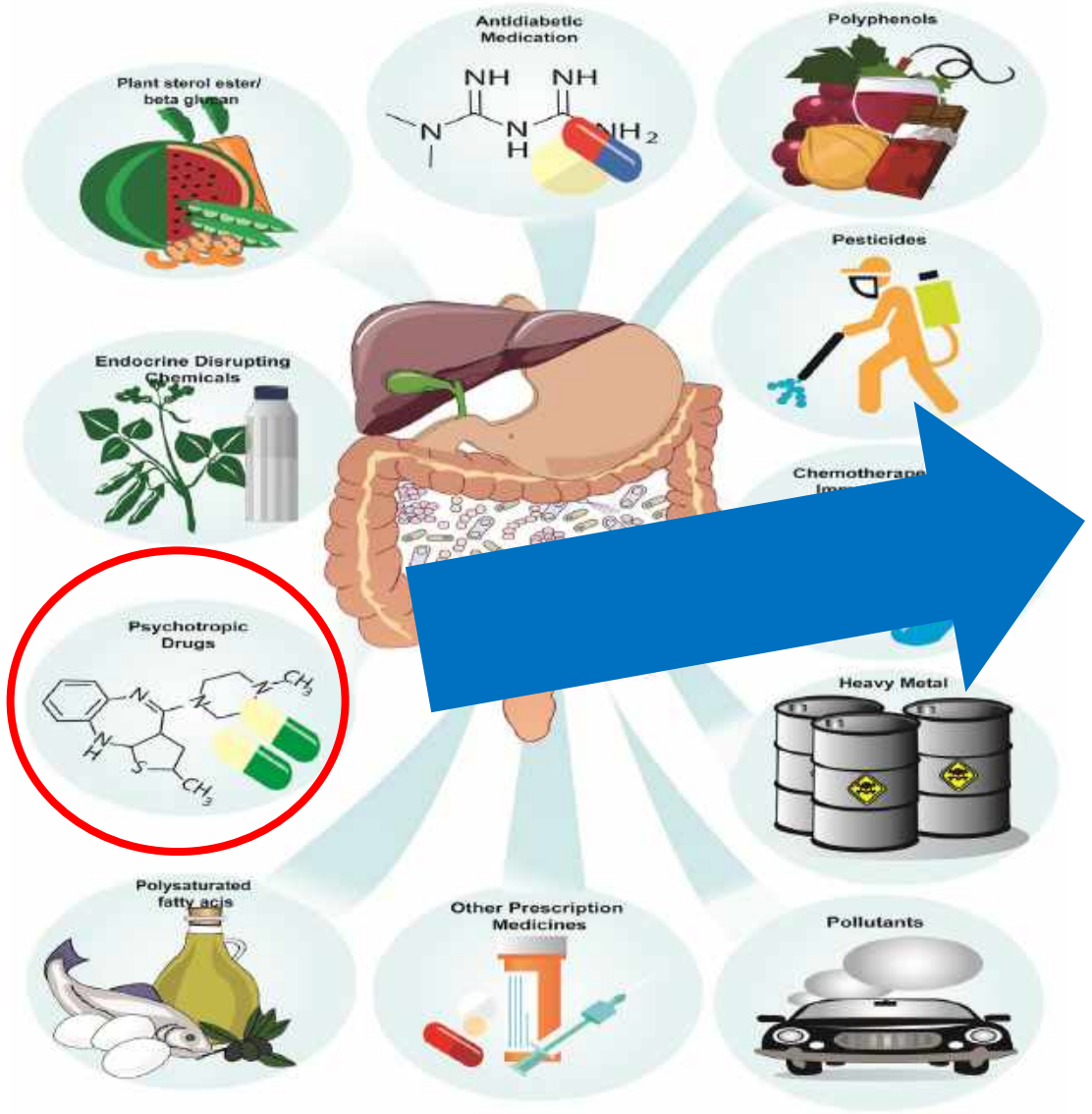


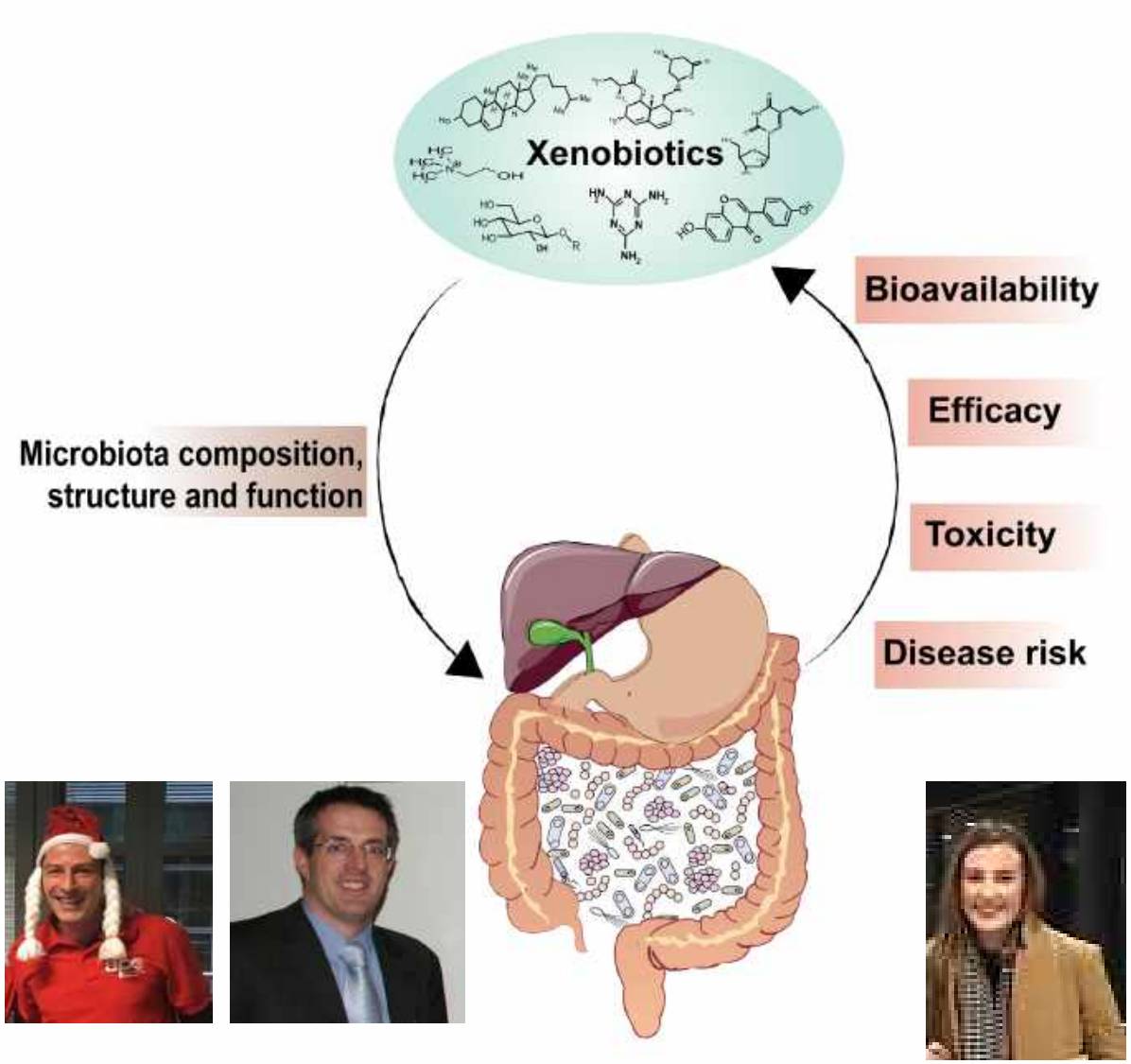
A cognitive neurobiological model of brain-gut axis dysfunction: Focus on IBS.

Adapted from: **Mayer E A et al.,** ***Am J Physiol Gastrointest Liver Physiol*** **(2001).**

Drug-Microbiome Interactions

http://apc.ucc.ie





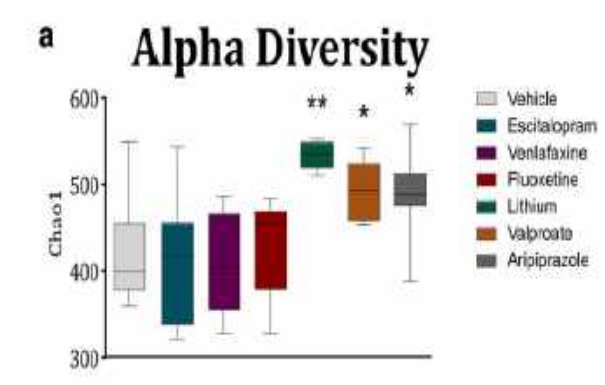
Clarke et al., Pharmacological Reviews 2019

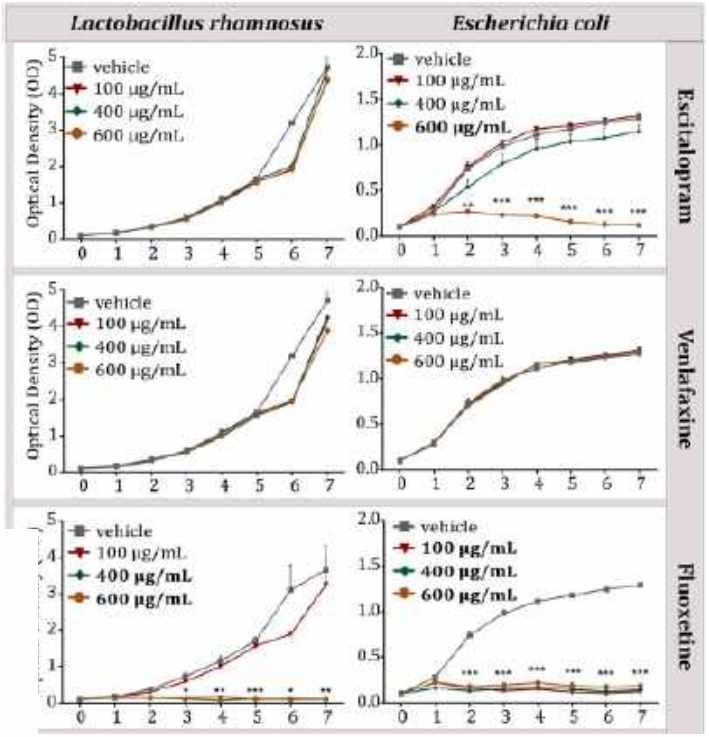
Psychopharmacology
https://doi.org/10.1007/s00213-018-5006-5

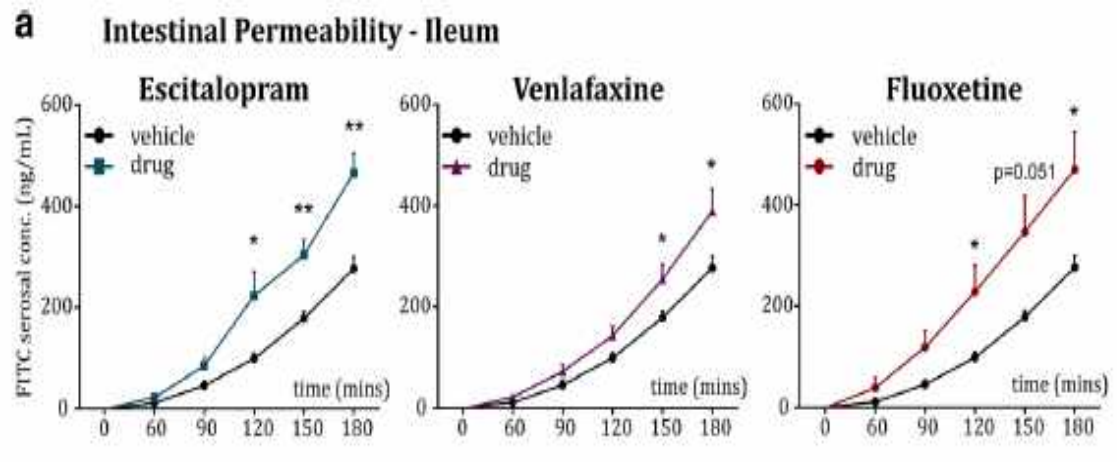
ORIGINAL INVESTIGATION

Differential effects of psychotropic drugs on microbiome composition and gastrointestinal function

