La revolución psicobiótica

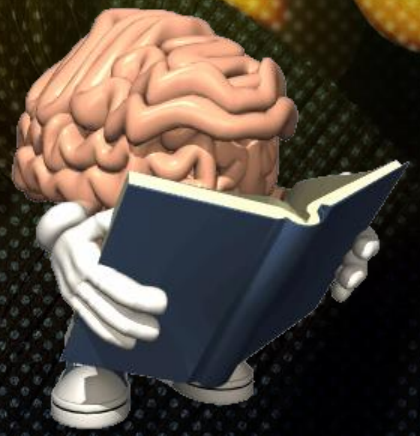
Eje intestino-cerebro y salud mental (cerebro, emociones y bacterias)

CFIE VALLADOLID

raul.espert@uv.es

@esperttortajada

Raul Espert



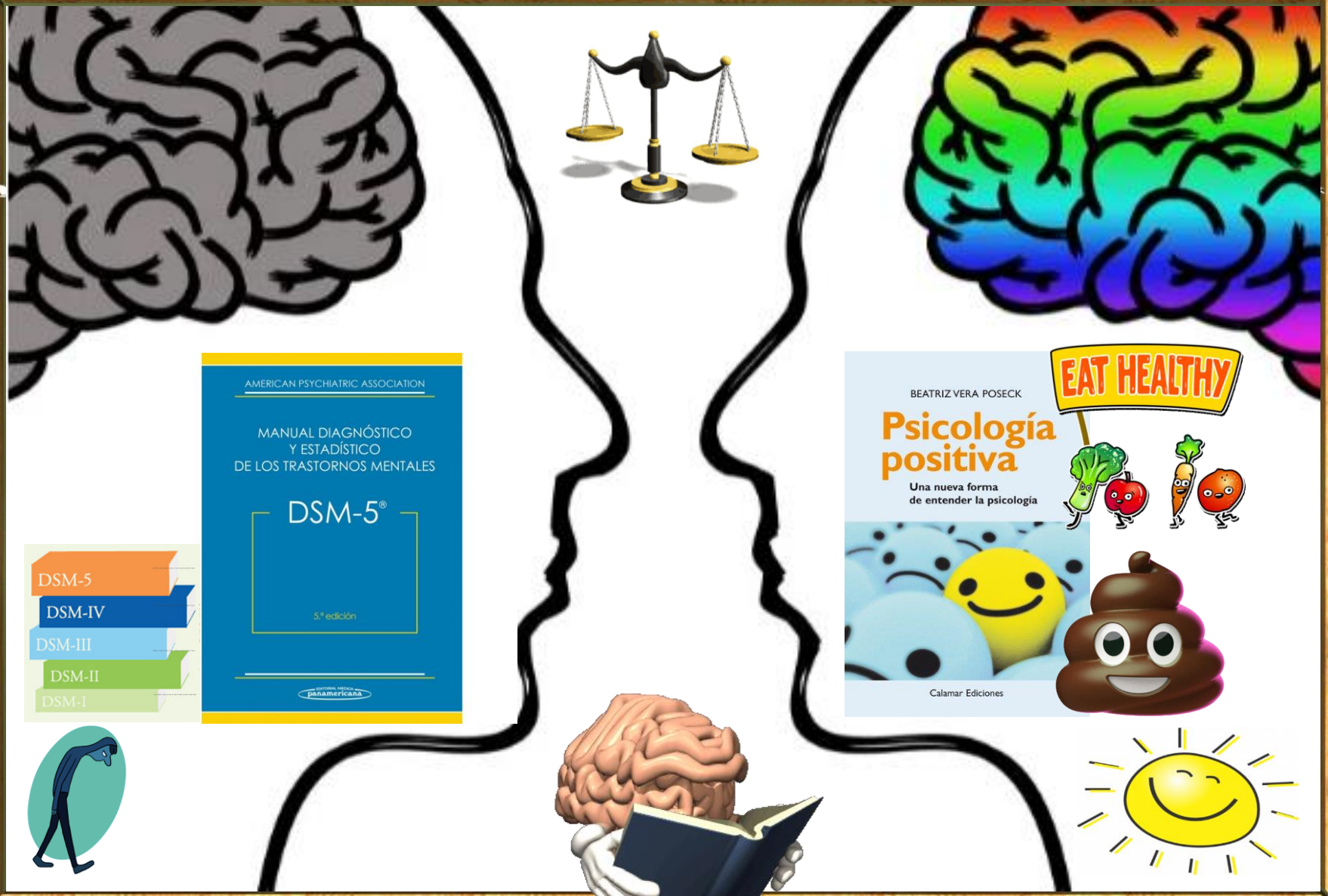
DR. RAÚL ESPERT

Dpto de Psicobiología (UV)

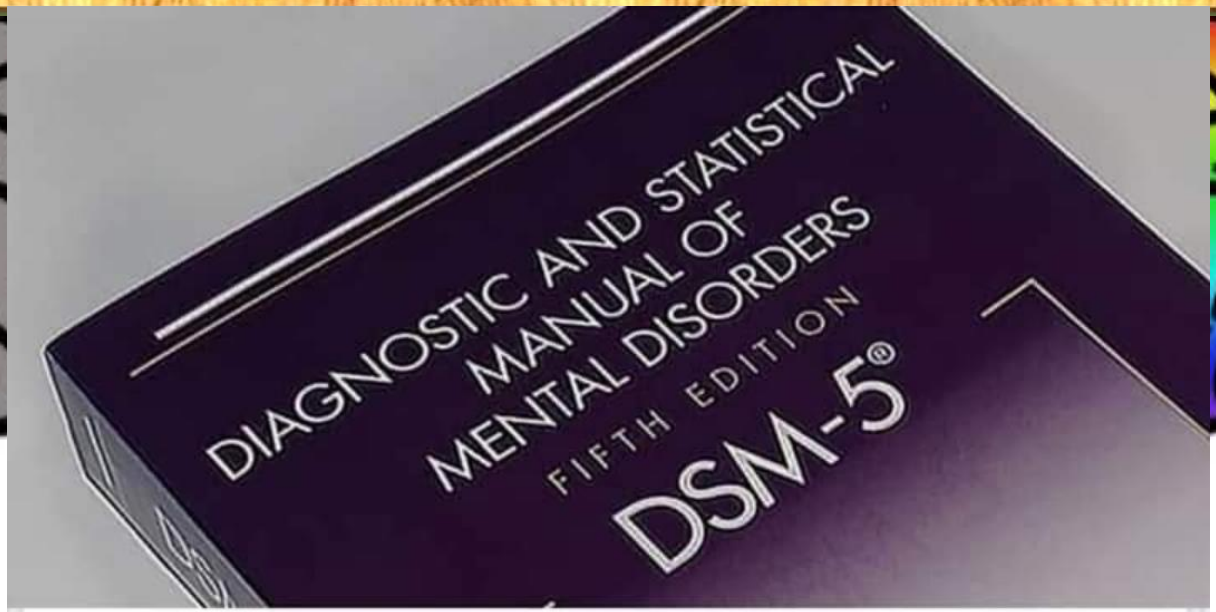
Unidad de Neuropsicología

(Hospital Clínico, València)

Psicología positiva vs. "negativa"



Psicología positiva vs. "negativa"



Evolución del DSM*

Versión	Año	Trastornos	Páginas
DSM-I	1952	128	132
DSM-II	1968	193	119
DSM-III	1980	228	494
DSM-III-R	1987	253	567
DSM-IV	1994	383	886
DSM-IV-TR	2000	383	943
DSM-5	2013	541	947

Hospital "Dr. Peset"

desde 1993 a 1999

Hospital Arnau de Vilanova

desde 1999-2007

Clinico desde 1999

Hospital Universitario La Fe. Valencia
Unidad de Neuropsicologia y Neurocirugía consciente (2015)

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Madrid, 23 de noviembre de 2018

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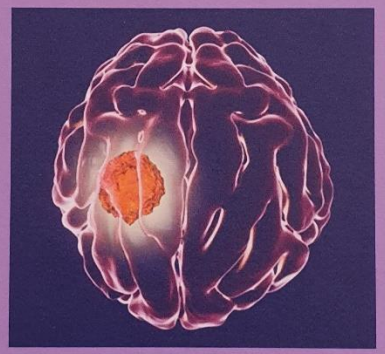
Facultat de Psicologia

Programa de Doctorado en Psicogerontología:
Perspectiva del Ciclo Vital

EVALUACIÓN NEUROPSICOLÓGICA Y EMOCIONAL EN NEUROCIRUGÍA CON PACIENTE DESPIERTO: UN ESTUDIO LONGITUDINAL

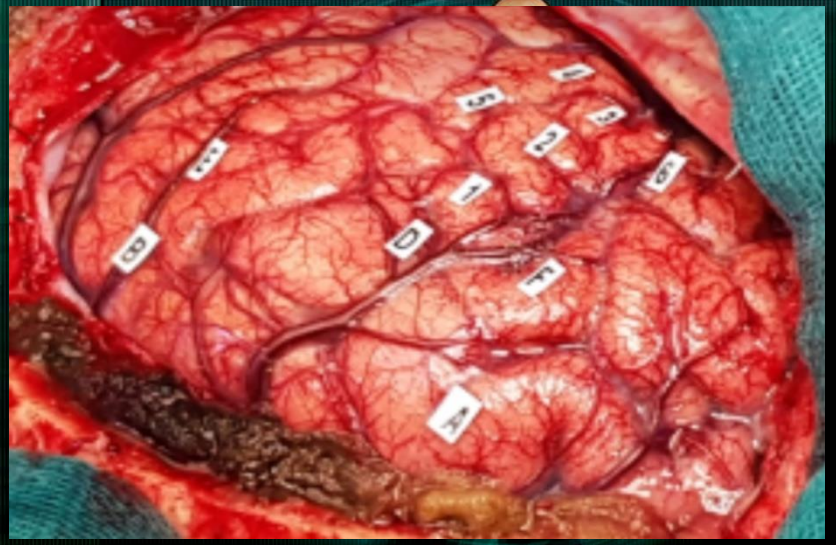


TESIS DOCTORAL

Presentada por:
PILAR LÓPEZ RUIZ

Dirigida por:
Dr. RAÚL ESPERT TORTAJADA
Dr. RICARDO PRAT ACÍN

VALENCIA 2020



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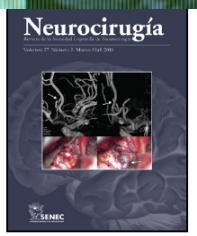

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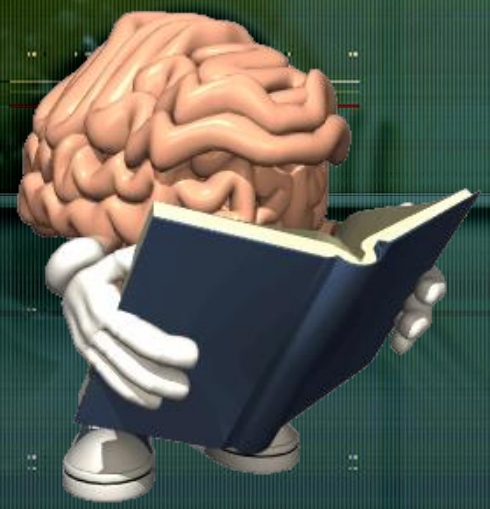
Intraoperative brain mapping during awake surgery in symptomatic supratentorial cavernomas

Ricardo Prat-Acín[a,d,*], *Inma Galeano-Senabre*[a,d], *Pilar López-Ruiz*[b], *Daniel García-Sánchez*[a], *Angel Ayuso-Sacido*[c], *Raul Espert-Tortajada*[b]

[a] *Servicio de Neurocirugía. Hospital Universitario I Politècnic La Fe, Valencia, Spain*
[b] *Departmento de Psicobiología, Universidad de Valencia, Spain*
[c] *Fundación de investigación HM Hospitales, Madrid, Spain*



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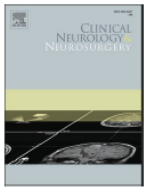

Intraoperative brain mapping of language, cognitive functions, and social cognition in awake surgery of low-grade gliomas located in the right non-dominant hemisphere

Ricardo Prat-Acín[a,*], Inma Galeano-Senabre[a], Pilar López-Ruiz[b], Angel Ayuso-Sacido[c], Raul Espert-Tortajada[b]

[a] *Department of Neurosurgery Hospital Universitario I Politècnic La Fe, Valencia, Spain*
[b] *Department of Psicobiology, University of Valencia, Spain*
[c] *Investigation Foundation HM Hospitals, Madrid, Spain*

II Congreso Internacional Virtual de Psicología ISEP
La psicología, ciencia aplicada a las situaciones de crisis y para la mejora del bienestar

RAUL ESPERT

NEUROPSYCHOLOGY AND PSYCHOBIOLOGY

PROFESOR TITULAR DE UNIVERSIDAD DEPARTAMENTO DE PSICOBIOLOGIA UNIVERSITAT DE VALENCIA (ESPAÑA) NEUROPSICOLOGO EN HOSPITAL CLINICO UNIVERSITARIO (VALENCIA) SERVICIO DE NEUROCIRUGIA. H...

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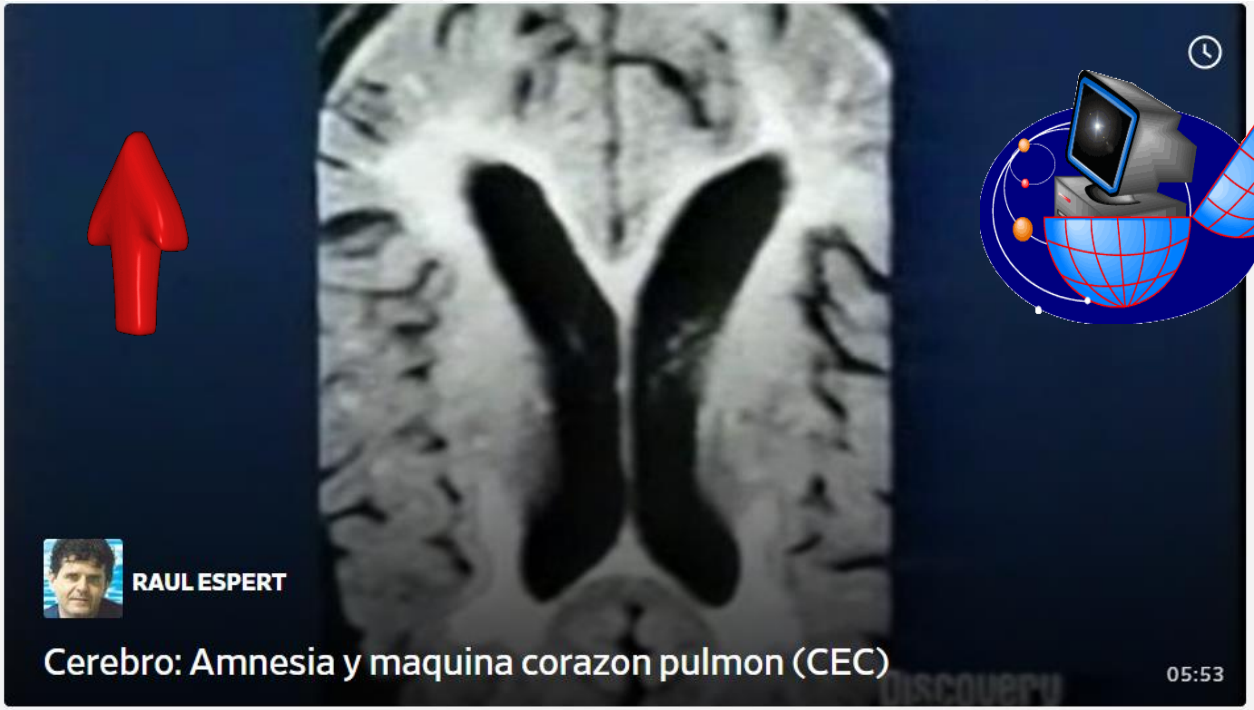

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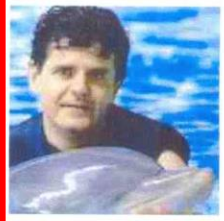

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Egas Moniz: Lobotomia — 0 votos — 1 vista | 0 com.


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MDMA: Alexander Shulgin — Por raulespert hace 5 horas — 1 vista


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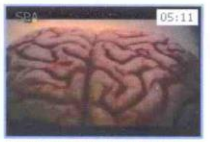
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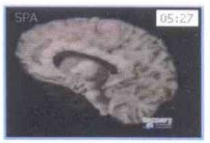
El extasis (MDMA) — Por raulespert hace 19 horas — 6 vistas


Vacuna contra la cocaina — Por raulespert hace 2 días — 5 vistas

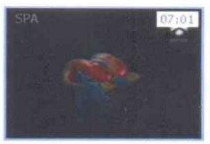

Cannabis y psicosis — Por raulespert ayer — 13 vistas


Cannabis y cerebro — Por raulespert hace 2 días — 13 vistas


Meth y cerebro — Por raulespert hace 3 días — 20 vistas


Nicotina y cerebro 2 — Por raulespert hace 3 días


Neurobiologia de las Benzodiacepinas — Por raulespert hace 3 días


Neurobiologia de los opiaceos — Por raulespert hace 3 días

ÍNDICE

Inteligencia emocional: 0

Tras pegar a Chris Rock

Will Smith ingresa en una clínica de rehabilitación para controlar su estrés

La reacción violenta que el actor tuvo durante la gala de los Oscar le ha llevado a tomar esta decisión

Will Smith reaparece en India un mes después de la agresión de los Oscars

• Diversos medios locales señalan que habría viajado para ver al líder espiritual Sadhguru Jaggi Vasudev

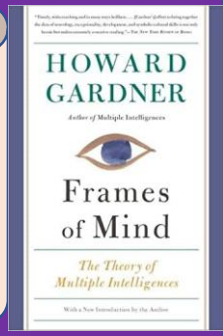
Inteligencia emocional: 0

Carlos III, berrinches y plumas

La estrafalaria sucesión de incidentes del nuevo rey de Inglaterra con los objetos de escritorio da mucho juego literario y semiótico

Inteligencia emocional

Desde 1983, con el Prof. **Howard Gardner** (*Frames of the Mind: The theory of multiple intelligences*), **la inteligencia (C.I.) dejaba de ser considerada un campo único** ligado al conocimiento para albergar diferentes espacios de la vida de una persona, su desarrollo y su capacidad de desempeño frente a estímulos y problemas de la realidad.

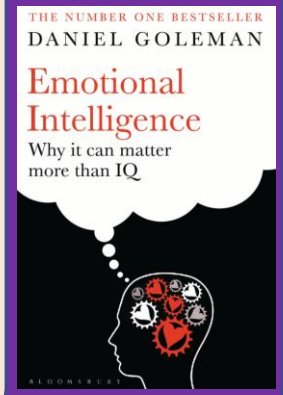


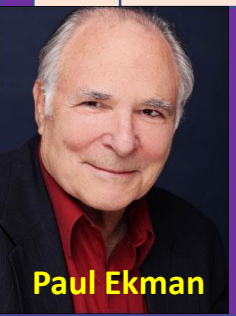
Dividió el C.I. en diferentes capacidades independientes, pero interrelacionadas entre sí, que definen a una persona. De esta manera, separó la inteligencia en **doce tipos distintos** para su análisis:

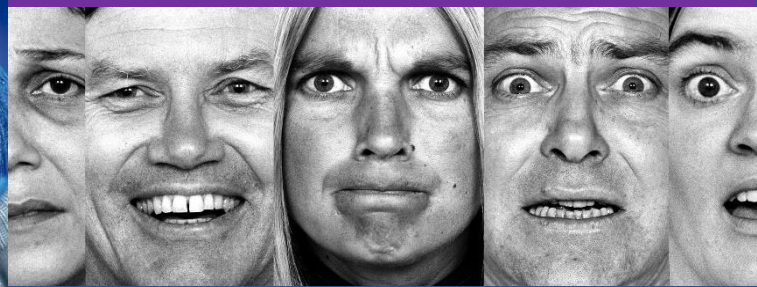
1. inteligencia lingüístico-verbal
2. lógico-matemática
3. visual-espacial
4. musical
5. corporal-kinestésica
6. intrapersonal
7. interpersonal
8. naturalista
9. **emocional**
10. existencial
11. creativa
12. colaborativa

Daniel Goleman

construyó el **concepto de inteligencia emocional**, profundizando en este tipo de inteligencia planteado por Gardner. Esta no depende necesariamente de las emociones, sino también de un correcto pensamiento y desarrollo emocional.







Inteligencia emocional

La **inteligencia emocional** se define como un **conjunto de habilidades que una persona adquiere por nacimiento o aprende durante su vida**, donde destaca la **empatía**, la **motivación** de uno mismo, el **autocontrol**, el **entusiasmo y el manejo de emociones**.

Peter Salovey & John Mayer

El concepto de **inteligencia emocional** fue utilizado por primera vez en el año **1990** con **Peter Salovey y John Mayer.** No consiste en alterar la capacidad de generación de emociones con respecto a diferentes estímulos del entorno, sino se relaciona más con **la reacción que una persona tiene frente a ellas.**

La **inteligencia emocional** no es una sola. Abarca diferentes tipos y características que definen el CI emocional: 5 categorías:

- **Empatía:** Consiste en entender cómo se sienten los demás y aprender a comunicarse correctamente para lograr un objetivo común.
- **Habilidades sociales:** las buenas relaciones interpersonales guían a las personas al éxito, ya que pueden lograr más cosas con liderazgo, gestión de conflictos, cooperación y trabajo en equipo.
- **Autoconocimiento:** Capacidad de reconocer los sentimientos que uno alberga y cómo estos pueden afectar las acciones que hacen. La conciencia emocional y la confianza son vitales para su desarrollo.
- **Motivación:** Se relaciona con el compromiso de llegar a los objetivos que uno se plantea, cómo se mantiene el positivismo ante las adversidades (resiliencia) y cuál es la iniciativa que una persona maneja para plasmar determinadas metas.
- **Autorregulación:** las técnicas de autocontrol son esenciales en la inteligencia emocional. Controlar la duración de nuestras emociones y que tanto influyen estas en nuestras decisiones es vital para este tipo de inteligencia emocional.

Inteligencia emocional

¿Qué características tienen las personas con alto grado de Inteligencia Emocional?:

1. **Prestan atención a sus emociones**: analizan sus emociones y las escuchan, no solo se limitan a sentirlas.

2. **Conocen sus sentimientos y no los reprimen**: estas personas son auténticas y sinceras, ya que expresan sus sentimientos de forma clara.
Analizan sus proyectos y sueños: no viven en un sueño constante, sino que saben razonar sobre lo que sienten y si alguna meta puede ser alcanzada o no.

3. **Tienen un balance constante en sus acciones**: saben que todo tiene su lado bueno o malo, por lo que dirigen su atención a las cosas que pueden solucionar o que pueden ser de utilidad para ellos mismos.

4. **No toman nada personal**: cuando una persona los altera o algo en su entorno no sale como lo tenían planeado, analizan qué pudieron haber hecho mal y qué cosas mejorar a futuro. No se concentran en algo que no pueden controlar.

5. **Son autocríticos con sus acciones**: las emociones no los controlan, ellos controlan lo que deciden hacer con ciertas emociones y reconocen cuando algo se les fue de las manos.

6. **Se fijan en las emociones de otras personas**: intentan ser siempre empáticos con sus semejantes para saber cómo expresan sus emociones. Así, se relacionan mejor con los demás.

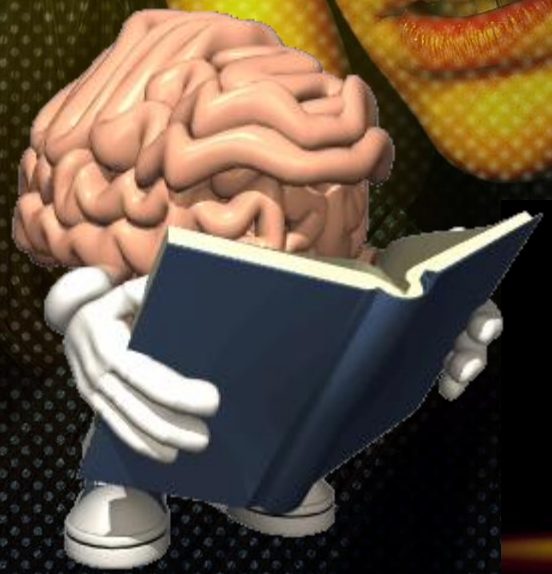
7. **Conocen siempre gente nueva pero se rodean de aquellos con los que tienen una conexión**: A través de otras personas, conocen diferentes puntos de vista y comparten más con aquellos que son compatibles con la suya. No pierden tiempo en relaciones tóxicas ahorrándose así una incomodidad innecesaria.

8. **Se motivan a sí mismos constantemente**: estas personas se emocionan cuando sucede algo que les gusta o realizan una acción determinada. No se enfrascan en por qué ya no les motivan cosas antiguas, sino que buscan siempre renovar su emoción con nuevas experiencias.

1. BREVE HISTORIA DE LAS EMOCIONES

BREVE HISTORIA DE LAS EMOCIONES

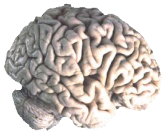
Corazón vs. cerebro



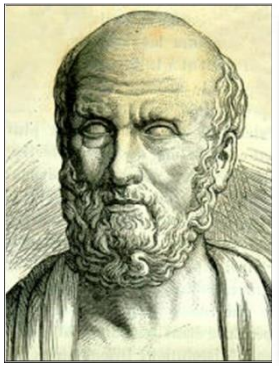
¿Qué es una emoción?¿Qué es un sentimiento?

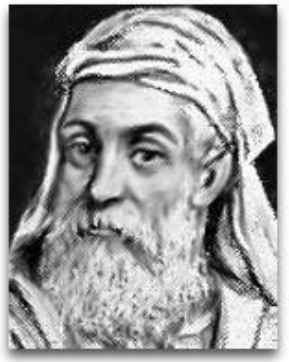
LAS EMOCIONES: BREVE HISTORIA

Comportamiento (mente) está controlado por un alma:



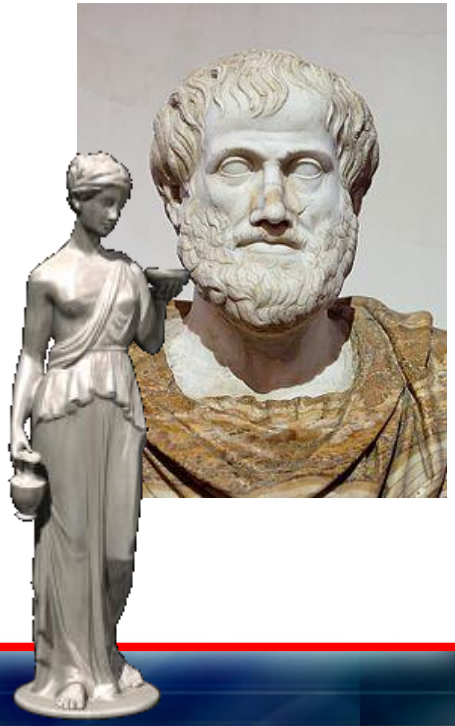
-Alcmeon de Crotona (500 años a. de C.): Cerebro





-Empédocles (490 a de C.): Corazón

Aristóteles: El corazón era la sede de las sensaciones de las pasiones y de la inteligencia. El cerebro compuesto de agua y tierra no tenía otro papel que refrigerar el organismo.



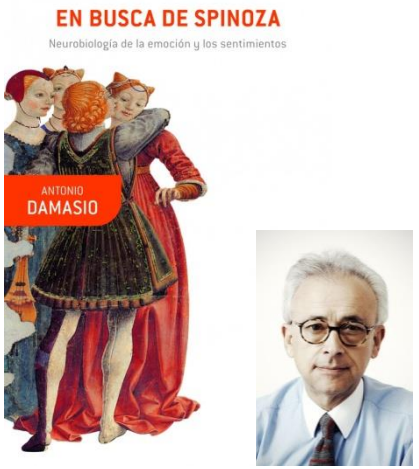
Ni en el Antiguo ni en el Nuevo Testamento se cita ni una sola vez la palabra cerebro, sin embargo sí citan cientos de veces el corazón y hacen referencia al hígado, intestino... como lugares de asiento de la pasión, el coraje y la compasión. “ *Te doy un corazón de sabiduría*” dijo el profeta.

Legado actual: Frases como “*me has roto el corazón*”

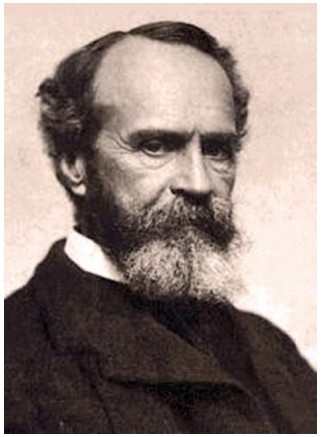
CORAZÓN vs. CEREBRO

HISTORIA

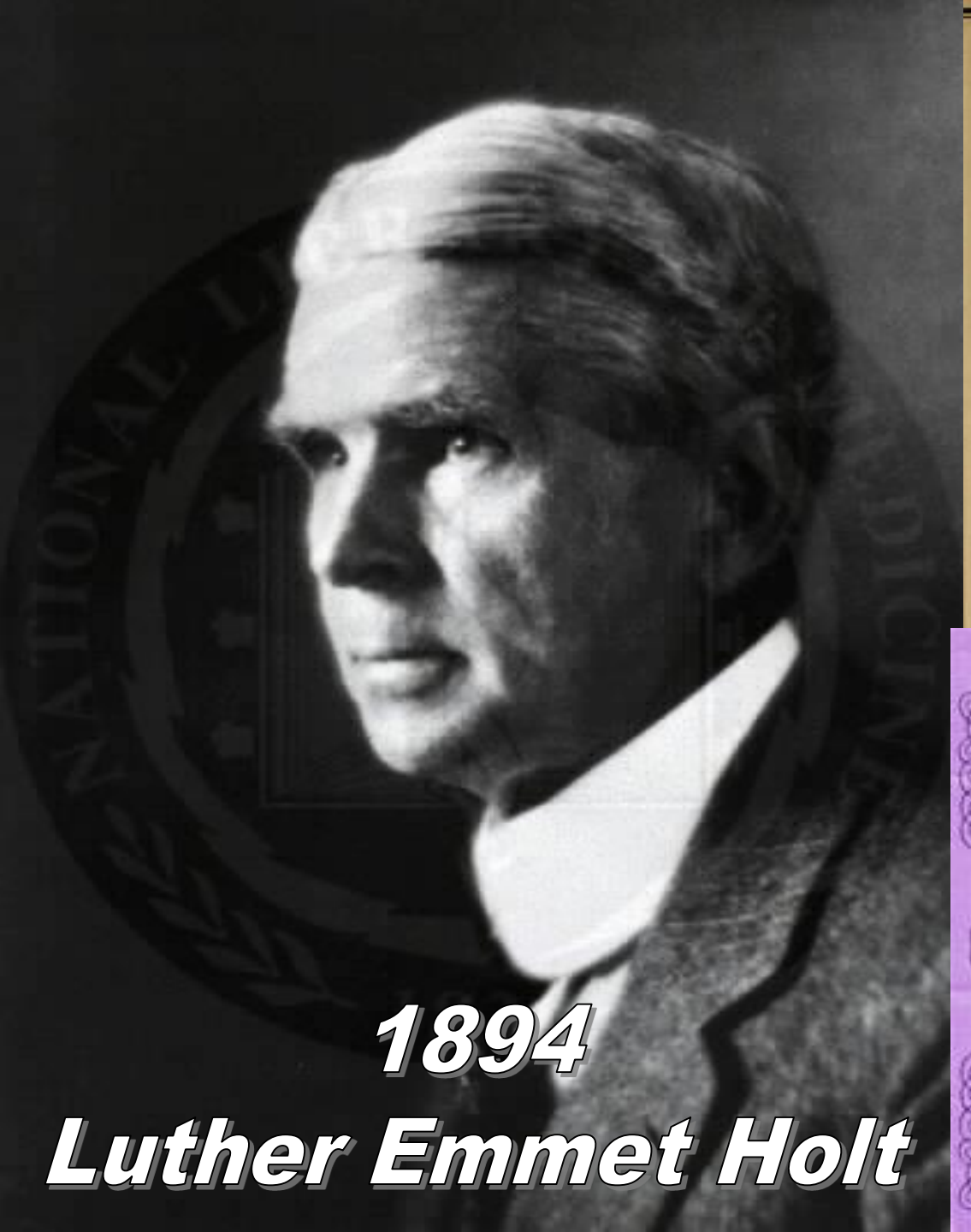
- ***Damasio* (2003): «las emociones se representan en el teatro del cuerpo». «Los sentimientos se representan en el teatro de la mente».**
- ***«Las emociones son el fundamento de los sentimientos».***



- ***William James* (1884): «como respuesta a las experiencias y estímulos, el sistema nervioso autónomo crea respuestas fisiológicas (tensión muscular, lagrimeo, aceleración cardiorrespiratoria…) a partir de las cuales se crean las emociones»**

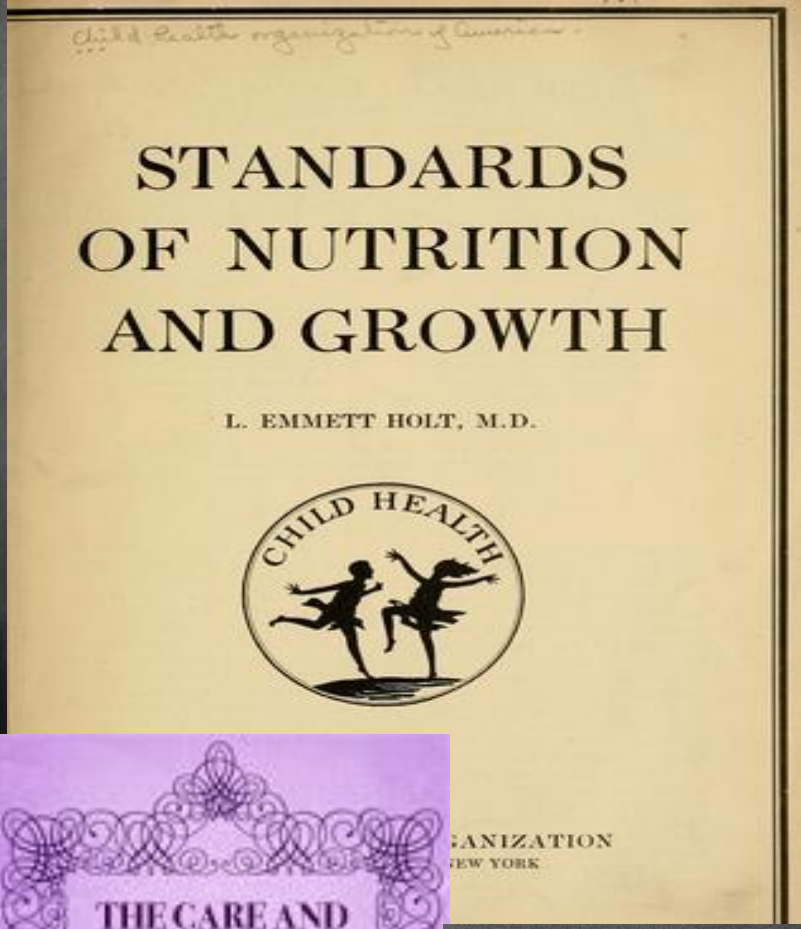


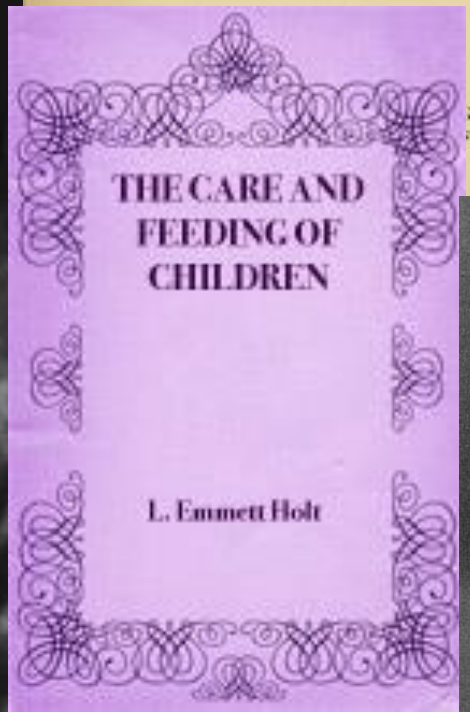
Damasio, A. (2003). En busca de Spinoza. Neurobiología de la emoción y los sentimientos. Barcelona: Booket.

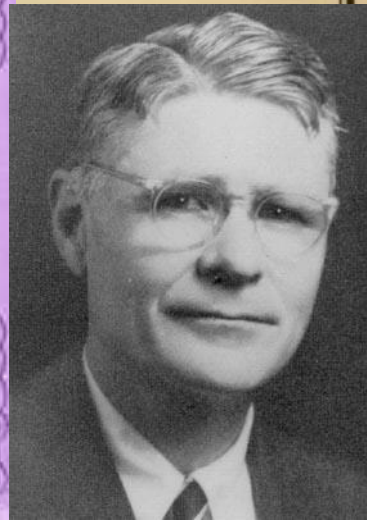


1894

Luther Emmet Holt







DEFINICIÓN

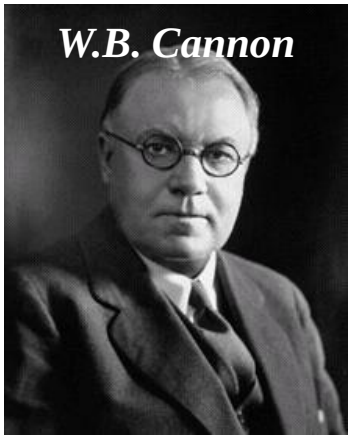
- ***DEFINICIÓN DE EMOCIÓN*** *(Damasio, 2003):*
- *«**conjunto complejo de respuestas químicas y neuronales automáticas que forman un patrón distintivo**». «Estas respuestas son **producidas por el cerebro sano cuando detecta un estímulo emocionalmente competente, ya sea de origen externo o interno**»*
- *«La mayoría de los estímulos nos provoca alguna reacción emocional (por pequeña que sea)»*

«El cerebro está preparado por la evolución para responder a determinados estímulos emocionalmente competentes con repertorios específicos de acción. Sin embargo, existen muchos otros que son aprendidos en toda una vida de experiencia. El resultado inmediato de todas estas respuestas es un cambio temporal en el estado del propio cuerpo»

Damasio, A. (2003). En busca de Spinoza. Neurobiología de la emoción y los sentimientos. Barcelona: Booket.