Sofia Cussotto[1,2] · Conall R. Strain[1,3] · Fiona Fouhy[1,3] · Ronan G. Strain[1,3] · Veronica L. Peterson[1,2] · Gerard Clarke[1,4] · Catherine Stanton[1,3,4] · Timothy G. Dinan[1,4] · John F. Cryan[1,2]







ARTICLE

OPEN

Citation: Transl Psychiatry (2013) 3, e309; doi:10.1038/tp.2013.83

www.nature.com/tp

ORIGINAL ARTICLE

Antipsychotics and the gut microbiome: olanzapine-induced metabolic dysfunction is attenuated by antibiotic administration in the rat

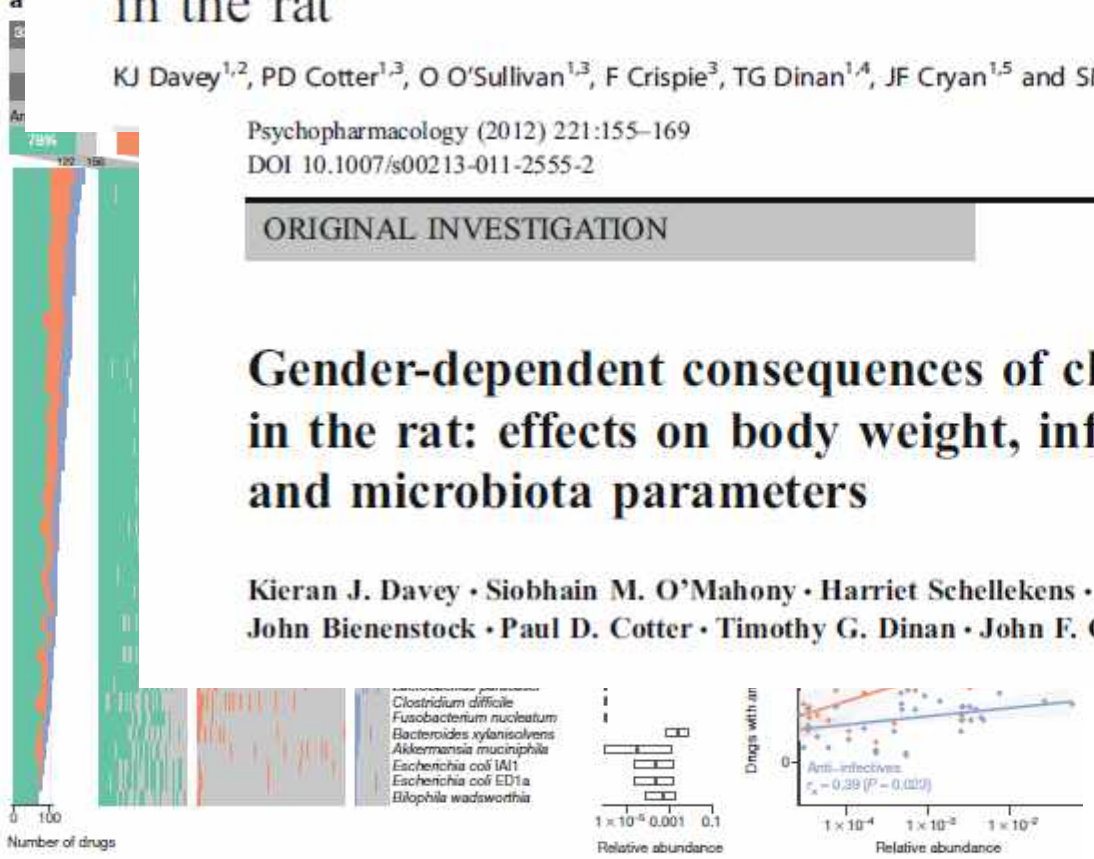
KJ Davey[1,2], PD Cotter[1,3], O O'Sullivan[1,3], F Crispie[3], TG Dinan[1,4], JF Cryan[1,5] and SM O'Mahony[1,5]

Psychopharmacology (2012) 221:155–169
DOI 10.1007/s00213-011-2555-2

ORIGINAL INVESTIGATION

Gender-dependent consequences of chronic olanzapine in the rat: effects on body weight, inflammatory, metabolic and microbiota parameters

Kieran J. Davey · Siobhain M. O'Mahony · Harriet Schellekens · Orla O'Sullivan · John Bienenstock · Paul D. Cotter · Timothy G. Dinan · John F. Cryan



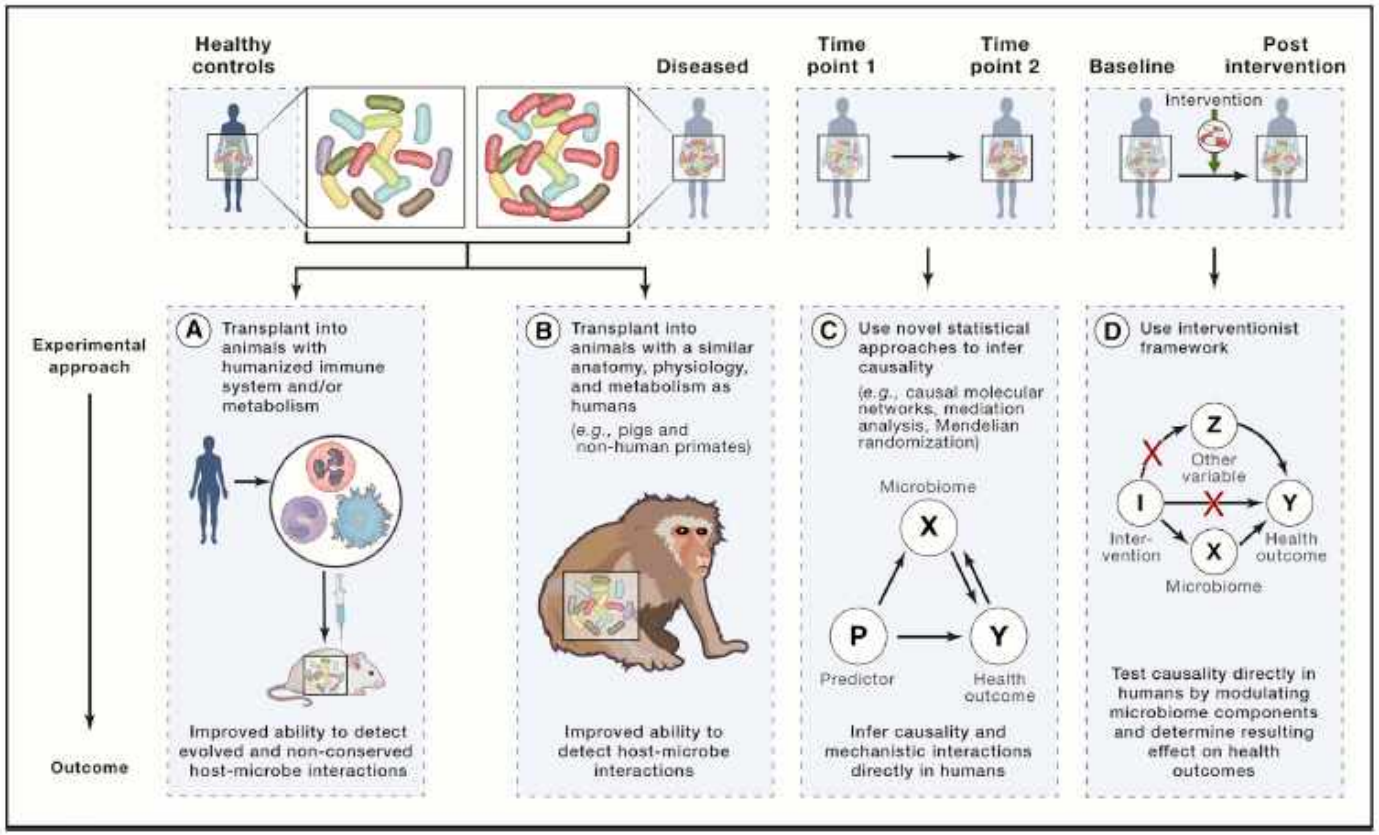
Cell 180, January 23, 2020

Leading Edge

Perspective

Establishing or Exaggerating Causality for the Gut Microbiome: Lessons from Human Microbiota-Associated Rodents

Jens Walter,[1,2,3,4,8,*] Anissa M. Armet,[1,8] B. Brett Finlay,[5,6,7] and Fergus Shanahan[3]



3 GOOD HEALTH AND WELL-BEING

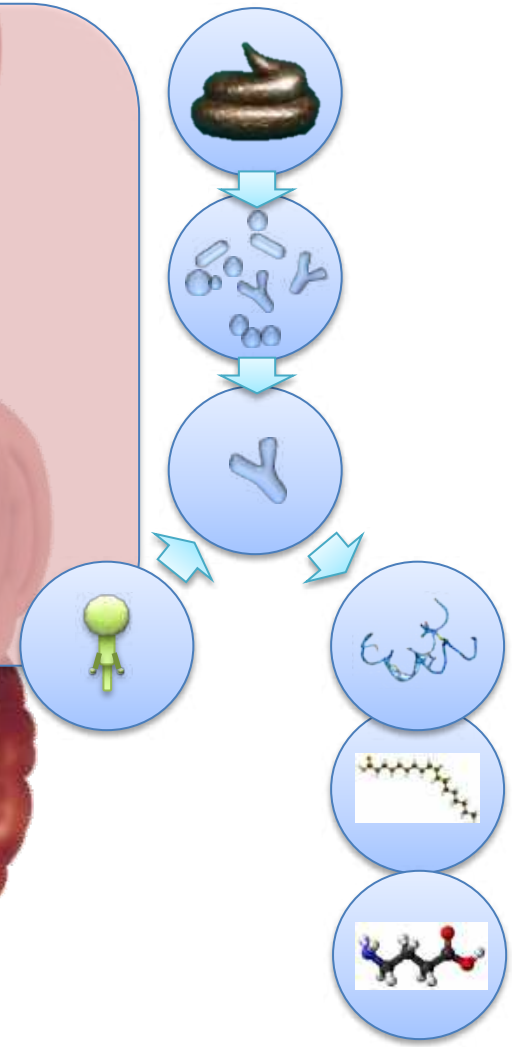
Are Gut Feelings the Real Deal?

Microbiome Ireland

Perspectives

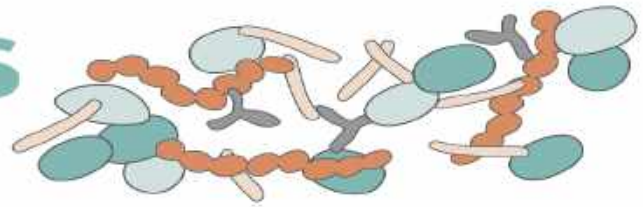
The gut microbiota plays a role in determining mental health - we can mine for, and target with, **psychobiotics**

- Probiotics
- Prebiotics
- Diet
- Faecal transplants
- Microbial consortia
- Metabolites



3 GOOD HEALTH AND WELL-BEING

Probiotics



Microbiome Ireland
Interfacing Food & Medicine
http://apc.ucc.ie

What are probiotics?

Scientists define probiotics as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. They can help support the bacteria that live with us, especially when our bacteria are challenged, for example by antibiotics, poor diet or traveling. Probiotics are present in numerous foods and dietary supplements.

What can probiotics do for you?

Probiotics can support health in different ways

- Help your immune system function properly
- Aid digestion by breaking down some of the food we can't digest
- Keep harmful microorganisms in check
- Produce vitamins and aid in nutrient absorption

Some probiotics may:

- Help reduce antibiotic-associated diarrhea
- Help manage digestive discomforts
- Help reduce colic symptoms and eczema in infants
- Help with the digestion of lactose
- Treat infectious diarrhea
- Decrease risk or duration of common infections, including respiratory tract, gut and vaginal tract

INTERNATIONAL SCIENTIFIC ASSOCIATION FOR PROBIOTICS AND PREBIOTICS

For more information visit **ISAPPscience.org**
Follow ISAPP on Twitter **@ISAPPscience**

Choosing a probiotic

Know your probiotic. Probiotics are known by their genus, species and strain (for example, *Lactobacillus acidophilus* ABC). Products should display each strain's designation.

Match the strain to the benefit you want. Not all strains are the same. See usprobioticguide.com or probioticchart.ca.

Amounts matter. Be sure the product contains at least the level of probiotics that was used in the study. Higher counts are not necessarily better. Levels of live probiotics should be provided through the 'best by' date (not time of manufacture).

Supplements or foods? More important than supplement vs food is getting an effective probiotic strain at an effective dose. Some yogurts, fermented milks and some other foods may contain probiotics. Look for added probiotics listed on the label and for a food that fits within your healthy diet.

Other fermented foods? Traditional yogurts contain live bacteria that can help digestion of lactose, but not all fermented foods contain live cultures that meet the definition of probiotic. See ISAPPscience.org/fermented-foods

Safety. Probiotics are safe for most people, but talk to your doctor if you suffer from an immune disorder, have a serious underlying illness, have short gut, or before giving to a young infant.

REVIEW

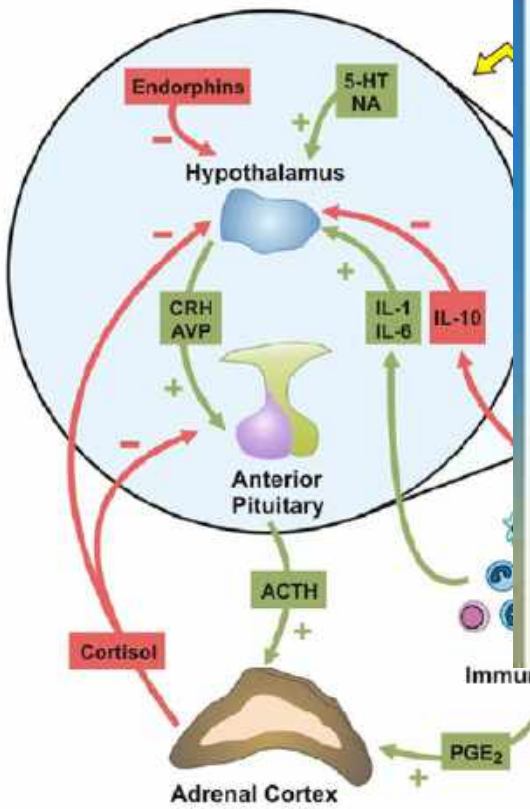
Psychobiotics:

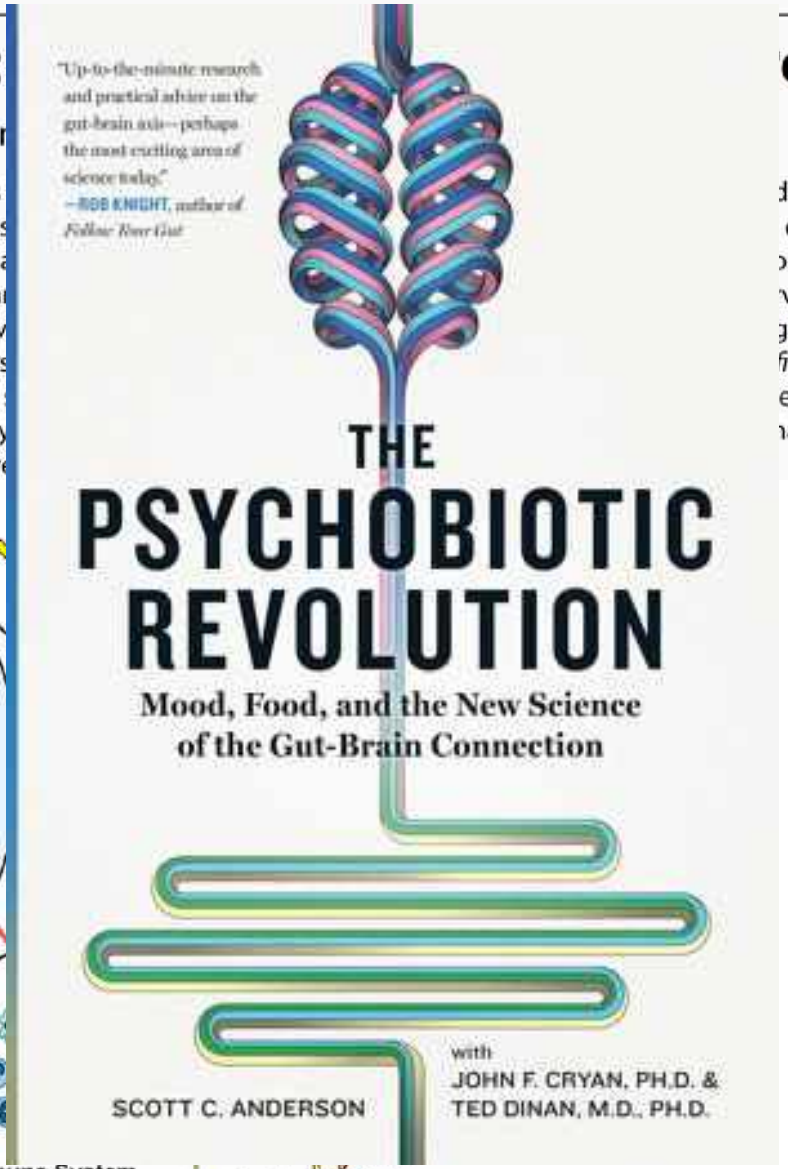
Timothy G. Dinan, Catherin

Here, we define a psychobiotic as
suffering from psychiatric illness. As
such as gamma-aminobutyric acid a
psychobiotics possess antidepressa
systems. So far, psychobiotics hav
syndrome, where positive benefits
emerging of benefits in alleviating
inflammatory actions of certain psy
scale placebo-controlled studies ar

opic

duces a health benefit in patients
delivering neuroactive substances
on in rodents suggests that certain
ve, spinal cord, or neuroendocrine
g in patients with irritable bowel
fidobacterium infantis. Evidence is
enefits may be related to the anti-
nal axis activity. Results from large

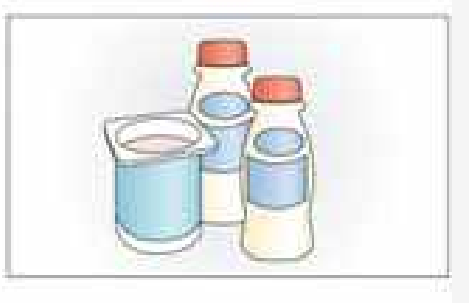


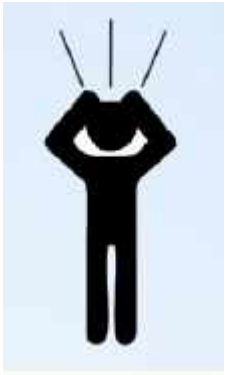


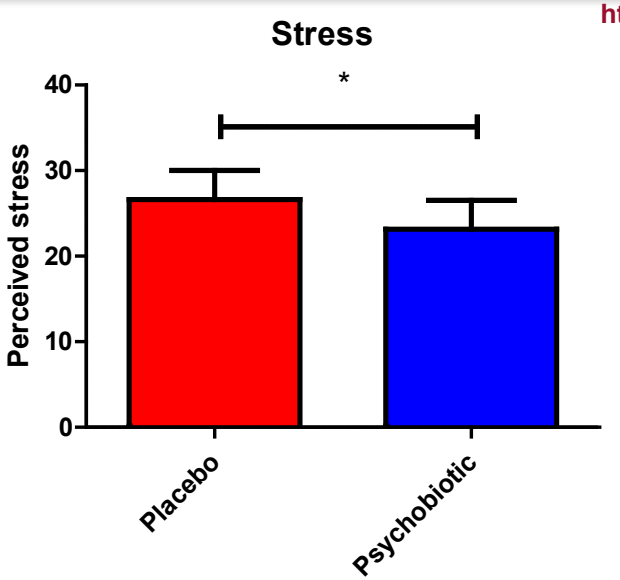
Elie Metchnikoff (1845-1916))
Nobel Prize 1908

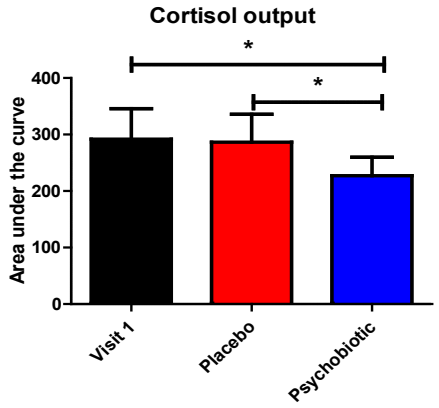
B. longum reduces stress response in healthy human volunteers

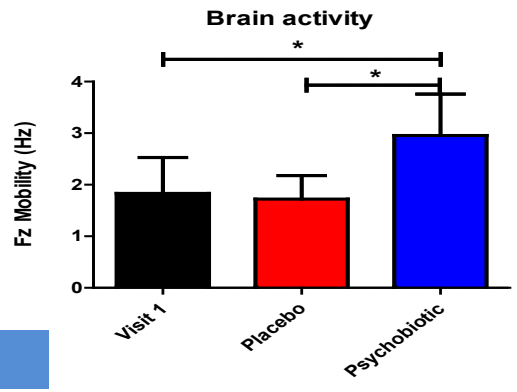
http://apc.ucc.ie

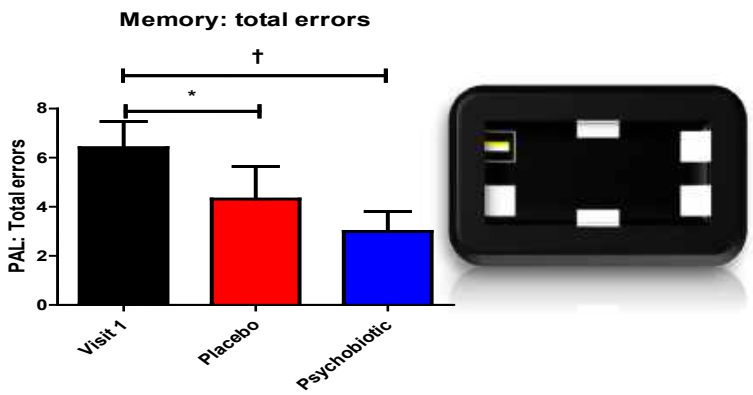












Allen et al., *2016*, Trans Psych

Brain, Behavior, and Immunity 61 (2017) 50–59

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Full-length Article

Lost in translation? The potential psychobiotic *Lactobacillus rhamnosus* (JB-1) fails to modulate stress or cognitive performance in healthy male subjects

John R. Kelly [a,b], Andrew P. Allen [a,b], Andriy Temko [c], William Hutch [d], Paul J. Kennedy [a], Niloufar Farid [b], Eileen Murphy [e], Geraldine Boylan [d], John Bienenstock [f], John F. Cryan [a,g], Gerard Clarke [a,b], Timothy G. Dinan [a,b,*]

Psychobioti eural activity and neu red using magnetoencepnalography, during social stress

NATURE REVIEWS | GASTROENTEROLOGY & HEPATOLOGY

CONSENSUS STATEMENT

OPEN

EXPERT CONSENSUS DOCUMENT

The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics

Glenn R. Gibson[1], Robert Hutkins[2], Mary Ellen Sanders[3], Susan L. Prescott[4], Raylene A. Reimer[5], Seppo J. Salminen[6], Karen Scott[7], Catherine Stanton[8], Kelly S. Swanson[9], Patrice D. Cani[10], Kristin Verbeke[11] and Gregor Reid[12]

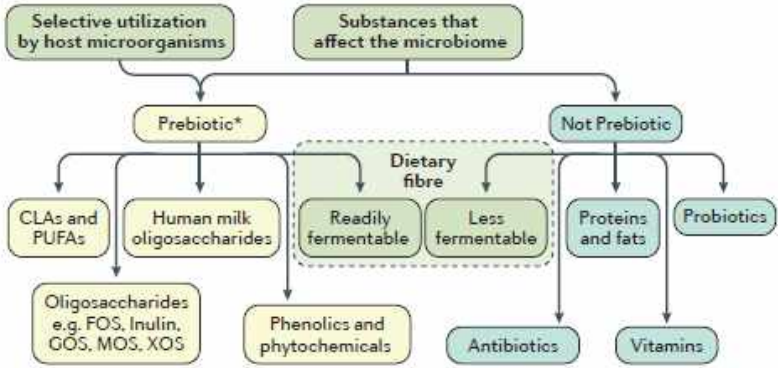


Figure 1 | **Distinguishing what is considered a prebiotic with the proposed definition.** Prebiotics must be selectively utilized and have adequate evidence of health benefit for the target host. Dietary prebiotics must not be degraded by the target host enzymes. *The figure shows candidate as well as accepted prebiotics in that levels of evidence currently vary, with FOS and GOS being the most researched prebiotics.CLA, conjugated linoleic acid; PUFA, polyunsaturated fatty acid; FOS, fructooligosaccharides; GOS, galactooligosaccharides; MOS, mannanoligosaccharide; XOS, xylooligosaccharide.