DEFINICIÓN

- *Todos los organismos vivos (desde una ameba hasta un ser humano), nacen con una maquinaria diseñada para resolver automáticamente, sin que se requiera el razonamiento adecuado, los problemas básicos de la vida (**homeostásis**): (emociones en animales)*



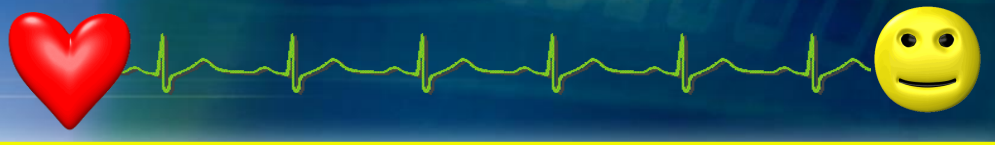
1. -Encontrar fuentes de energía; mantener un equilibrio químico del interior compatible con el proceso vital

2. -Conservar la estructura del organismo mediante la reparación del desgaste natural.

3. -Detener los agentes externos de enfermedad y daño físico.

Sapolsky, R.M. (1995). ¿Por qué las cebras no tienen úlcera? La guía del estrés. Madrid, Alianza.

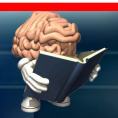
LAS EMOCIONES



- *Niveles de **regulación homeostática**, desde lo simple a lo complejo:*

- ***-Regulación metabólica.** Mantener el equilibrio de las **señales químicas** internas (acidez y alcalinidad; síntesis y transporte de proteínas, lípidos y carbohidratos, etc.).*
- ***-Reflejos básicos.** **Reflejo de sobresalto**: los organismos responden ante un ruido fuerte o contacto. **Tropismos** que hacen los organismos para alejarse del frío y acercarse al calor, o bien para alejarse de la oscuridad y acercarse a la luz.*
- ***-El sistema inmune**. Preparado para detectar virus, parásitos, bacterias y moléculas de sustancias químicas tóxicas que invaden el organismo.*
- ***-Comportamientos de dolor y placer**. Cuando hay o una lesión inminente de tejidos del cuerpo, las células de la región afectada emiten señales químicas nociceptivas. En respuesta, el organismo reacciona automáticamente con comportamientos de dolor o comportamientos de enfermedad (cioquinas). Placer: endorfinas.*
- ***-Instintos y motivaciones**. Hambre, sed, curiosidad, exploración, juego y sexo.*
- ***-Emociones propiamente dichas**. Desde la alegría, la pena y el miedo hasta el orgullo, la vergüenza y la simpatía. En esta misma cúspide también encontraríamos los sentimientos.*

Sapolsky, R.M. (1995). ¿Por qué las cebras no tienen úlcera? La guía del estrés. Madrid, Alianza.

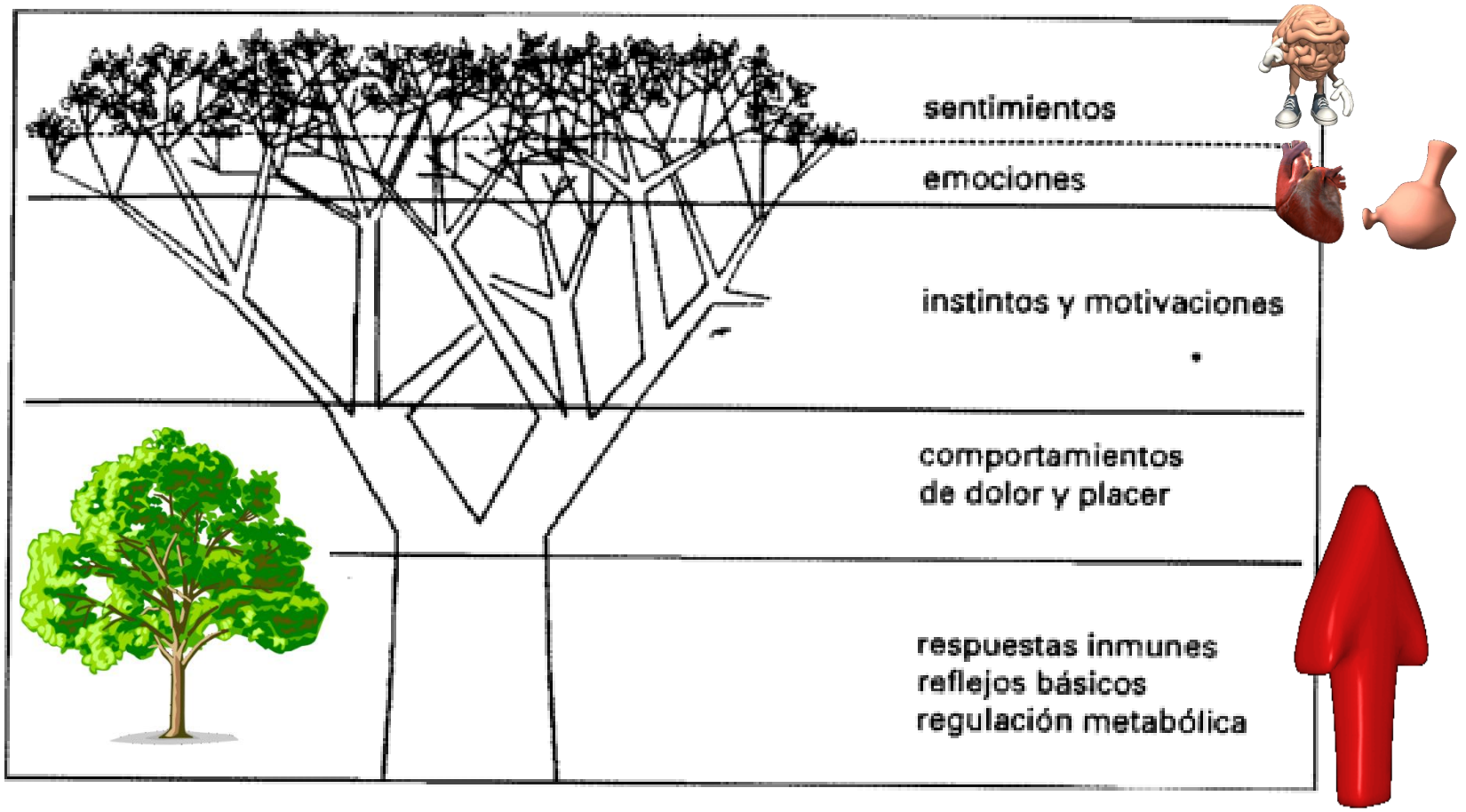


DEFINICION

http://www.dailymotion.com/video/x72wcw_panksepp-emociones-en-animales_school

http://www.dailymotion.com/video/x2b6d0k_la-risa-de-las-ratas-jaak-pankseep_school

LAS EMOCIONES



Niveles de regulación homeostática automatizada, desde lo simple a lo complejo. Los sentimientos son una expresión mental de todos los demás niveles de regulación homeostática

Damasio, A. (2003). En busca de Spinoza. Neurobiología de la emoción y los sentimientos. Barcelona: Booket.

LAS EMOCIONES

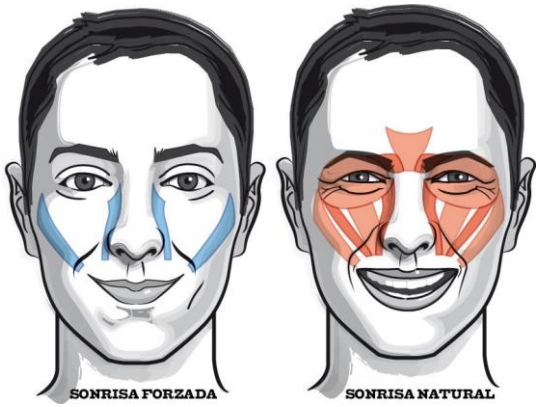
Taxonomía de los sentimientos

Protoemociones	Bienestar		Malestar					
Emociones básicas	Alegría		Miedo		Enfado		Tristeza	
Emociones cognitivas primarias (ejemplos)	Buen humor	Satisfacción	Amenaza	Angustia	Disgusto	Frustración	Decepción	Abatimiento
Emociones cognitivas secundarias (ejemplos)	Amor Suerte		Vergüenza Celos Envidia		Cólera Desprecio		Luto	

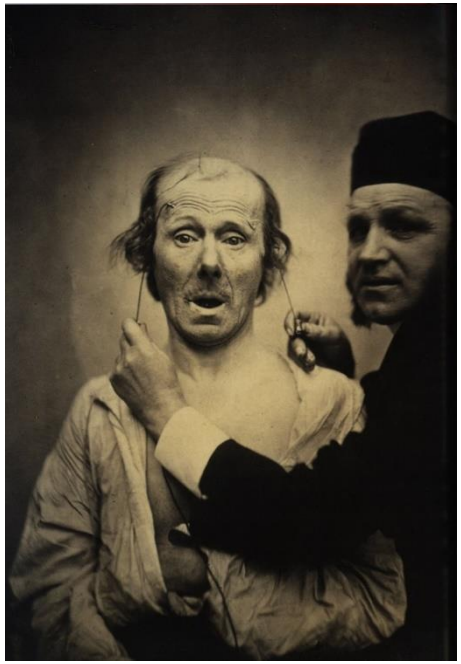
Ekman, P.(2012). El rostro de las emociones. RBA Libros.

LAS EMOCIONES (Sonrisa de Duchenne)

-La sonrisa de Duchenne (Guillaume Duchenne), es un tipo de sonrisa que involucra la contracción de los músculos cigomático mayor y menor cerca de la boca, los cuales elevan la comisura de los labios, y el músculo orbicular cerca de los ojos, cuya contracción eleva las mejillas y produce arrugas alrededor de los ojos (indica una emoción espontánea y genuina ya que la mayor parte de las personas no pueden contraer a voluntad el músculo orbicular).



-La respuesta muscular que genera una sonrisa espontánea (o de Duchenne) es producto de un impulso generado en los ganglios basales como respuesta a procesos del sistema límbico. En cambio, la sonrisa voluntaria tiene origen en la corteza motora. Activar voluntariamente, desde la corteza motora, la cantidad de músculos que implica una sonrisa espontánea y no predominantemente el risorio tiene un grado de complejidad que impide que sea realizado exitosamente sin entrenamiento.



http://www.dailymotion.com/video/x17v0ki_cerebro-mentiroso-sonrisa-de-duchenne_school

http://www.dailymotion.com/video/x3hijd5_mentiras-lobulo-frontal-y-sonrisa-falsa_school

Maps of subjective feelings

PNAS | September 11, 2018 | vol. 115 | no. 37 |

Lauri Nummenmaa[a,b,1], Riitta Hari[c,1], Jari K. Hietanen[d], and Enrico Glerean[a]

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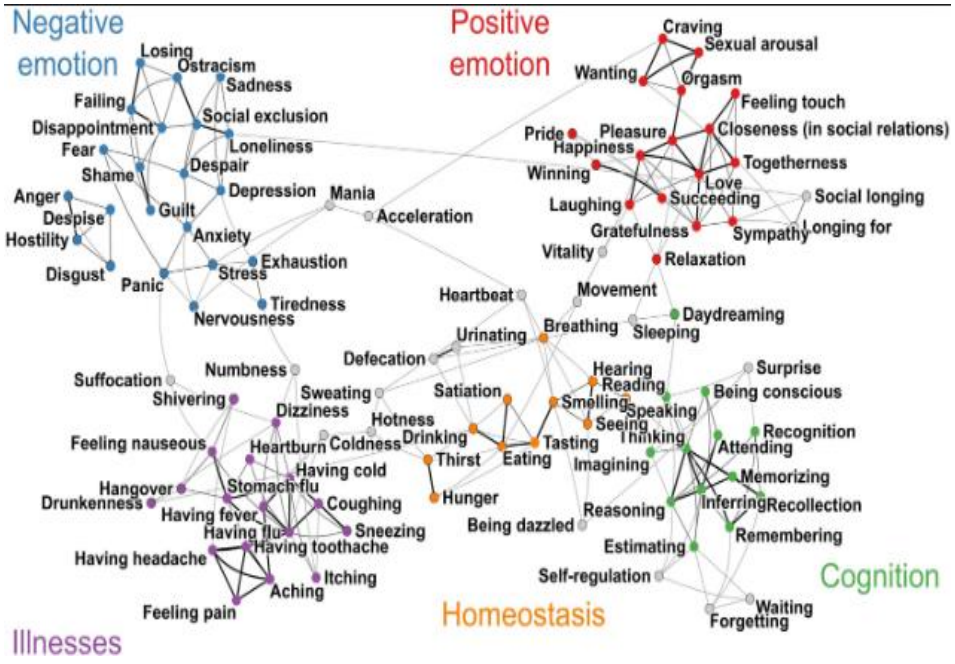
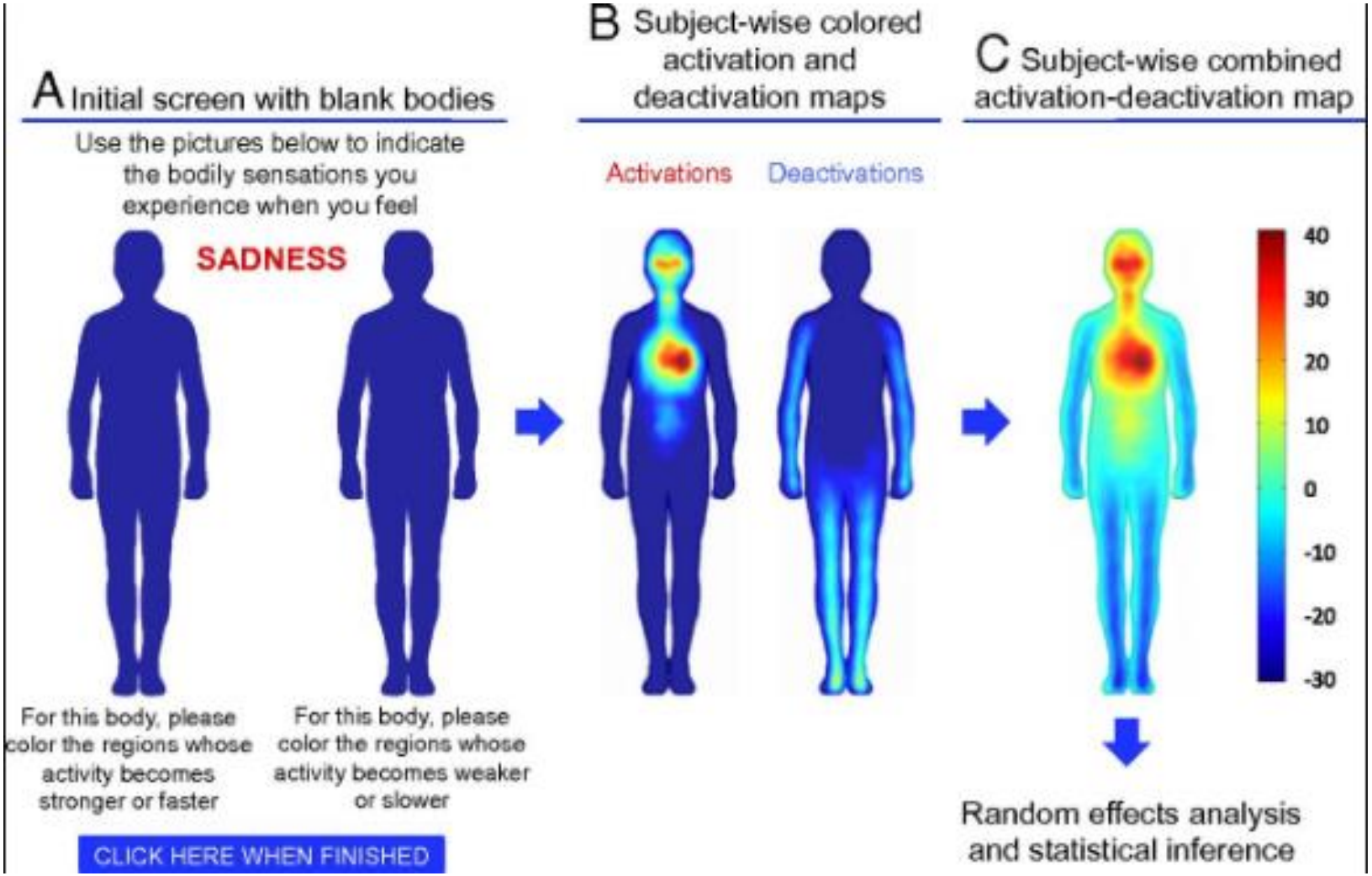
Subjective feelings are a central feature of human life. We defined the organization and determinants of a feeling space involving 100 core feelings that ranged from cognitive and affective processes to somatic sensations and common illnesses. The feeling space was determined by a combination of basic dimension rating, similarity mapping, bodily sensation mapping, and neuroimaging meta-analysis. A total of 1,026 participants took part in online surveys where we assessed (*i*) for each feeling, the intensity of four hypothesized basic dimensions (mental experience, bodily sensation, emotion, and controllability), (*ii*) subjectively experienced similarity of the 100 feelings, and (*iii*) topography of bodily sensations associated with each feeling. Neural similarity between a subset of the feeling states was derived from the NeuroSynth meta-analysis database based on the data from 9,821 brain-imaging studies. All feelings were emotionally valenced and the saliency of bodily sensations correlated with the saliency of mental experiences associated with each feeling. Nonlinear dimensionality reduction revealed five feeling clusters: positive emotions, negative emotions, cognitive processes, somatic states and illnesses, and homeostatic states. Organization of the feeling space was best explained by basic dimensions of emotional valence, mental experiences, and bodily sensations. Subjectively felt similarity of feelings was associated with basic feeling dimensions and the topography of the corresponding bodily sensations. These findings reveal a map of subjective feelings that are categorical, emotional, and embodied.

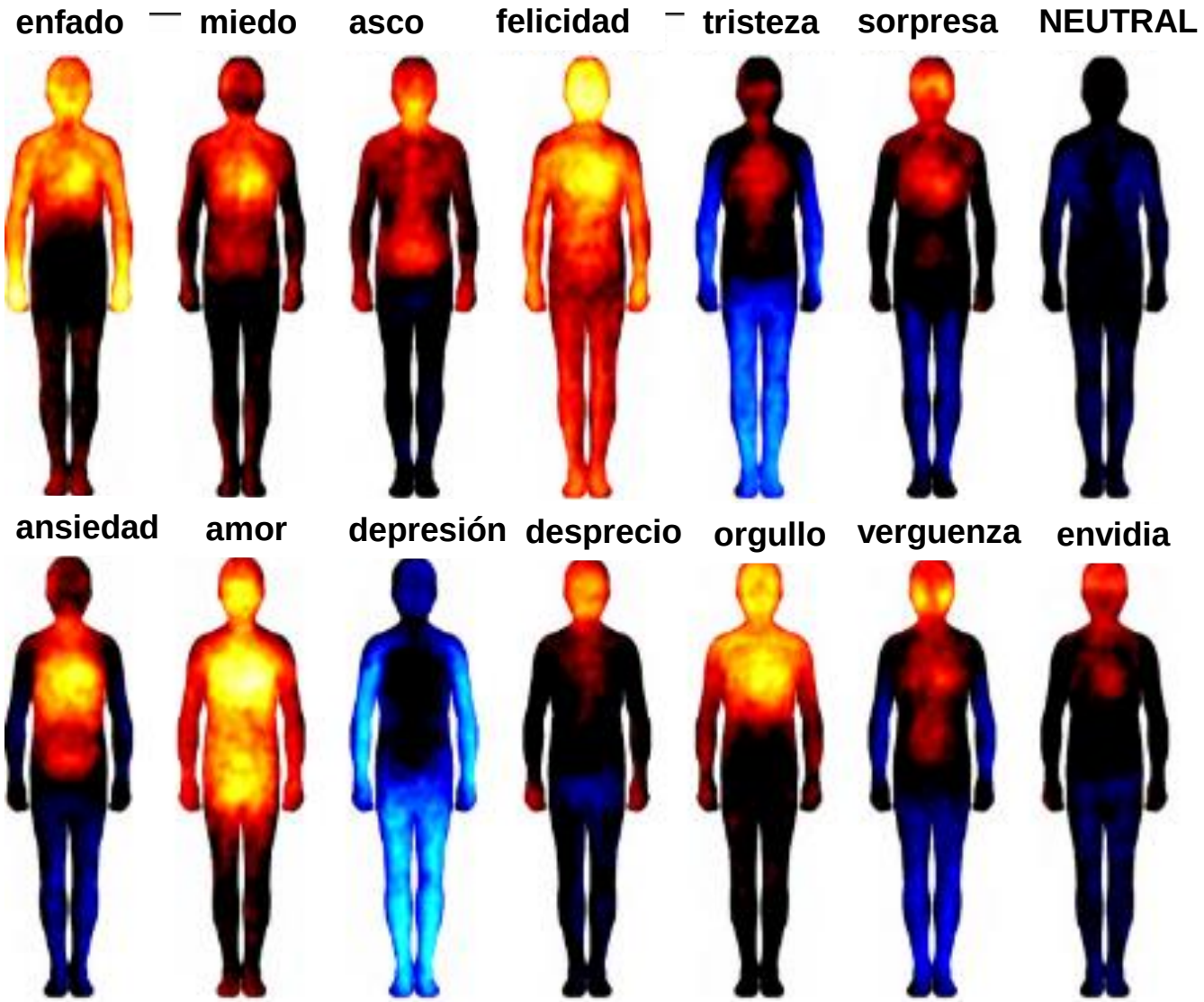


CEREBRO EMOCIONAL



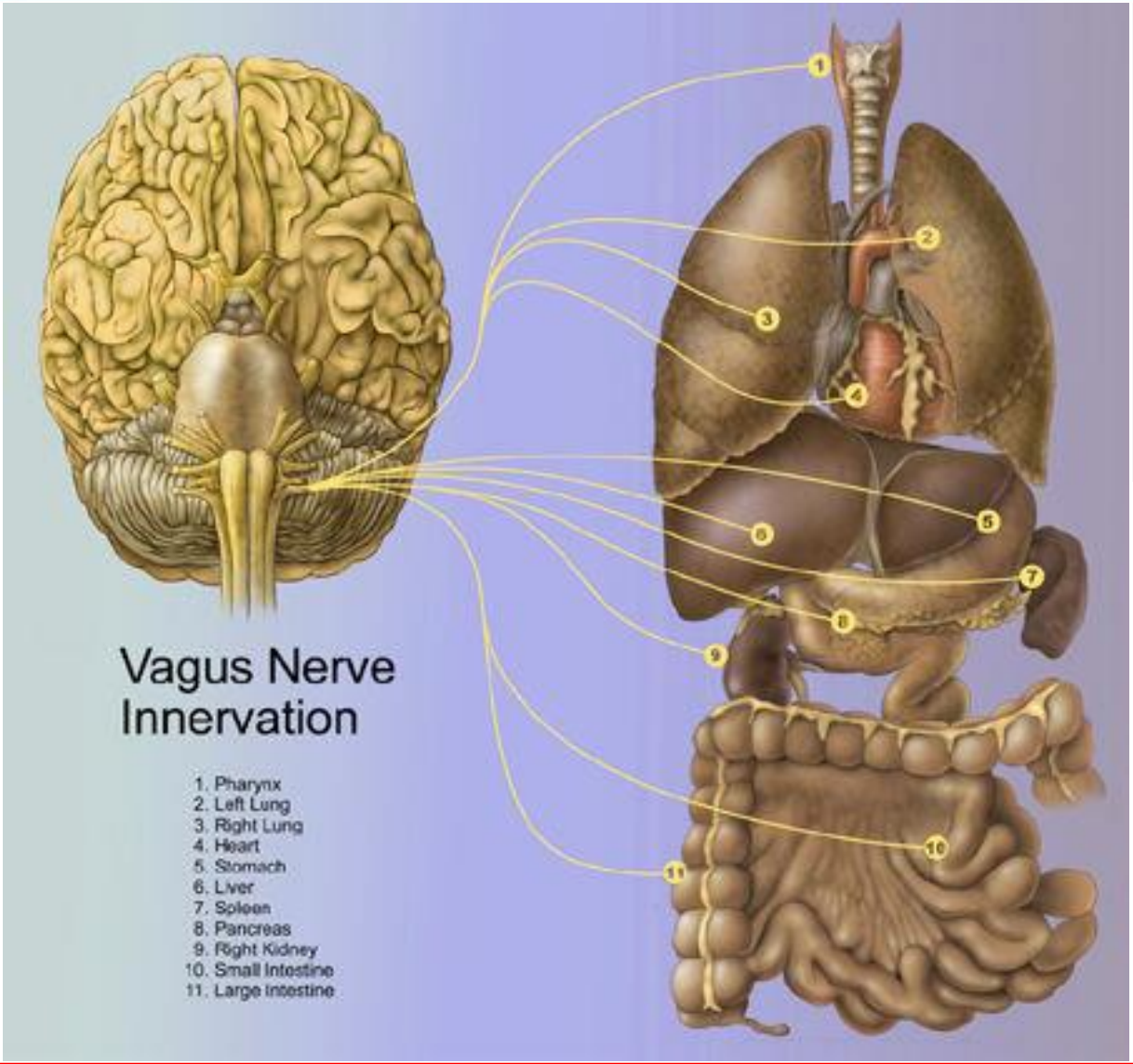
www.pnas.org/cgi/doi/10.1073/pnas.1807390115

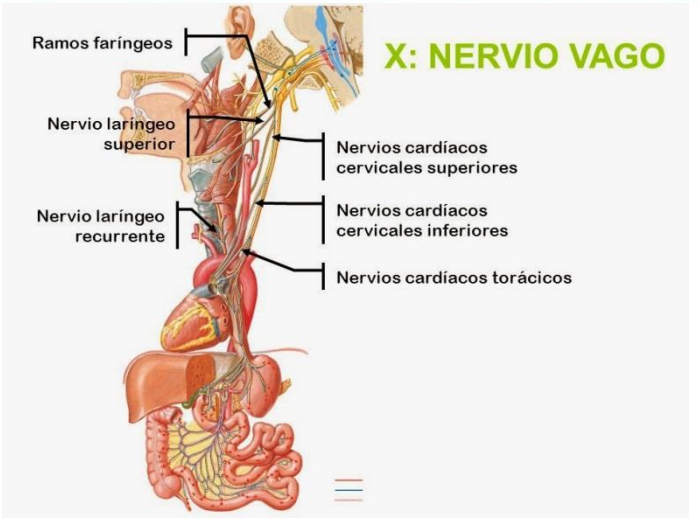
CEREBRO EMOCIONAL

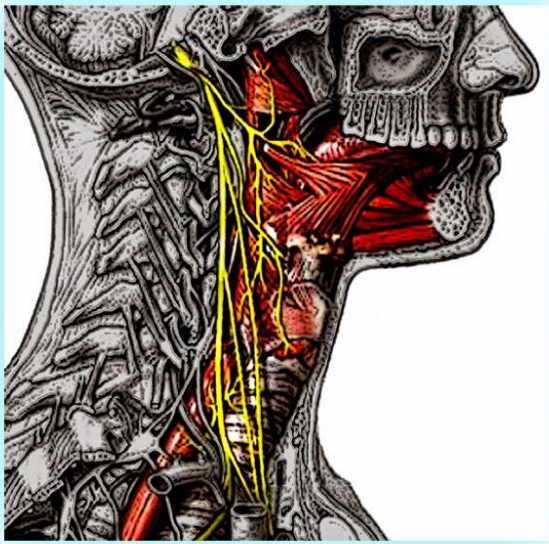


www.pnas.org/cgi/doi/10.1073/pnas.1807390115

LAS EMOCIONES: NERVIO VAGO







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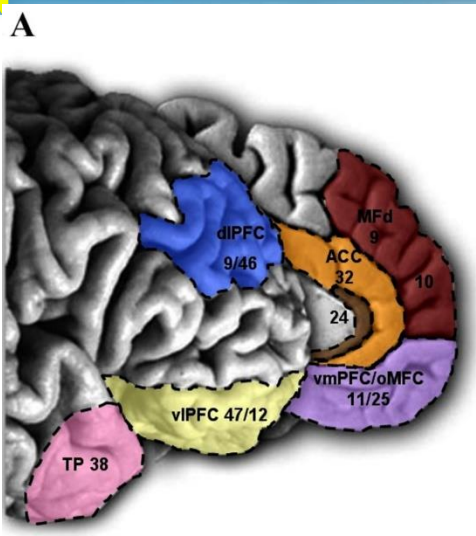
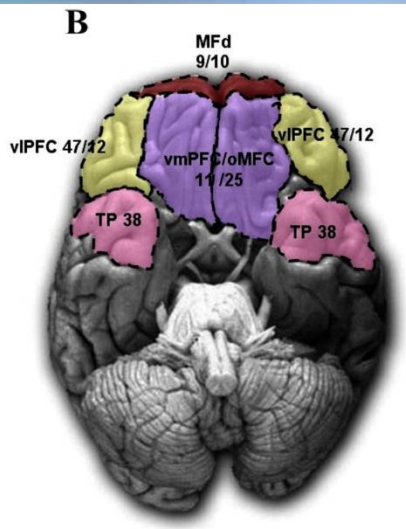
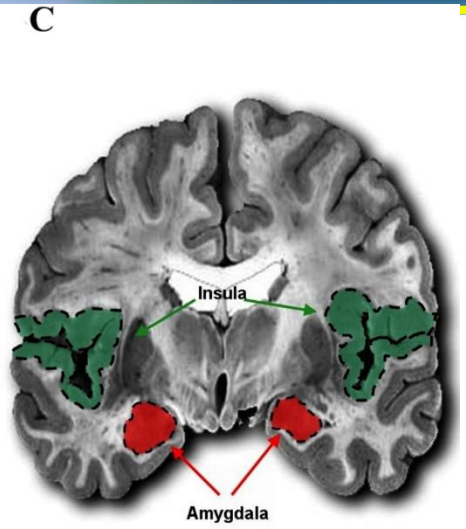






Mobbs D, Lau HC, Jones OD, Frith CD (2007)- Law, Responsibility, and the Brain. PLoS Biol 5(4): April 17,

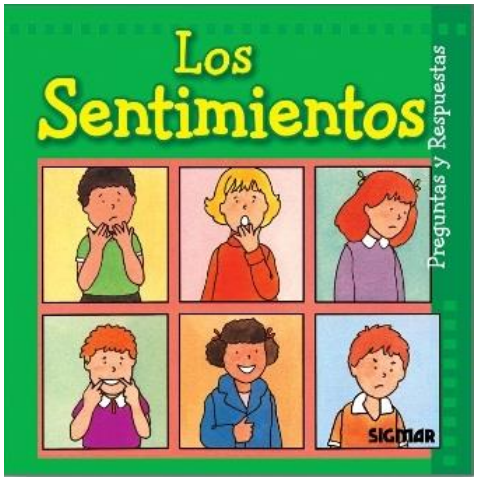
Brain Region	Pro-Social Behaviour
Anterior cingulate cortex	Empathy [71,72]
Orbital PFC	Regret [24]
Ventromedial PFC	Ethical decisions [73,74]
Ventrolateral PFC	Inhibition of behaviour [75]
Dorsolateral PFC	Reasoning [46,76]

doi:10.1371/journal.pbio.0050103.t001

MARCADORES SOMÁTICOS

LOS SENTIMIENTOS

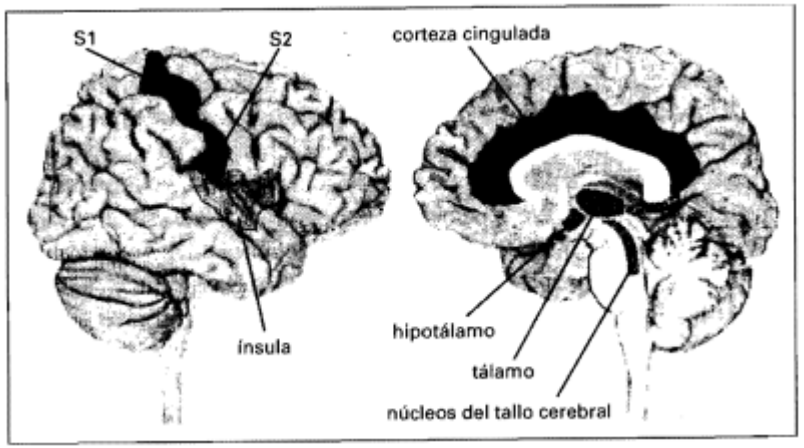
-Damasio (2003) define los ***sentimientos*** *como la* ***percepción de un determinado estado del cuerpo junto con la percepción de un determinado modo de pensar*** *(percepción o cognitivización de la emoción a un nivel consciente).*



-Los sentimientos surgen cuando la acumulación absoluta de detalles cartografiados por el cerebro alcanza una fase determinada (el sustrato de sentimientos es el conjunto de patrones neurales que cartografían el estado corporal y del que puede surgir una imagen mental del estado del cuerpo).

-En resumen, el sentimiento implica la ***percepción de un determinado estado corporal y la de un determinado estado mental acompañante****.*

-Marcadores somáticos: Cortex somatosensorial primario, Insulas, corteza cingulada y nn. Troncoencefálicos (la elaboración de sentimientos requiere de la integridad de todas estas estructuras cerebrales



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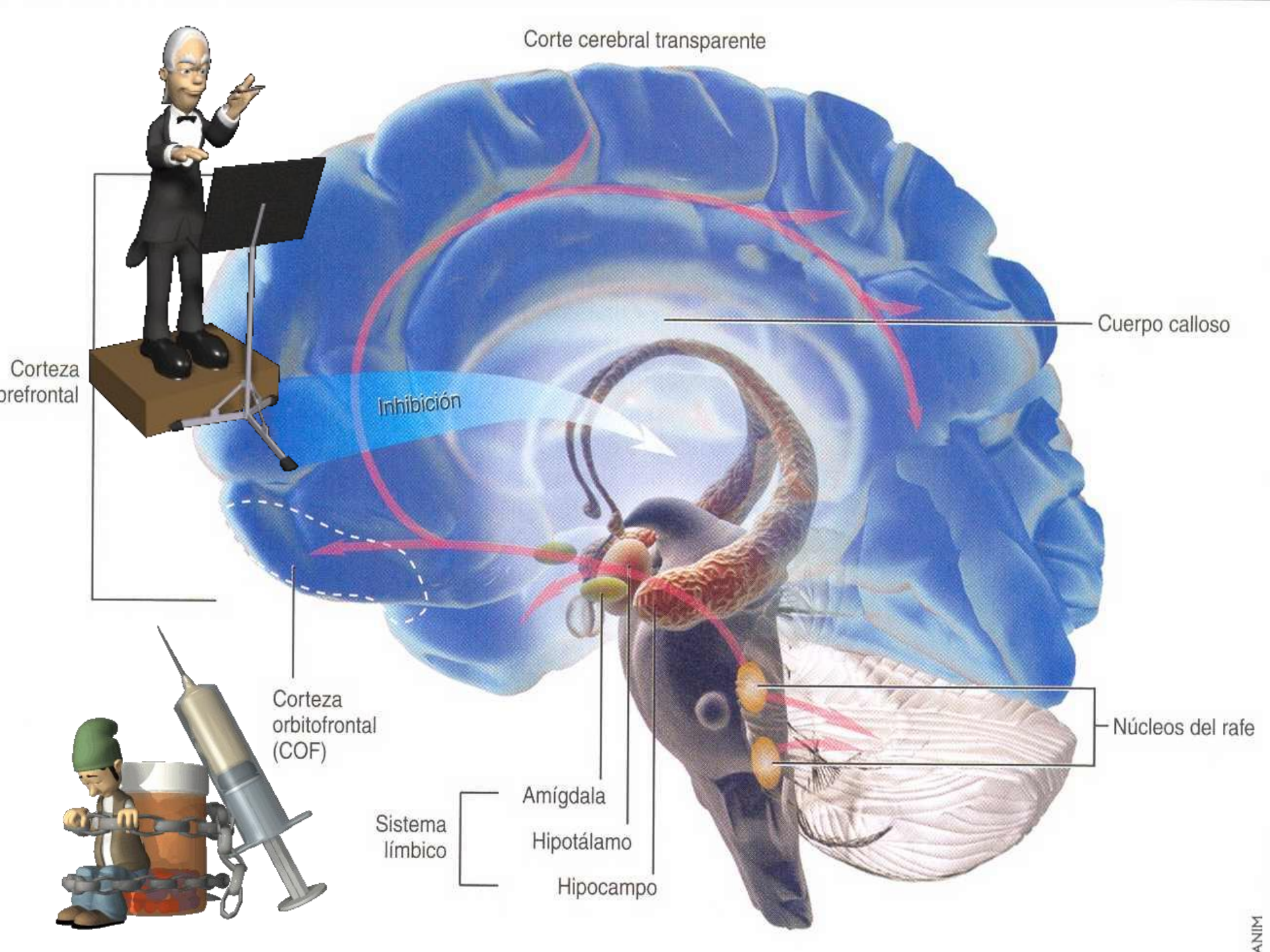
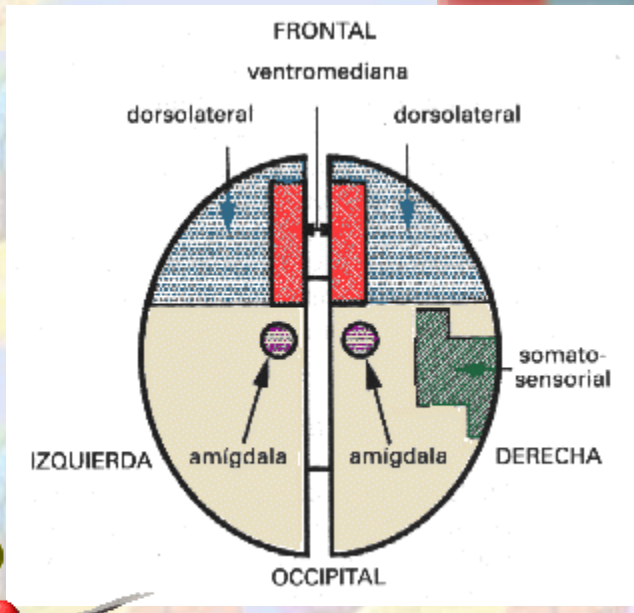

Corte cerebral transparente
Cuerpo calloso
Corteza prefrontal
Inhibición
Corteza orbitofrontal (COF)
Núcleos del rafe
Amígdala
Sistema límbico
Hipotálamo
Hipocampo

CEREBRO EMOCIONAL

Marcadores somáticos

El marcador somático

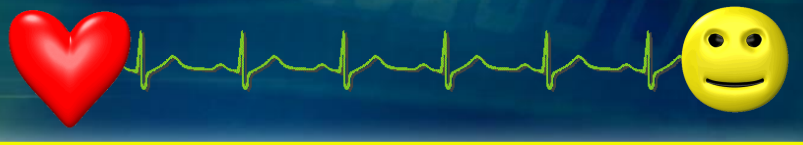
Las cortezas prefrontales serían las encargadas de la adquisición de las señales de los marcadores somáticos. Sus múltiples y variadas conexiones con todas las regiones sensoriales (incluidas las cortezas somatosensoriales), con los núcleos del troncoencéfalo y del prosencéfalo basal, con la amígdala, la ínsula anterior, con el cortex cingulado anterior y el hipotálamo, le mantienen actualizada de lo que ocurre al organismo.

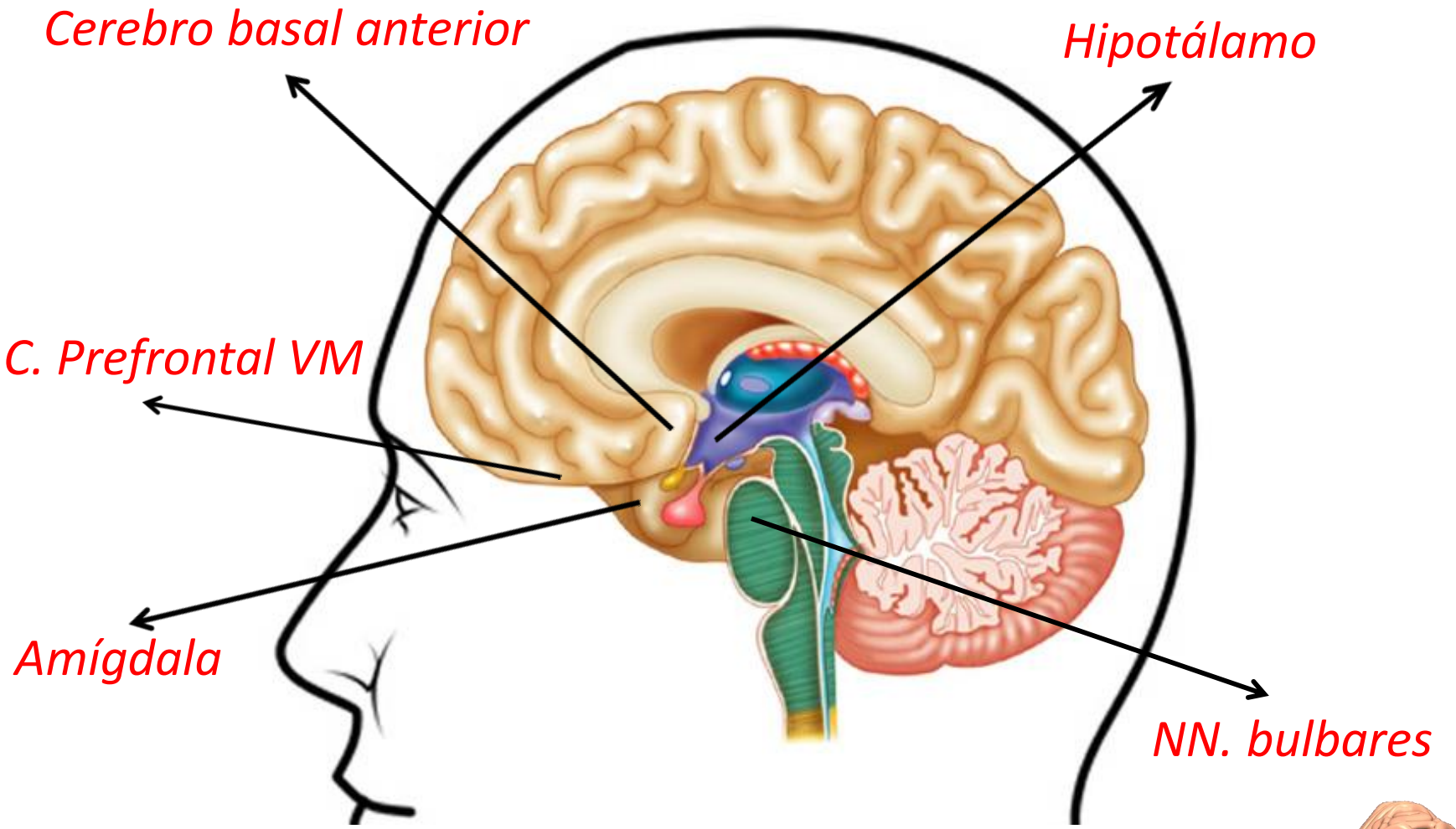


*La **región prefrontal ventromedial** cumple una función crítica en la representación somatosensorial, interpretando las sensaciones de nuestro cuerpo, asociadas a los eventos emocionales (generan respuestas inmediatas mediadas por el SNA)*

Las cortezas prefrontales establecen categorizaciones de las distintas situaciones que ha debido enfrentar el organismo, creando así una especie de "banco de datos" ordenado sobre nuestras distintas experiencias y a partir de cómo ha reaccionado nuestro cuerpo en aquellas situaciones.

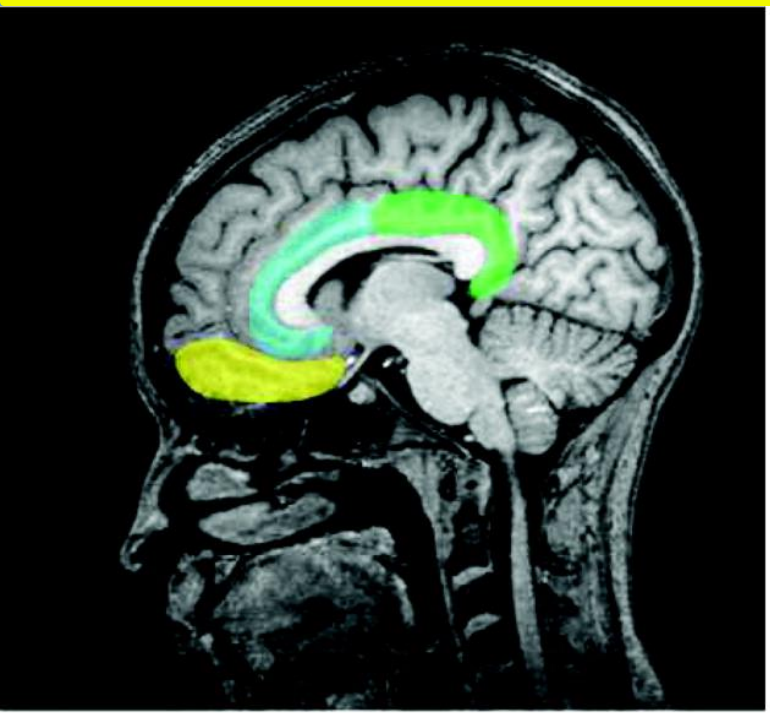
CEREBRO EMOCIONAL

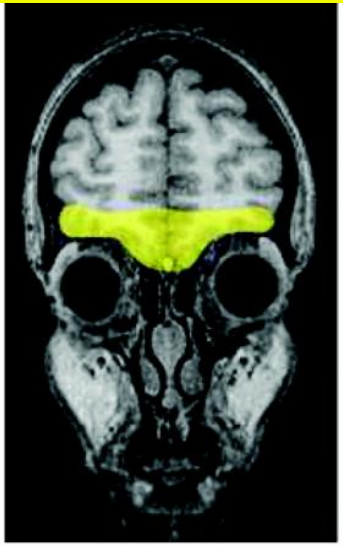


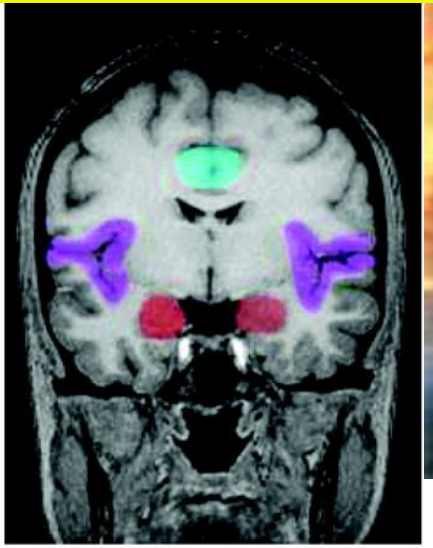


«la emoción resulta de la participación combinada de varios lugares de un sistema cerebral» (Damasio, 2003).

CEREBRO EMOCIONAL







Science 8 November 2007: Vol. 298. no. 5596, pp. 1191 – 119
Review NEUROSCIENCE AND PSYCHOLOGY:
Emotion, *COGNITION****, and Behavior R. J. Dolan***

Brain regions implicated in emotional experience include orbitofrontal cortex (yellow), insular cortex (purple), and anterior (blue) and posterior (green) cingulate cortices. The amygdala (red) is involved in linking perception with automatic emotional responses and memory

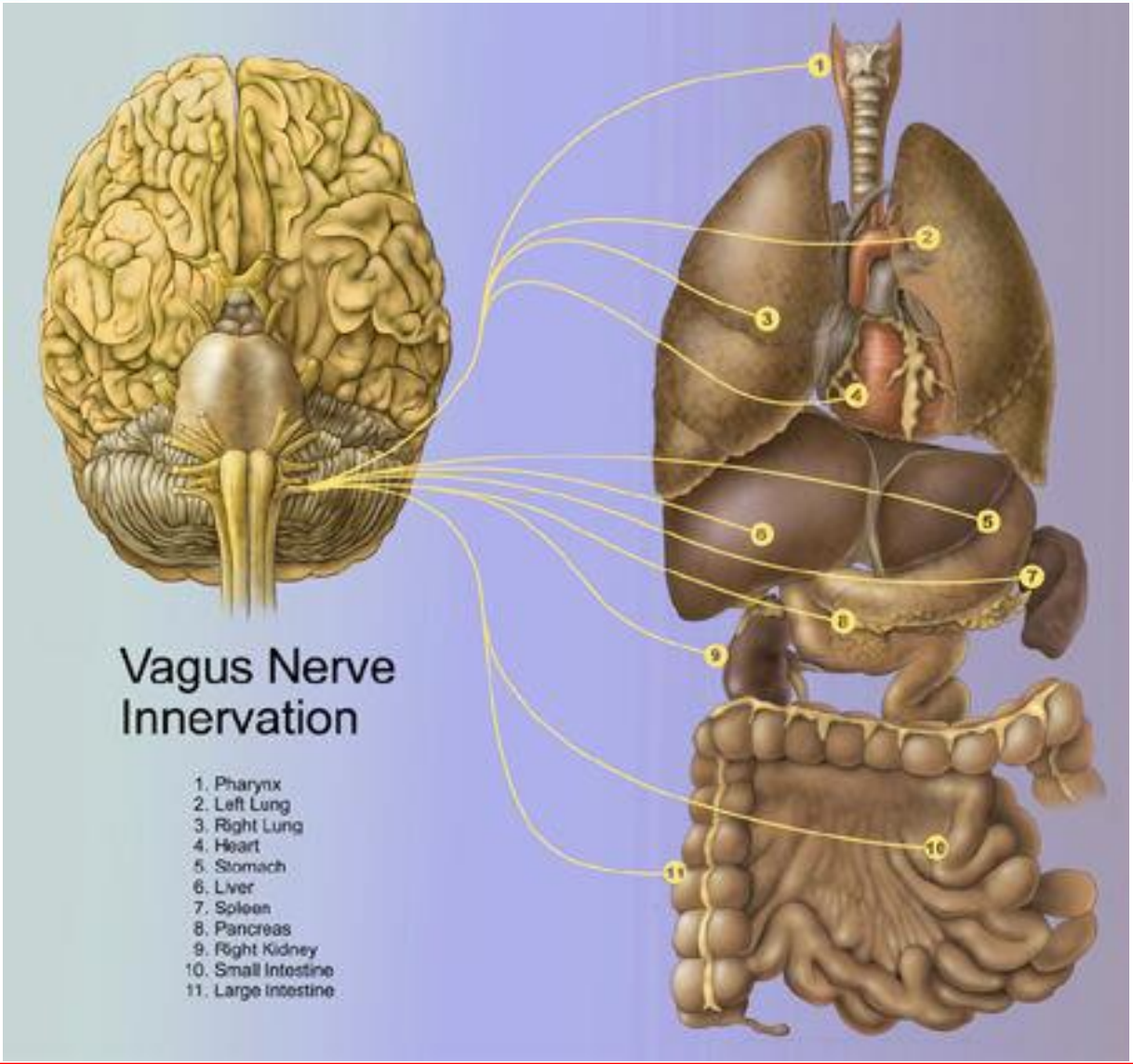
MARCADORES SOMÁTICOS

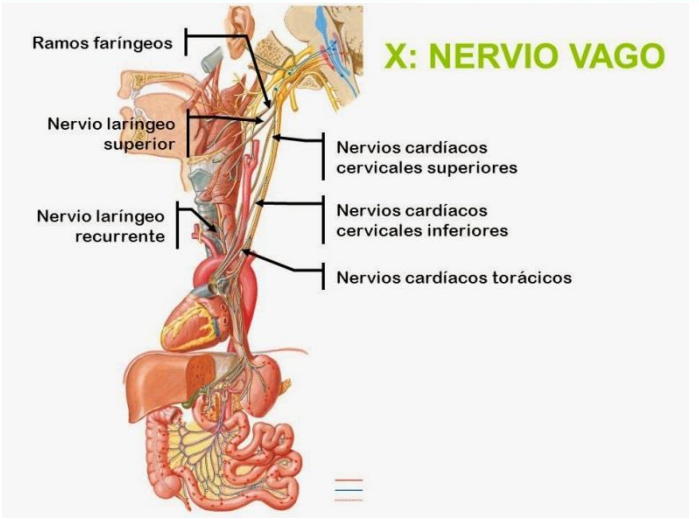
CEREBRO EMOCIONAL: Marcadores somáticos

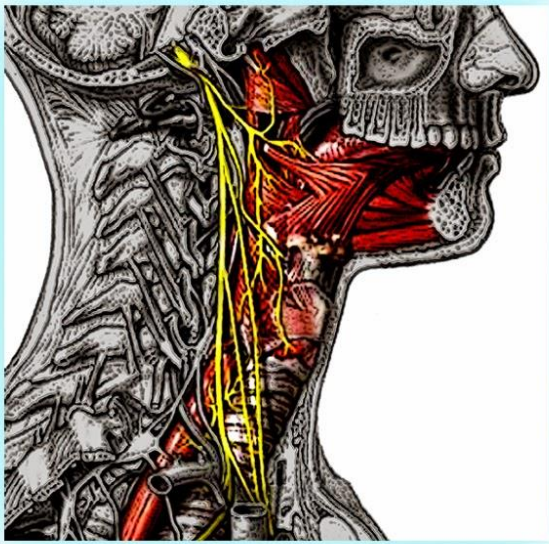
Evaluación y definición de un estímulo emocional (miedo)	1	Corteza cerebral sensorial asociativa (superior)
Disparo (inducción)	2	Amígdala
Ejecución	3	Cerebro basal anterior Hipotálamo Troncoencéfalo
Estado emocional	4	Cambios transitorios en el medio interno (vísceras y sistema musculoesquelético)

Damasio, A. (2003). En busca de Spinoza. Neurobiología de la emoción y los sentimientos. Barcelona: Booket.

LAS EMOCIONES: NERVIO VAGO







SNA: Parasimpático

VNS: PARASYMPATHETIC DIVISION.

CORTICAL EFF.A
HYPOTHALAMUSB( )
ANT. NUC.B1
PERIVENT. NUC.B2
DORSAL LONG. FASC.C

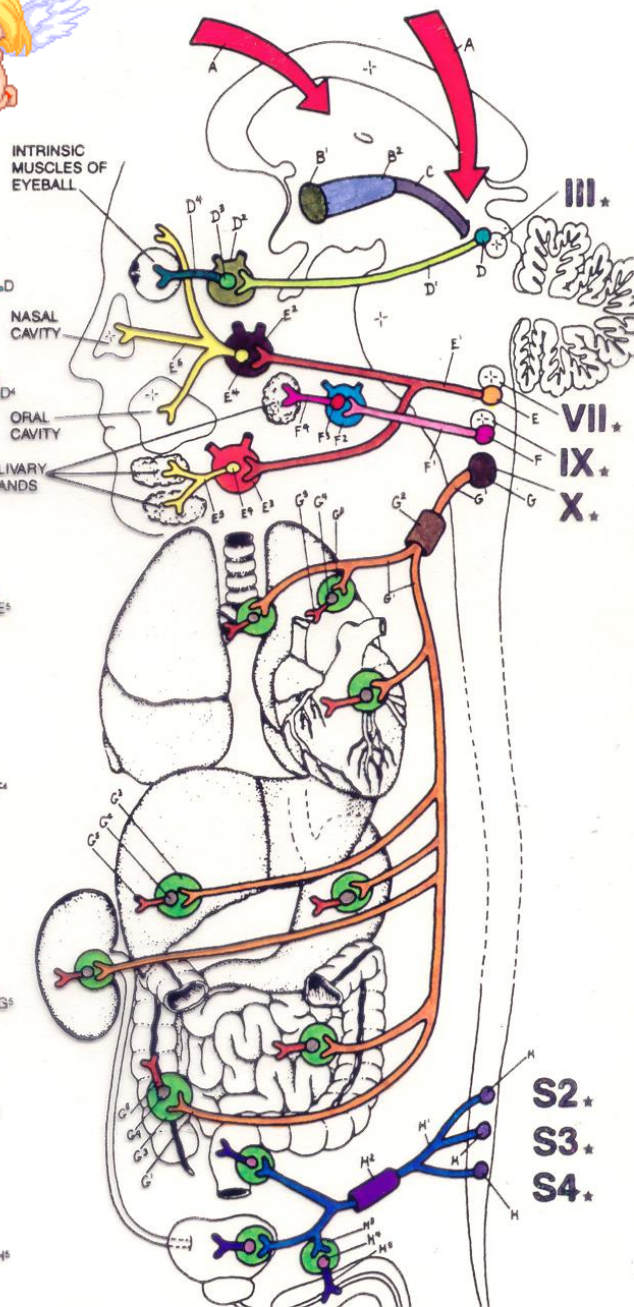
CRANIAL OUTFLOW.
NUC. EDINGER WESTPHALD
PREGANG. FIBERD1
CILIARY GANG.D2
POSTGANG. NEUR.D3/FIBERD4

SUP. SALIV. NUC.E
PREGANG. FIBERE1
PTERYGOPAL. GANG.E2
SUBMANDIB. GANG.E3
POSTGANG. NEUR.E4/FIBERE5

INF. SALIV. NUC.F
PREGANG. FIBERF1
OTIC GANG.F2
POSTGANG. NEUR.F3/FIBERF4

DORSAL MOTOR NUC.G
PREGANG. FIBERG1
VAGUS N.G2
INTRAMURAL GANG.G3
POSTGANG. NEUR.G4/FIBERG5

SACRAL OUTFLOW.
LAT. HORN MOTOR NEUR.H
PREGANG. FIBERH1
PELVIC SPLANCH. N.H2
INTRAMURAL GANG.H3
POSTGANG. NEUR.H4/FIBERH5

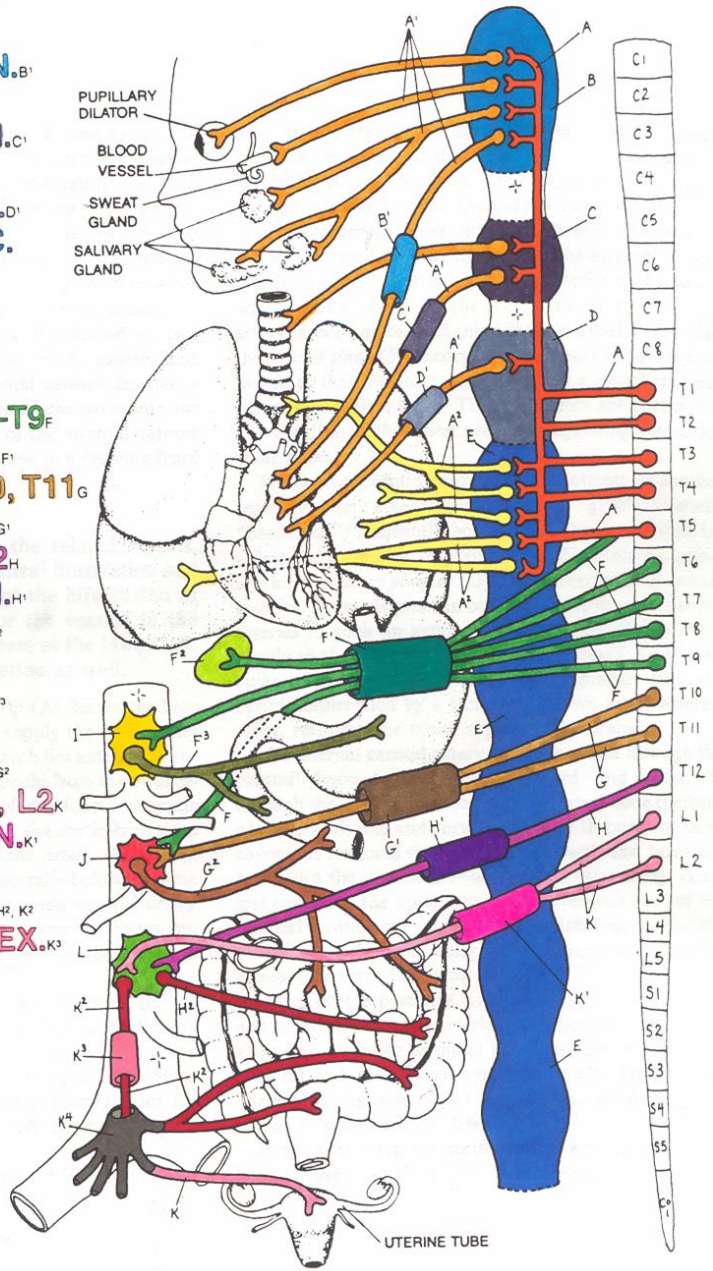


SNA: Simpático

VNS: SYMPATHETIC DIVISION.

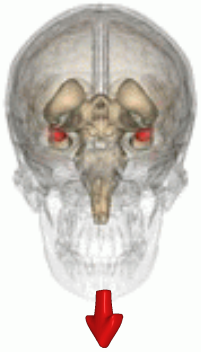
PREGANG. NEUR. T1–T5A
POSTGANG. NEUR.A'
SUP. CERV. GANG.B
SUP. CERV. CARD. N.B'
MID. CERV. GANG.C
MID. CERV. CARD. N.C'
INF. CERV. GANG.D
INF. CERV. CARD. N.D'
THORACOLUMBOSAC. CHAINE
POSTGANG. NEUR./ PULM. PLEXUSA²

PREGANG. NEUR. T5–T9F
GRTR. SPLANCH. N.F'
PREGANG. NEUR. T10, T11G
LESS. SPLANCH. N.G'
PREGANG. NEUR. T12H
LEAST SPLANCH. N.H'
ADRENAL MEDULLAF²
CELIAC GANG.I
POSTGANG. NEUR.F³
SUP. MES. GANG.J
POSTGANG. NEUR.G²
PREGANG. NEUR. L1, L2K
LUMBAR SPLANCH. N.K'
INF. MES. GANG.L
POSTGANG. NEUR.H², K²
SUP. HYPOGAST. PLEX.K³
PELVIC PLEX.K⁴



CEREBRO EMOCIONAL

http://www.dailymotion.com/video/x8upy4_cerebro-emocional-amigdala_school

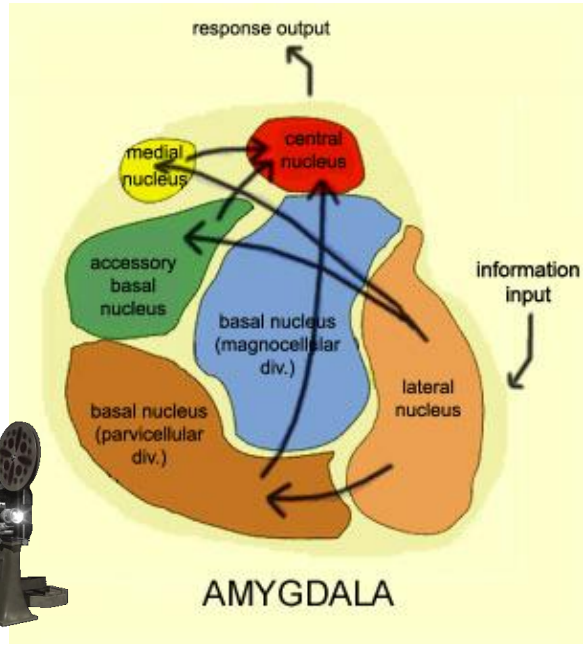


Amígdala

*-La **hipótesis amígdala-miedo** ha sido la más popularizada por la neurociencia apoyando que la amígdala (en particular el núcleo central) provoca cambios cardiovasculares en ratas en respuesta a sobresaltos (tonos asociados a pequeñas descargas eléctricas) (LeDoux et al., 1990).*

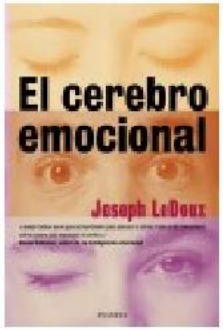
*-Pacientes con **lesiones en la amígdala** (LaBar et al., 1995) o **atrofia** (Bechara et al., 1995) mostraron dificultades para percibir el miedo y deterioro en las respuestas de la conductancia de la piel.*

Feinstein et al. (2011) estudiaron un individuo con lesión amigdalina bilateral que no informó sentir miedo cuando se le expuso en contacto directo con serpientes y arañas.



LeDoux, J., Ciccetti, P., Xagoraris, A., Romanski, L. (1990). The lateral amygdaloid nucleus: Sensory interface of the amygdala in fear conditioning. Journal of Neuroscience, 10, 1062–69.

CEREBRO EMOCIONAL



http://www.dailymotion.com/video/xpfvzf_cerebro-el-circuito-del-miedo-joseph-ledoux_school

http://www.dailymotion.com/video/xpovem_cerebro-y-emociones-joseph-ledoux_school

http://www.dailymotion.com/video/xpql27_cerebro-el-sistema-del-miedo-joseph-ledoux_school

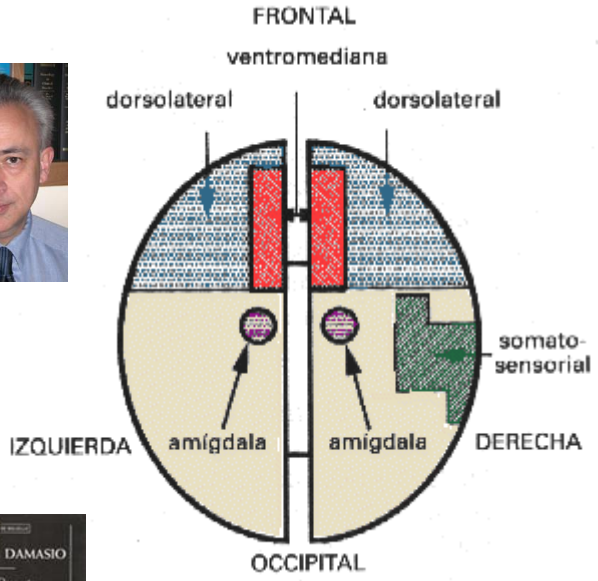
http://www.dailymotion.com/video/xbbrnj_vias-cerebrales-del-miedo-joseph-le_school

http://www.dailymotion.com/video/x6nf05_amigdala-vs-lobulo-frontal_school

Le Doux, J. (1999). El cerebro emocional. Editorial Planeta

CEREBRO EMOCIONAL: Los marcadores somáticos

Las cortezas prefrontales *serían las encargadas de la adquisición de las señales de los marcadores somáticos. Sus múltiples y variadas conexiones con todas las regiones sensoriales (incluidas las cortezas somatosensoriales), con los núcleos del troncoencéfalo y del prosencéfalo basal, con la amígdala, la ínsula anterior, con el cortex cingulado anterior y el hipotálamo, le mantienen actualizada de lo que ocurre al organismo a través del* ***nervio vago****.*

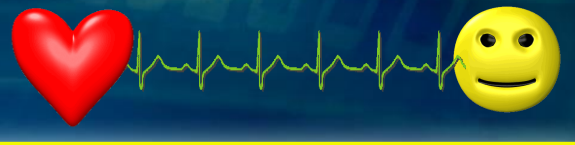


La ***región prefrontal ventromedial*** *cumple una función crítica en la representación somatosensorial, interpretando las sensaciones de nuestro cuerpo, asociadas a los eventos emocionales (generan respuestas inmediatas mediadas por el SNA)*

Las cortezas prefrontales establecen categorizaciones de las distintas situaciones que ha debido enfrentar el organismo, creando así una especie de "banco de datos" ordenado sobre nuestras distintas experiencias y a partir de cómo ha reaccionado nuestro cuerpo en aquellas situaciones.

Damasio, A. (2011). El error de Descartes. Editorial Destino

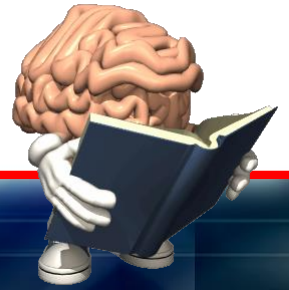
EMOCIONES: Miedo y amígdalas



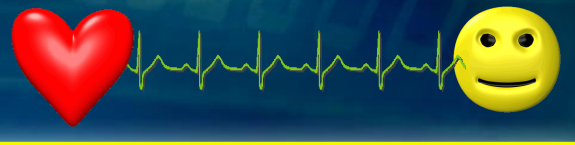
La amígdala también está implicada en algunas psicopatologías (ansiedad y la psicopatía). La RMf ha puesto de manifiesto que en el caso de la ansiedad, la amígdala se encontraría ***hiperreactiva****, en cambio, en la psicopatía la amígdala está* ***hipofuncional*** *(junto con la corteza prefrontal orbitofrontal), por ello, estos individuos son incapaces de empatizar emocionalmente con el resto de seres humanos.*

Otra función muy importante de la amígdala es la ***focalización de la atención a estímulos aversivos*** *(Anderson y Phelps, 2001) y a* ***estímulos socialmente relevantes*** *(Kennedy y Adolphs, 2010). Esto nos sugiere la idea de que la amígdala está implicada en la* ***atención hacia estímulos salientes*** *(Lindquist et al., 2012) y su estimulación eléctrica produce una gama de experiencias en los humanos que no únicamente se reducen al miedo (Bancaud et al., 1994).*

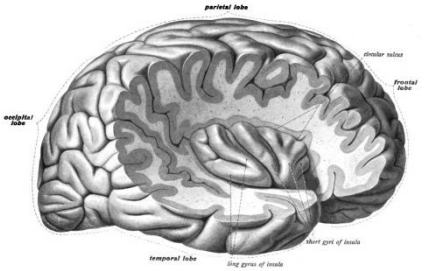
*Según el neurocientífico Joseph Ledoux: «****la amígdala es útil para desencadenar respuestas rápidas ante situaciones de peligro»****. De modo que si está enfrentada a un peligro, sabe que lo es y lo racionaliza.*



EMOCIONES: La ínsula anterior



-La **hipótesis de la ínsula anterior y asco** es la más reconocida hasta la actualidad: Tienen dificultades para percibir asco o disgusto en caras (Adolphs et al., 2003). Estos individuos experimentan menos repugnancia cuando se les exponen a insectos, excrementos u otros estímulos que normalmente provocan asco a personas con la ínsula intacta (Calder et al., 2000).



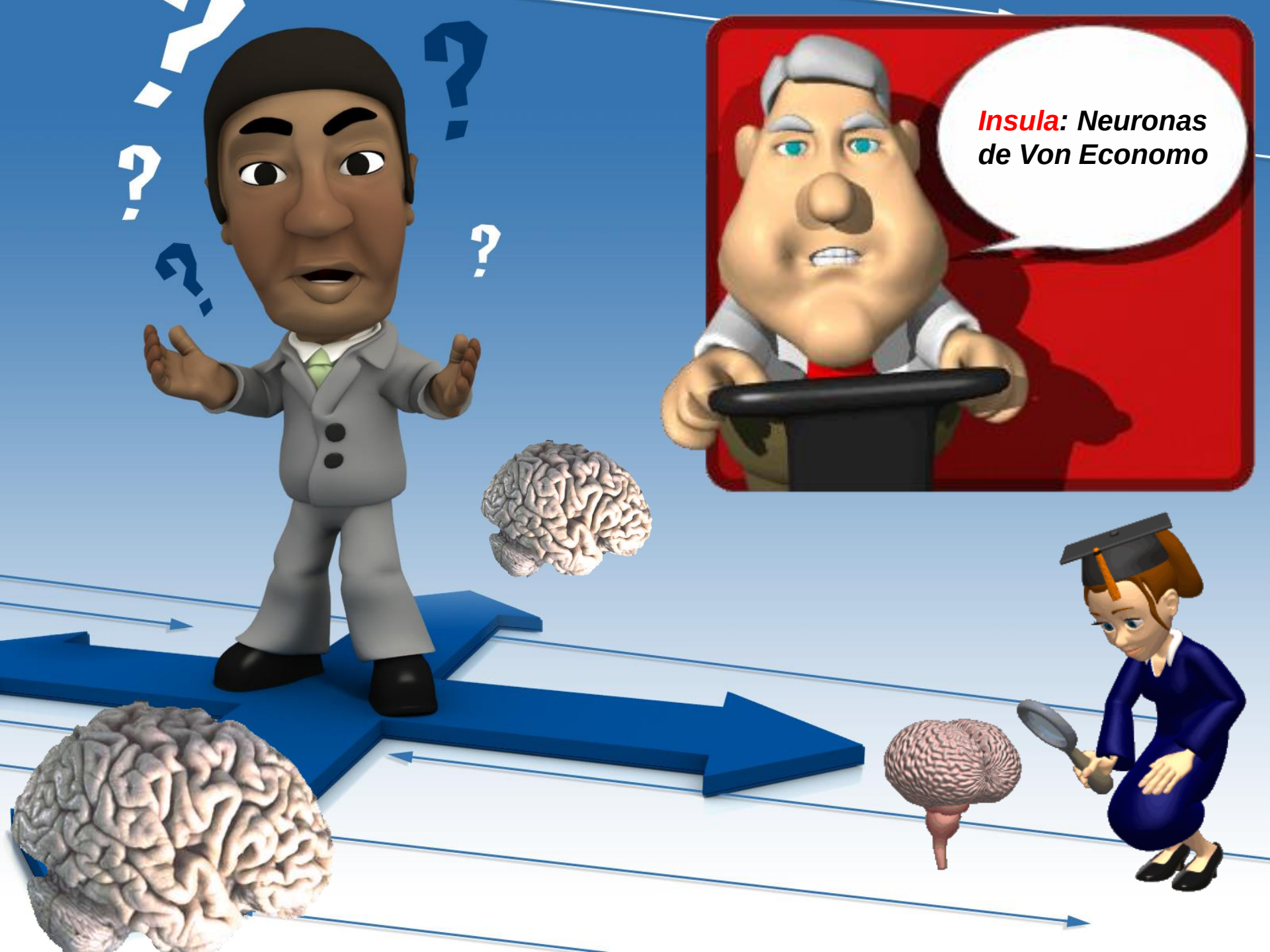
-Enfermedades neurodegenerativas que afectan a la ínsula y ganglios basales (v.g. Corea de Huntington y Parkinson) muestran un menor asco o disgusto ante estímulos malolientes (Mitchell et al., 2005).

-Pacientes con estimulación eléctrica en la ínsula anterior informaron sensaciones viscerales consistentes con la experiencia de asco (por ejemplo, sensaciones en el estómago y garganta, náuseas; Penfield y Faulk, 1995).

-Está implicada en la **toma de conciencia de las sensaciones corporales** (Craig, 2002) y del **estado afectivo principal** (Craig, 2009). La ínsula anterior muestra una mayor activación cuando tomamos conciencia del movimiento de nuestro cuerpo, la distensión gástrica, durante el orgasmo, movimiento, espasmos, calor y hormigueo en los labios, la lengua, los dientes, los brazos, las manos y los dedos (no solo asco).