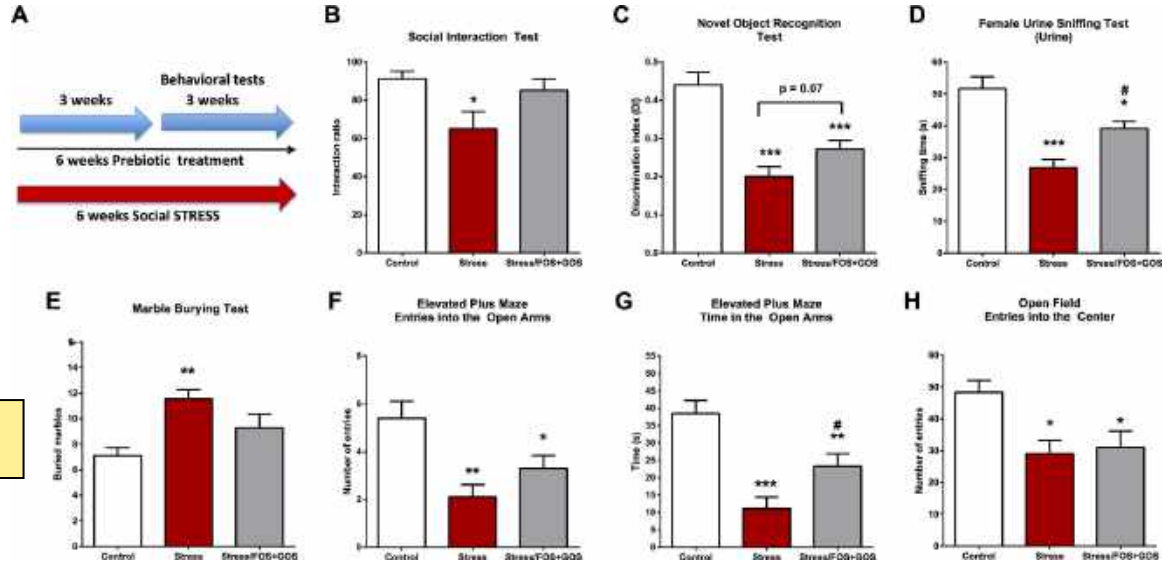
Biological Psychiatry October 1, 2017; 82:472–487 www.sobp.org/journal

Archival Report

Targeting the Microbiota-Gut-Brain Axis: Prebiotics Have Anxiolytic and Antidepressant-like Effects and Reverse the Impact of Chronic Stress in Mice

Aurelijus Burokas, Silvia Arboleya, Rachel D. Moloney, Veronica L. Peterson, Kiera Murphy, Gerard Clarke, Catherine Stanton, Timothy G. Dinan, and John F. Cryan

Prebiotic reverses consequences of chronic stress



Social behaviour and cognition

Anxiety

Kao et al. *Translational Psychiatry* (2018)8:66
DOI 10.1038/s41398-018-0116-8

Translational Psychiatry

ARTICLE Open Access

Prebiotic attenuation of olanzapine-induced weight gain in rats: analysis of central and peripheral biomarkers and gut microbiota

Amy Chia-Ching Kao[1], Sonia Spitzer[1], Daniel C. Anthony[2], Belinda Lennox[1] and Philip W. J. Burnet[1]

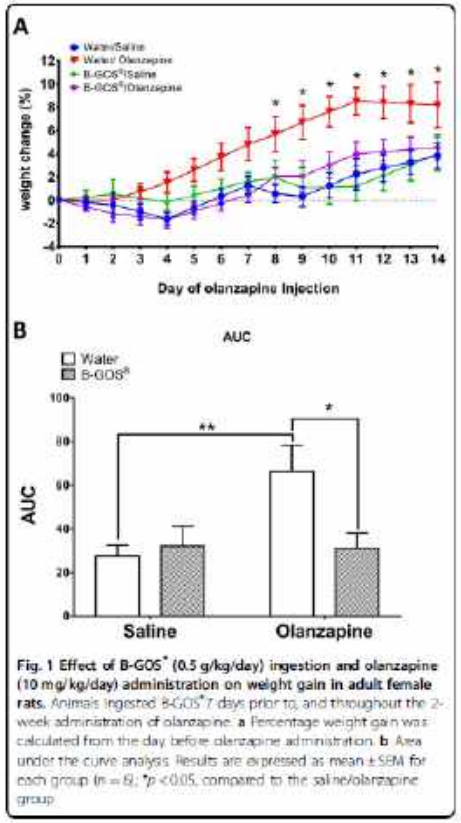


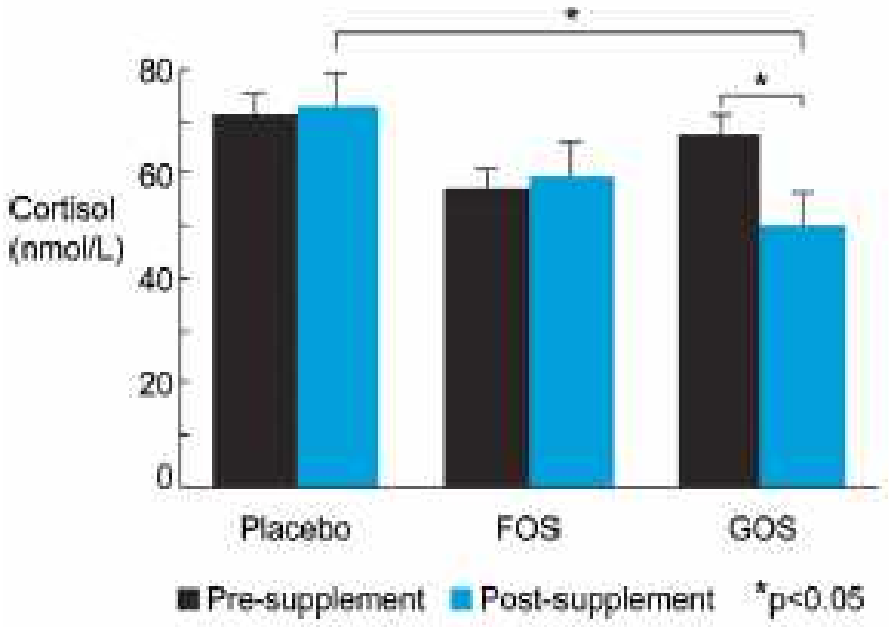
Fig. 1 Effect of B-GOS® (0.5 g/kg/day) ingestion and olanzapine (10 mg/kg/day) administration on weight gain in adult female rats. Animals ingested B-GOS® 7 days prior to, and throughout the 2-week administration of olanzapine. **a** Percentage weight gain was calculated from the day before olanzapine administration. **b** Area under the curve analysis. Results are expressed as mean ± SEM for each group ($n = 6$); $^{*}p < 0.05$, compared to the saline/olanzapine group

Psychopharmacology
DOI 10.1007/s00213-014-3810-0

ORIGINAL INVESTIGATION

Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers

Kristin Schmidt · Philip J. Cowen · Catherine J. Harmer · George Tzortzis · Steven Errington · Philip W. J. Burnet



Let food be thy medicine

224 Sandhu et al

Translational Research
January 2017

Feeding the microbiota-gut-brain axis: diet, microbiome, and neuropsychiatry

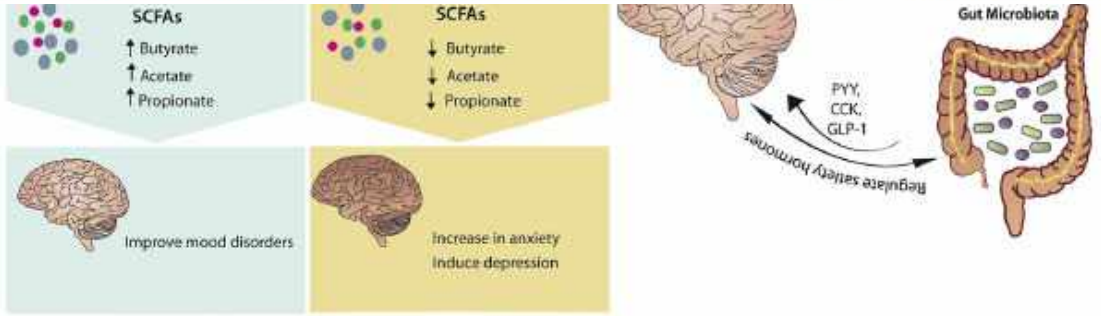
KIRAN V. SANDHU, EOIN SHERWIN, HARRIËT SCHELLEKENS, CATHERINE STANTON,

Nutritional medicine as mainstream in psychiatry

Jerome Sarris, Alan C Logan, Tasnime N Akbaraly, G Paul Amminger, Vicent Balanzá-Martínez, Marlene P Freeman, Joseph Hibbeln, Yutaka Matsuoka, David Mischoulon, Tetsuya Mizoue, Akiko Nanri, Daisuke Nishi, Drew Ramsey, Julia J Rucklidge, Almudena Sanchez-Villegas, Andrew Scholey, Kuan-Pin Su, Felice N Jacka, on behalf of The International Society for Nutritional Psychiatry Research

Psychiatry is at an important juncture, with the current pharmacologically focused model having achieved modest

Lancet Psychiatry 2015



Jacka et al. BMC Medicine (2017) 15:23
DOI 10.1186/s12916-017-0791-y

BMC Medicine

RESEARCH ARTICLE Open Access

A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial)

Felice N. Jacka[1,4,9,10,13*], Adrienne O'Neil[1,2,13], Rachelle Opie[5,13], Catherine Itsiopoulos[5], Sue Cotton[3], Mohammedreza Mohebbi[1], David Castle[4,11], Sarah Dash[1,13], Cathrine Mihalopoulos[7], Mary Lou Chatterton[7], Laima Brazionis[5,6], Olivia M. Dean[1,4,12,13], Allison M. Hodge[8] and Michael Berk[1,3,12,13]

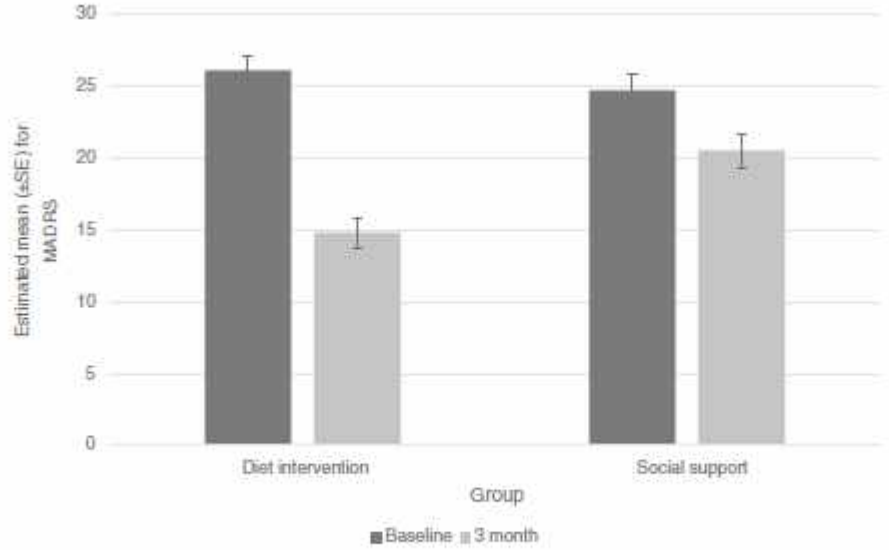


Fig. 2 MADRS scores for dietary support and social support control groups at baseline and endpoint. Effect size: Cohen's $d = -1.16$ (95% CI −1.73, −0.59). Baseline data $n = 67$; 12 week data $n = 56$

Fermented foods

What are fermented foods?