LAS EMOCIONES: Asco e insula anterior

http://www.dailymotion.com/video/x8fowh_asco-en-el-cerebro-rmf_school


Insula: Neuronas de Von Economo

Opinion TRENDS in Cognitive Sciences Vol.9 No.8 August 2005

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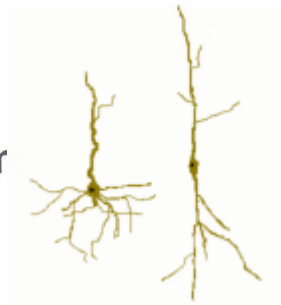
SCIENCE DIRECT

Intuition and autism: a possible role for Von Economo neurons

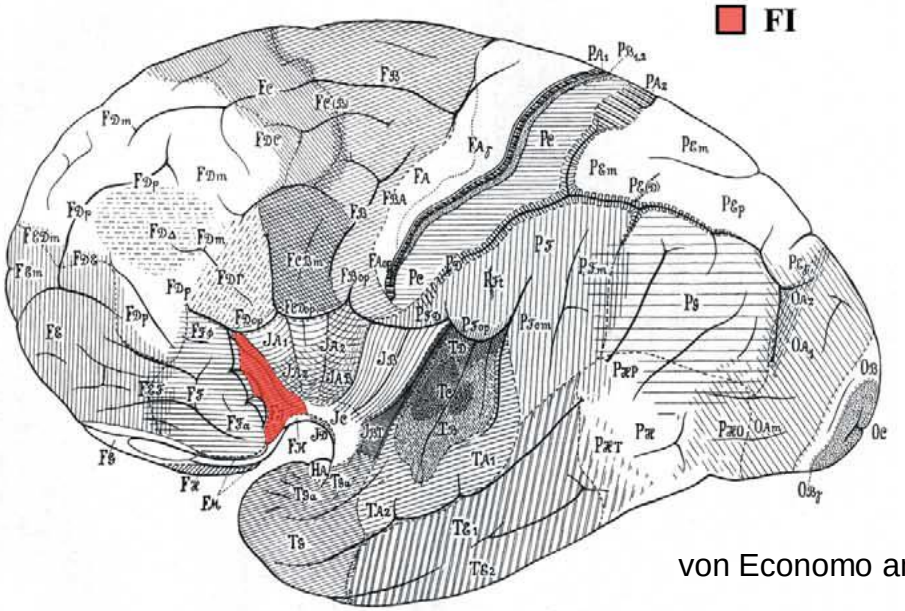
John M. Allman, Karli K. Watson, Nicole A. Tetreault and Atiya Y. Hakeem

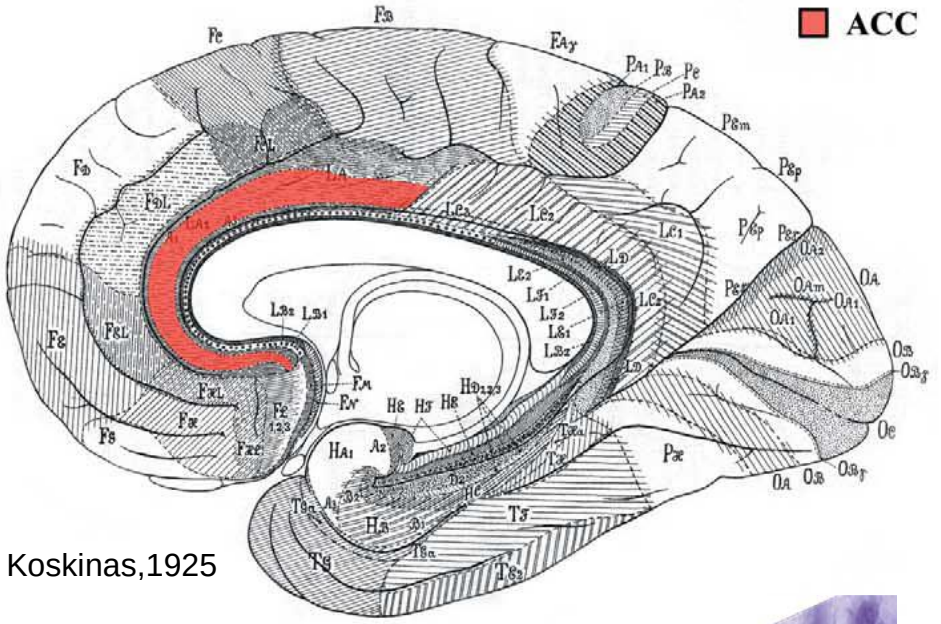
Division of Biology, M. C. 216-76, California Institute of Technology, Pasadena, CA 91125, USA



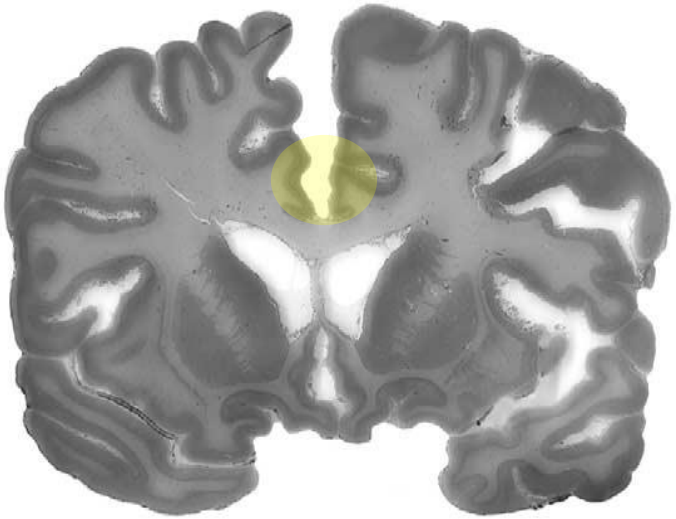
Von Economo neurons (VENs) are a recently evolved cell type which may be involved in the fast intuitive assessment of complex situations. As such, they could be part of the circuitry supporting human social networks. We propose that the VENs relay an output of fronto-insular and anterior cingulate cortex to the parts of frontal and temporal cortex associated with theory-of-mind, where fast intuitions are melded with slower, deliberative judgments. The VENs emerge mainly after birth and increase in number until age 4 yrs. We propose that in autism spectrum disorders the VENs fail to develop normally, and that this failure might be partially responsible for the associated social disabilities that result from faulty intuition.

mapped in humans by Von Economo and Koskinas [2]. Elsewhere we have referred to them as the 'spindle' neurons, but because of potential confusion with other uses of this term, we now refer to them by the first author of the best description of these cells. They are found only in humans and great apes [3] and are far more abundant in humans than in apes (see Figure 2). They are thus a phylogenetic specialization that has arisen within the last 15 million years in hominoids and have proliferated greatly within the human line of descent. Because of this late emergence in phylogeny, natural selection has had only a relatively short time to shape VEN functioning and integration with other cell populations. Consequently the VENs might be particularly vulnerable to dysfunction in a manner analogous to the propensity of humans to suffer

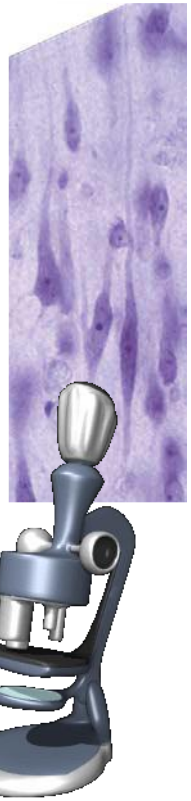




von Economo and Koskinas,1925



Regions of the brain containing Von Economo neurons (VENs).
(a) A lateral view of the brain, with fronto-insular cortex (FI) shown in red. (b) A medial view of the brain, with anterior cingulate cortex (ACC) shown in red. Adapted from Von Economo and Koskinas [2]. (c) FI and the spindle-cell-containing region of ACC indicated on coronal sections through a human brain (50-year-old female) and (d) a common chimpanzee brain (sections shown with the right hemisphere of the brain on the right of the figure). Sections are from the Yakovlev Brain Collection at the National Museum of Health and Medicine, and were scanned by the authors. Note that FI is much larger in the human than in the chimpanzee. (e) A Von Economo neuron and a pyramidal neuron in layer 5 of FI. Both types of neuron have a single apical dendrite, but note that the VEN also has only a single basal dendrite, in contrast to the pyramidal neuron's multiple basal dendrites. Photomicrograph by the authors of a section fromthe 50-year-old human brain shown in part (c).



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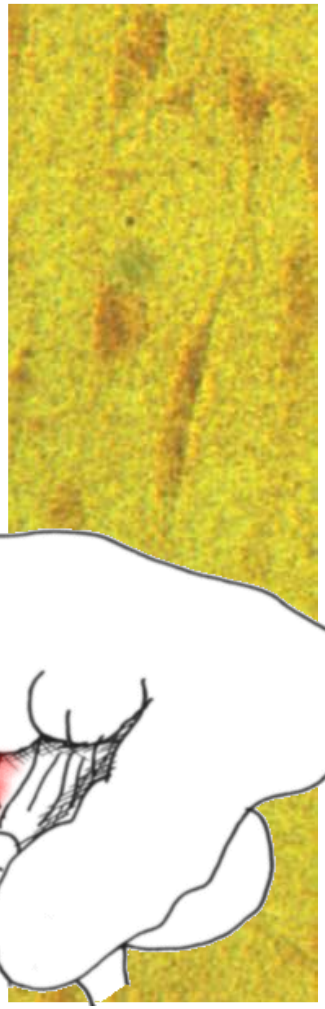
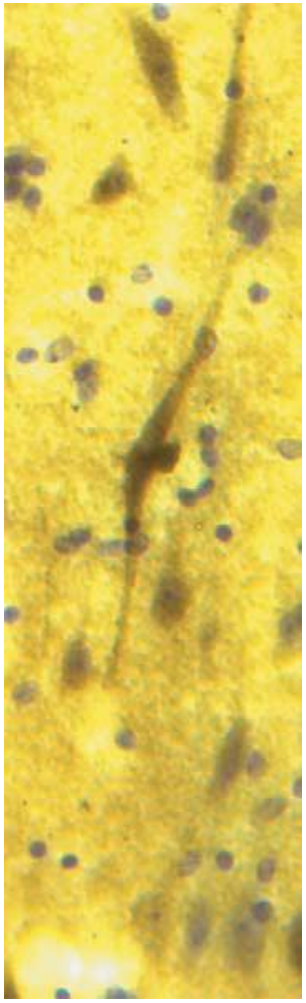
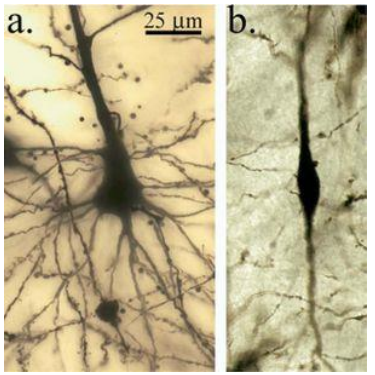
Vasopressin 1a

Dopamine d3

Serotonin 2b







Immunocytochemistry of Von Economo neurons. VENs in ACC of male humans, labeled with antibodies to:

(a) the vasopressin 1a receptor, which has been linked to the formation of social bonds in rodents

(b) the dopamine d3 receptor, a high-affinity receptor potentially linked to the anticipation of reward under conditions of uncertainty;

(c) the serotonin 2b receptor which may be linked to the anticipation of punishment.

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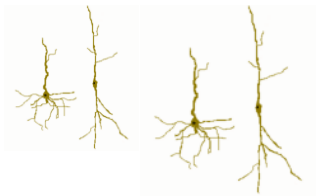
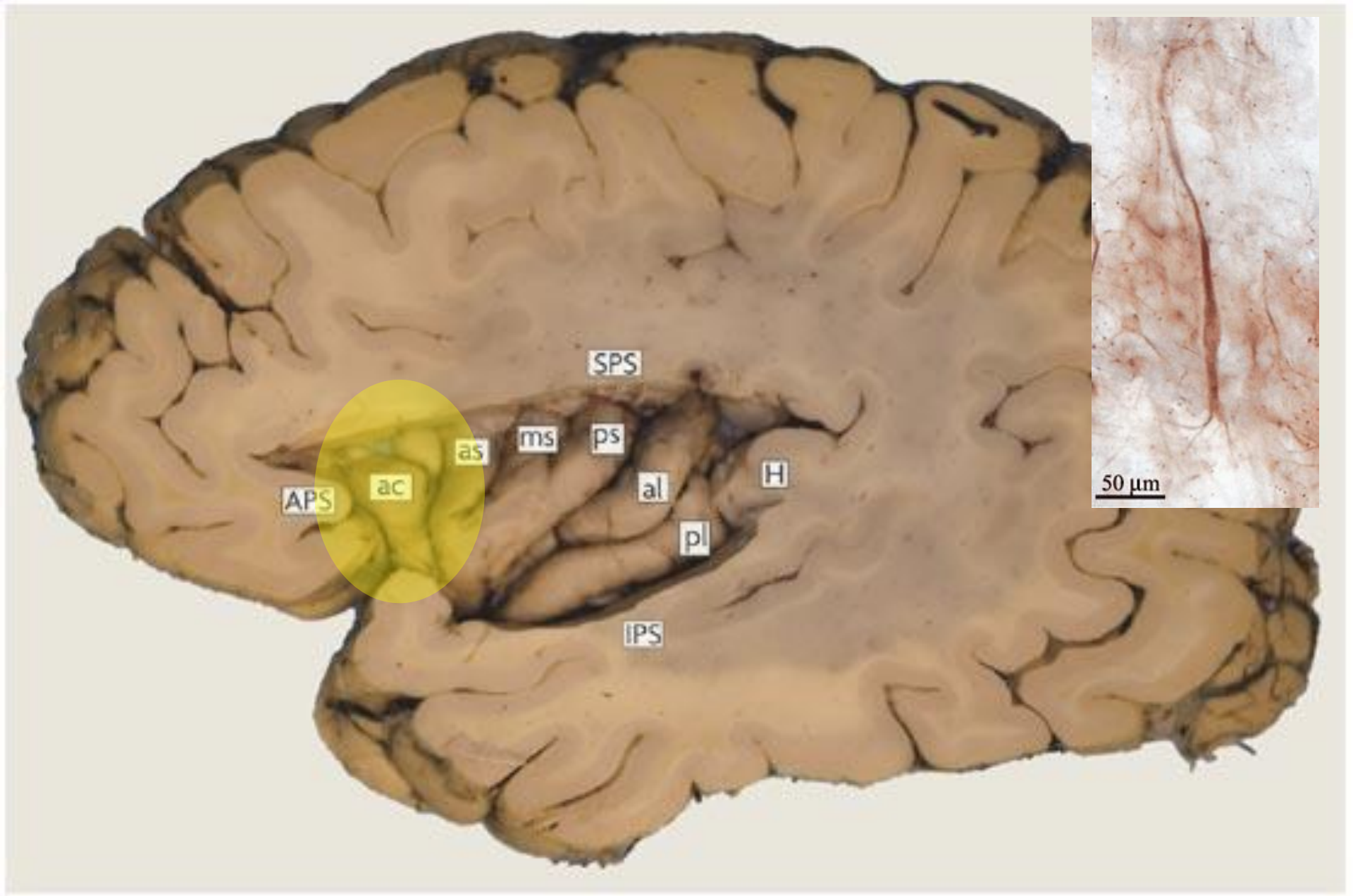




Insula

Nature Reviews | Neuroscience

Early Frontotemporal Dementia Targets Neurons Unique to Apes and Humans

William W. Seeley, MD,[1] Danielle A. Carlin, BA,[1] John M. Allman, PhD,[2] Marcelo N. Macedo, BS,[1] Clarissa Bush, BA,[3] Bruce L. Miller, MD[1] and Stephen J. DeArmond, MD, PhD,[3]

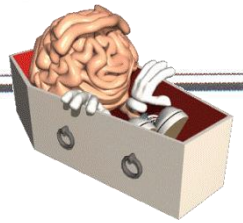
Objective: Frontotemporal dementia (FTD) is a neurodegenerative disease that erodes uniquely human aspects of social behavior and emotion. The illness features a characteristic pattern of early injury to anterior cingulate and frontoinsular cortex. These regions, though often considered ancient in phylogeny, are the exclusive homes to the von Economo neuron (VEN), a large bipolar projection neuron found only in great apes and humans. Despite progress toward understanding the genetic and molecular bases of FTD, no class of selectively vulnerable neurons has been identified.

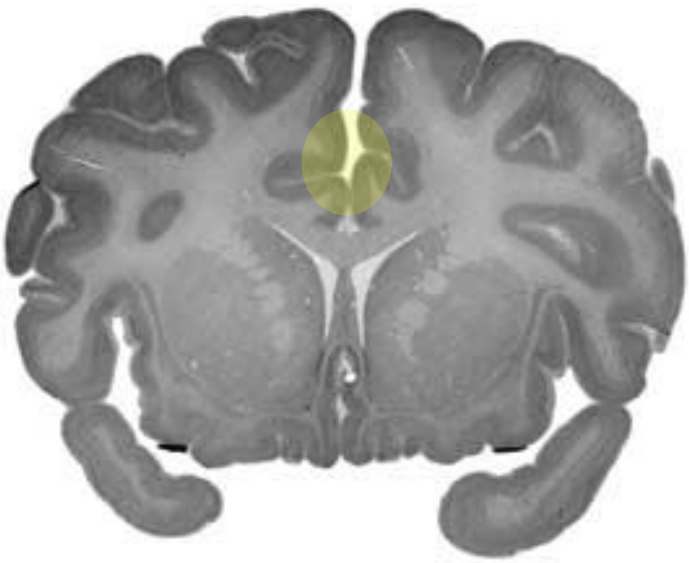
Methods: Using unbiased stereology, we quantified anterior cingulate VENs and neighboring Layer 5 neurons in FTD (n = 7), Alzheimer's disease (n = 5), and age-matched nonneurological control subjects (n = 7). Neuronal morphology and immunohistochemical staining patterns provided further information about VEN susceptibility.

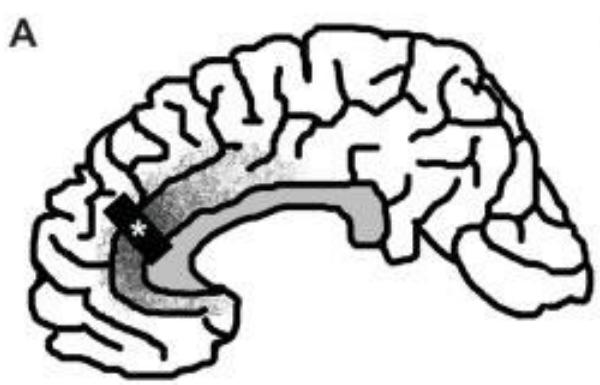
Results: FTD was associated with early, severe, and selective VEN losses, including a 74% reduction in VENs per section compared with control subjects. VEN dropout was not attributable to general neuronal loss and was seen across FTD pathological subtypes. Surviving VENs were often dysmorphic, with pathological tau protein accumulation in Pick's disease. In contrast, patients with Alzheimer's disease showed normal VEN counts and morphology despite extensive local neurofibrillary pathology.

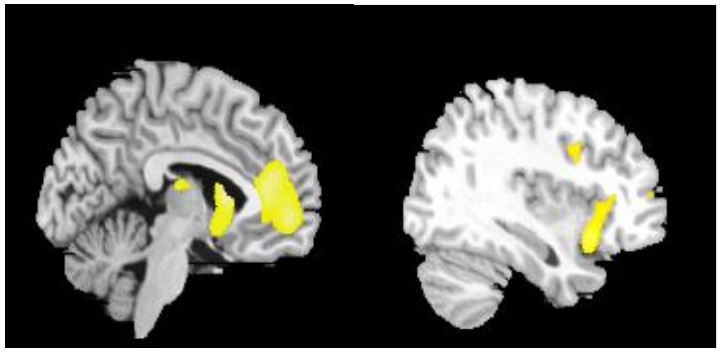
Interpretation: VEN loss links FTD to its signature regional pattern. The findings suggest a new framework for understanding how evolution may have rendered the human brain vulnerable to specific forms of degenerative illness.

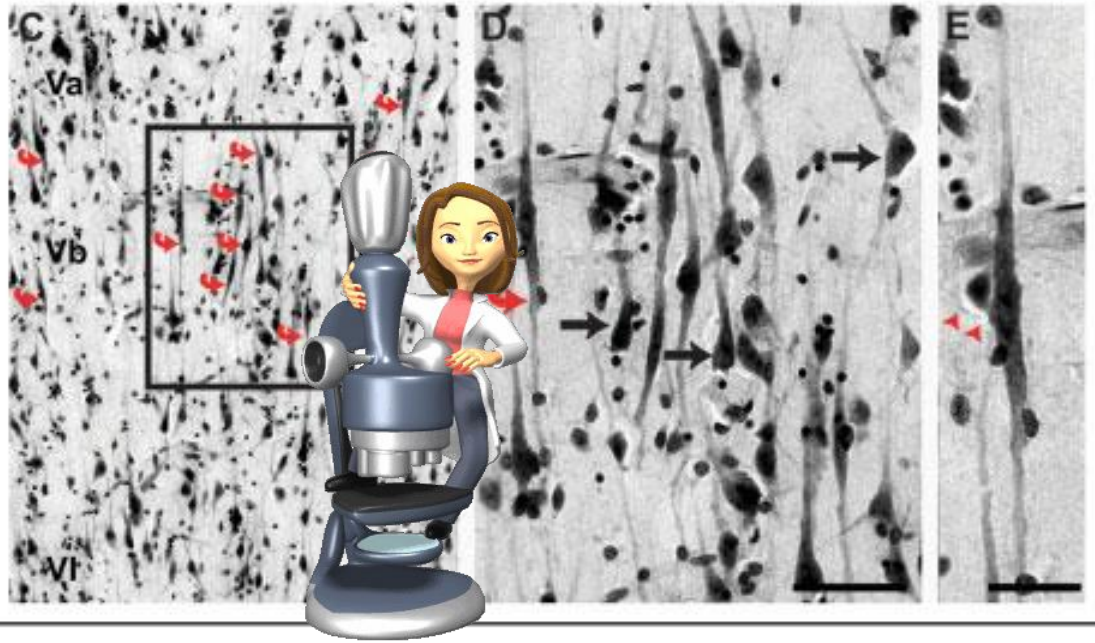
Ann Neurol 2006;60:660–667











Anterior cingulate sampling site and von Economo neuron (VEN) characteristics in control subjects. (A) VENs are distributed throughout the mid- and anterior cingulate cortex. Dots, *drawn schematically based on previous work,31 highlight the increasing posterior-to-anterior VEN gradient in the normal brain. For this study, tissue blocks were cut from the pregenual anterior cingulate cortex (ACC)* (asterisk). *(B) ACC VEN distribution in a representative nonneurological control subject. Overlaid contours of the ACC (outer) and Layer 5 (red, inner) were manually traced on 5 to 10 sections per subject.* Dots *represent VENs, which are concentrated in the crowns of the gyrus. (C–E) VENs (curved red arrows in C) are located in Layer 5b and are distinguished from neighboring neurons (e.g.* straight black arrows *in D) by their large size and bipolar dendritic architecture. VENs form vertically oriented clusters, often adjacent to small arterioles. Box in (C) is magnified in (D). One of six VENs in (D) is highlighted* (curved red arrow) *and magnified in (E) to show the typical VEN morphology, including a large VEN axon* (red arrowheads). *Cresyl violet stain.*

Early Frontotemporal Dementia Targets Neurons Unique to Apes and Humans
William W. Seeley, et al, Ann Neurol 2006;60:660–667

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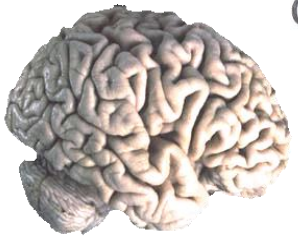
Von Economo neurons are present in the dorsolateral (dysgranular) prefrontal cortex of humans



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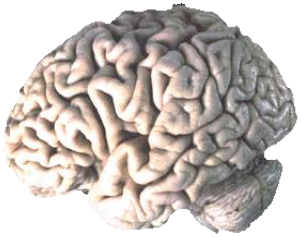
[a] *Centro de Estudios Cerebrales, Facultad de Salud, Universidad del Valle, Cali, Valle, Colombia*
[b] *University of Lousville, Department of Psychiatry, Louisville, KY, United States*

Received 10 January 2008; received in revised form 12 February 2008; accepted 18 February 2008



Abstract

Von Economo neurons (VENs), also known as spindle cells, have been described in layer V of the anterior cingulate (BA 24) and frontoinsular cortex (FI) of humans and other great apes. In the present study we used immunohistochemistry against two specific neuronal markers (NeuN and MAP2) in order to establish the presence of these cell types in Brodmann area 9 (BA 9) of the human prefrontal cortex. We evaluated tissue samples of eight human postmortem brains (age range 26–50) from BAs 9, 24, 4, 46, 45, 10 and 17. We identified a group of cells with similar morphology to that previously described for VENs in all specimens of BA 9 examined, albeit less frequently than in BA 24. This is the first description of this cell type in a human brain area with well developed granular layers (BA 9).
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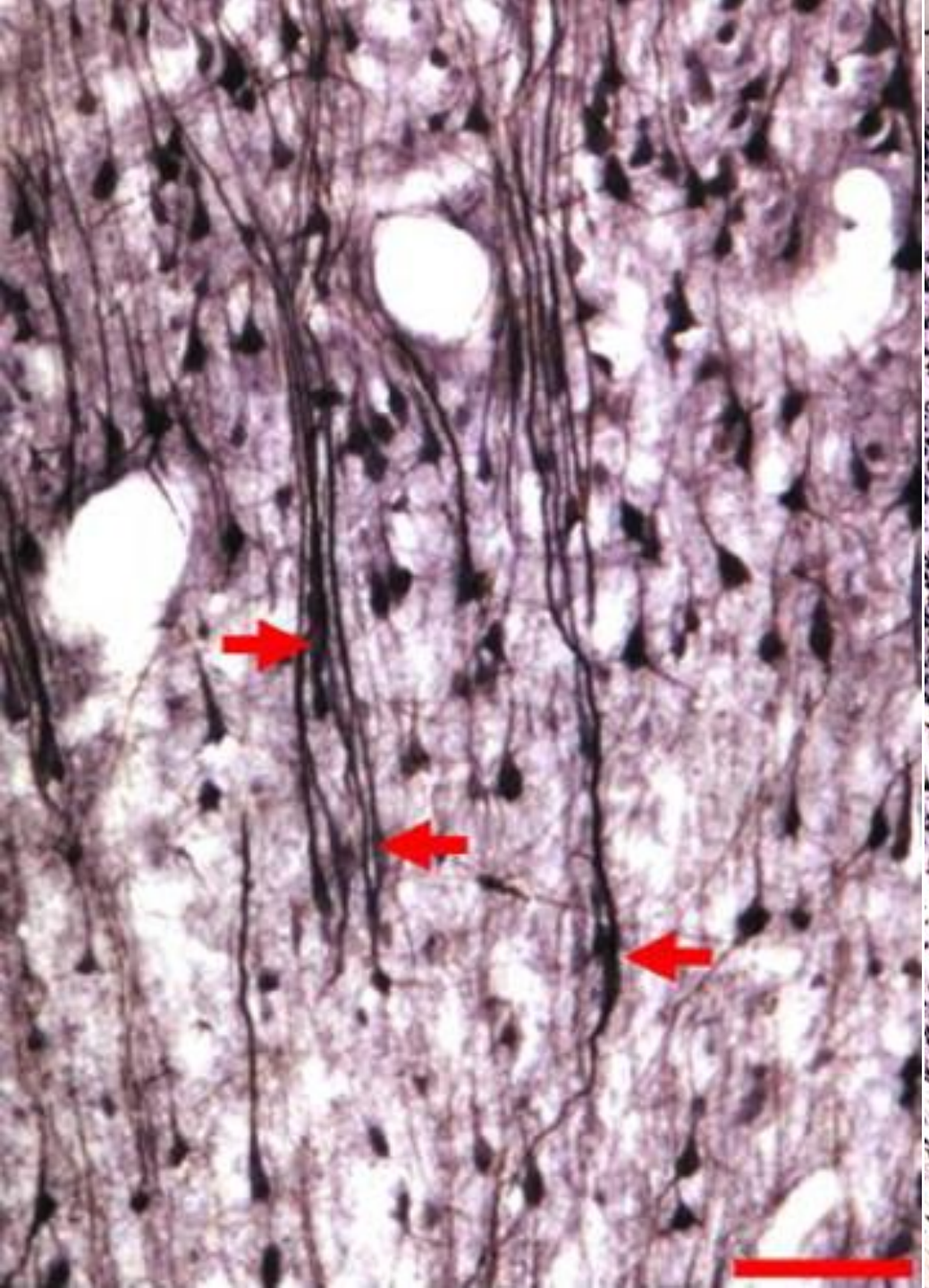
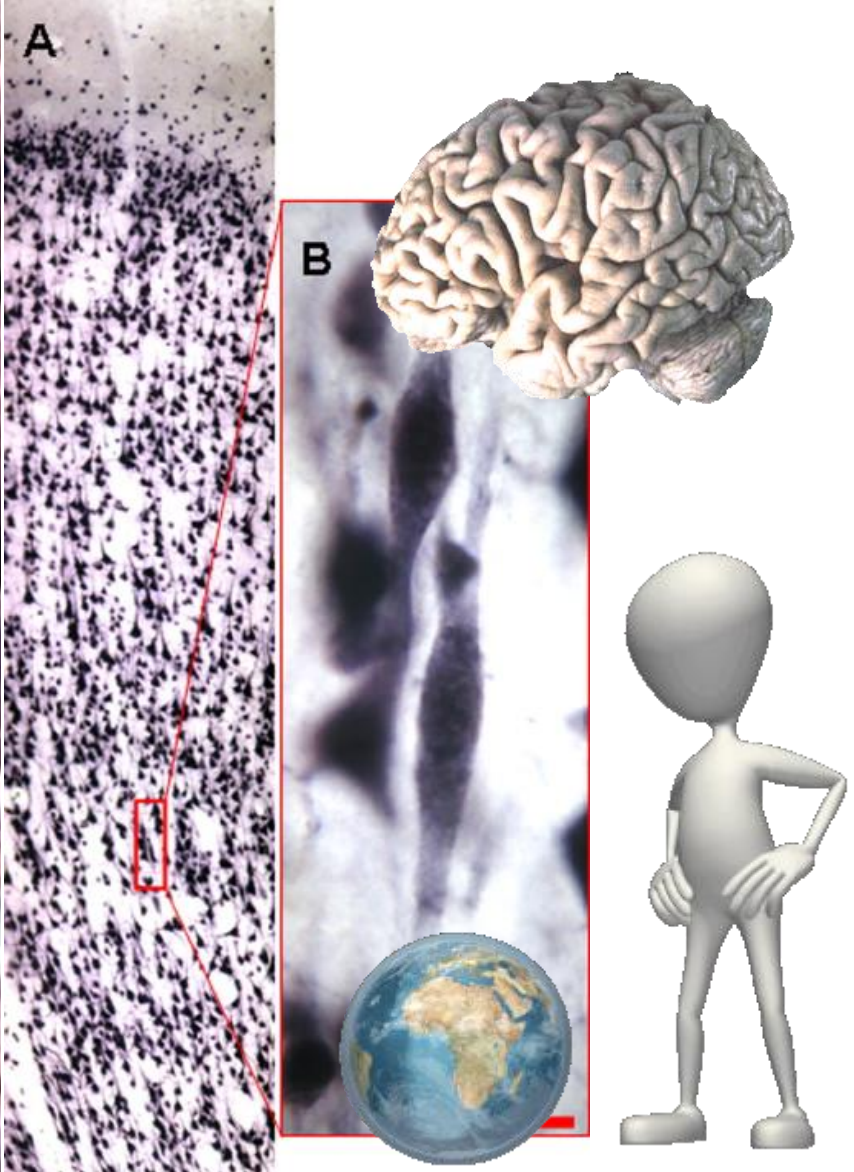
Keywords: Von Economo neurons; Spindle cells; Anterior cingulate gyrus; Frontoinsular cortex; Dorsolateral prefrontal cortex





Neuroscience Letters
Volume 435, Issue 3, 25 April 2008, 215-218
Von Economo neurons are present in the dorsolateral (dysgranular) prefrontal cortex of humans **C. Fajardo et al.**

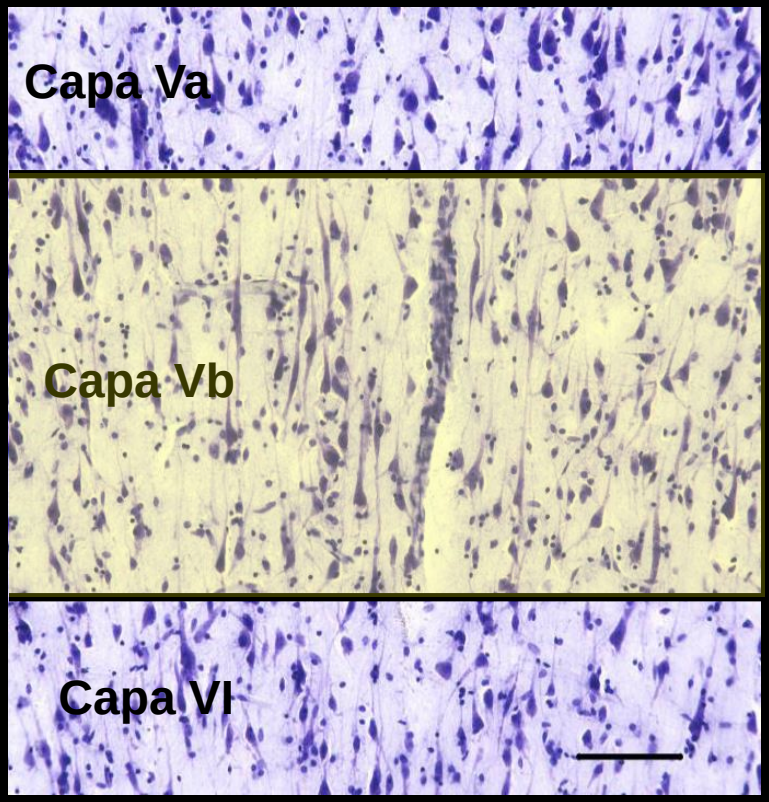
Neuronas de Von Economo

Estructura

Arquitectura simple
Capa Vb, FI>>ACC
Agrupaciones columnares paralelas a pequeñas arteriolas
Hemisferio D/I = 3:1

Ontogenia

Surgen entre la semana 34-38 de gestación
Pico máximo = 8m-4 años
Recién nacido: 28.200
A los 4 años: 184.000
Humano adulto: 193.000



Filogenia

Ausente en en monos y pequeños simios
Orangutan<Gorila<Chimp.
Grandes simios<Humanos
cetáceos-elefantes
Media en simios: 6.950 neuronas

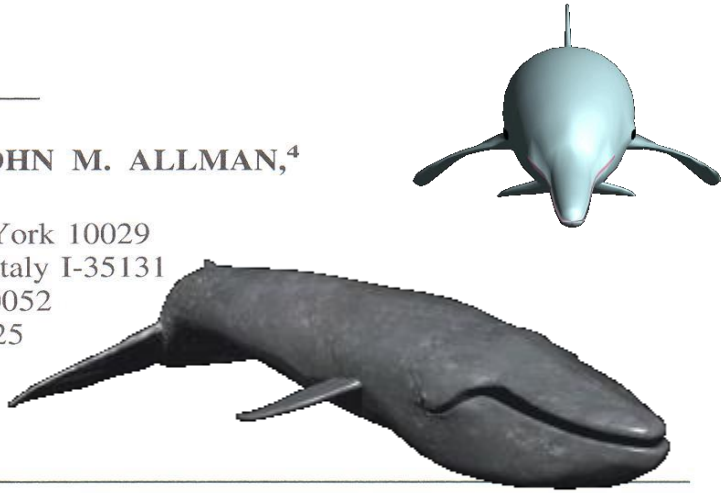
Neuroquímica

Los somas y dendritas proximales expresan receptores:

D3
5HT1b/2b
Vasopresina 1a

The Journal of Comparative Neurology 515:243–259 (2009)
Research in Systems Neuroscience

Total Number and Volume of Von Economo Neurons in the Cerebral Cortex of Cetaceans



CAMILLA BUTTI,[1,2] CHET C. SHERWOOD,[3] ATIYA Y. HAKEEM,[4] JOHN M. ALLMAN,[4] AND PATRICK R. HOF[1,5]*

[1]Department of Neuroscience, Mount Sinai School of Medicine, New York, New York 10029
[2]Department of Experimental Veterinary Sciences, University of Padova, Padova, Italy I-35131
[3]Department of Anthropology, George Washington University, Washington, DC 20052
[4]Division of Biology, California Institute of Technology, Pasadena, California 91125
[5]New York Consortium in Evolutionary Primatology, New York, New York

ABSTRACT

Von Economo neurons (VENs) are a type of large, layer V spindle-shaped neurons that were previously described in humans, great apes, elephants, and some large-brained cetaceans. Here we report the presence of Von Economo neurons in the anterior cingulate (ACC), anterior insular (AI), and frontopolar (FP) cortices of small odontocetes, including the bottlenose dolphin (*Tursiops truncatus*), the Risso's dolphin (*Grampus griseus*), and the beluga whale (*Delphinapterus leucas*). The total number and volume of VENs and the volume of neighboring layer V pyramidal neurons and layer VI fusiform neurons were obtained by using a design-based stereologic approach. Two humpback whale (*Megaptera novaeangliae*) brains were investigated for comparative purposes as representatives of the suborder Mysticeti. Our results show that the distribution of VENs in these cetacean species is comparable to that reported in humans, great apes, and elephants. The number of VENs in these cetaceans is also comparable to data available from great apes, and stereologic estimates indicate that VEN volume follows in these cetacean species a pattern similar to that in hominids, the VENs being larger than neighboring layer V pyramidal cells and conspicuously larger than fusiform neurons of layer VI. The fact that VENs are found in species representative of both cetacean suborders in addition to hominids and elephants suggests that these particular neurons have appeared convergently in phylogenetically unrelated groups of mammals possibly under the influence of comparable selective pressures that influenced specifically the evolution of cortical domains involved in complex cognitive and social/emotional processes. J. Comp. Neurol. 515:243–259, 2009.

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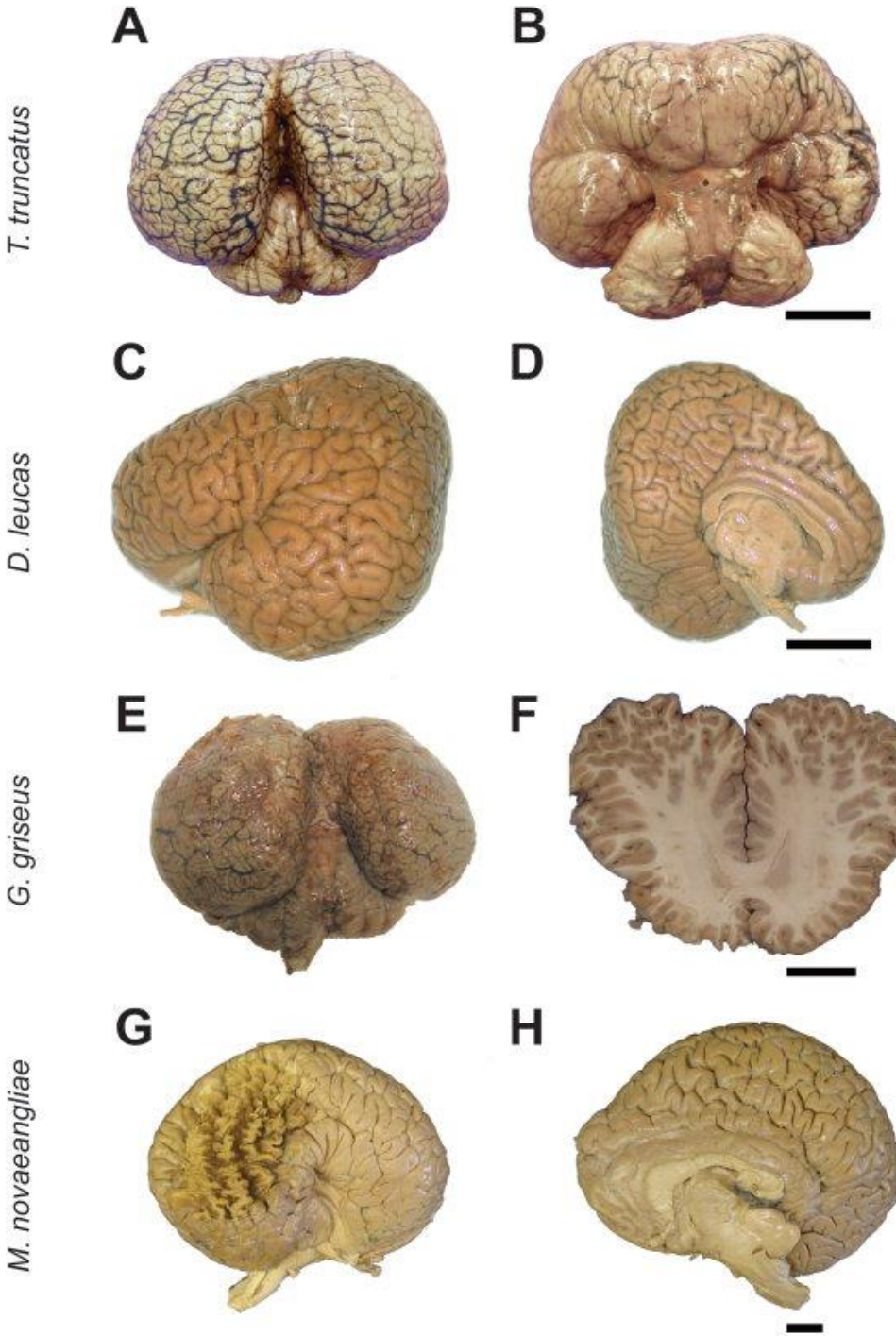
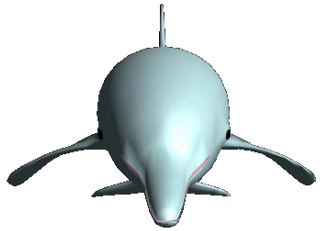
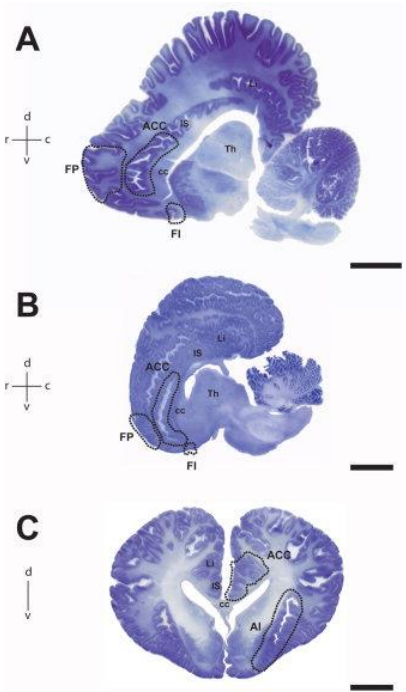
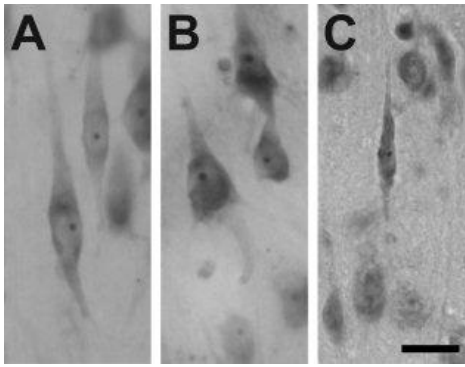


Macroscopic views of the brains of the cetacean species analyzed in the present study. Dorsal (**A**) and ventral (**B**) views of the brain of a bottlenose dolphin; lateral (**C**) and midline (**D**) views of the left hemisphere of the brain of a beluga whale; dorsal view (**E**) and coronal slab at the level of the genu of the corpus callosum (**F**) of the brain of a Risso's dolphin; lateral (**G**) and midline view (**H**) of the right hemisphere of the brain of a humpback whale. Note the large size of the brains and the complex gyral pattern. The lateral aspect of the parietal lobe of the humpback whale brain sustained damage when the specimen was removed from the skull (G). This, however, did not affect the present study. The brains are not shown to scale.