A fermented food or beverage is a type of food made by extensive microbial growth. These foods are nothing new. They've been around for thousands of years. To understand how fermented foods are made, let's look at yogurt.

Yogurt is a fermented food made from milk. During yogurt fermentations, lactic acid-producing bacteria grow on the sugars and other nutrients in milk. As they multiply, the bacteria produce compounds that change the flavor, texture, and nutrients in the milk to give us what we know as yogurt.

The value of fermented foods

- Source of live, active microbes
- Improve food taste, texture, and food digestibility
- Increase concentrations of vitamins and bioactive compounds in foods
- Remove/ reduce toxic or anti-nutrients in raw foods
- Increase food safety and shelf-life

The fermentation process

This same type of process happens in all fermented foods. Depending on the food, certain species of bacteria, yeasts and/or molds carry out the fermentation. Those microbes are still alive when we eat yogurt, kefir, cheeses, kimchi and some other fermented foods. But some foods that undergo fermentation are further processed (by pasteurization, baking, or filtering) so they are no longer sources of active microbes.

Fermented foods retaining living cultures:

- fresh kimchi
- water or brine cured olives
- kefir
- traditional salami
- yogurt
- some cheeses
- fresh sauerkraut
- fresh sour dill pickles

Fermented foods consumed without living cultures:

- tempeh
- most soy sauce
- most beer
- most wine
- sourdough bread
- chocolate

Fermented foods and gut health

The human digestive tract contains 100 trillion bacterial cells. These bacteria, termed our intestinal microbiota, are important to our health.

Modern practices, such as sanitation, antibiotic use, caesarean birth, formula feeding and eating foods devoid of live cultures, may be leading to a poorly functioning intestinal microbiota.

Fermented foods containing living cultures add beneficial bacteria to the digestive tract.

These fermented foods may benefit human health by reducing risk for some acute and chronic diseases and helping maintain a healthy intestinal microbiota.

ISAPP

International Scientific Association for Probiotics and Prebiotics

For more information visit **ISAPPscience.org/fermented-foods**
or follow us on Twitter **@ISAPPscience**

Received: 18 October 2018 | First decision: 27 November 2018 | Accepted: 14 December 2018
DOI: 10.1111/apt.15129
WILEY APT Alimentary Pharmacology & Therapeutics

Review article: dietary fibre in the era of microbiome science

John O'Grady[1,2] | Eibhlís M. O'Connor[1,3] | Fergus Shanahan[1,2]

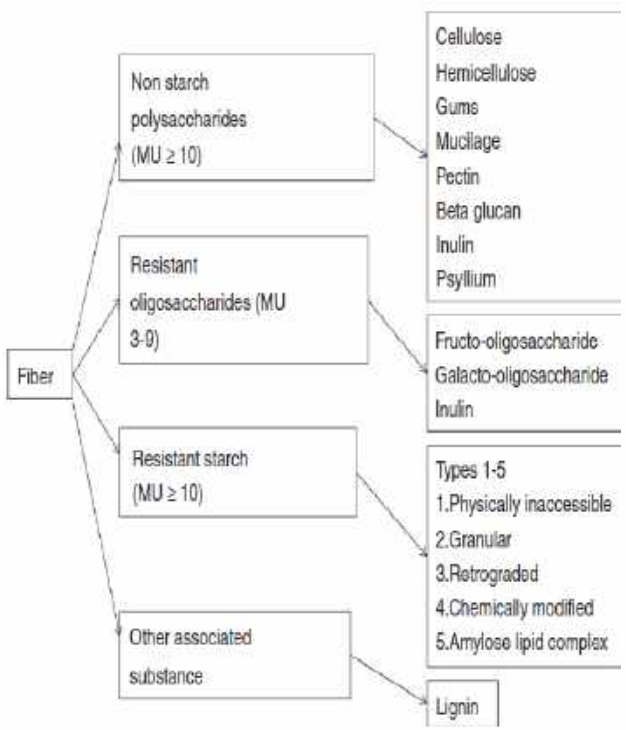


TABLE 1 Fibre subtypes[8,13,14,18]

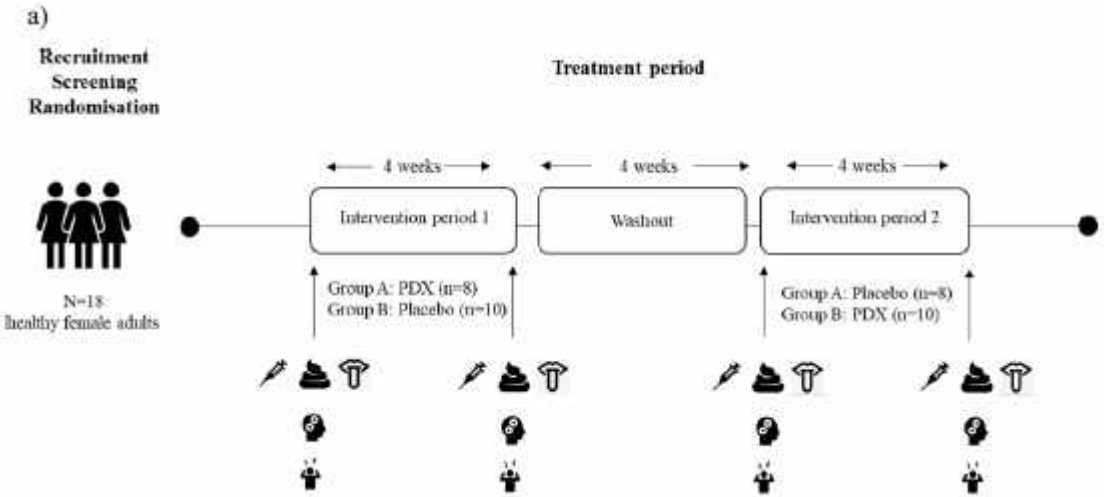
Fibre subtype	Structure	Source	Metabolic effect
Cellulose	Linear chains of glucose units with beta-1, 4 glucosidic linkage	Cereals, legumes, nuts	Increases stool bulk and stimulates peristalsis
Hemicellulose	As cellulose with xylose, galactose, mannose and arabinose sugar branches	Cereals, cell walls of fruits, vegetables	Varies with source; mix of insoluble, soluble and viscous properties
Lignan	Complex polymer of aromatic alcohols. Not a polysaccharide	Cereals, plant cell walls	Increases stool bulk and stimulates peristalsis
Gums	Mannose backbone with galactose side chains	Legumes, nuts	Cholesterol and glucose lowering effects, slow digestion and absorption. Fermentation by microbiota
Pectin	Polygalacturonic acid, D-galacturonic acid unit backbone, substituted with arabinans, galactin, arabinogalactin side chains	Fruit peel, legumes, beetroot	Cholesterol and glucose lowering effects, Slow digestion and absorption, Fermentation by microbiota
Beta glucan	Beta-D glucose linear backbone with 1-3 beta glycosidic linkage	Cereals and grains, yeasts, fungi and bacteria	Cholesterol and glucose lowering effects, Fermentation by microbiota
Inulin	Beta 1-2-fructan residue backbone, often glucosyl units as chain terminating moieties	Chicory root, onion, cereals	Lower triglyceride concentration, Fermentation by microbiota
Psyllium	Heteroxylan with 1:4, 1:3 linkage backbone, side chains of arabinose, xylose, galactose and rhamnose	*Plantago Ovata*	Cholesterol and glucose lowering, Stool forming effects
Oligosaccharides	Beta- fructo- oligosaccharides (FOS) Alpha and beta-galactooligosaccharides (GOS)	Polymers derived from polysaccharides by hydrolysis	Fermentation by microbiota
Resistant starch (RS1-5)	Alpha-1,4-D-glucan links	Cereals, legumes, fruits	Cholesterol and glucose lowering, Fermentation by microbiota

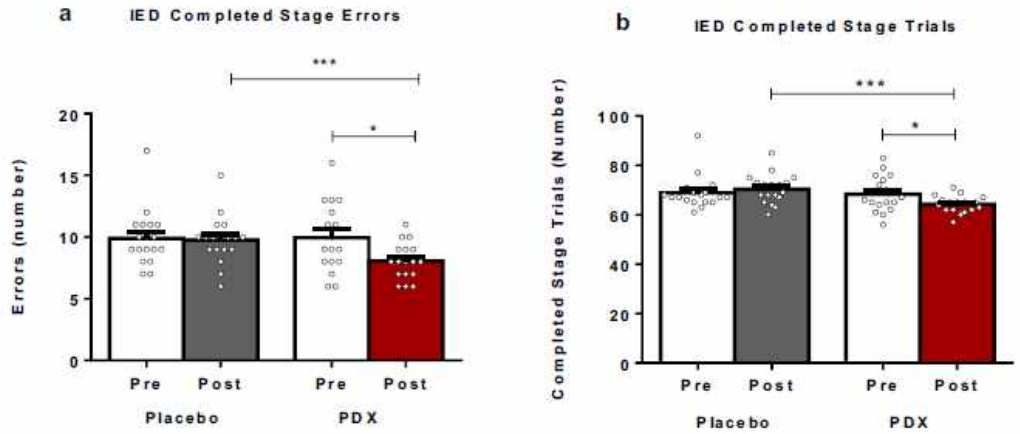
Psychopharmacology
https://doi.org/10.1007/s00213-020-05665-y

ORIGINAL INVESTIGATION

A specific dietary fibre supplementation improves cognitive performance—an exploratory randomised, placebo-controlled, crossover study

Kirsten Berding[1] · Caitriona M. Long-Smith[1] · Carina Carbia[1] · Thomaz F. S. Bastiaanssen[1,2] · Marcel van de Wouw[1] · Niamh Wiley[1,3,4] · Conall R. Strain[1,4] · Fiona Fouhy[1,4] · Catherine Stanton[1,3,4] · John F. Cryan[1,2] · Timothy G. Dinan[1,3]





GUT MICROBES
2017, VOL. 8, NO. 3, 253–267
http://dx.doi.org/10.1080/19490976.2017.1293224

Taylor & Francis
Taylor & Francis Group

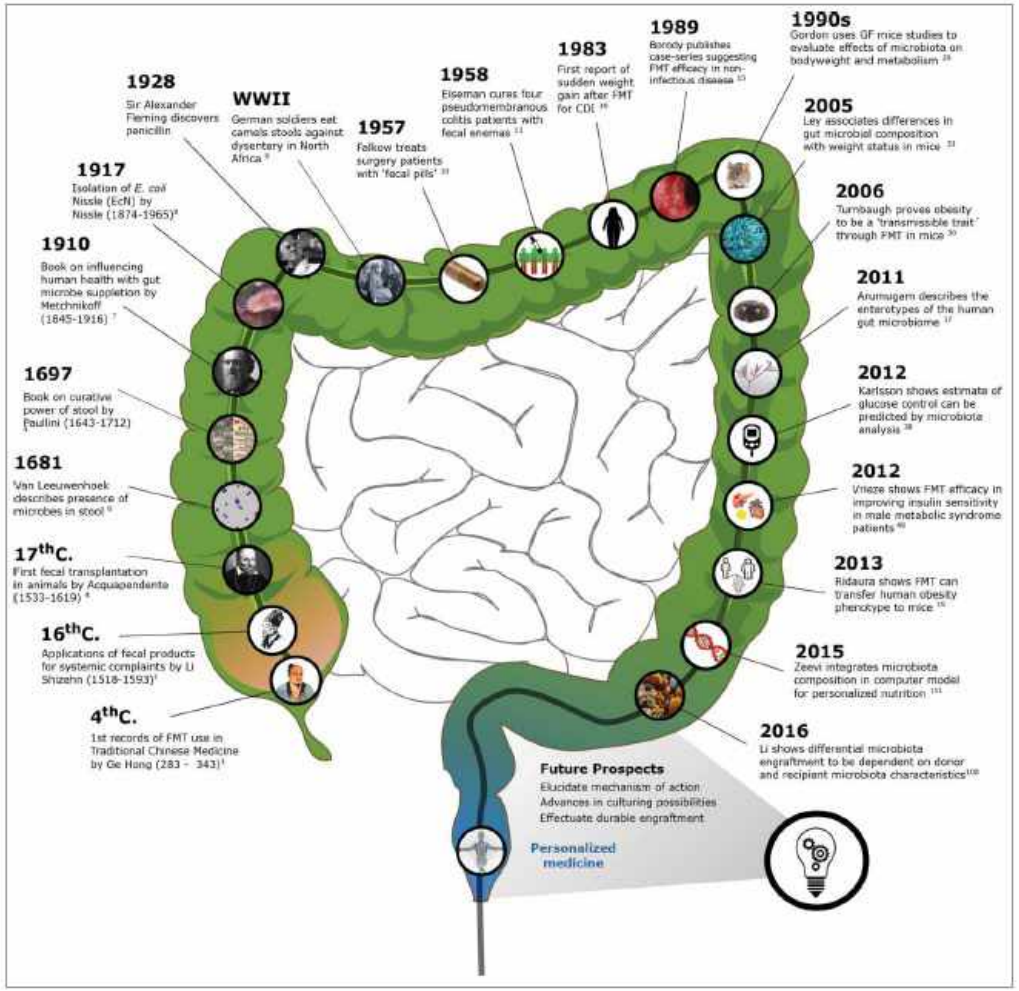
REVIEW

OPEN ACCESS

Fecal microbiota transplantation in metabolic syndrome: History, present and future

P. F. de Groot[a], M. N. Frissen[a], N. C. de Clercq[a], and M. Nieuwdorp[a,b,c,d]

Andrea Levy, The Plain



The New Yo

HEALTH

A Promising

By PAM BELLUCK OCT. 11, 2014

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Thursday, October 25, 2012

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ecal transplants?

OPEN ACCESS

European consensus conference on faecal microbiota transplantation in clinical practice

Giovanni Cammarota,[1] Gianluca Ianiro,[1] Herbert Tilg,[2] Mirjana Rajilić-Stojanović,[3] Patrizia Kump,[4] Reetta Satokari,[5] Harry Sokol,[6] Perttu Arkkila,[7] Cristina Pintus,[8] Ailsa Hart,[9] Jonathan Segal,[9] Marina Aloi,[10] Luca Masucci,[11] Antonio Molinaro,[12] Franco Scaldaferri,[1] Giovanni Gasbarrini,[1] Antonio Lopez-Sanroman,[13] Alexander Link,[14] Pieter de Groot,[15] Willem M de Vos,[5,16] Christoph Högenauer,[4] Peter Malfertheiner,[14] Eero Mattila,[17] Tomica Milosavljević,[18] Max Nieuwdorp,[12,15,19] Maurizio Sanguinetti,[11] Magnus Simren,[20] Antonio Gasbarrini,[1] The European FMT Working Group

Box 1 Key issues to select potential donors at the preliminary interview

INFECTIOUS DISEASES

- History of, or known exposure to, HIV, HBV or HCV, syphilis, human T-lymphotropic virus I and II, malaria, trypanosomiasis, tuberculosis
- Known systemic infection not controlled at the time of donation
- Use of illegal drugs
- Risky sexual behaviour (anonymous sexual contacts; sexual contacts with prostitutes, drug addicts, individuals with HIV, viral hepatitis, syphilis; work as prostitute; history of sexually transmittable disease)
- Previous reception of tissue/organ transplant
- Previous (<12 months) reception of blood products
- Recent (<6 months) needle stick accident
- Recent (<6 months) body tattoo, piercing, earring, acupuncture
- Recent medical treatment in poorly hygienic conditions
- Risk of transmission of diseases caused by prions
- Recent parasitosis or infection from rotavirus, *Giardia lamblia* and other microbes with GI involvement
- Recent (<6 months) travel in tropical countries, countries at high risk of communicable diseases or traveller's diarrhoea
- Recent (<6 months) history of vaccination with a live attenuated virus, if there is a possible risk of transmission
- Healthcare workers (to exclude the risk of transmission of multidrug-resistant organisms)
- Individual working with animals (to exclude the risk of transmission of zoonotic infections)

GI, METABOLIC AND NEUROLOGICAL DISORDERS

- History of IBS, IBD, functional chronic constipation, coeliac disease, other chronic GI disorders
- History of chronic, systemic autoimmune disorders with GI involvement
- History of, or high risk for, GI cancer or polyposis
- Recent appearance of diarrhoea, hematochezia
- History of neurological/neurodegenerative disorders
- History of psychiatric conditions
- Overweight and obesity (body mass index >30)

DRUGS THAT CAN IMPAIR GUT MICROBIOTA COMPOSITION

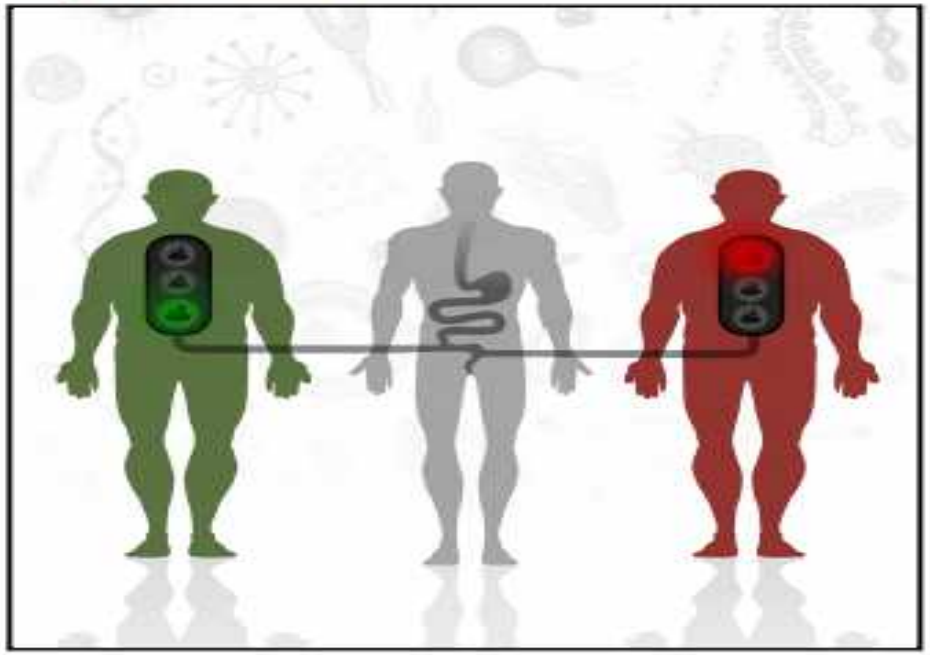
- Recent (<3 months) exposure to antibiotics, immunosuppressants, chemotherapy
- Chronic therapy with proton pump inhibitors

Clinical and Translational Report

Cell Metabolism

Improvement of Insulin Sensitivity after Lean Donor Feces in Metabolic Syndrome Is Driven by Baseline Intestinal Microbiota Composition

Graphical Abstract



Authors

Ruud S. Kootte, Evgeni Levin, Jarkko Salojärvi, ..., Erik S.G. Stroes, Albert K. Groen, Max Nieuwdorp

Correspondence

m.nieuwdorp@amc.uva.nl

In Brief

Kootte et al. show that fecal microbiota transplantation from lean donors to obese patients with metabolic syndrome improves insulin sensitivity, a transient effect associated with changes in microbiota composition and fasting plasma metabolites. Baseline fecal microbiota composition in recipients predicts the response to lean donor fecal microbiota transplantation.

Highlights

- Lean donor FMT in obese metabolic syndrome patients improves insulin sensitivity
- Beneficial effects of lean donor FMT are transient
- Improvement in insulin sensitivity is linked to changes in plasma metabolites
- Response to lean donor FMT is driven by baseline fecal microbiota composition

Early Life Factors

ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Paediatrica ISSN 0803-5253

REVIEW ARTICLE

Priming for health: gut microbiota acquired in early life regulates physiology, brain and behaviour

G Clarke (g.clarke@ucc.ie)[1,2]*, SM O'Mahony[1,3]*, TG Dinan[1,2], JF Cryan[1,3]

1.Alimentary Pharmabiotic Centre, University College Cork, Cork, Ireland
2.Department of Psychiatry, University College Cork, Cork, Ireland
3.Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

Keywords
Behaviour, Brain Development, Breastfeeding, Early Life, Microbiota

Correspondence
G Clarke, Department of Psychiatry/Alimentary Pharmabiotic Centre, 1.15 Biosciences Institute, University College Cork, Cork, Ireland.
Tel: +353 214 901 408 |

ABSTRACT
The infant gut microbiome is dynamic, and radical shifts in composition occur during the first 3 years of life. Disruption of these developmental patterns, and the impact of the microbial composition of our gut on brain and behaviour, has attracted much recent attention. Integrating these observations is an important new research frontier.
Conclusion: Early-life perturbations of the developing gut microbiota can impact on the central nervous system and potentially lead to adverse mental health outcomes.

Drug Discovery Today • Volume 17, Numbers 9/10 • May 2012 REVIEWS

ELSEVIER

Can we vaccinate against depression?

Graham A.W. Rook[1], Charles L. Raison[2] and Christopher A. Lowry[3]

Reviews • GENE TO SCREEN

MICROBIOLOGY

Maternal microbiota in pregnancy and early life

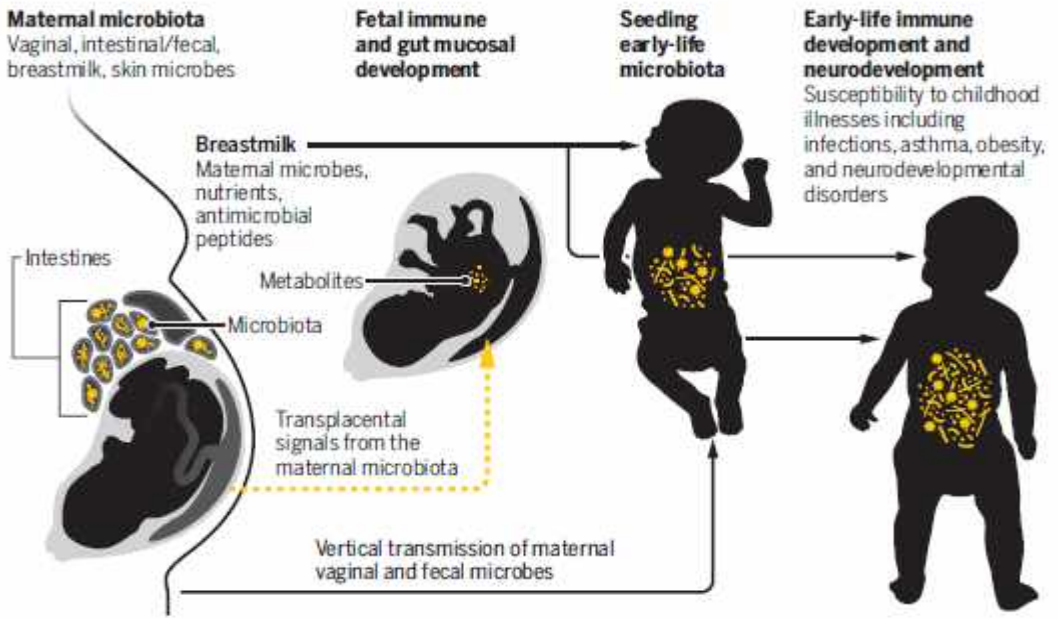
The maternal microbiota shape offspring development, including susceptibility to some illnesses

By **Braedon McDonald**[1] *and* **Kathy D. McCoy**[2]

remains the subject of debate. In support of this, a recent study found that the human pla-

Effects of the maternal microbiota in pregnancy and early life

Through effects on early-life colonization, immune development, and neurodevelopment, the maternal microbiota regulates susceptibility to a number of childhood illnesses and can vertically transmit dysbiosis-mediated pathologies.