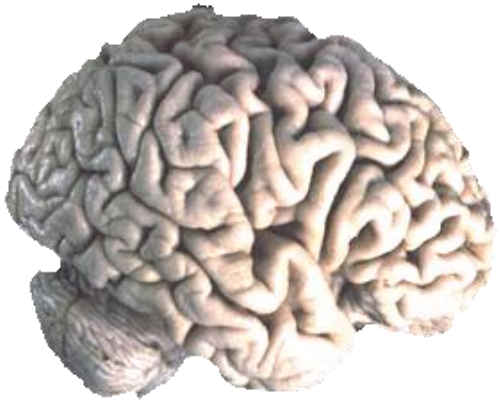
The Journal of Comparative Neurology, 2009, Volume 515, Issue 2, Pages 243-259
Total number and volume of Von Economo neurons in the cerebral cortex of cetaceans. C. Butti et al.







THE ANATOMICAL RECORD 292:242–248 (2009)



Von Economo Neurons in the Elephant Brain

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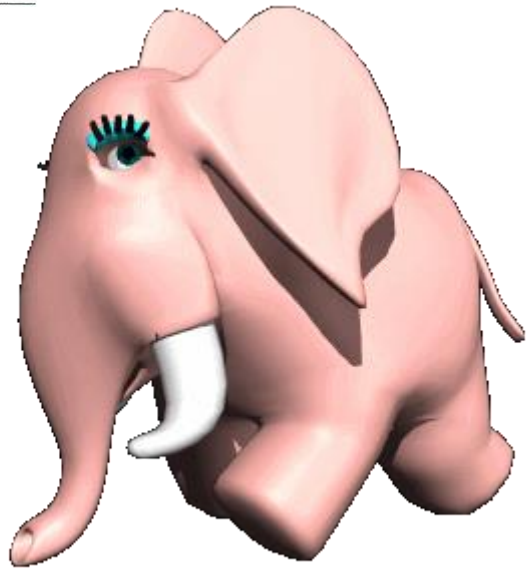
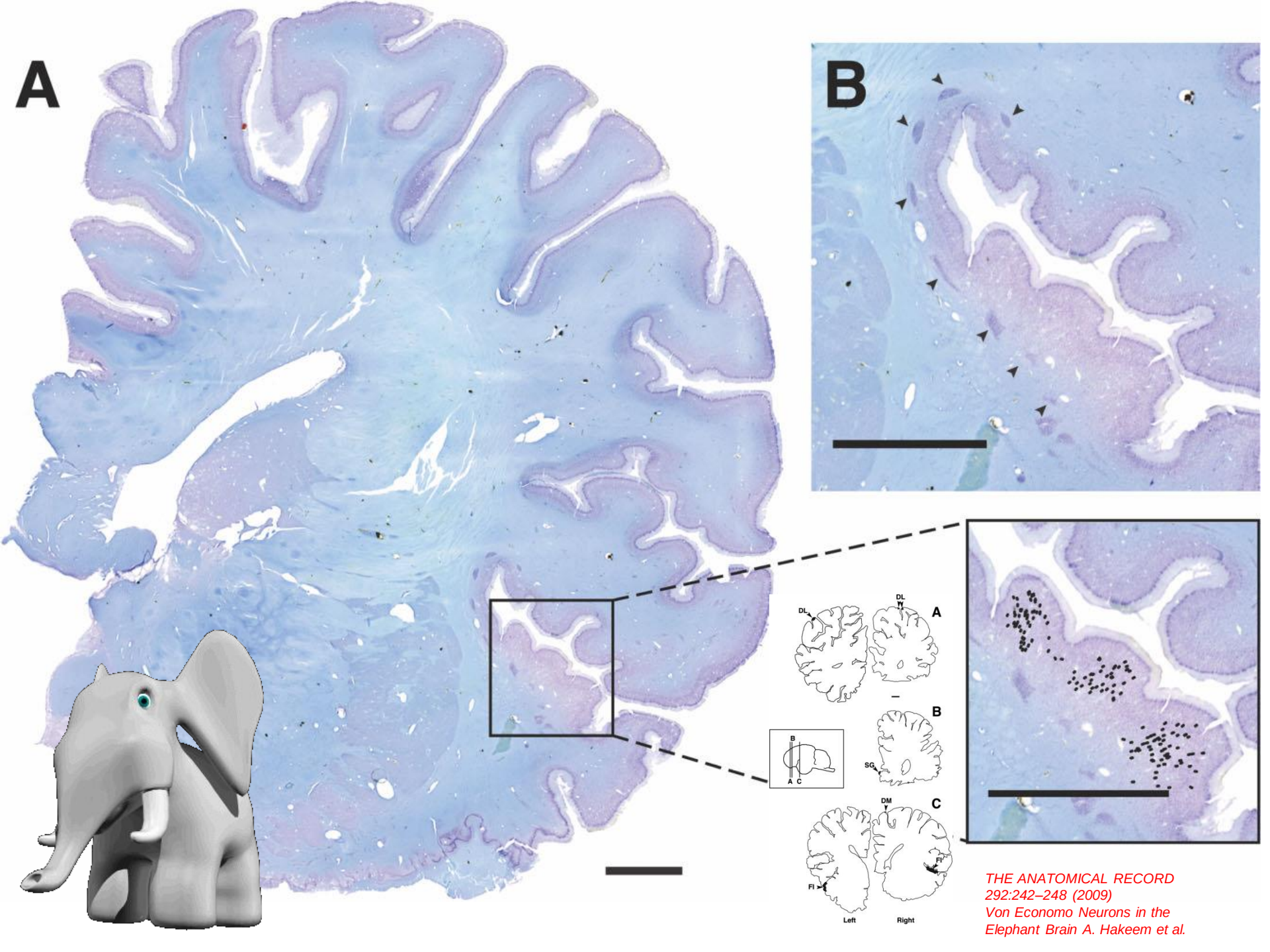


ABSTRACT

Von Economo neurons (VENs), previously found in humans, all of the great ape species, and four cetacean species, are also present in African and Indian elephants. The VENs in the elephant are primarily found in similar locations to those in the other species. They are most abundant in the frontoinsular cortex (area FI) and are also present at lower density in the anterior cingulate cortex. Additionally, they are found in a dorsolateral prefrontal area and less abundantly in the region of the frontal pole. The VEN morphology appears to have arisen independently in hominids, cetaceans, and elephants, and may reflect a specialization for the rapid transmission of crucial social information in very large brains. Anat Rec, 292:242–248, 2009. © 2008 Wiley-Liss, Inc.

Key words: elephant; Von Economo neuron; frontoinsular cortex; cetacean; large brains

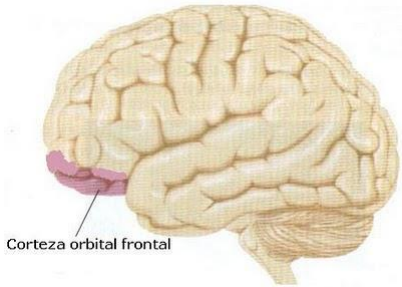


THE ANATOMICAL RECORD
292:242–248 (2009)
Von Economo Neurons in the
Elephant Brain A. Hakeem et al.

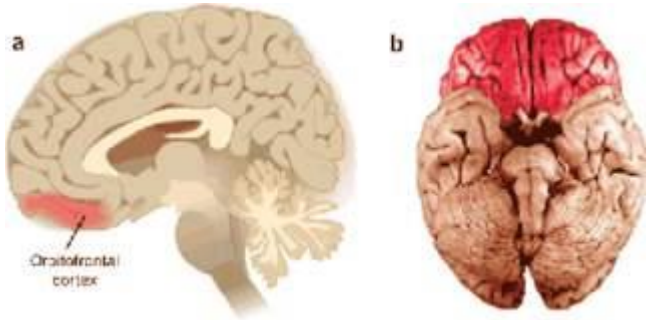
2. EMOCIONES: Corteza orbitofrontal (COF)

-La **hipótesis localizacionista relaciona la COF con la IRA** *(Vytal & Hamann, 2010)*
-***Lesión cerebral en COF****: Cambios de personalidad y aplanamiento afectivo (ira más verbal que física)*

-*La COF es una estructura (entre otras) que integra la información exteroceptiva e interoceptiva para guiar el comportamiento (**marcador somático**).*

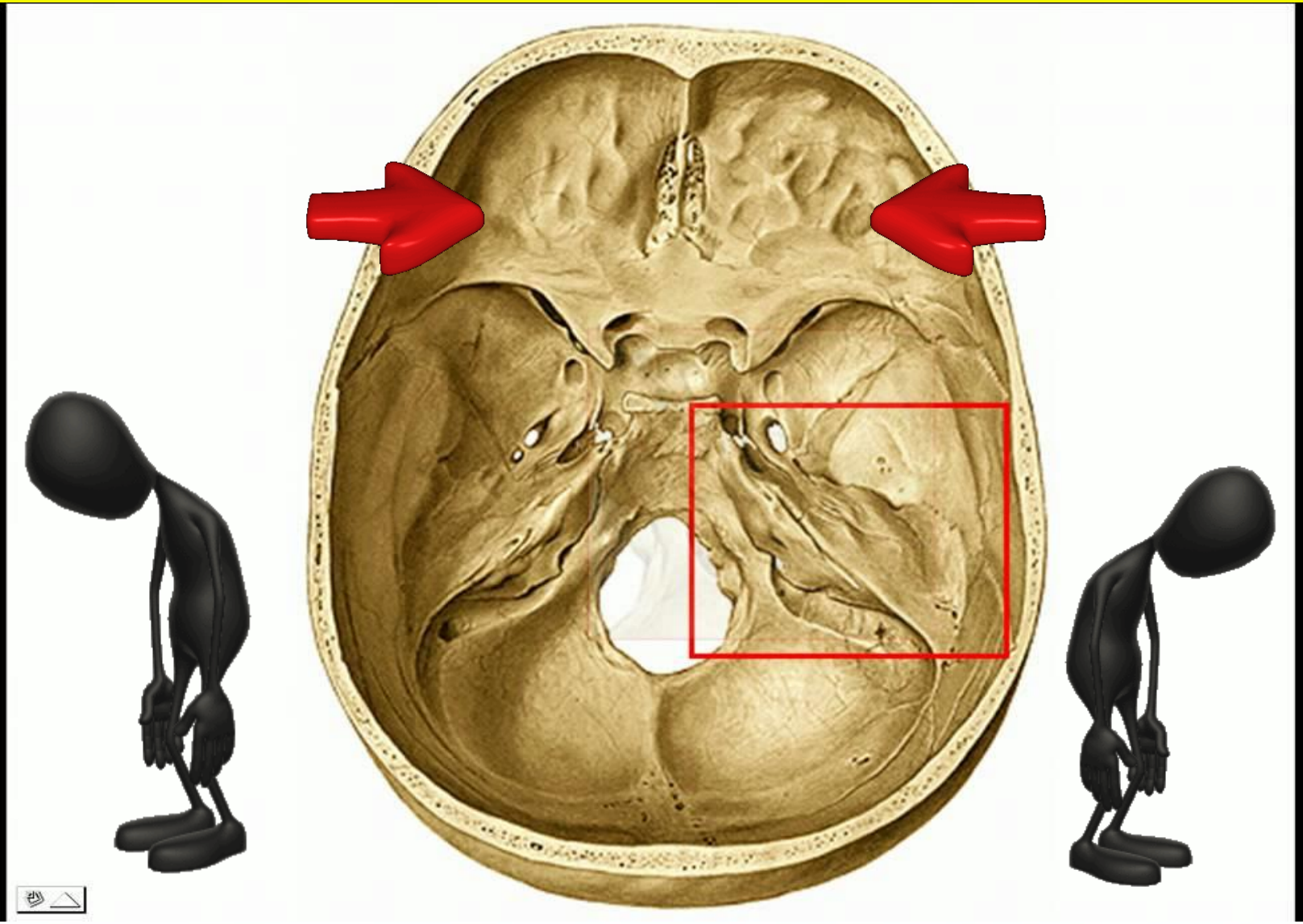


-***La hipótesis del marcador somático de Damasio*** *(1994) dice que la COF es la estructura cerebral que asocia una situación con su consecuencia y con la emoción primaria que desencadena dicha consecuencia.*
De tal manera, una lesión en esta estructura provoca una incapacidad para asociar una conducta con el estado interno que producen sus consecuencias.



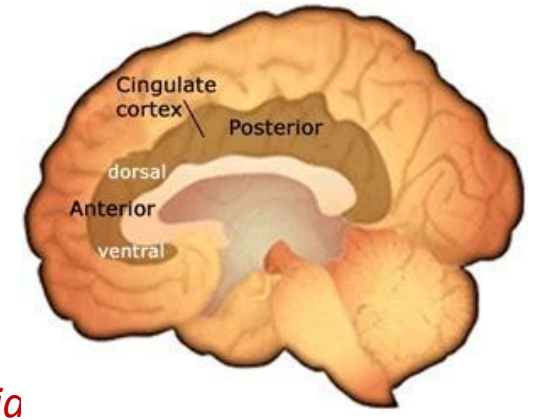
Vytal, K., Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: A voxel-based meta-analysis. Journal of Cognitive Neuroscience, 22(12), 2864–85.

2. EMOCIONES: Corteza orbitofrontal (COF)



Vytal, K., Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: A voxel-based meta-analysis. Journal of Cognitive Neuroscience, 22(12), 2864–85.

2. EMOCIONES: Corteza cingulada anterior



-La hipótesis localizacionista asocia la corteza cingulada anterior pregenual (CCAP) y la corteza cingulada anterior subgenual (CCAS) área 25 de Brodmann) o ventral con la ***tristeza*** *(**función afectiva: dolor emocional**) (**Tania Singer**). La **depresión clínica** se caracteriza por cambios estructurales y funcionales en la CCAS (25). La estimulación Eléctrica TDCS de estas zonas alivia los síntomas de apatía y anhedonia*

*-Un **estudio en humanos** encontró que lesiones en la CCAP (incluyendo daños en la corteza prefrontal dorsomedial) provocaban hipersensibilidad y una mayor tendencia al llanto en eventos tristes (Hornak et al., 2003). Si la CCAP estuviera implicada en crear experiencias de tristeza, **daños en esta estructura** deberían abolir la tendencia a llorar ante eventos tristes.*

-La CCAP también está implicada en el dolor y en la vergüenza

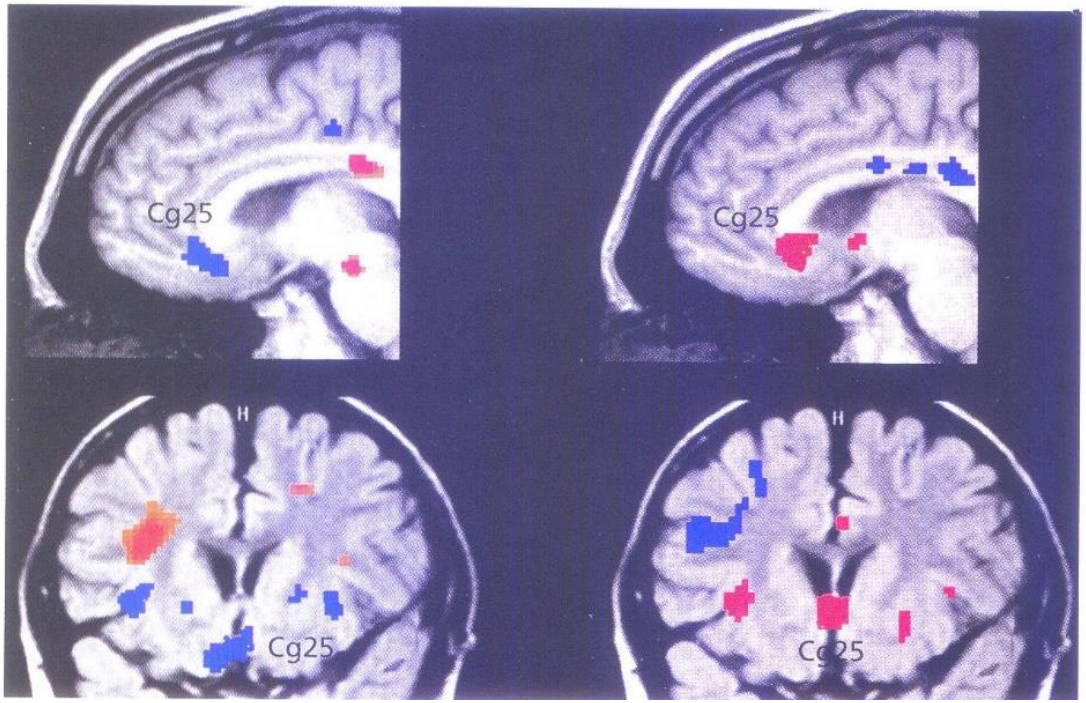
*-La parte **más dorsal de la corteza cingulada** parece que desempeña un papel importante en **la atención ejecutiva.** Desde este punto de vista, esta estructura ofrece fuentes de información sensorial exteroceptiva (desde proyecciones talámicas) junto con información sensorial interna (desde la ínsula) para dirigir la atención y dar respuestas motoras (**marcador somático**).*

-Hornak, J., Bramham, J., Rolls, E., Morris, R., O'Doherty, J., Bullock, P. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. Brain: 126, 1691–712.

2. EMOCIONES: Corteza cingulada anterior

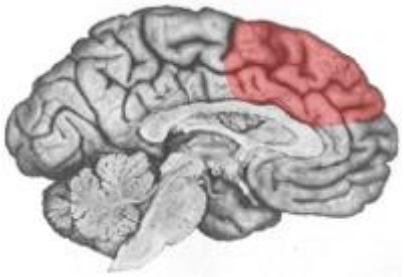
EL ÁREA 25, UNA DE LAS CLAVES

Las imágenes de tomografía por emisión de positrones muestran cómo en los individuos que se curan de la depresión disminuye el metabolismo en el área 25 de Brodmann (imágenes a la izquierda, con tonalidades azules en el área 25 que indican un metabolismo adecuado en ese área), mientras aumenta en aquellos que son sometidos a estímulos tristes (imágenes a la derecha, con tonalidades en rojo, indicando un hipermetabolismo en esa región).



-Hornak, J., Bramham, J., Rolls, E., Morris, R., O'Doherty, J., Bullock, P. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulate cortices. Brain: 126, 1691–712.

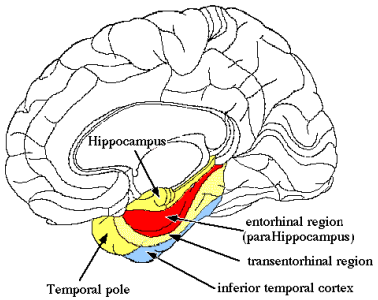
2. EMOCIONES: Corteza DM, temporal medial, retrosplenial, cíngulo posterior

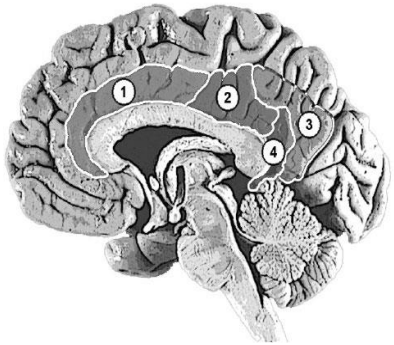


-Estas áreas cerebrales utilizan experiencias anteriores para crear un nuevo significado de nuestro estado afectivo principal, viniendo estas señales de nosotros mismos u observando a otros (evaluación de situaciones).

-Experiencias de tristeza y de felicidad fueron asociadas a una activación consistente en la CPF DM

-El miedo se ha asociado a un incremento en la activación del lóbulo temporal medial. Este hallazgo está más relacionado con la codificación de estímulos Salientes, ya que la amígdala se activa durante experiencias de miedo y tiene una conexión funcional muy fuerte con el hipocampo durante la codificación de estímulos.





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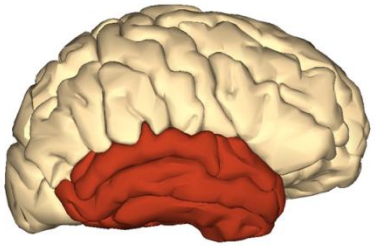
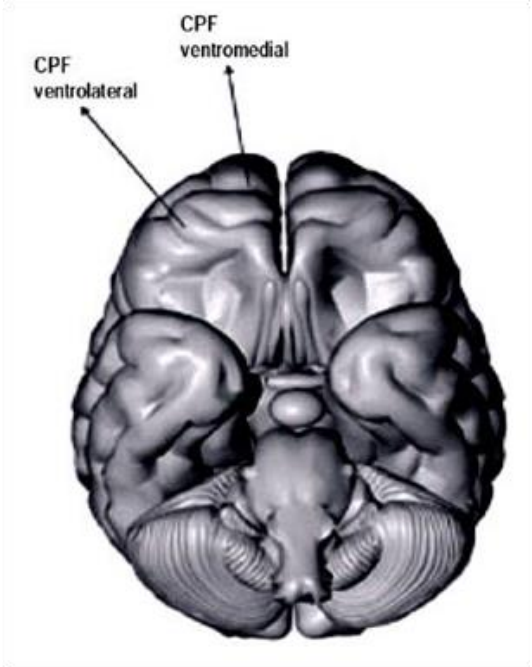
2. EMOCIONES: Lóbulo temporal anterior (LTA) y corteza prefrontal ventrolateral (CPVL)

*-Pacientes con demencia semántica tienen atrofia local en el **LTA**, dificultad para utilizar y asociar conceptos semánticos, y también tienen **dificultad para la percepción de emociones y empatía.***



*-El LTA (especialmente el izquierdo) está implicado en la **ira.***

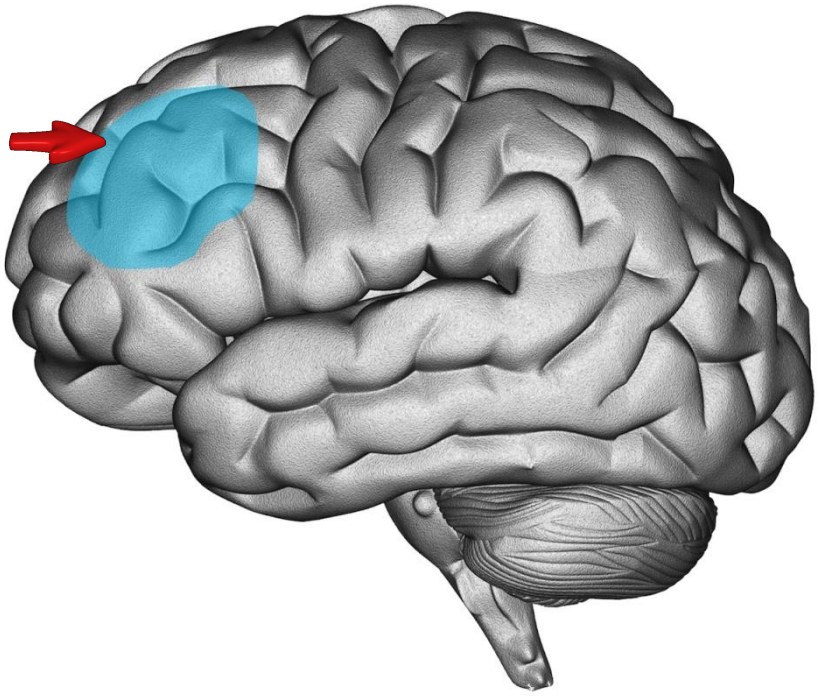


*-La **CPFVL** está implicada en tareas de **procesamiento semántico categorización de objetos, abstracción, atención y la inhibición de respuestas.***

Corbetta, M., Patel, G., Shulman, G. (2008). The reorienting system of the human brain: From environment to theory of mind. Neuron, 58, 306–24.

2. EMOCIONES: Corteza prefrontal dorsolateral (CFDL)

*-La corteza **prefrontal dorsolateral (CPFDL)** forma parte de la red frontoparietal dorsal que está implicada en el procesamiento arriba-abajo: atención y memoria de trabajo*



-Lindquist et al. (2012), refieren que esta región cerebral se activaba cuando, por ejemplo, los participantes tenían que mantener información afectiva en la mente para categorizarla.

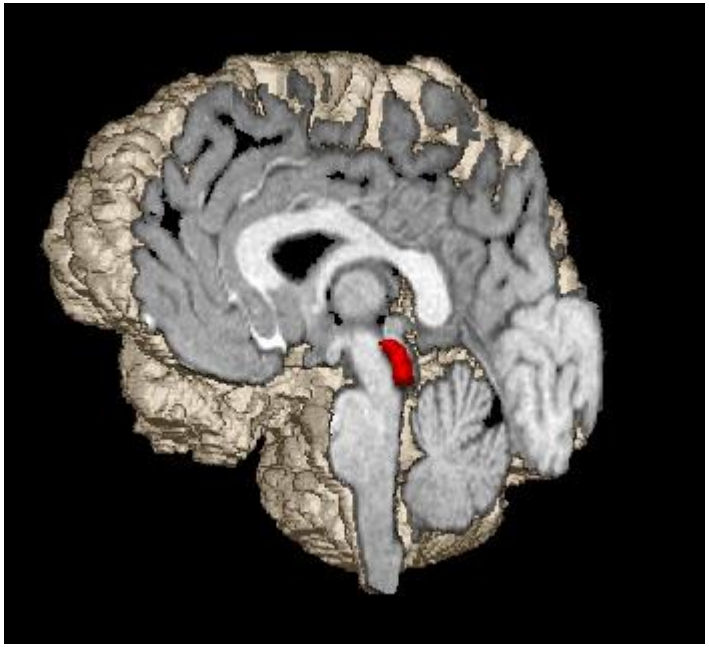
Además, había una mayor activación en la CPFDL cuando percibían estados emocionales relacionados con la ira.

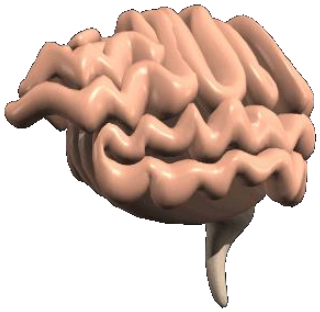
Lindquist, K., Wager, T., Kober, H., Bliss-Moreau, E. (2012). The brain bases of emotion: A meta-analytic review. Behavioral and brain sciences, 35, 121-202.

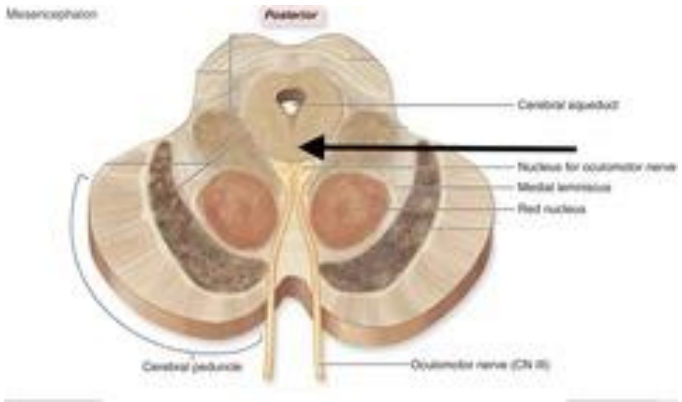
2. EMOCIONES: Sustancia gris periacueductal (SGPA)

-Está implicada en la regulación de los sustratos autonómicos que nos permiten adaptaciones conductuales tales como quedarnos paralizados, huir, vocalizar y comportamiento reproductivo (Mobbs et al., 2007).

-Un enfoque localizacionista ha vinculado la SGPA a distintos circuitos correspondientes con varias categorías de emoción: ***rabia, miedo, alegría, angustia, amor y lujuria.***



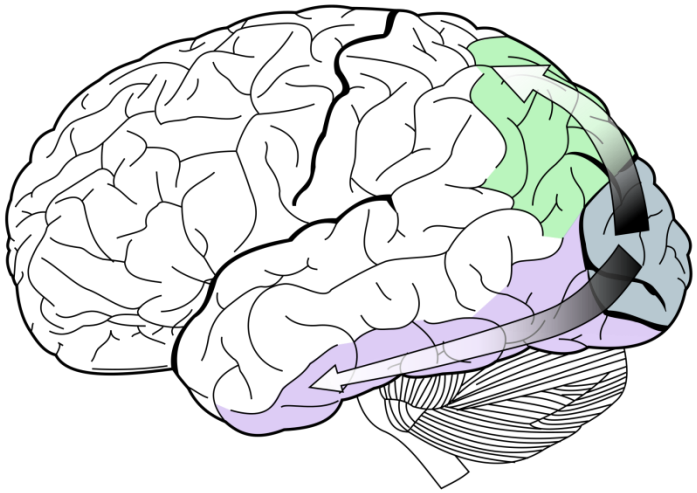




Mobbs, D., Petrovic, P., Marchant, J., Hassabis, D., Weiskopf, N., Seymour, B., Dolan, R., Frith, C. (2007). When fear is near: Threat imminence elicits prefrontal periaqueductal gray shifts in humans. Science, 317(5841), 1079–83

2. EMOCIONES: Cortex visual

-Lindquist et al. (2012): La emoción surge como una conceptualización de sensaciones internas del cuerpo y sensaciones externas del mundo para crear una experiencia unificada de nuestro yo en un contexto determinado.

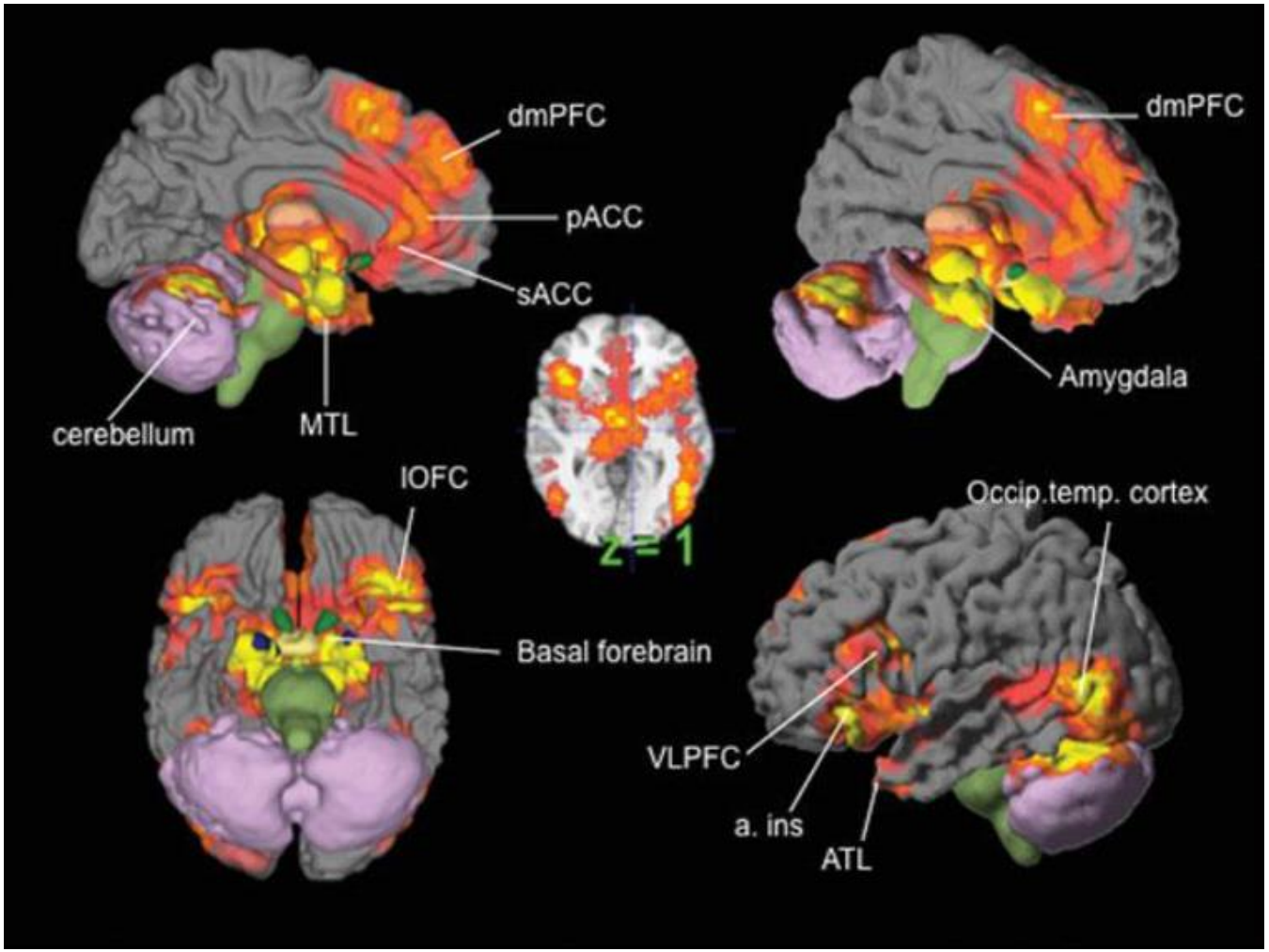


El aumento en la activación de la corteza visual se produjo cuando los participantes realizaban tareas con métodos visuales (por ejemplo, ver imágenes, rostros, etc.). Por lo tanto, no es de extrañar que la corteza visual y otras regiones encargadas en el procesamiento sensorial aumenten su actividad en tareas de este tipo.

Lindquist, K., Wager, T., Kober, H., Bliss-Moreau, E. (2012). The brain bases of emotion: A meta-analytic review. Behavioral and brain sciences, 35, 121-202.

2. EMOCIONES: Resumen bases cerebrales

Regiones cerebrales activadas en todos los estudios evaluativos de la experiencia o la percepción de ira, asco, miedo, felicidad y tristeza. Las regiones cerebrales en amarillo superaron el umbral de p<0.05; las regiones naranjas superaron el umbral de p<0.01, y las regiones en rosa y magenta no cuentan con una significación tan evidente. La corteza cerebral es de color gris, el núcleo accumbens azul y el cerebelo púrpura (Lindquist et al., 2012).



Lindquist, K., Wager, T., Kober, H., Bliss-Moreau, E. (2012). The brain bases of emotion: A meta-analytic review. Behavioral and brain sciences, 35, 121-202.

SISTEMA NERVIOSO ENTÉRICO
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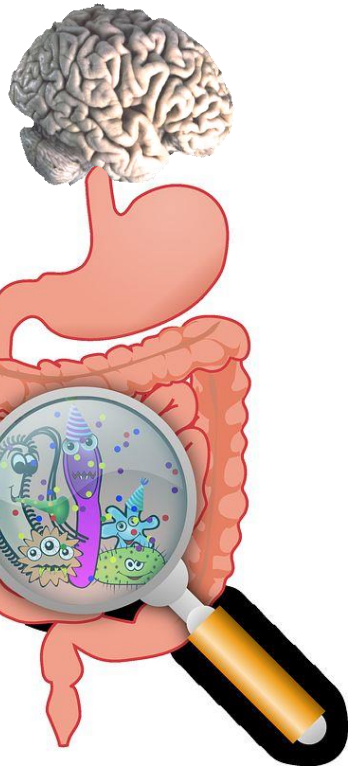
CFIE VALLADOLID



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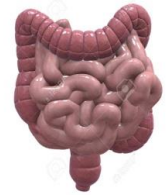

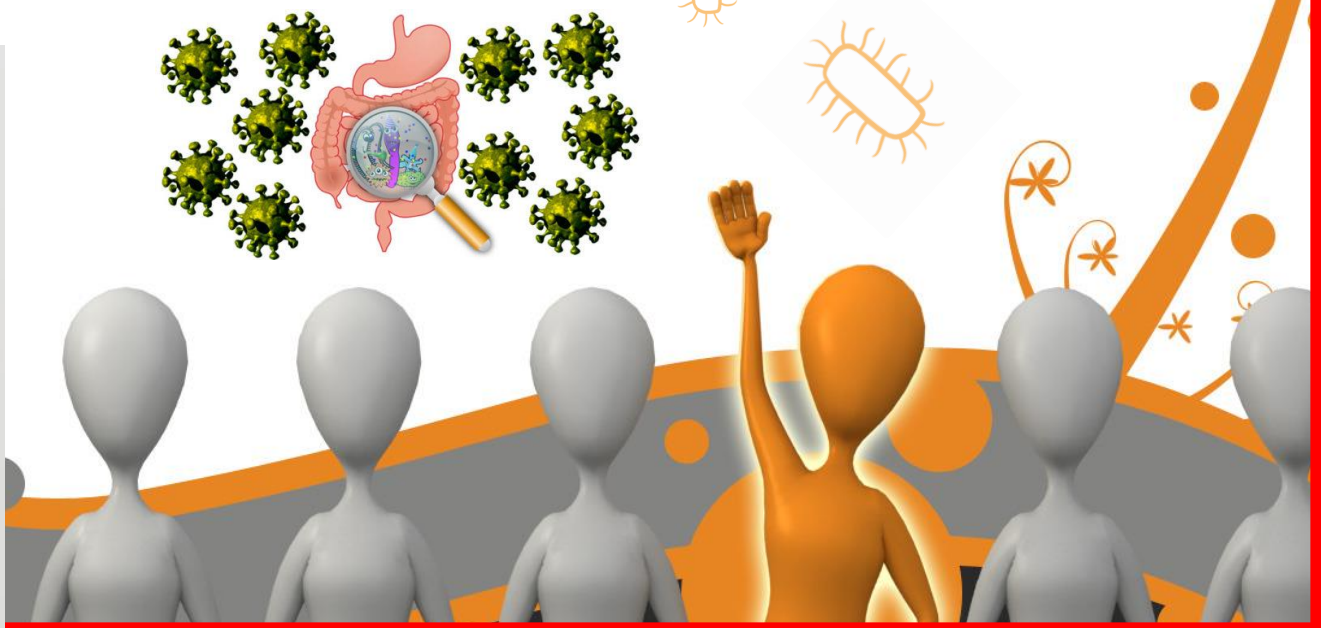

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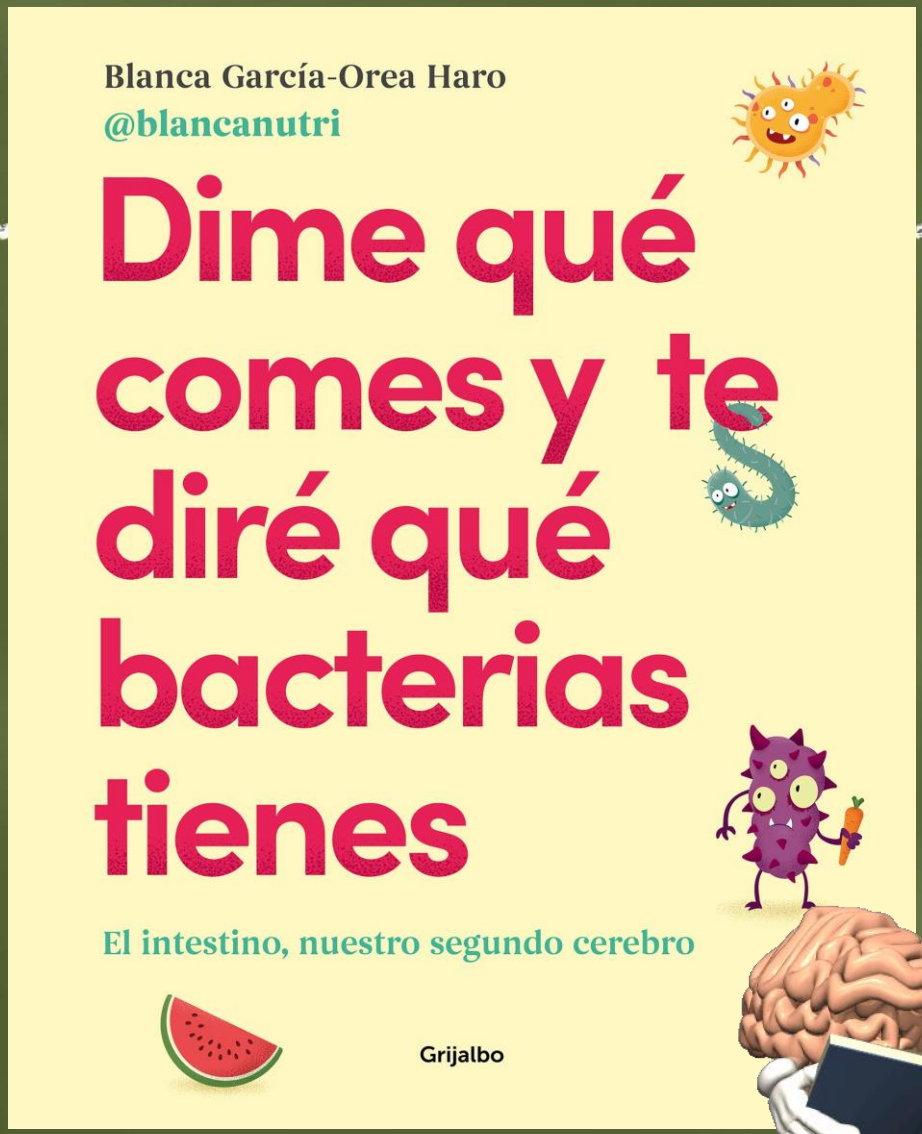

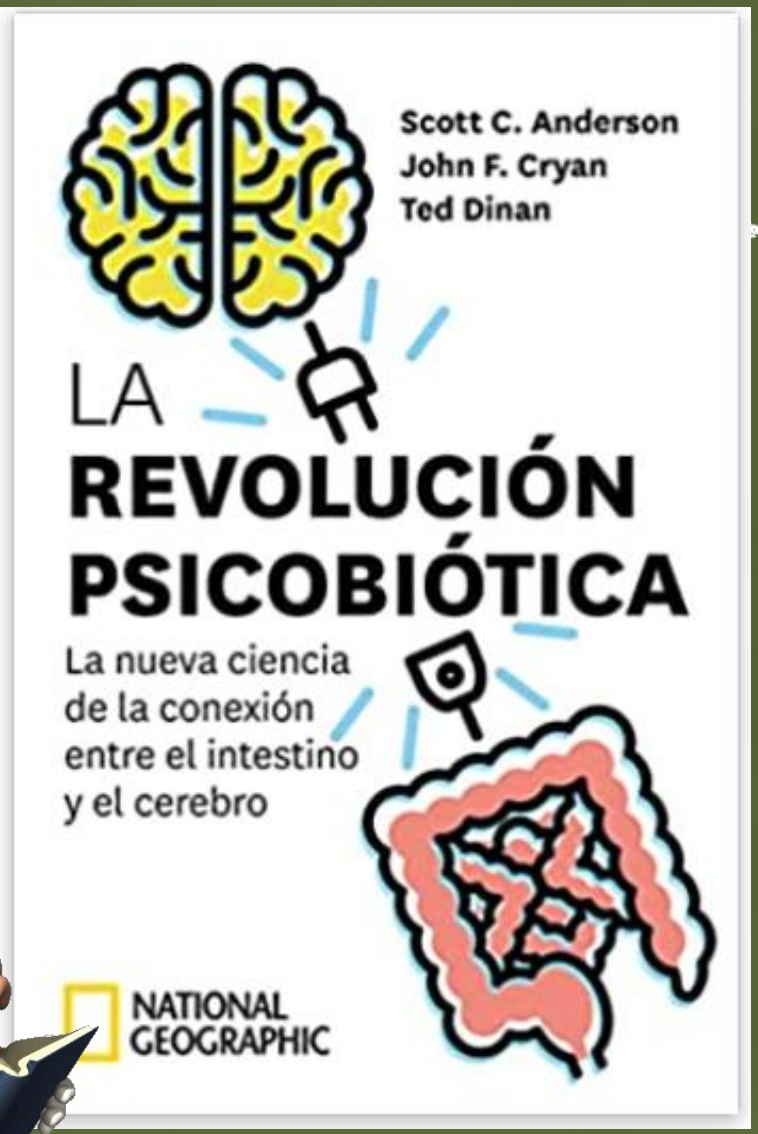

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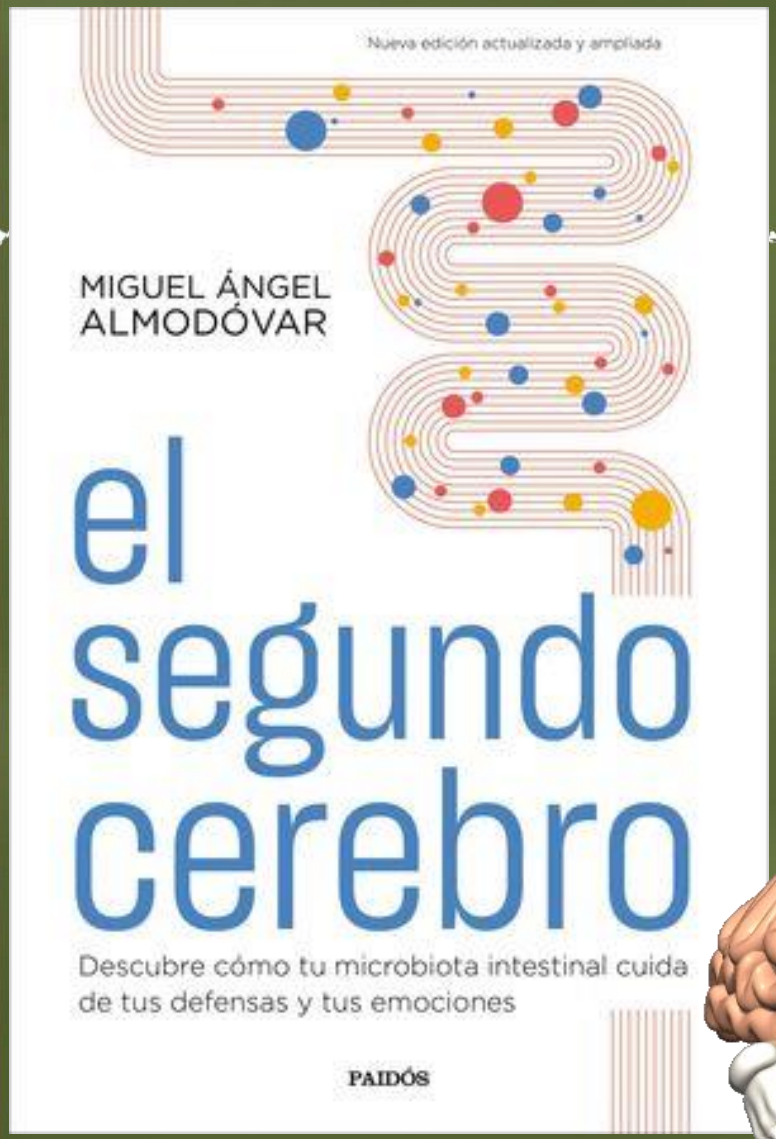

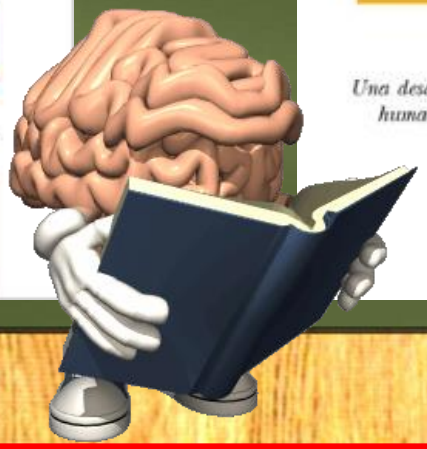

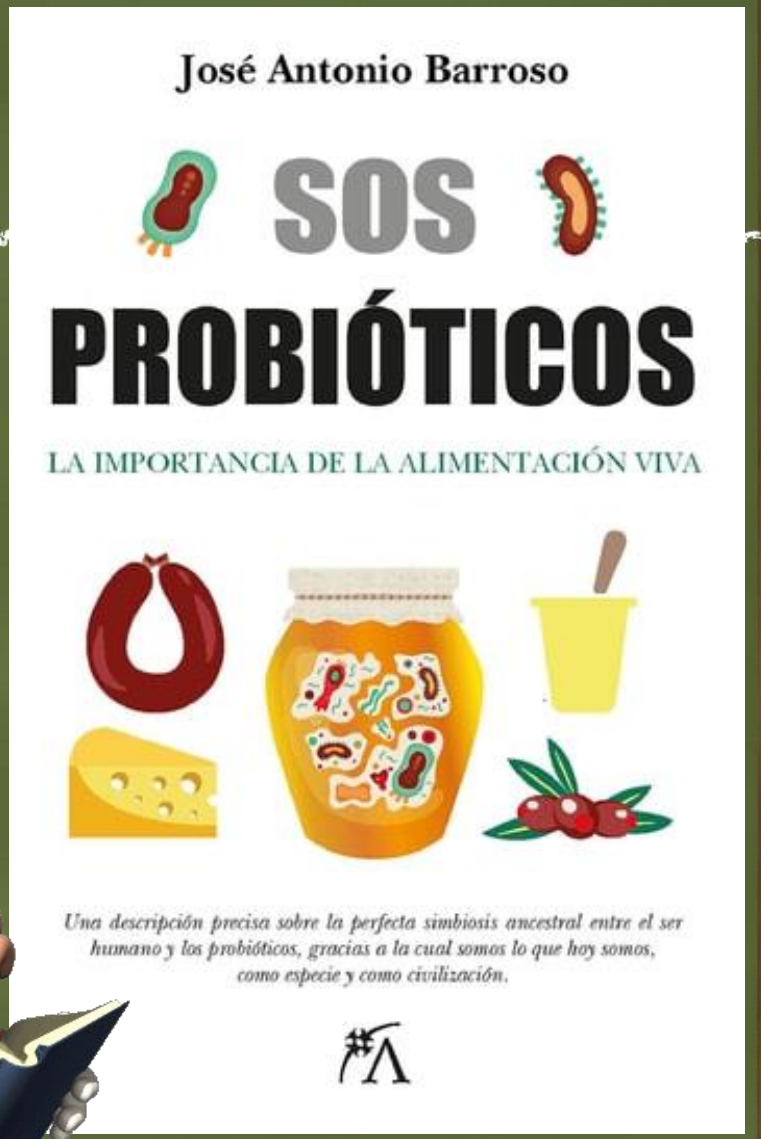

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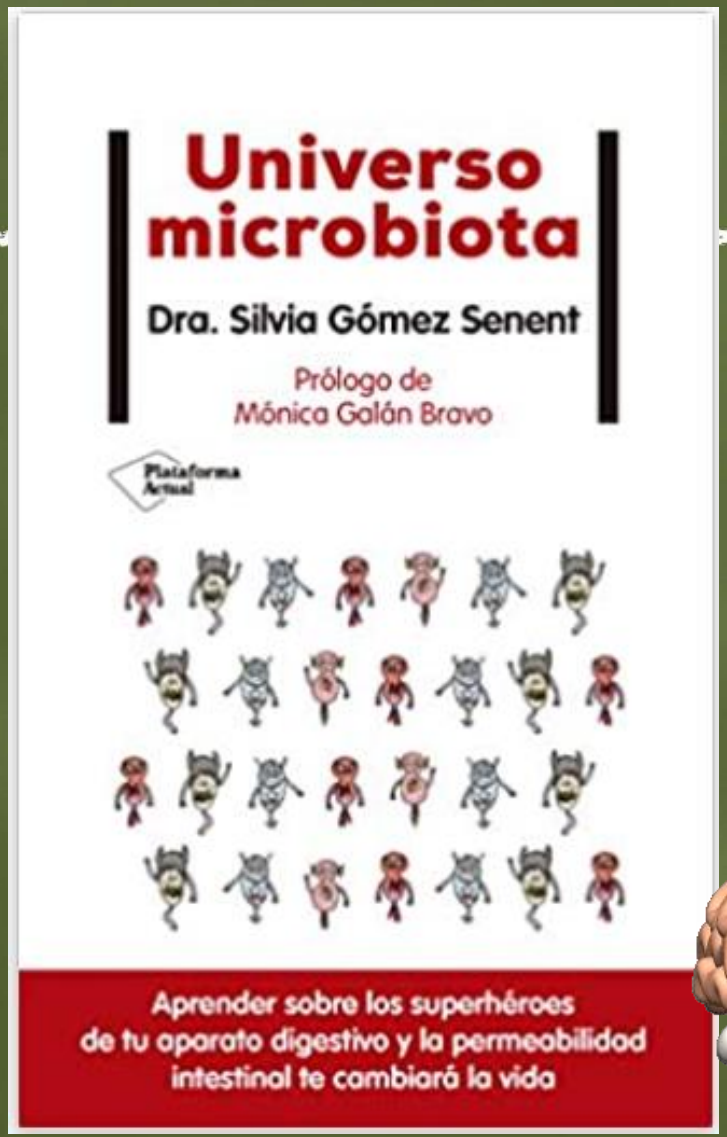

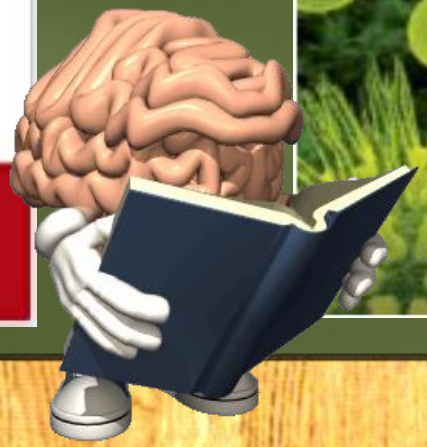

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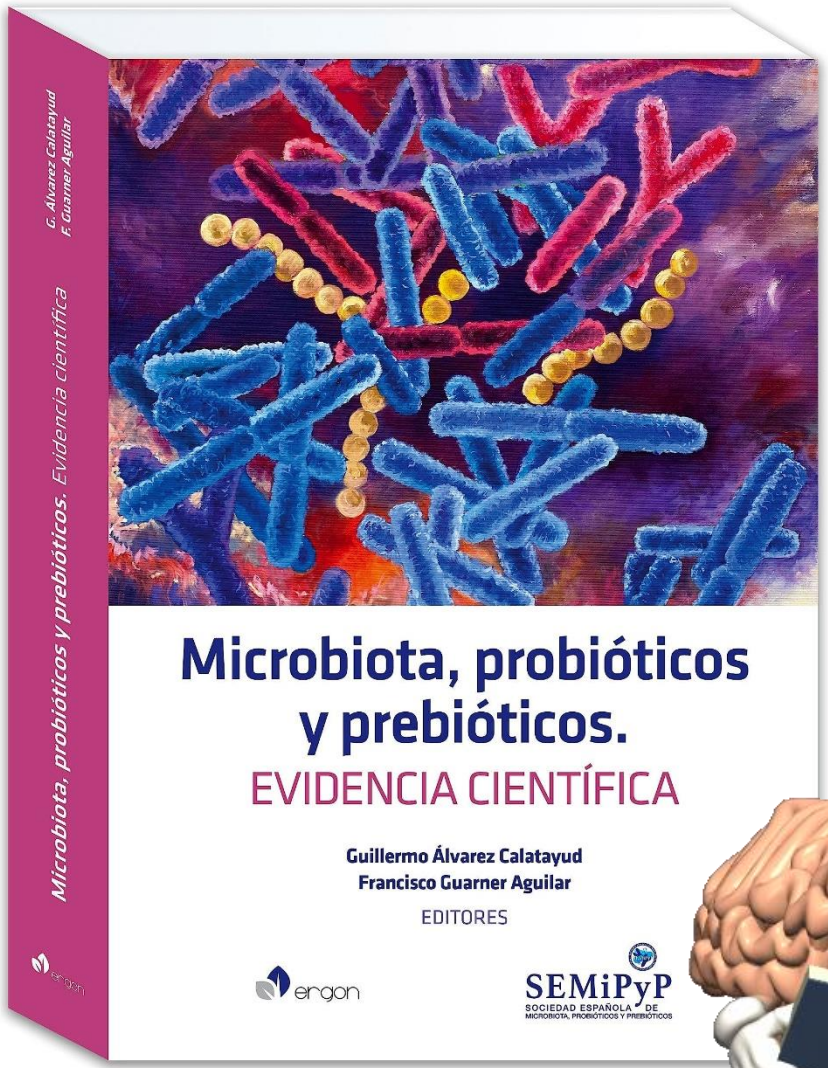

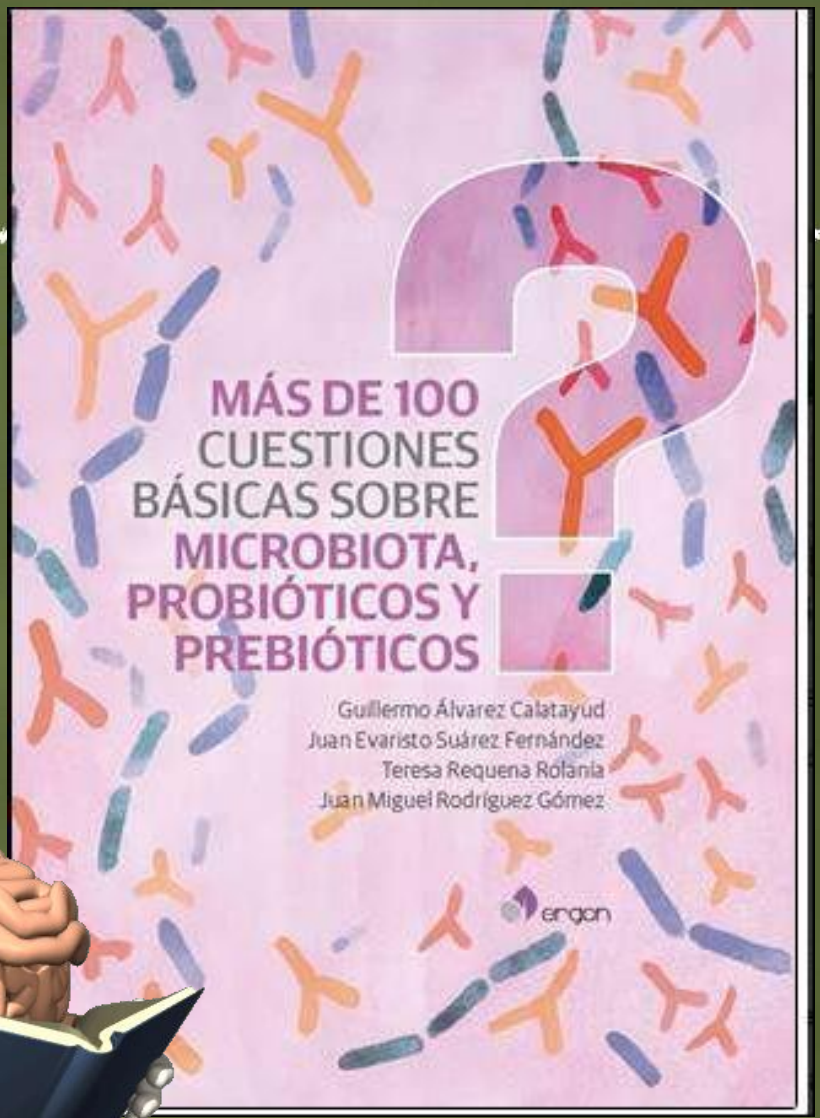

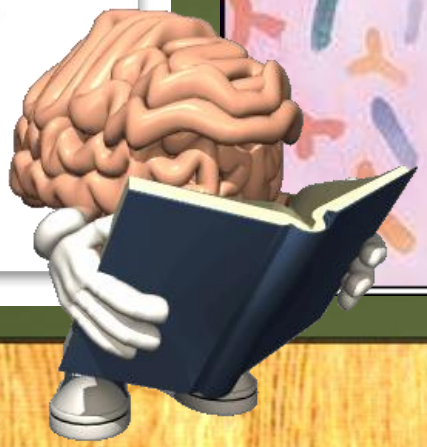

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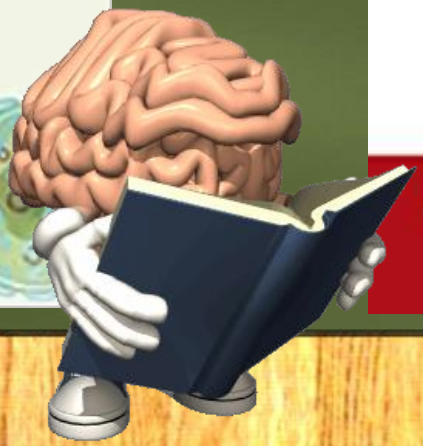

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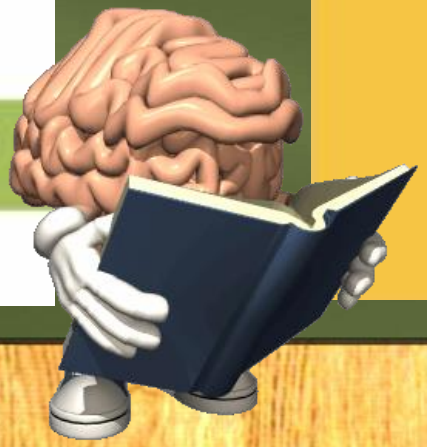

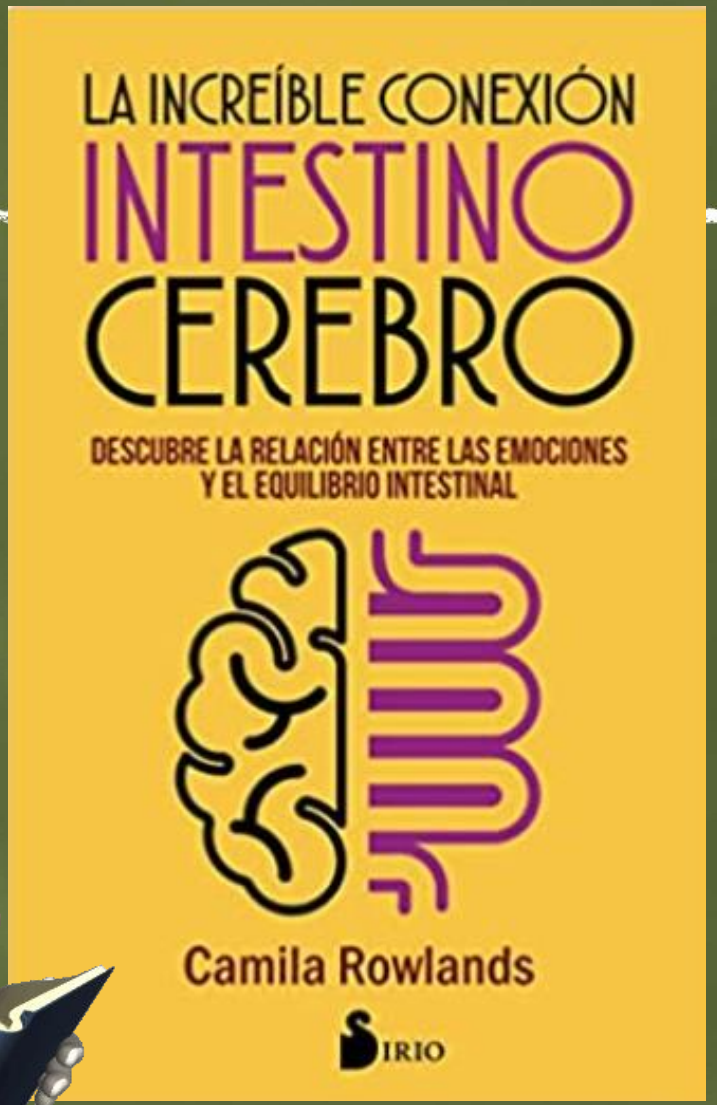

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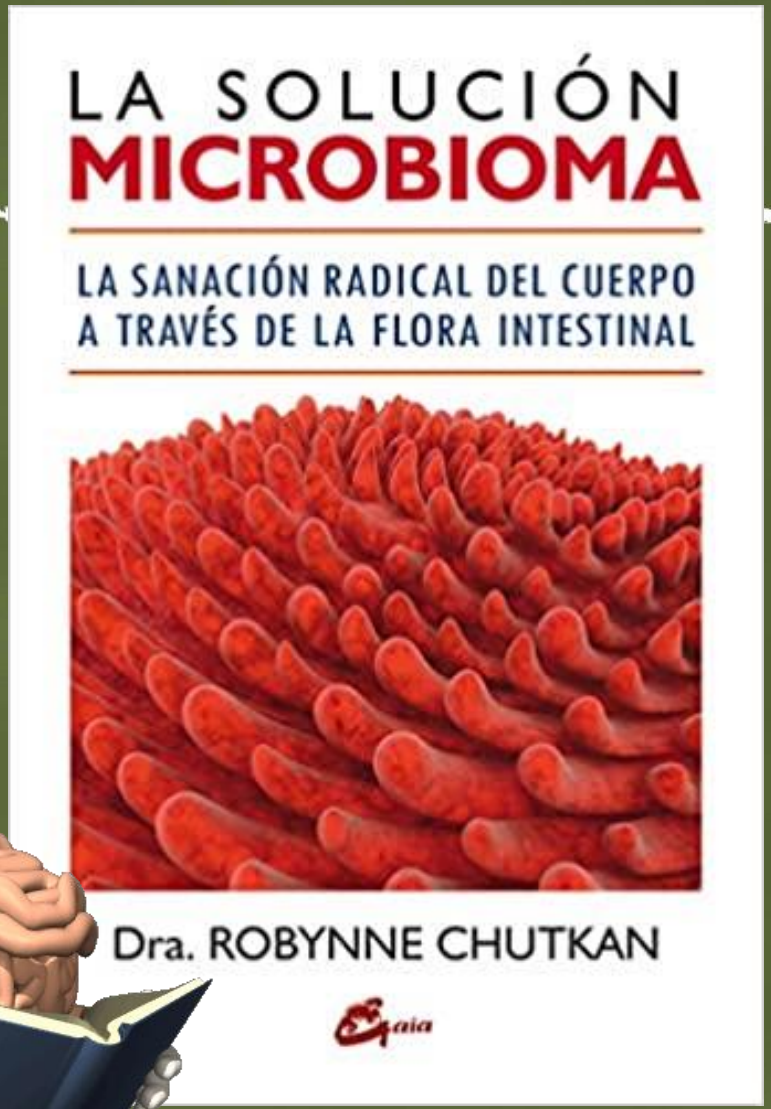

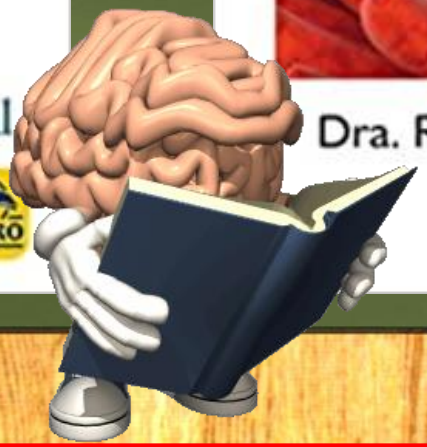

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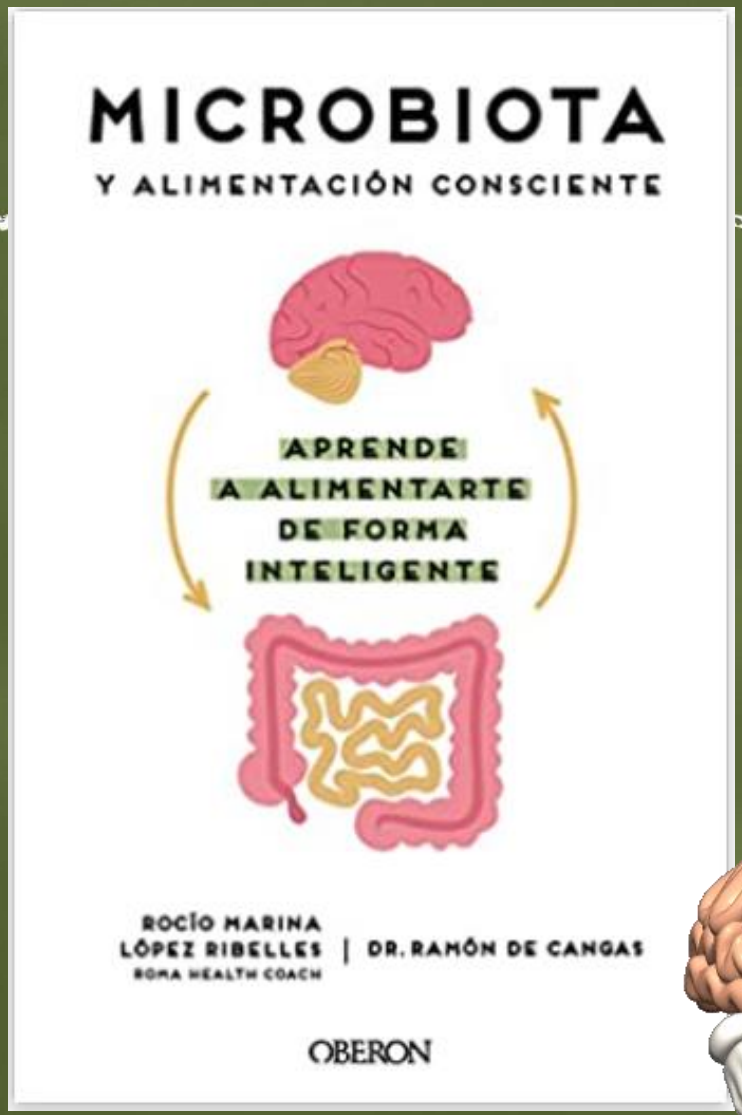

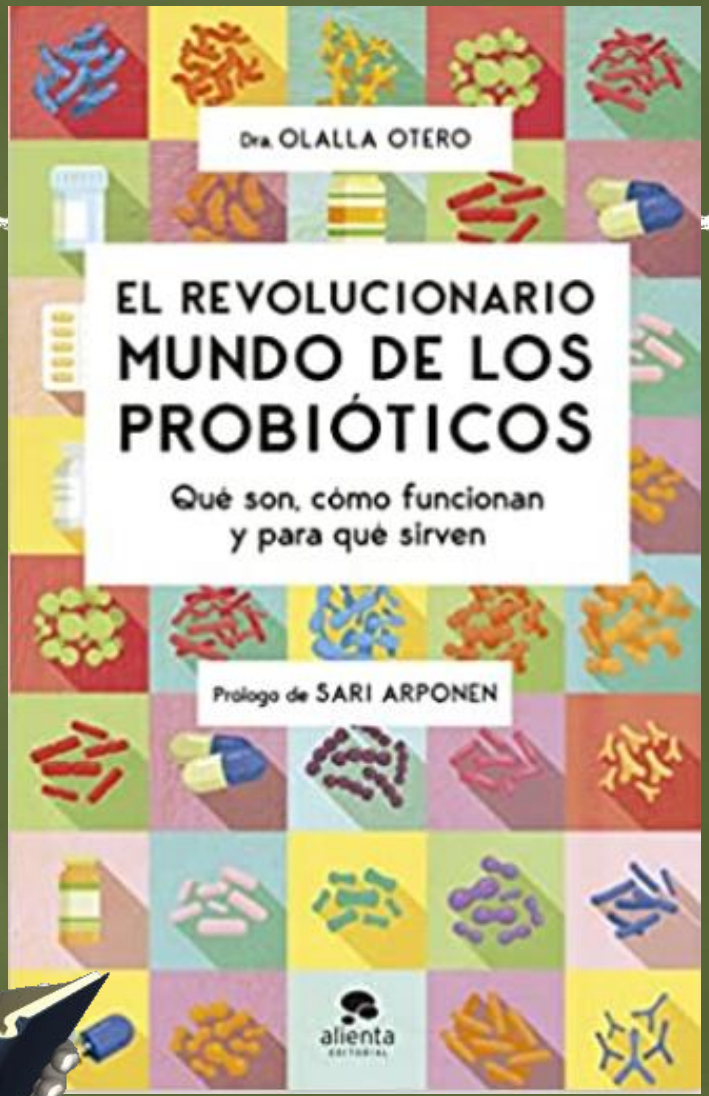

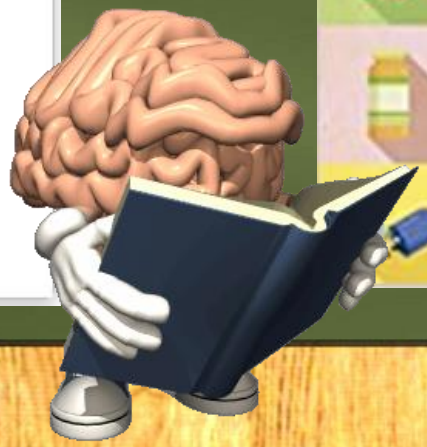

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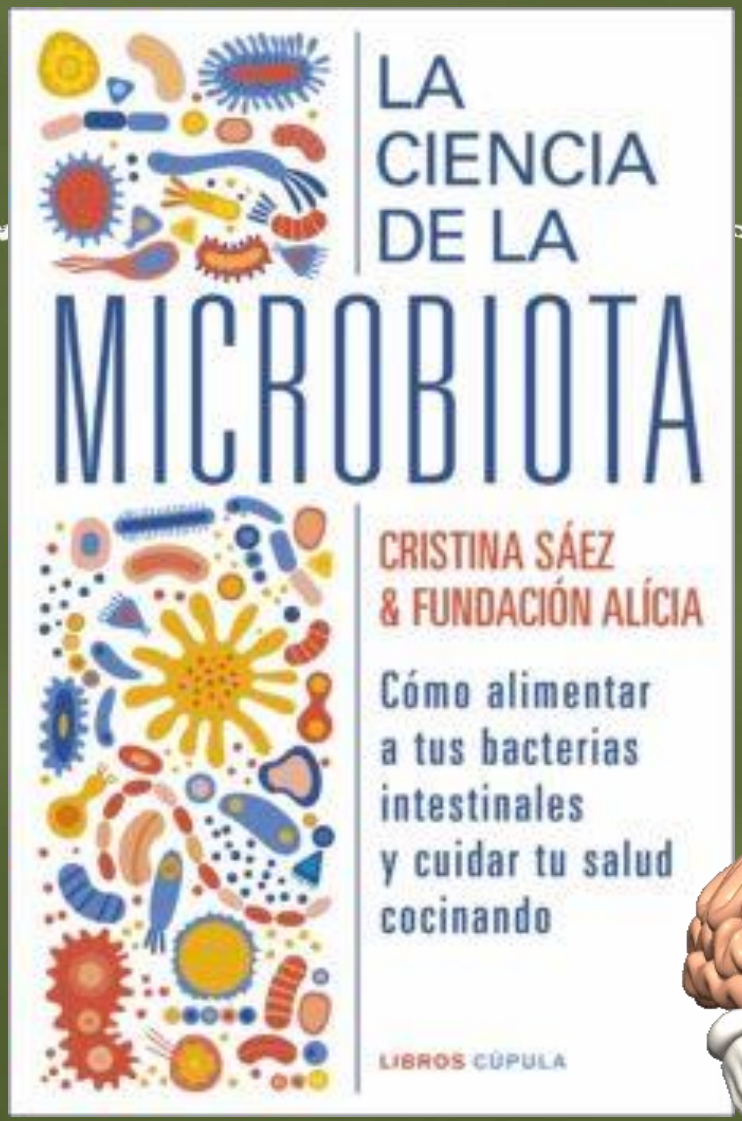