Review

CellPress

Special Issue: Nurturing the Next Generation

The infant microbiome development: mom matters

Noel T. Mueller[1,2], Elizabeth Bakacs[3], Joan Combellick[4], Zoya Grigoryan[3], and Maria G. Dominguez-Bello[3]

[1] Department of Epidemiology, Mailman School of Public Health, Columbia University Medical Center, New York, NY, USA
[2] Institute of Human Nutrition and Department of Medicine, College of Physicians and Surgeons, Columbia University Medical Center, New York, NY, USA
[3] Division of Translational Medicine, New York University School of Medicine, New York, NY, USA

Table 1. Perturbations to the assembly of the neonatal microbiome, prevention strategies, and approaches for microbiome restoration

Perturbation to microbiome assembly	Prevention strategies	Restoration approaches
C-section delivery	Support efforts to increase use of midwives Champion evidence-based labor management Optimize managing labor (reduce pain, increase maternal comfort) Educate women about the potential consequences of C-section delivery Change policies around physician incentives and malpractice insurance	Inoculation of neonate with maternal vaginal flora immediately following C-section delivery Breastfeeding Pre- and probiotic supplementation of neonate
Gestational, perinatal, or postnatal antibiotics	Implement robust antimicrobial stewardship programs (http://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria) Develop safe strategies that limit use of antibiotics in women in labor (e.g., rapid PCR testing for group B *Streptococcus* at the time of admission to the delivery unit) During C-section delivery, give antibiotics after cord clamping to eliminate fetal exposure to antibiotics Use more prudency in antibiotic administration during pregnancy	Breastfeeding Pre- and probiotic supplementation of mother during pregnancy and neonate after birth
Formula feeding	Adopt WHO/UNICEF Baby Friendly Hospital Initiative Develop other policies that incentivize breastfeeding Do not offer formula to newborns without request or medical indication Promote use of donor breast milk rather than formula when maternal milk is not an option	Reintroduce breastfeeding Pre- and probiotic supplementation

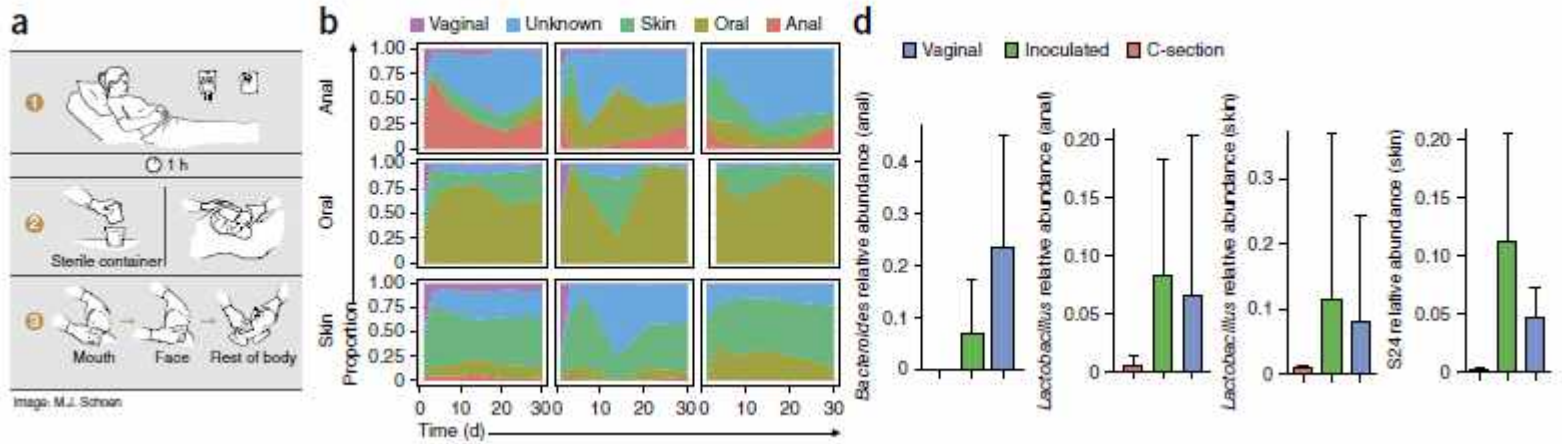
nature medicine

Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello[1,2], Kassandra M De Jesus-Laboy[2], Nan Shen[3], Laura M Cox[1], Amnon Amir[4], Antonio Gonzalez[4], Nicholas A Bokulich[1], Se Jin Song[4,5], Marina Hoashi[1,6], Juana I Rivera-Vinas[7], Keimari Mendez[7], Rob Knight[4,8] & Jose C Clemente[3,9]

estimated 15% of births that require C-section delivery to protect the health of the mother or baby[11].

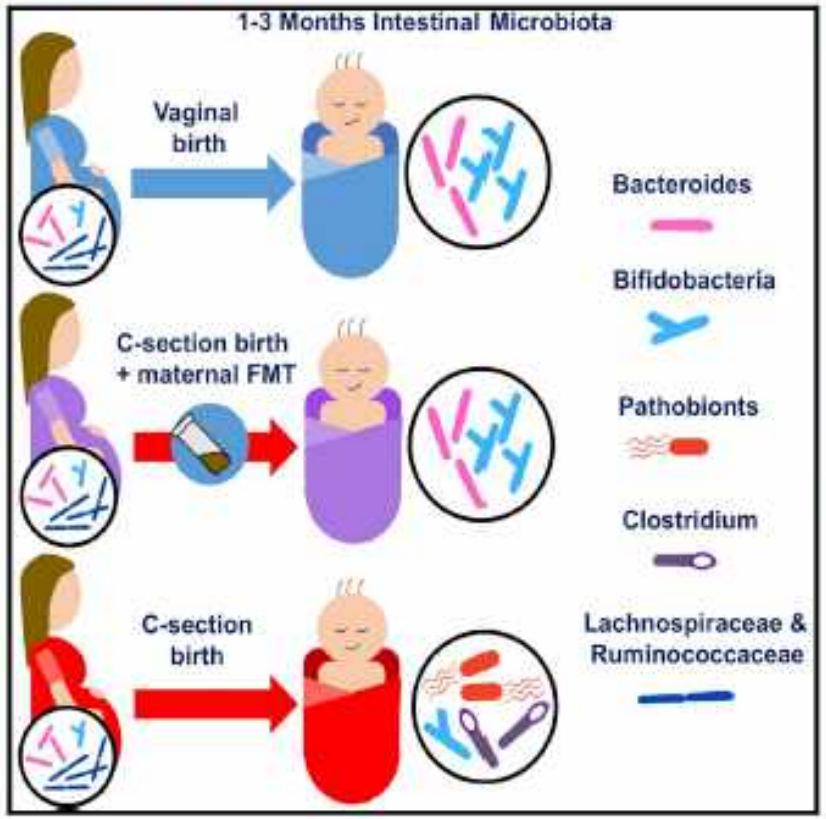
Here we exposed C-section–delivered infants to their maternal vaginal fluids at birth and longitudinally determined the composition of their microbiota to assess whether it developed more similarly to vaginally born babies than to unexposed C-section–delivered infants. We collected samples from 18 infants and their mothers, including 7 born vaginally and 11 delivered by scheduled C-section, of which four were exposed to the maternal vaginal fluids at birth (**Supplementary Table 1**). Briefly, the microbial restoration procedure, or vaginal microbial transfer, consists of incubating sterile gauze in the vagina of moth-



Cell

Maternal Fecal Microbiota Transplantation in Cesarean-Born Infants Rapidly Restores Normal Gut Microbial Development: A Proof-of-Concept Study

Graphical Abstract



Authors

Katri Korpela, Otto Helve, Kaija-Leena Kolho, ..., Anne Salonen, Sture Andersson, Willem M. de Vos

Correspondence

willem.devos@wur.nl

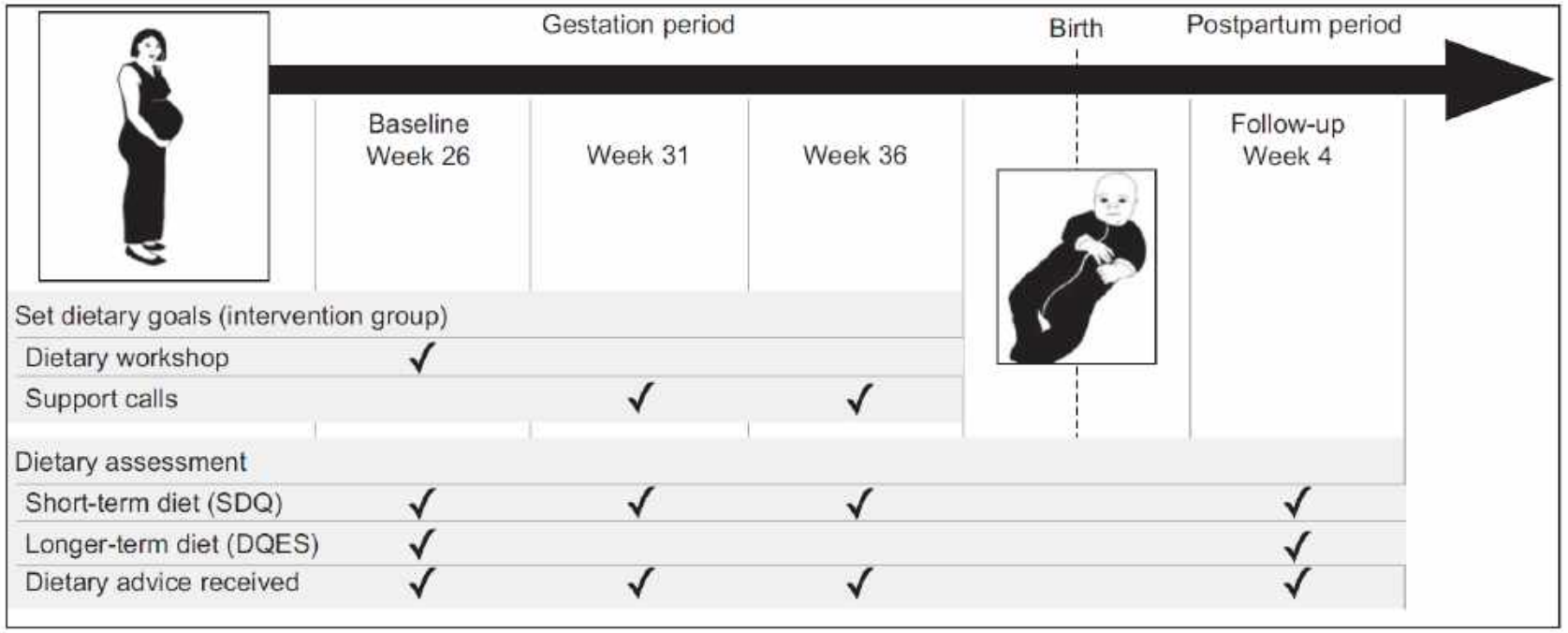
In Brief

A proof-of-concept safety study shows that oral fecal transplantation can shift the microbiome composition of infants who are born via cesarean section to a profile that is more similar to those born via vaginal delivery.