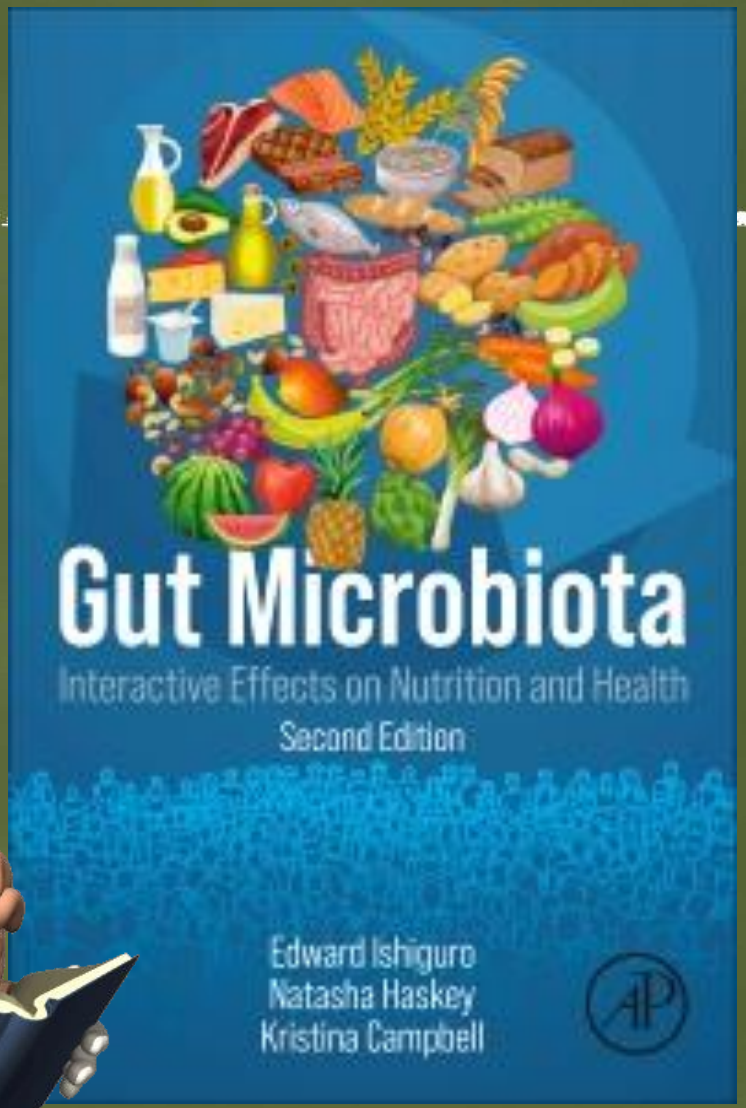

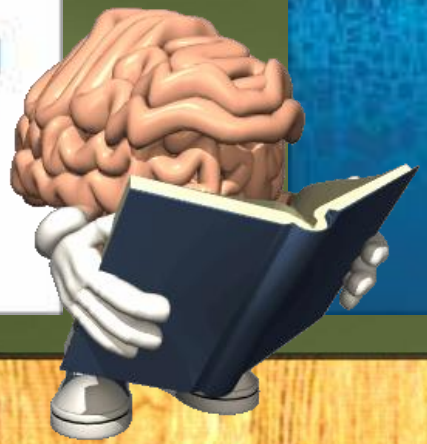

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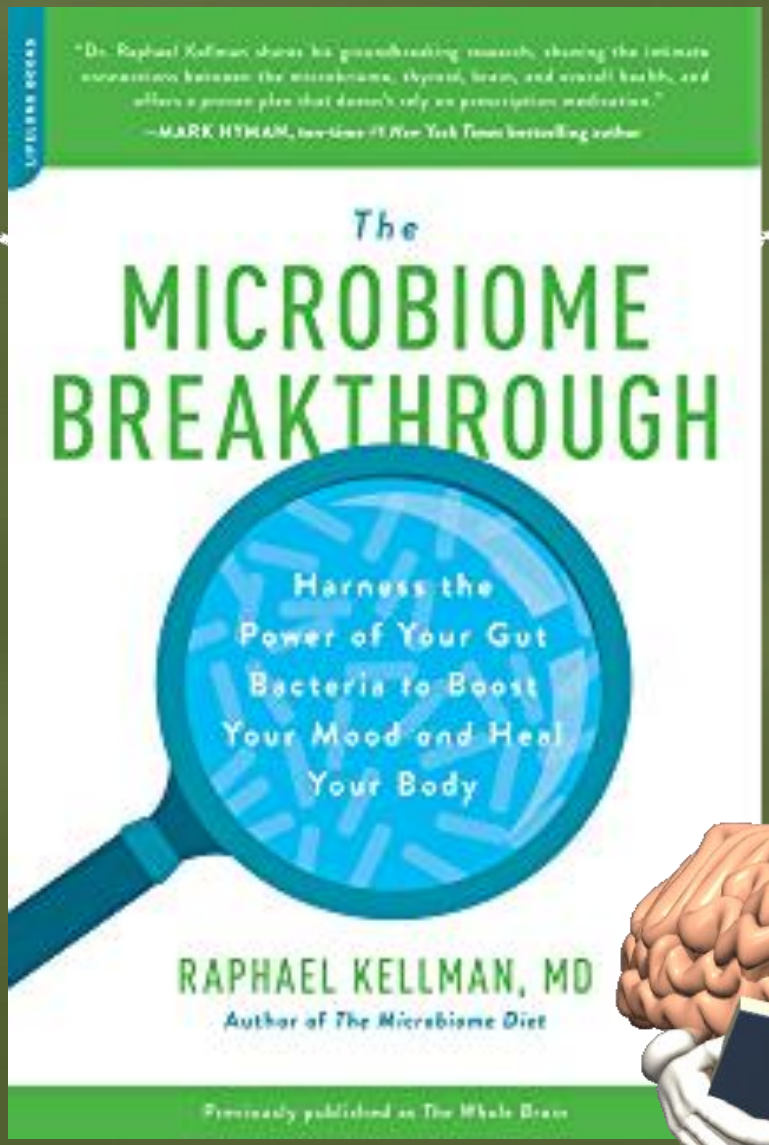

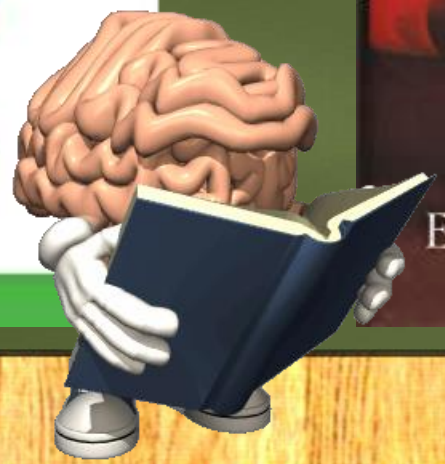

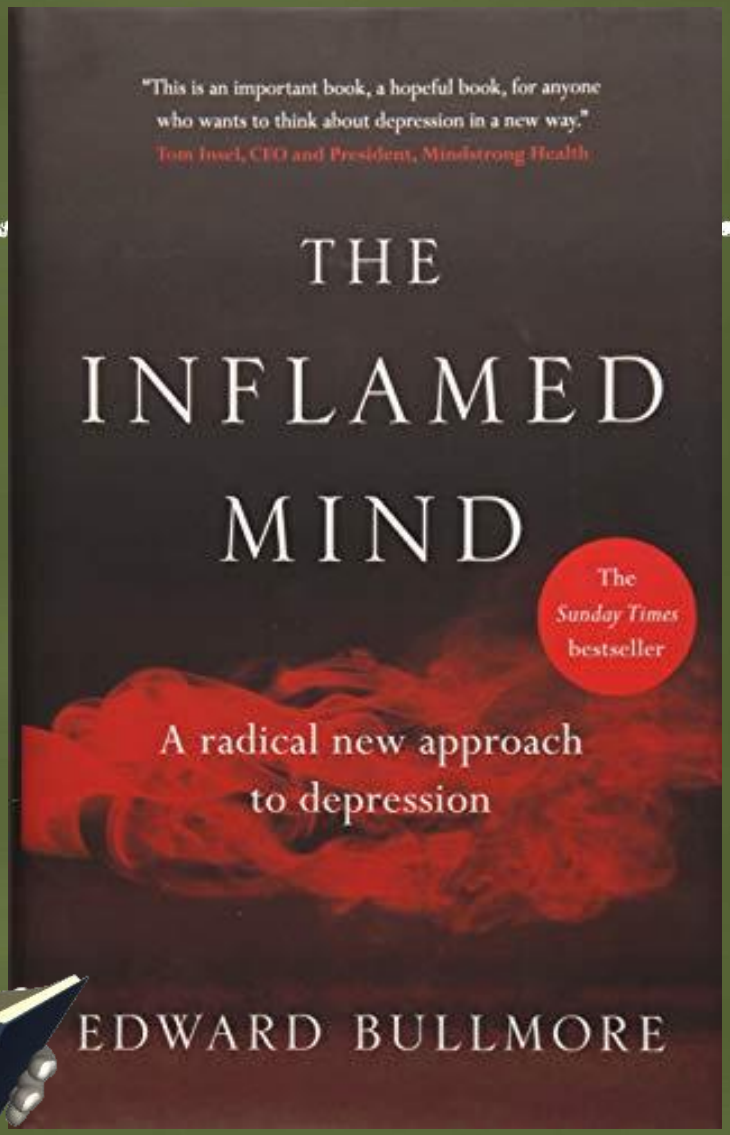

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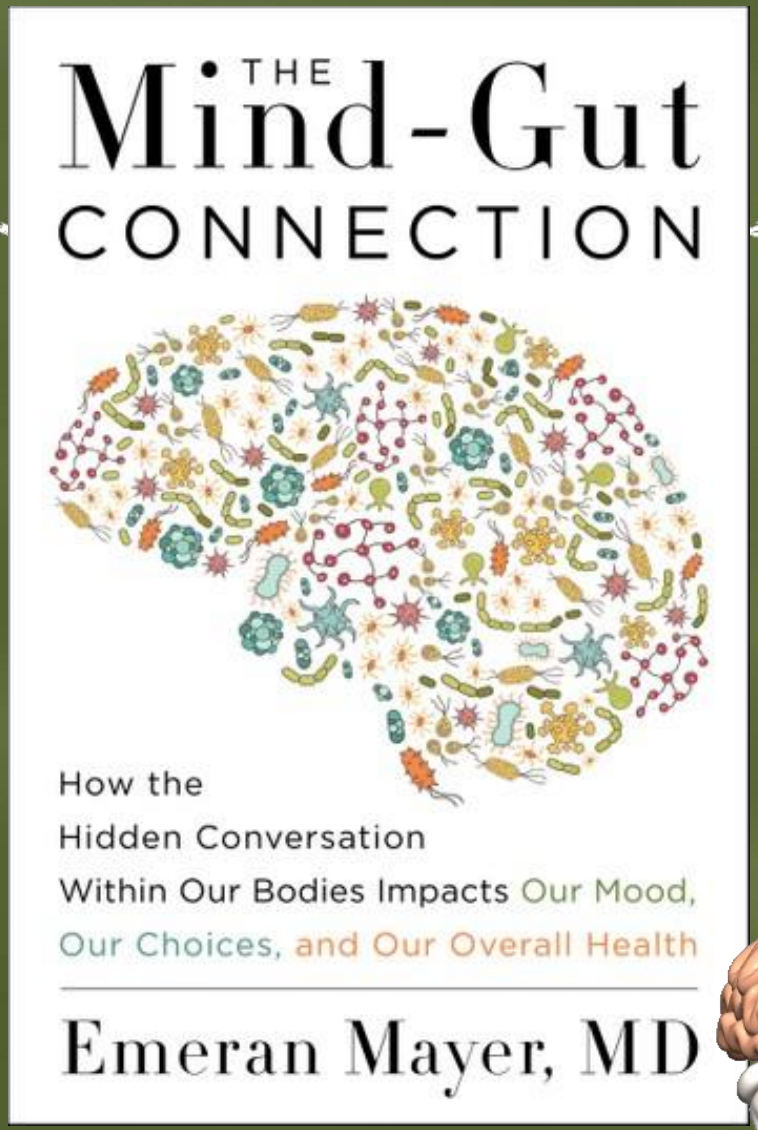

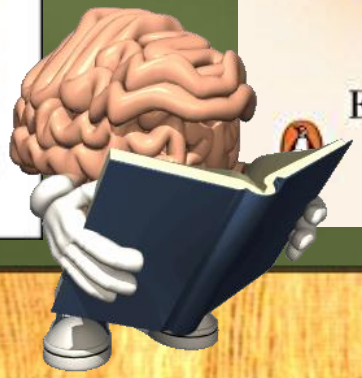

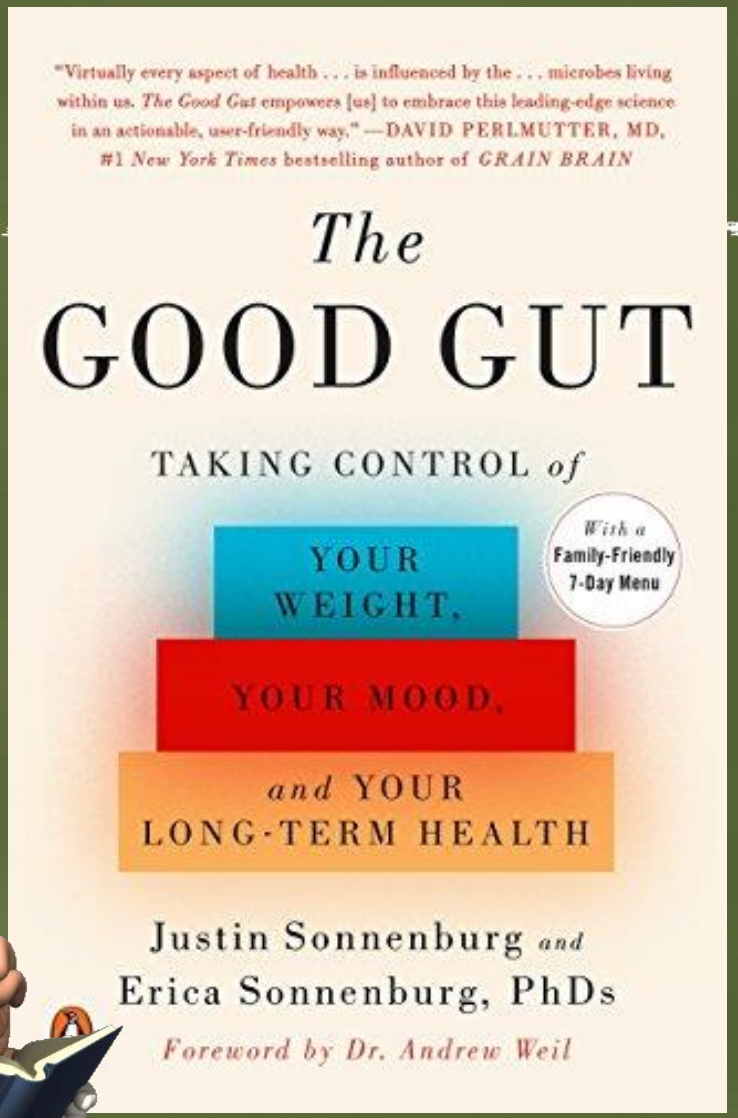

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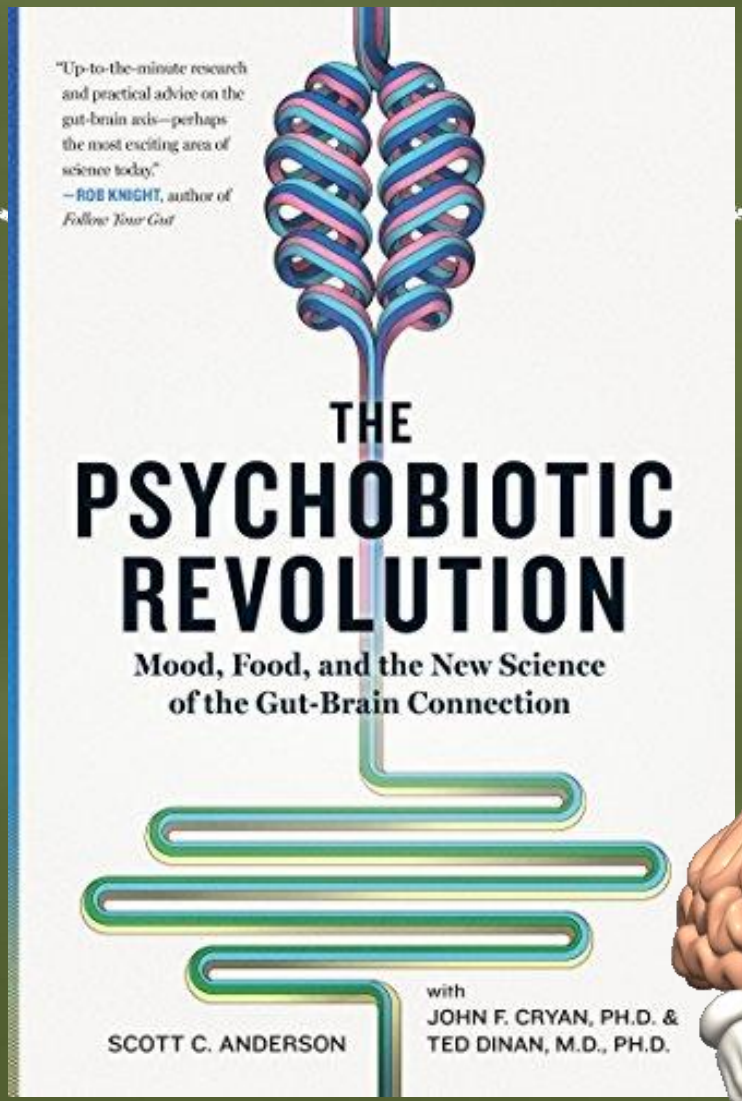
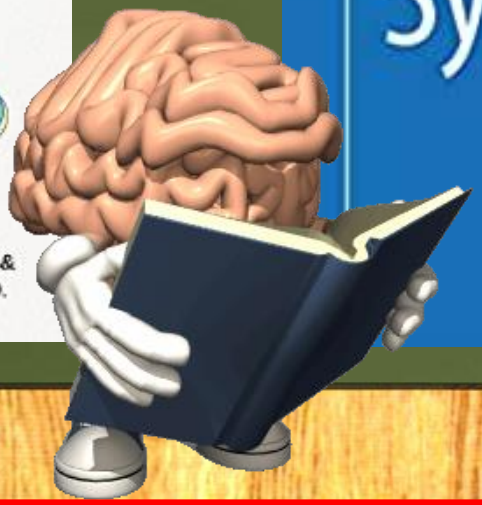
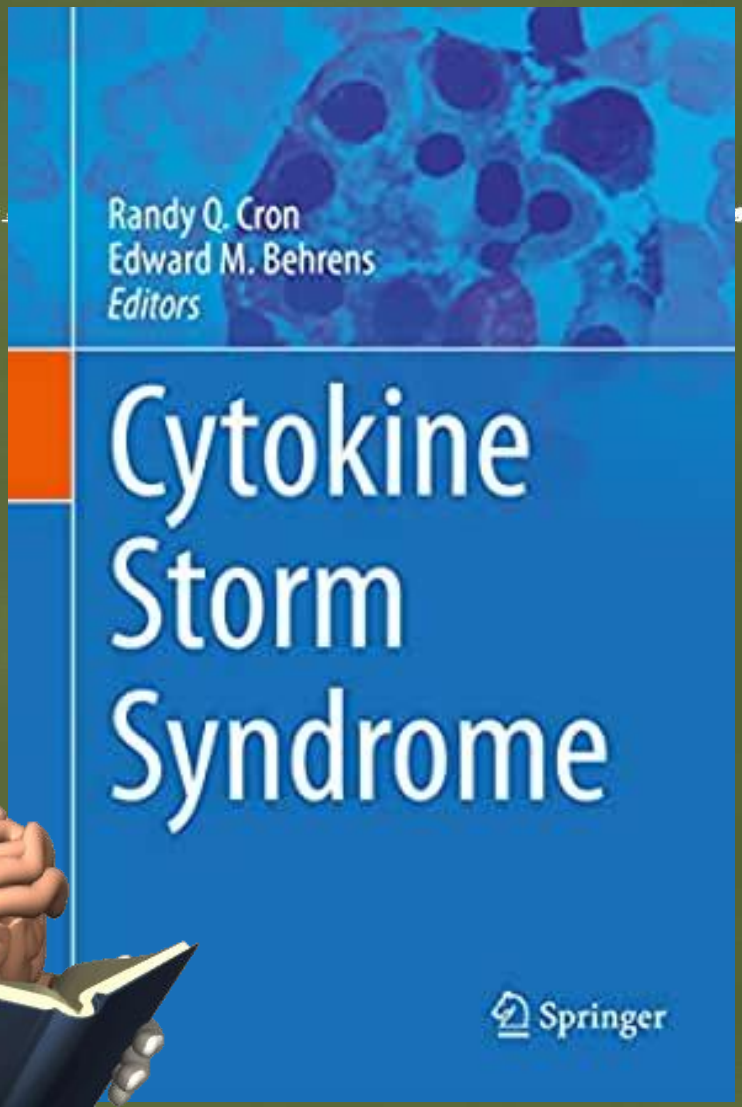


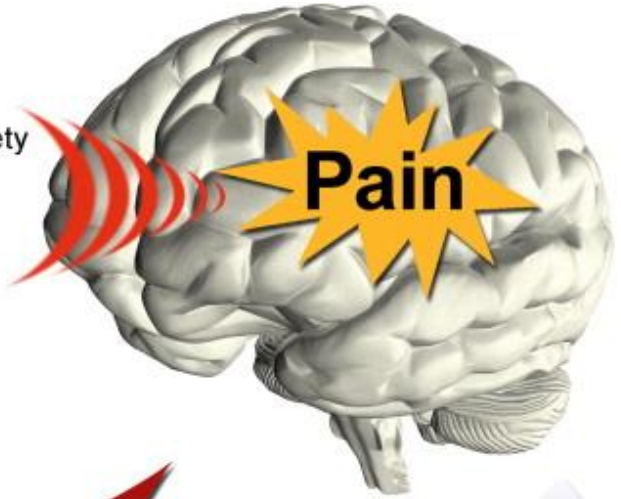




¿Pueden las bacterias intestinales (dieta) modular nuestro estado de ánimo?

¿Qué necesitan nuestros dos cerebros?

- Stress & Anxiety
- Depression
- Attention
- Expectation
- Conditioning

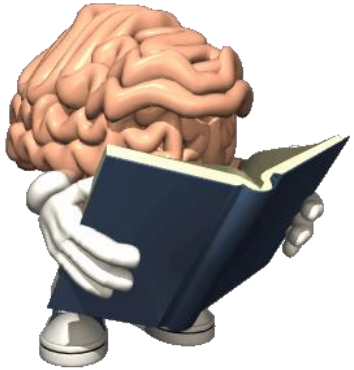


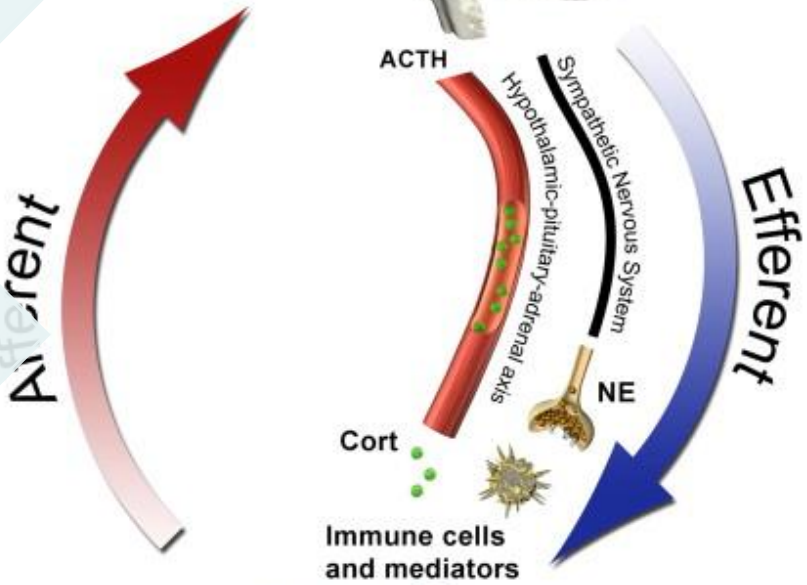
Genética
Sentidos (EE)
Oxígeno
Alimentos

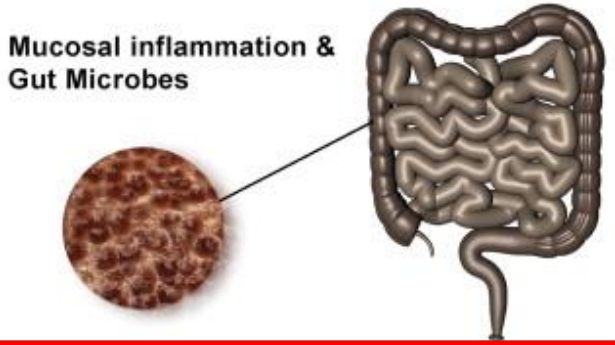
- *Primer cerebro*

Genética
Dieta (pre y probiótica)
Parto
Antibióticos
Higiene
Relaciones interpersonales

- *Segundo cerebro*
- *(Sistema N. entérico)*







The person-to-person transmission landscape of the gut and oral microbiomes

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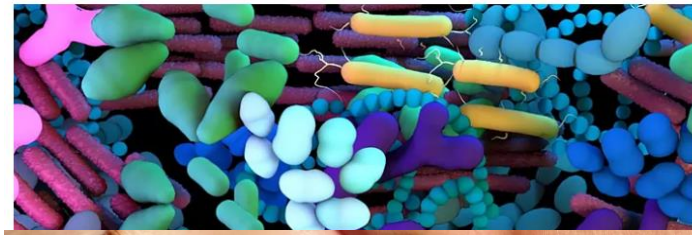
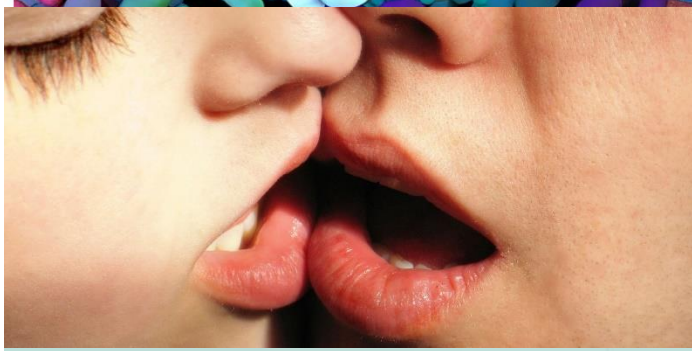
The human microbiome is an integral component of the human body and a co-determinant of several health conditions[1,2]. However, the extent to which interpersonal relations shape the individual genetic makeup of the microbiome and its transmission within and across populations remains largely unknown[3,4]. Here, capitalizing on more than 9,700 human metagenomes and computational strain-level profiling, we detected extensive bacterial strain sharing across individuals (more than 10 million instances) with distinct mother-to-infant, intra-household and intra-population transmission patterns. Mother-to-infant gut microbiome transmission was considerable and stable during infancy (around 50% of the same strains among shared species (strain-sharing rate)) and remained detectable at older ages. By contrast, the transmission of the oral microbiome occurred largely horizontally and was enhanced by the duration of cohabitation. There was substantial strain sharing among cohabiting individuals, with 12% and 32% median strain-sharing rates for the gut and oral microbiomes, and time since cohabitation affected strain sharing more than age or genetics did. Bacterial strain sharing additionally recapitulated host population structures better than species-level profiles did. Finally, distinct taxa appeared as efficient spreaders across transmission modes and were associated with different predicted bacterial phenotypes linked with out-of-host survival capabilities. The extent of microorganism transmission that we describe underscores its relevance in human microbiome studies[5], especially those on non-infectious, microbiome-associated diseases.

Tu pareja, tus compañeros de piso o tus amigos influyen en las bacterias de tu boca y tu intestino

Además de la herencia materna y de factores exógenos como la dieta, la microbiota también puede estar modulada por las relaciones personales, a través de la transmisión horizontal



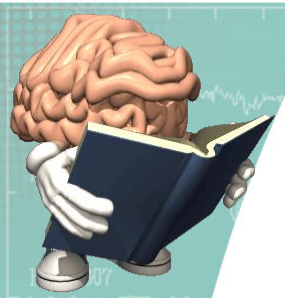


Microbiota Involvement in the Gut–Brain Axis

*Flavia Indrio, †Giuseppe Riezzo, ‡Francesco Raimondi, *Antonio Di Mauro, and *Ruggiero Francavilla

JPGN • Volume 57, Supplement 1, December 2013

FIGURE 1. The interaction among the immune, neuronal, and endocrine components of the communication between the central nervous system and the gastrointestinal tract.



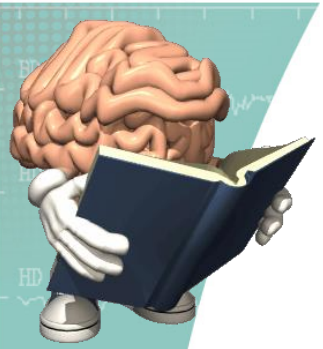
PROBIÓTICOS Y PREBIÓTICOS

https://www.dailymotion.com/video/x6svpa?playlist=x4t2zs

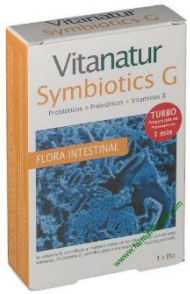
PROBIÓTICOS: Los alimentos probióticos son microorganismos vivos añadidos que permanecen activos en el intestino en cantidad suficiente (a pesar del Ph ácido del estómago) como para alterar la microbiota intestinal del huésped, tanto por implantación como por colonización. Pueden tener efectos beneficiosos cuando son ingeridos en cantidades suficientes. Pueden atravesar el aparato digestivo y recuperarse vivos en los excrementos, pero también se adhieren a la mucosa intestinal.

https://www.dailymotion.com/video/x6yuoac?playlist=x4t2zs

PREBIÓTICOS: Los prebióticos son una clase de alimentos funcionales, definidos como ingredientes de la comida no digeribles (almidón resistente y fibra) que son utilizados por la microbiota intestinal, estimulando el crecimiento de una o más cepas de las bacterias presentes en el tracto intestinal, modificando su composición y actividad, logrando una mejora en la salud y el bienestar del huésped (fibras dietéticas insolubles)



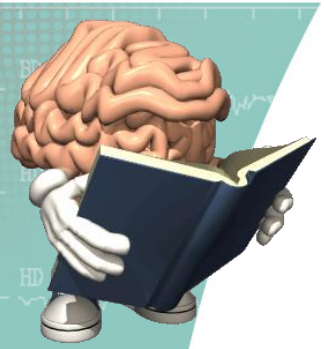
SIMBIÓTICOS



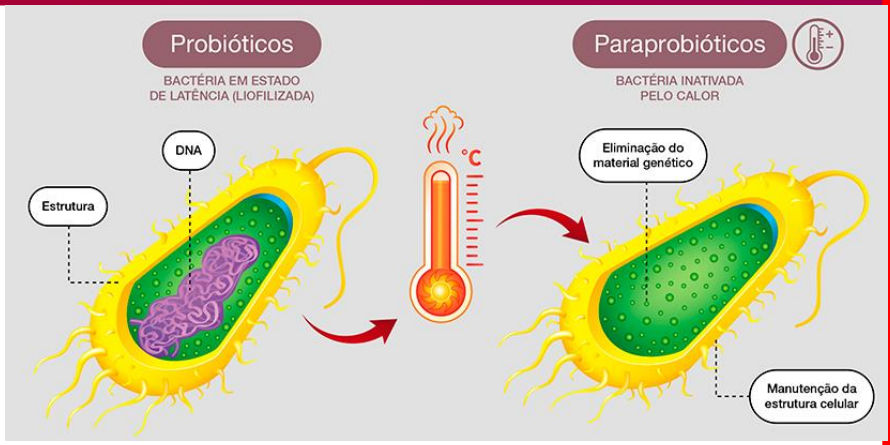
SIMBIÓTICOS: Un simbiótico es una preparación farmacéutica o alimentaria que contiene una o más especies de probióticos e ingredientes prebióticos. Así, un producto simbiótico ejerce un efecto probiótico y prebiótico.

Recientemente (agosto de 2020), la *International Scientific Association of Probiotics and Prebiotics* (ISAPP) publicó un documento de consenso en el que indica que **sólo se deberían denominar simbióticos a aquellos preparados cuya combinación queda confirmada científicamente que presenta eficacia**. Por lo tanto, la eficacia de una mezcla simbiótica no podrá atribuirse al beneficio clínico que ha sido demostrado por una cepa probiótica estudiada individualmente.

La definición actualizada de simbiótico es "*mezcla que comprende microorganismos vivos y sustratos utilizados selectivamente por los microorganismos del hospedador que confiere un beneficio para la salud del hospedador*".



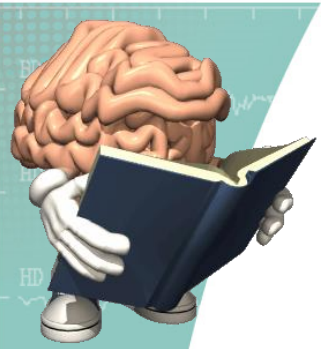
PARAPROBIÓTICOS



"Material no viable de origen microbiano (microorganismos inactivos o fracciones celulares)" que habrían demostrado que pueden tener beneficios para la salud humana y/o animal".
(procesos de pasteurización de probióticos)

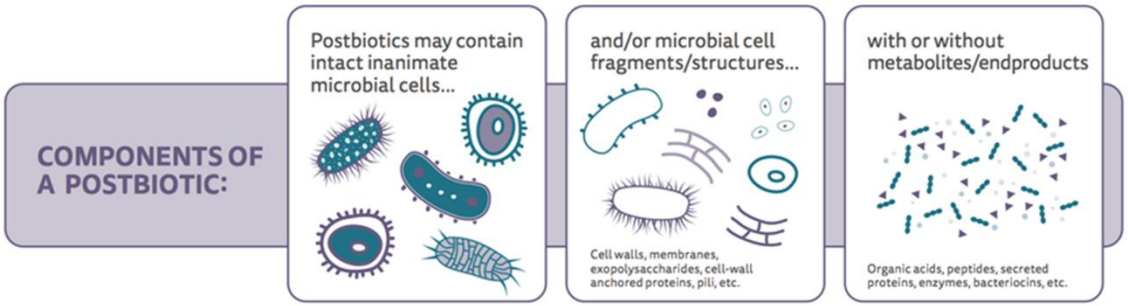
Bacterias probióticas inactivas con efecto biológico sobre la salud y un buen perfil de seguridad, estabilidad y tolerancia que induce una respuesta biológica "diferente" a la que generaría la bacteria viva y metabólicamente activa.

Un estudio publicado en *Nature Medicine* en 2019 prueba que en un ensayo con pacientes con sobrepeso y resistencia a la insulina, la suplementación con *Akkermansia mucinisphila* en un preparado con bacteria viva y pasteurizada (inactivada) fue segura y mejoró varios parámetros metabólicos (buena tolerancia y sin efectos secundarios)



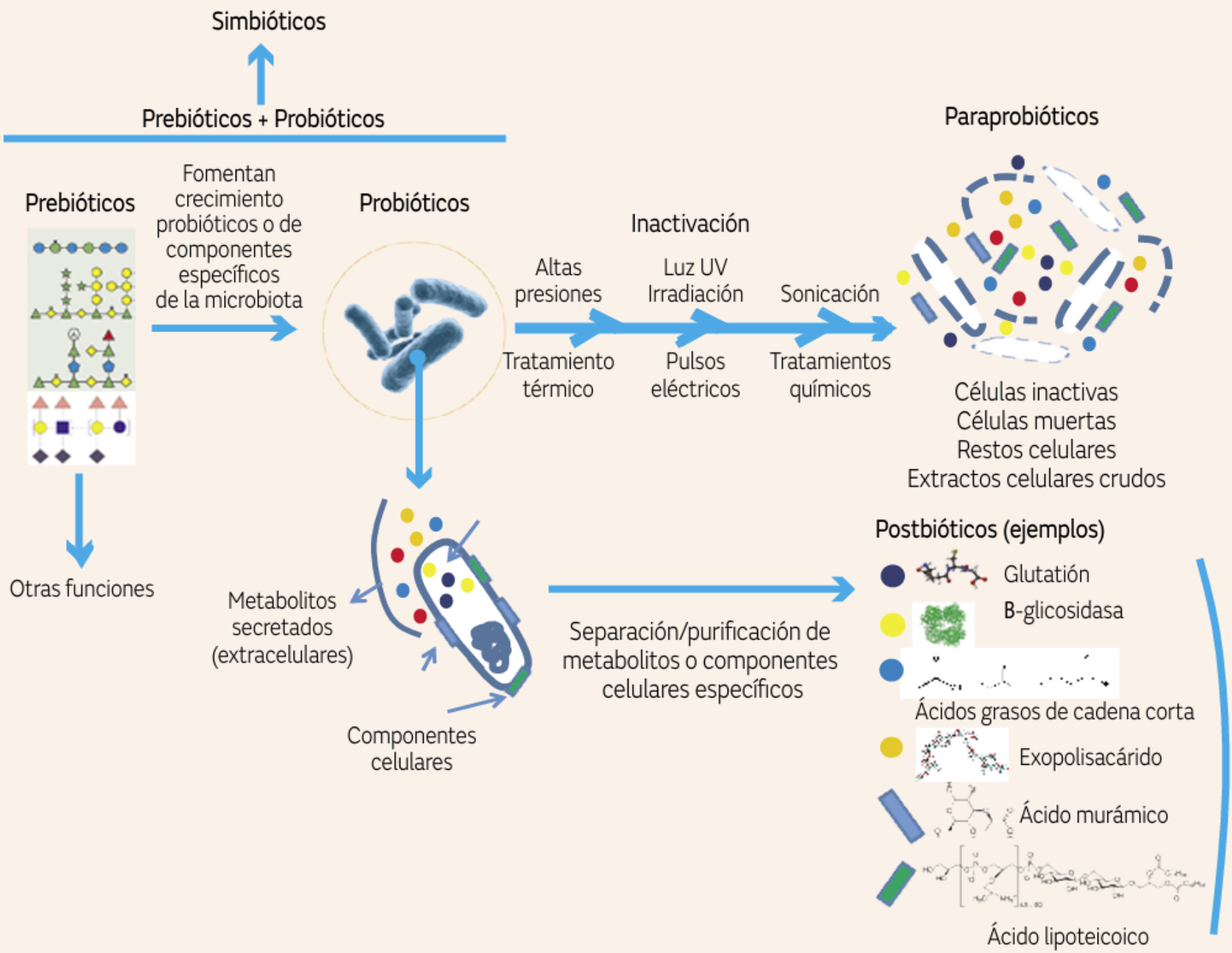
Postbiotics

A postbiotic is a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.