Public Health Nutrition: page 1 of 13 doi:10.1017/S1368980020003511

Targeting the perinatal diet to modulate the gut microbiota increases dietary variety and prebiotic and probiotic food intakes: results from a randomised controlled trial

Samantha L Dawson[1,2,*], Mohammadreza Mohebbi[3], Jeffrey M Craig[2,4], Phillip Dawson[5], Gerard Clarke[6,7,8], Mimi LK Tang[9,10] and Felice N Jacka[1,11,12,13]



ARTICLE

doi:10.1038/nature11319

Gut microbiota composition correlates with diet and health in the elderly

Marcus J. Claesson[1,2*], Ian B. Jeffery[1,2*], Susana Conde[3], Susan E. Power[1], Eibhlís M. O'Connor[1,2], Siobhán Cusack[1], Hugh M. B. Harris[1], Mairead Coakley[4], Bhuvaneswari Lakshminarayanan[4], Orla O'Sullivan[4], Gerald F. Fitzgerald[1,2], Jennifer Deane[1], Michael O'Connor[5,6], Norma Harnedy[5,6], Kieran O'Connor[6,7,8], Denis O'Mahony[5,6,8], Douwe van Sinderen[1,2], Martina Wallace[9], Lorraine Brennan[9], Catherine Stanton[2,4], Julian R. Marchesi[10], Anthony P. Fitzgerald[3,11], Fergus Shanahan[2,12], Colin Hill[1,2], R. Paul Ross[2,4] & Paul W. O'Toole[1,2]

Alterations in intestinal microbiota composition are associated with several chronic conditions, including obesity and inflammatory diseases. The microbiota of older people displays greater inter-individual variation than that of younger adults. Here we show that the faecal microbiota composition from 178 elderly subjects formed groups, correlating with residence location in the community, day-hospital, rehabilitation or in long-term residential care. However, clustering of subjects by diet separated them by the same residence location and microbiota groupings. The separation of microbiota composition significantly correlated with measures of frailty, co-morbidity, nutritional status, markers of inflammation and with metabolites in faecal water. The individual microbiota of people in long-stay care was significantly less diverse than that of community dwellers. Loss of community-associated microbiota correlated with increased frailty. Collectively, the data support a relationship between diet, microbiota and health status, and indicate a role for diet-driven microbiota alterations in varying rates of health decline upon ageing.

Feature Review

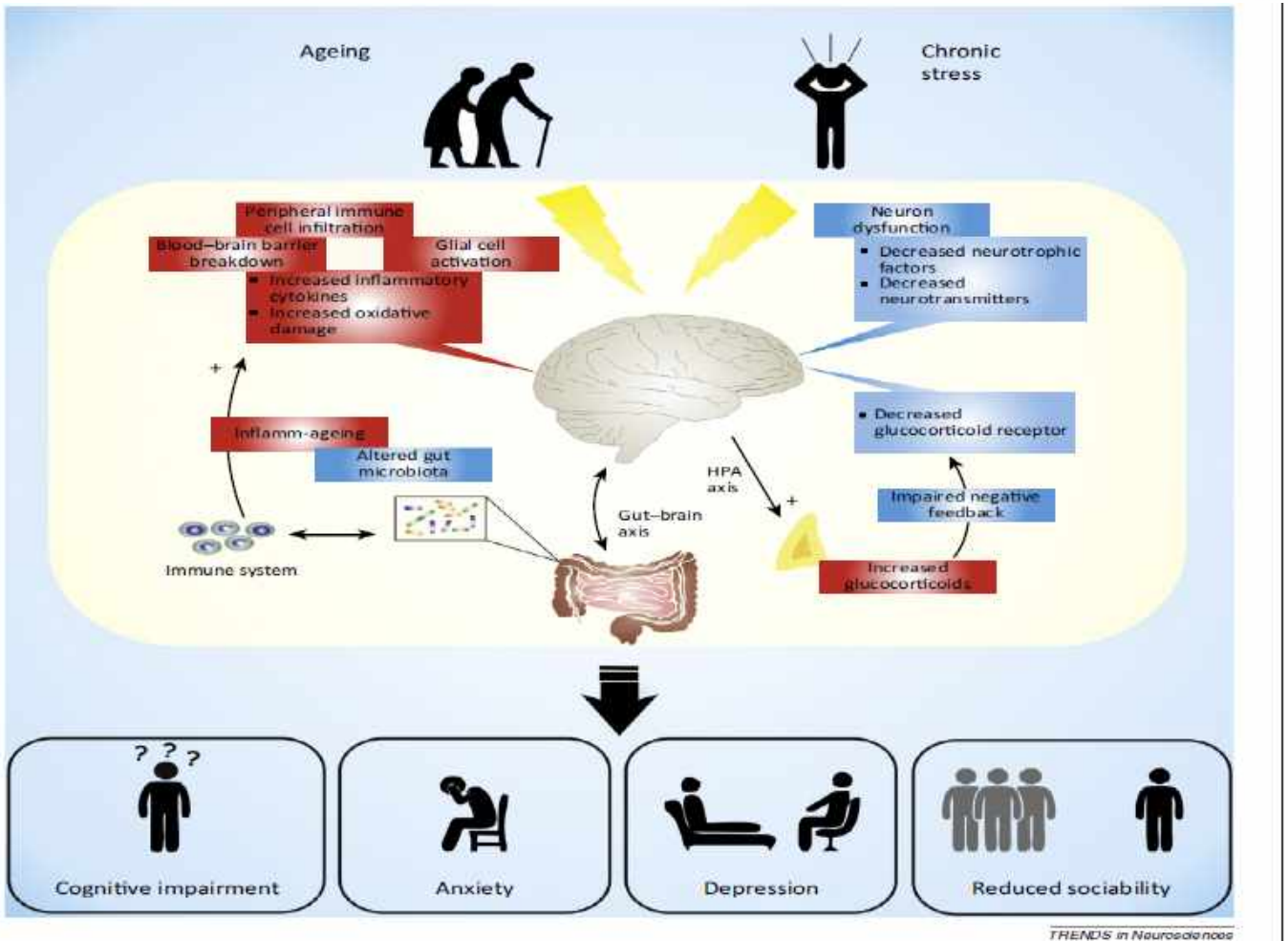
Trends in Neurosciences January 2015, Vol. 38, No. 1

CellPress

http://apc.ucc.ie

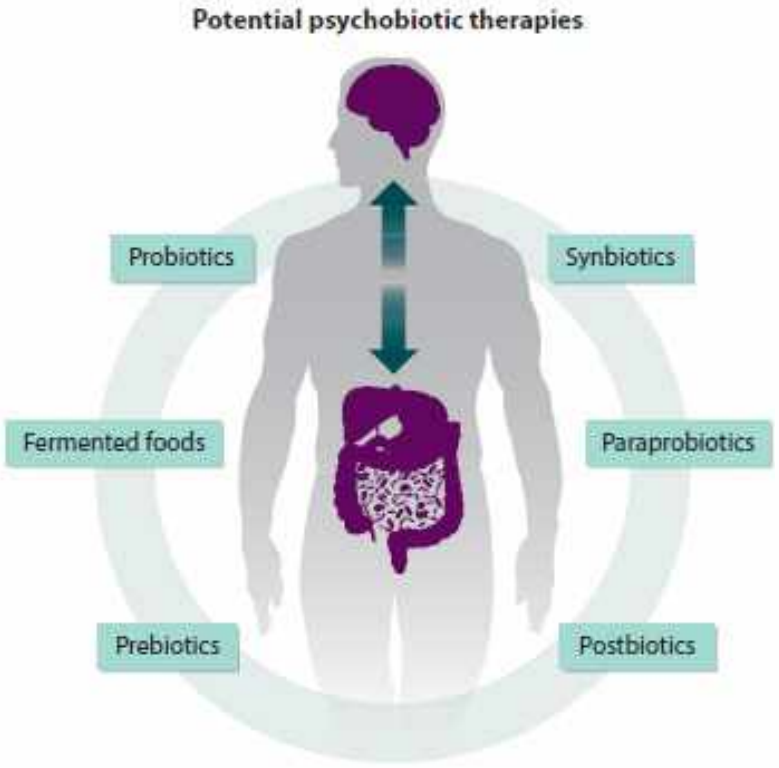
Adding fuel to the fire: the impact of stress on the ageing brain

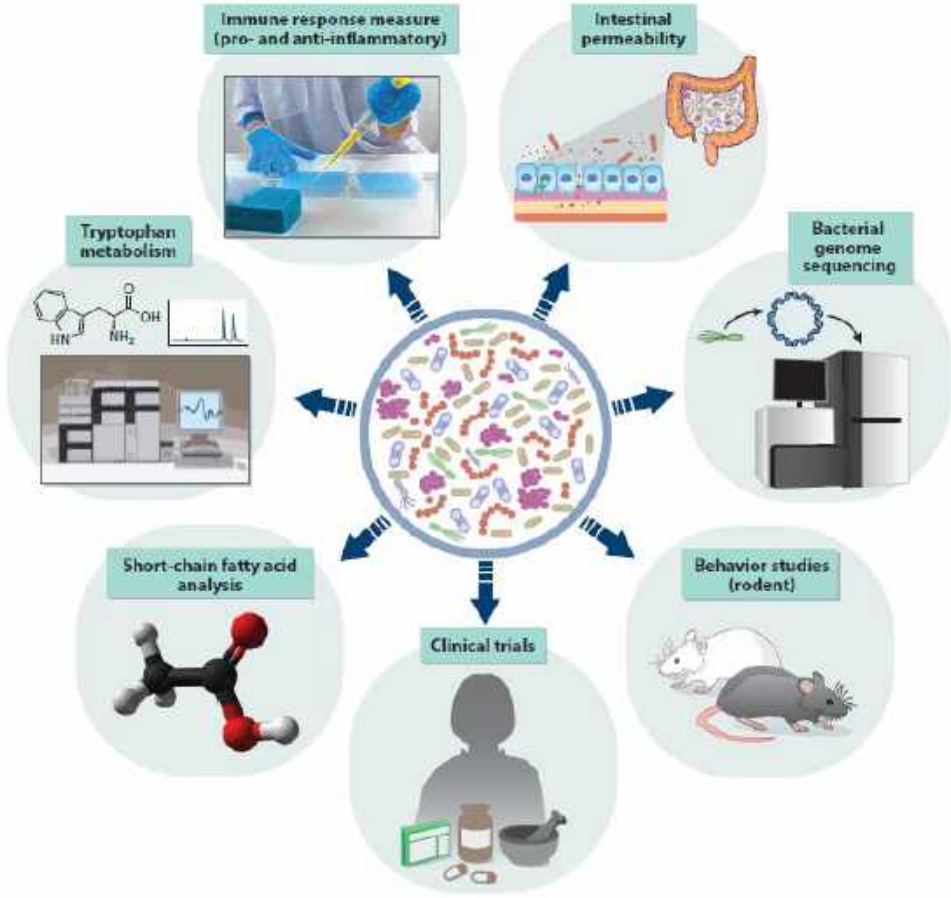
Jack A. Prenderville[1], Paul J. Kennedy[1], Timothy G. Dinan[1,2], and John F. Cryan[1,3]



Towards Psychobiotics: Focus on Mechanisms

The New Yorker



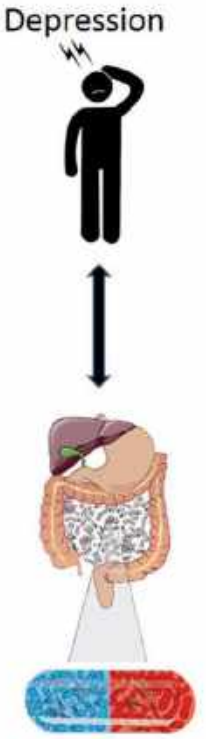


Long-Smith et al 2019, Annual Review Pharmacology and Toxicology

Summary & Conclusions

http://apc.ucc.ie

- Promising preclinical and clinical research
- Regulates behaviours and physiology relevant to neurogastroenterology
- Increasing translational efforts
- Mechanistic insights and focus on causation
- Fact or fiction: Expect some attrition along the way
- Microbial-based strategies for the treatment of stress-related gut-brain axis disorders?



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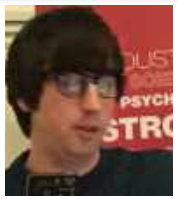





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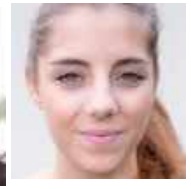

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GENIEUR.EU
Genes in irritable bowel syndrome

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MONDAY , 22 JANUARY 2018 | About

The allium
Science news you won't read nowhere else

Pope Francis To Award Sainthood To All Microbiome Researchers

Vatican City – Pope Francis announced today that he was going to award automatic sainthood t all microbiome researchers worldwide for "Doing God's Work".

3 GOOD HEALTH AND WELL-BEING

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Thank you

g.clarke@ucc.ie

"I told him as an expert in the field I strongly recommend wearing it, but he just kept bringing up his 'rights'."

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