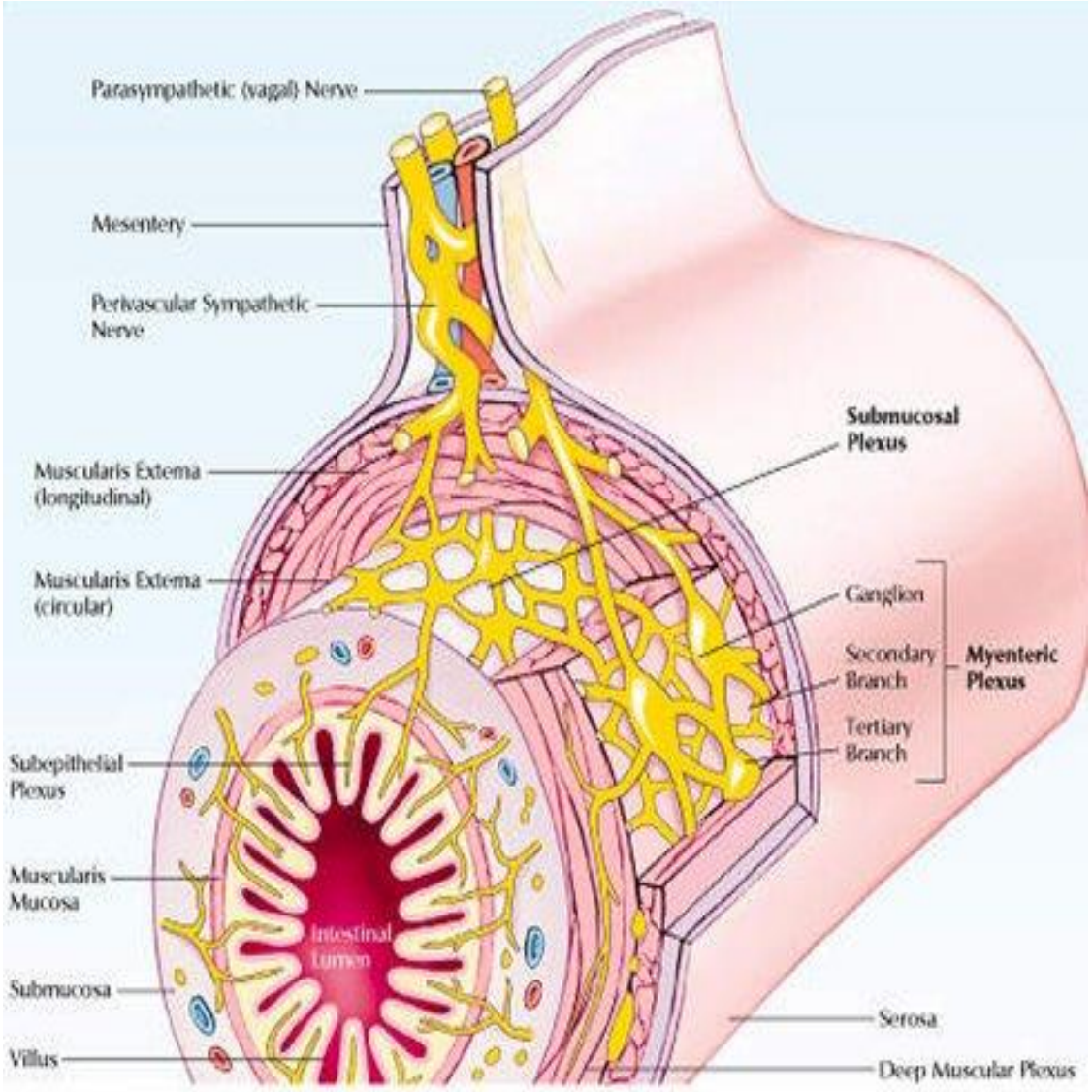
POSTBIÓTICOS

Se denomina 'posbióticos' a las sustancias producidas por los probióticos que ejercen efectos metabólicos y/o inmunomoduladores en el huésped, es decir, son factores solubles generados del metabolismo de los probióticos y liberados al medio extracelular, y que tendrían actividad beneficiosa sobre la salud.


Simbióticos
Prebióticos + Probióticos
Prebióticos
Fomentan crecimiento probióticos o de componentes específicos de la microbiota
Probióticos
Inactivación
Altas presiones
Tratamiento térmico
Luz UV Irradiación
Pulsos eléctricos
Sonicación
Tratamientos químicos
Paraprobióticos
Células inactivas
Células muertas
Restos celulares
Extractos celulares crudos
Otras funciones
Metabolitos secretados (extracelulares)
Componentes celulares
Separación/purificación de metabolitos o componentes celulares específicos
Postbióticos (ejemplos)
Glutatión
B-glicosidasa
Ácidos grasos de cadena corta
Exopolisacárido
Ácido murámico
Ácido lipoteicoico
Cada uno con sus funciones específicas

3. LAS EMOCIONES: SISTEMA ENTÉRICO

- *Es la única agrupación de neuronas fuera del SNC que forma circuitos con actividad autónoma refleja (parte más compleja del SNP)*
- *Está incrustado en la pared del tracto gastrointestinal*
- *Humanos: 200 millones de neuronas, de 20 tipos diferentes, 8 m. (400 m2)*
- *"Segundo cerebro": por su tamaño, complejidad, células gliales y afectación en múltiples trastornos congénitos y adquiridos*

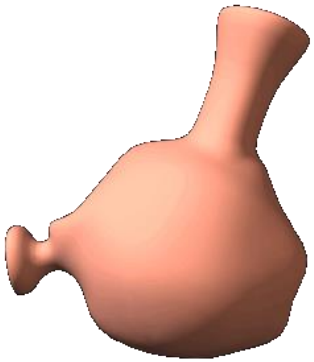


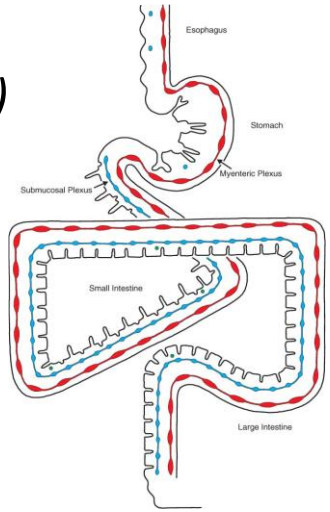
https://www.dailymotion.com/video/x6s75s7?playlist=x4t2zs

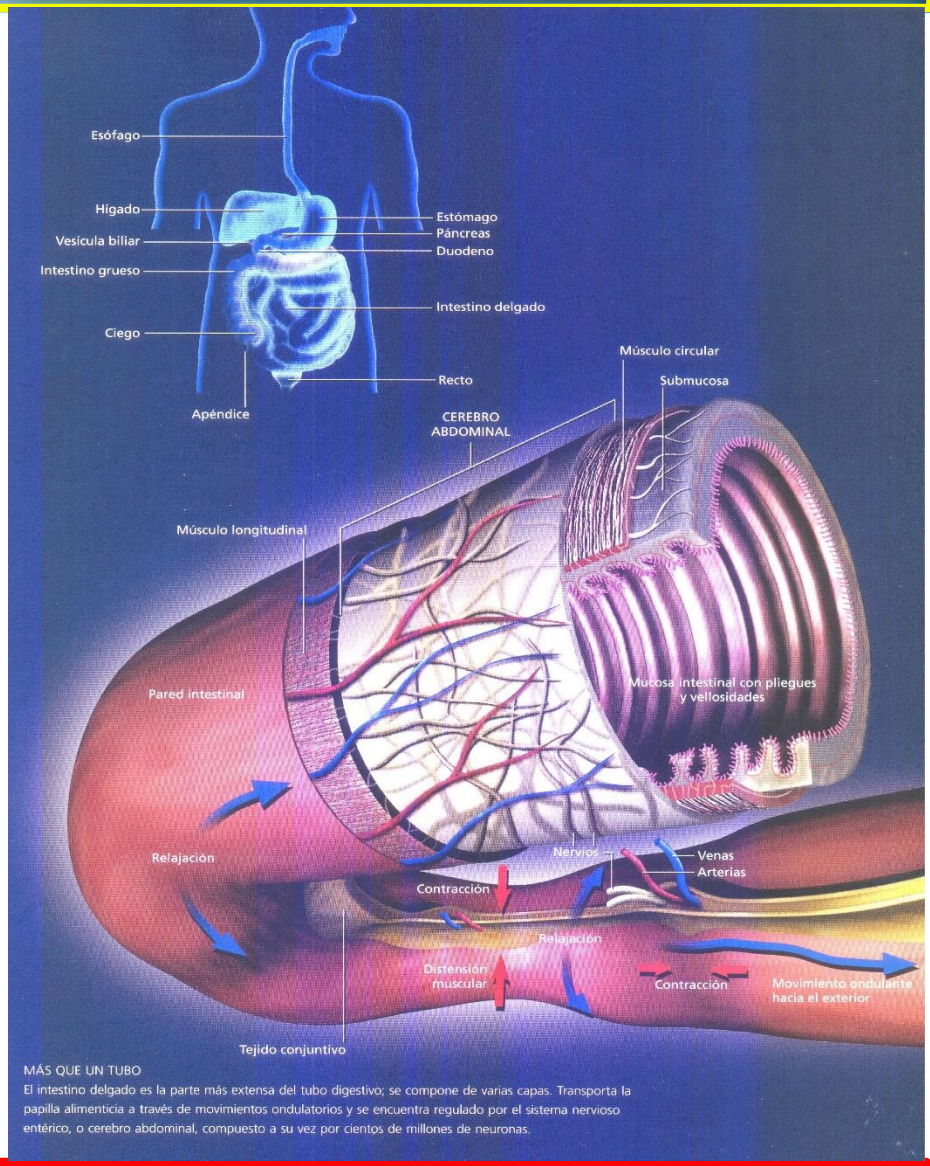
3. LAS EMOCIONES: SISTEMA N. ENTÉRICO

Es el sistema nervioso propio del tubo digestivo: se encuentra en su totalidad en la pared, desde el esófago hasta el ano.

- *Función principal: controlar movimientos y secreciones gastrointestinales*
- *Está formado por dos plexos:*
- *Plexo mientérico (rojo)*
- *Plexo submucoso (azul)*







MÁS QUE UN TUBO

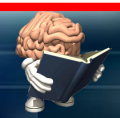
El intestino delgado es la parte más extensa del tubo digestivo; se compone de varias capas. Transporta la papilla alimenticia a través de movimientos ondulatorios y se encuentra regulado por el sistema nervioso entérico, o cerebro abdominal, compuesto a su vez por cientos de millones de neuronas.

Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO

SNE está formado por dos plexos:

- *Plexo mientérico o de Auerbach: movimientos gastrointestinales (entre capas musculares circular y longitudinal). Cadenas lineales de muchas neuronas interconectadas a lo largo de todo el tubo digestivo (desde el esófago hasta el esfínter anal externo.*
- *Efectos principales de su estimulación: aumento de la contracción tónica, aumento de la intensidad de las contracciones rítmicas, aumento de la frecuencia de las contracciones…*
- *Pero no es solo excitador, también tiene neuronas inhibidoras, que relajan algunos esfínteres musculares intestinales para que pasen los alimentos de un segmento del tubo digestivo al siguiente.*
- *Plexo submucoso o de Meissner: secreción y flujo sanguíneo local (de cada segmento minúsculo del intestino). Más desarrollado en intestino delgado y grueso. Ej: integra señales sensitivas del epitelio gastrointestinal para efectuar el control de la secreción intestinal local, la absorción local y la contracción local del músculo submucoso.*



3. LAS EMOCIONES: SISTEMA N. ENTÉRICO

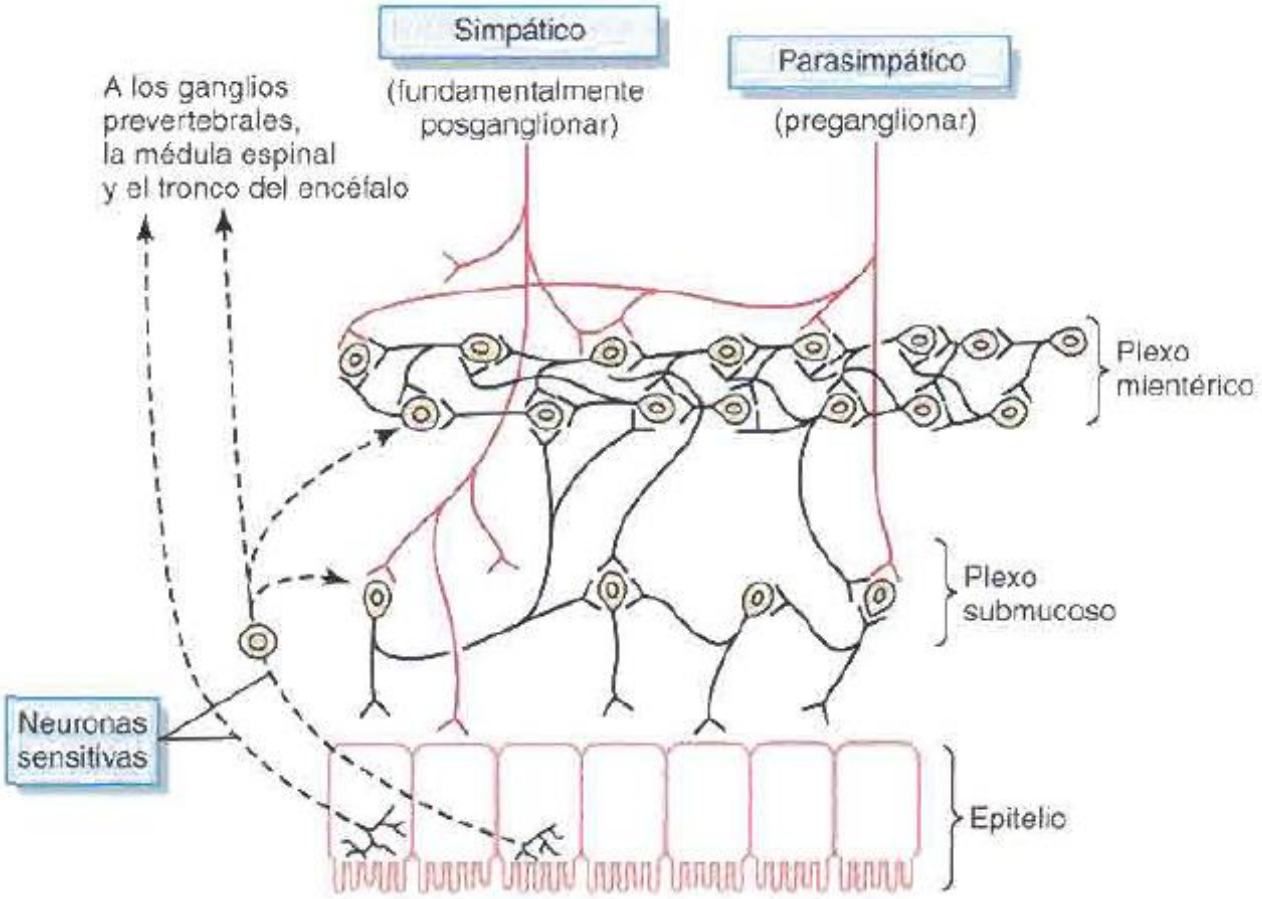


Figura 62-4

Control nervioso de la pared intestinal. Se observan los plexos mientéricos y submucoso *(fibras negras)*, el control extrínseco de estos plexos por los sistemas nerviosos simpático y parasimpático *(fibras rojas)*, y las fibras sensitivas que se dirigen desde el epitelio luminal y la pared intestinal a los plexos entéricos y desde ellos a los ganglios prevertebrales de la médula espinal y luego, directamente, a la médula espinal y al tronco del encéfalo *(fibras intestinales discontinuas)*.

SISTEMA NERVIOSO ENTÉRICO

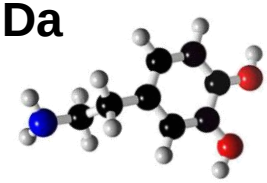
Terminaciones nerviosas sensitivas (originadas en epitelio gastrointestinal o pared intestinal): envían fibras aferentes a ambos plexos del SNE y a:

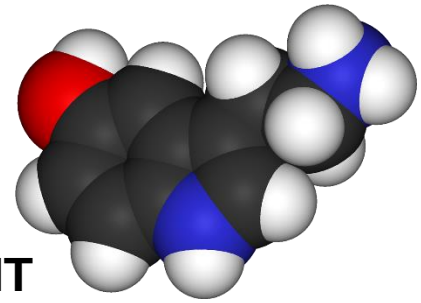
Ganglios prevertebrales del SN Simpático

Médula espinal

Por el nervio vago, en dirección al troncoencéfalo

Da





5-HT

Terminaciones nerviosas de las neuronas entéricas liberan más de 12 neurotransmisores, péptidos y hormonas:

Acetilcolina *(estimula actividad gastrointestinal),* ***Noradrenalina*** *(la inhibe), Adrenalina, Trifosfato de adenosina,* ***Serotonina (90%)****,* ***Dopamina****, Colecistocinina, Sustancia P, Polipéptido intestinal vasoactivo, Somatostatina, Leu-encefalina, Metencefalina, Bombesina…*

SISTEMA NERVIOSO ENTÉRICO (SNE)

The Gut Immune Barrier and the Blood-Brain Barrier: Are They So Different?

Immunity
Review

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[1]University of California, San Francisco, Department of Anatomy, San Francisco, CA 94143-0452, USA
[2]European Institute of Oncology, Department of experimental Oncology, 20139 Milan, Italy
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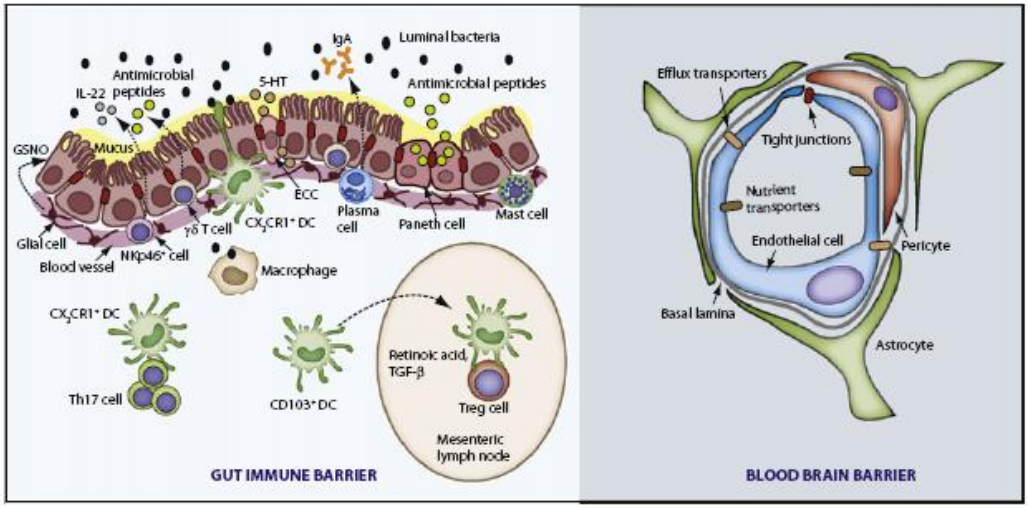
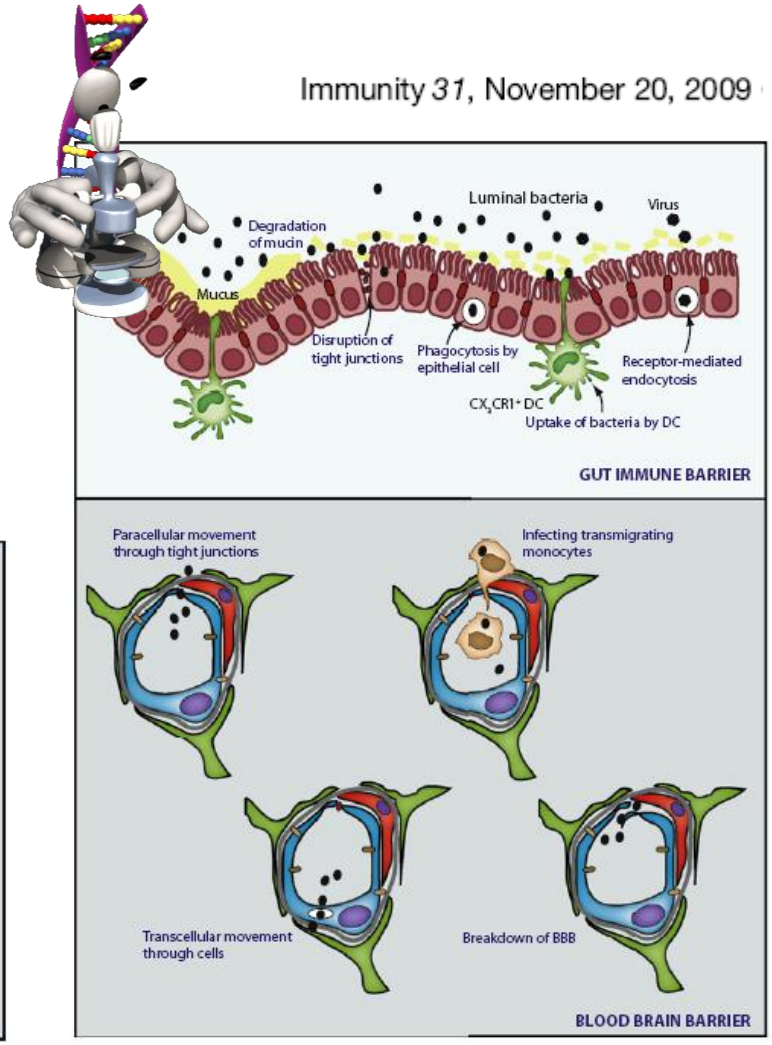
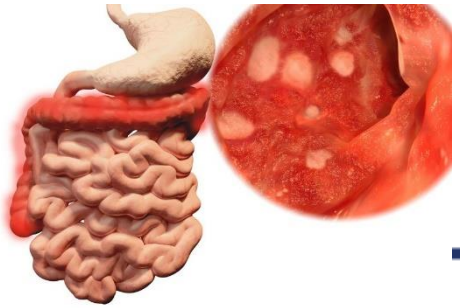
DOI 10.1016/j.immuni.2009.09.012

In order to protect itself from a diverse set of environmental pathogens and toxins, the body has developed a number of barrier mechanisms to limit the entry of potential hazards. Here, we compare two such barriers: the gut immune barrier, which is the primary barrier against pathogens and toxins ingested in food, and the blood-brain barrier, which protects the central nervous system from pathogens and toxins in the blood. Although each barrier provides defense in very different environments, there are many similarities in their mechanisms of action. In both cases, there is a physical barrier formed by a cellular layer that tightly regulates the movement of ions, molecules, and cells between two tissue spaces. These barrier cells interact with different cell types, which dynamically regulate their function, and with a different array of immune cells that survey the physical barrier and provide innate and adaptive immunity.



Immunity 31, November 20, 2009

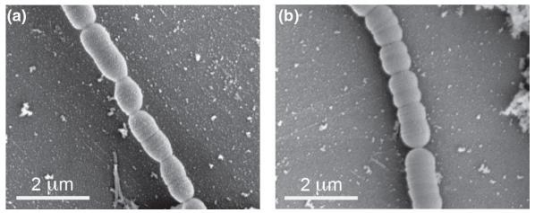




RESEARCH ARTICLE

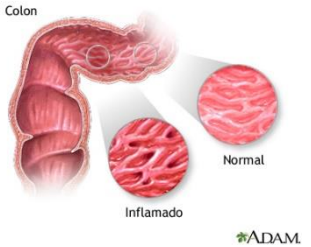
van Muijlwijk *et al.*, *Int. J. Syst. Evol. Microbiol.* 2023;73:005635

DOI 10.1099/ijsem.0.005635



Allobaculum mucilyticum sp. nov. and *Allobaculum fili* sp. nov., isolated from the human intestinal tract

Guus H. van Muijlwijk[1]†, Tyler A. Rice[2]†, Richard A. Flavell[2], Noah W. Palm[2,*] and Marcel R. de Zoete[1,*]



Abstract

As part of a culturomics study to identify bacterial species associated with inflammatory bowel disease, a large collection of bacteria was isolated from patients with ulcerative colitis. Two of these isolates were tentatively identified as members of the family *Erysipelotrichaceae*. Following phylogenetic analysis based on 16S rRNA gene sequence and genome sequences, both strain 128^T and 539^T were found to be most closely related to *Allobaculum stercoricanis*, with G+C contents of 48.6 and 50.5 mol%, respectively, and the genome sizes of 2864314 and 2580362 base pairs, respectively. Strains 128^T and 539^T were strict anaerobe rods that grew in long chains between 37 and 42 °C. Scanning electron microscopy did not reveal flagella, fimbriae or visible endospores. Biochemical analysis showed nearly identical results for both strains with enzymatic activity of C4 and C8 esterases, acid phosphatase, naphthol-AS-BI-phosphohydrolase, β-glucuronidase, *N*-acetyl-β-glucosaminidase and arginine arylamidase. In addition, both strains produced indole and reduced nitrate. Major fatty acids were identified as $C_{18:1}$ $\omega 9c$ (oleic acid, 64.06% in 128^T and 74.35% in 539^T), $C_{18:1}$ $\omega 7c$/$C_{18:1}$ $\omega 9t$/$C_{18:1}$ $\omega 12t$/UN17.834 (16.18% in 128^T and 6.22% in 539^T) and $C_{16:0}$ (6.23% in 128^T and 7.37% in 538^T). Based on these analyses two novel species are proposed, *Allobaculum mucilyticum* sp. nov. with the type strain 128^T (=NCTC 14626^T=DSM 112815^T) and *Allobaculum fili* sp. nov. with the type strain 539^T (=NCTC 14627^T=DSM 112814^T).

Gut epithelial barrier damage caused by dishwasher detergents and rinse aids

Ismail Ogulur, PhD,[a] Yagiz Pat, MD,[a,b] Tamer Aydin, BSc,[a] Duygu Yazici, PhD,[a] Beate Rückert, MSc,[a] Yaqi Peng, MD, PhD,[a,c] Juno Kim, BSc,[a] Urszula Radzikowska, MSc,[a,d] Patrick Westermann, MSc,[a] Milena Sokolowska, MD, PhD,[a,d] Raja Dhir, BSc,[e] Mubeccel Akdis, MD, PhD,[a] Kari Nadeau, MD, PhD,[f] and Cezmi A. Akdis, MD[a,d]

Davos, Switzerland; Aydin, Turkey; Guangzhou, China; and Los Angeles and Stanford, Calif

Background: The increased prevalence of many chronic inflammatory diseases linked to gut epithelial barrier leakiness has prompted us to investigate the role of extensive use of dishwasher detergents, among other factors.
Objective: We sought to investigate the effects of professional and household dishwashers, and rinse agents, on cytotoxicity, barrier function, transcriptome, and protein expression in gastrointestinal epithelial cells.
Methods: Enterocytic liquid-liquid interfaces were established on permeable supports, and direct cellular cytotoxicity, transepithelial electrical resistance, paracellular flux, immunofluorescence staining, RNA-sequencing transcriptome, and targeted proteomics were performed.
Results: The observed detergent toxicity was attributed to exposure to rinse aid in a dose-dependent manner up to 1:20,000 v/v dilution. A disrupted epithelial barrier, particularly by rinse aid, was observed in liquid-liquid interface cultures, organoids, and gut-on-a-chip, demonstrating decreased transepithelial electrical resistance, increased paracellular flux, and irregular and heterogeneous tight junction immunostaining. When individual components of the rinse aid were investigated separately, alcohol ethoxylates elicited a strong toxic and barrier-damaging effect. RNA-sequencing transcriptome and proteomics data revealed upregulation in cell death, signaling and communication, development, metabolism, proliferation, and immune and inflammatory responses of epithelial cells. Interestingly, detergent residue from professional dishwashers demonstrated the remnant of a significant amount of cytotoxic and epithelial barrier–damaging rinse aid remaining on washed and ready-to-use dishware.
Conclusions: The expression of genes involved in cell survival, epithelial barrier, cytokine signaling, and metabolism was altered by rinse aid in concentrations used in professional dishwashers. The alcohol ethoxylates present in the rinse aid were identified as the culprit component causing the epithelial inflammation and barrier damage. (J Allergy Clin Immunol 2022;■■■:■■■-■■■.)

Key words: *Alcohol ethoxylates, Caco-2, cytotoxicity, dishwasher detergents, epithelial barrier, inflammation, rinse aid*

The intestinal epithelium barrier holds a strong defense against foreign substances while at the same time regulating the absorption of nutrients, water, and electrolytes.[1,2] This passage of molecules is controlled by intercellular tight junction (TJ) proteins located at the apical domain of the epithelial cells. TJs form a multiprotein complex including transmembrane proteins (eg, occludin [OCLN], claudins [CLDNs], junctional adhesion molecule, and tricellulin) and intracellular plaque proteins (eg, zonula occludens [ZOs], ie, ZO-1, ZO-2, and ZO-3).[3,4]

Disruption of the gut epithelial TJ barrier has been proposed as a central pathogenic factor leading to the systemic inflammation observed in obesity, inflammatory bowel disease, and a long list of other chronic noninfectious inflammatory diseases of distant organs.[5,6] The recently postulated "Epithelial Barrier Hypothesis"

REVIEWS

NATURE REVIEWS | NEUROSCIENCE

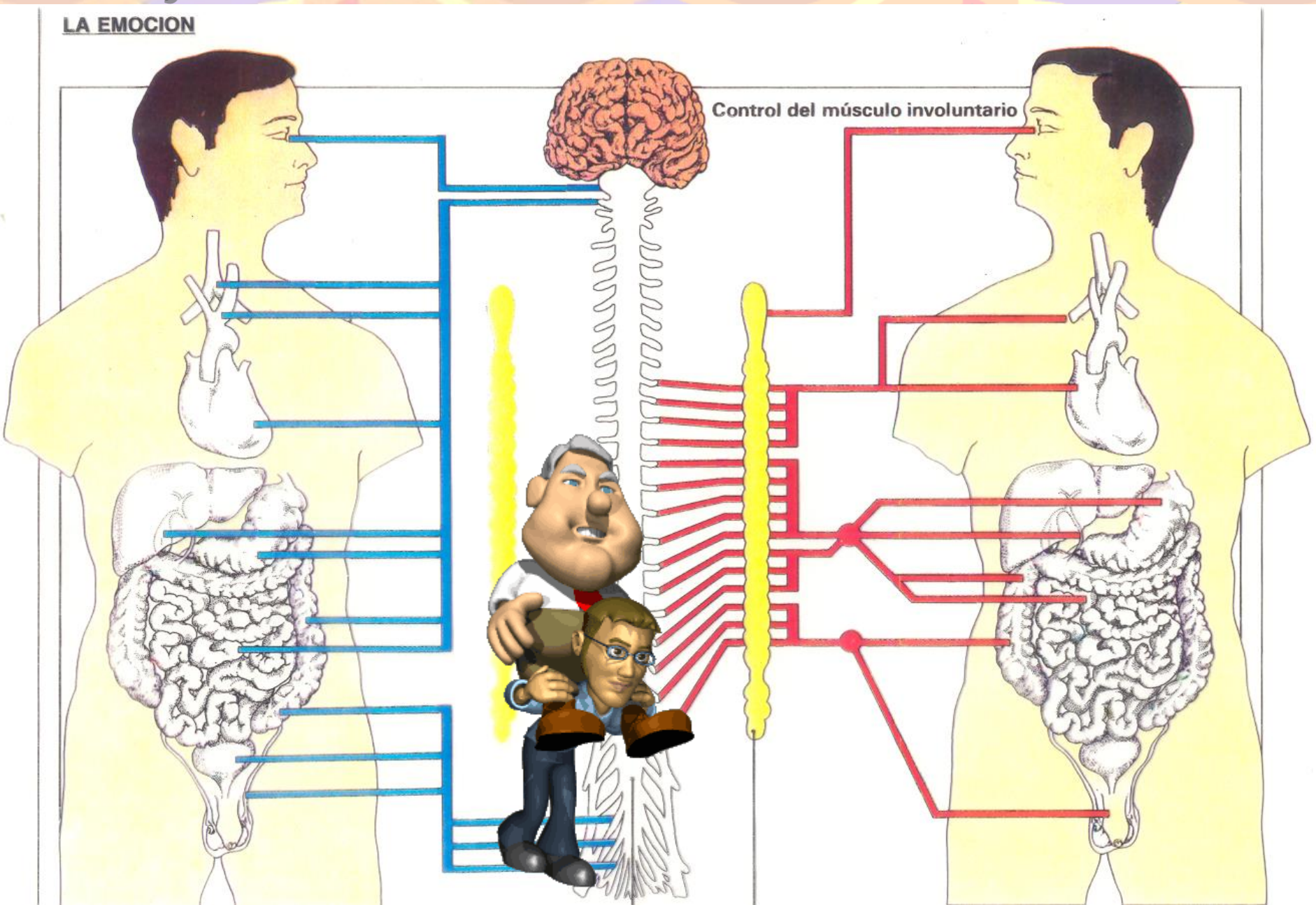
VOLUME 13 | OCTOBER 2012 |

Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour

John F. Cryan[1,2] and Timothy G. Dinan[1,3]

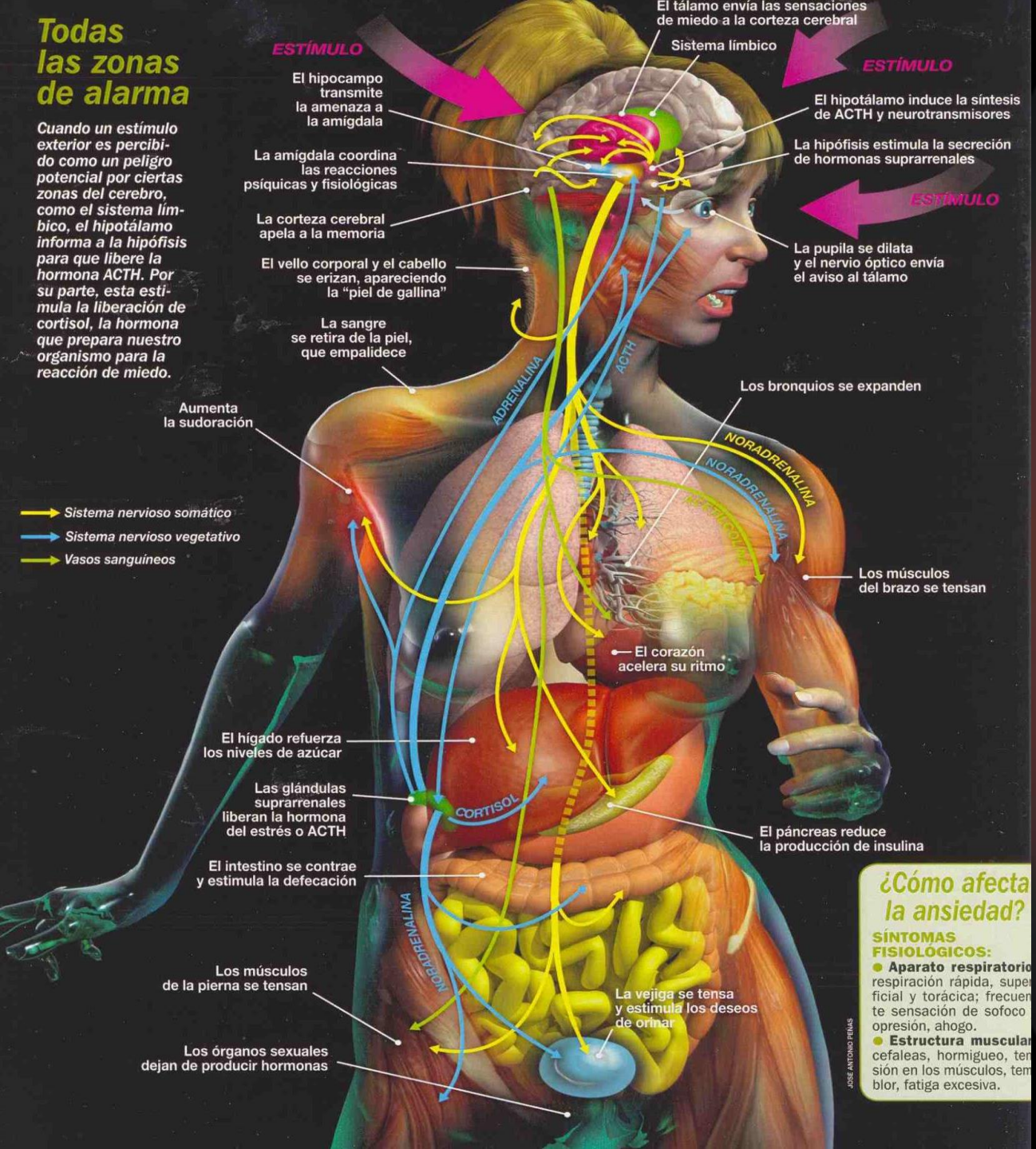
Abstract | Recent years have witnessed the rise of the gut microbiota as a major topic of research interest in biology. Studies are revealing how variations and changes in the composition of the gut microbiota influence normal physiology and contribute to diseases ranging from inflammation to obesity. Accumulating data now indicate that the gut microbiota also communicates with the CNS — possibly through neural, endocrine and immune pathways — and thereby influences brain function and behaviour. Studies in germ-free animals and in animals exposed to pathogenic bacterial infections, probiotic bacteria or antibiotic drugs suggest a role for the gut microbiota in the regulation of anxiety, mood, cognition and pain. Thus, the emerging concept of a microbiota–gut–brain axis suggests that modulation of the gut microbiota may be a tractable strategy for developing novel therapeutics for complex CNS disorders.

Estrés y Sistema Nervioso Autónomo



Todas las zonas de alarma

Cuando un estímulo exterior es percibido como un peligro potencial por ciertas zonas del cerebro, como el sistema límbico, el hipotálamo informa a la hipófisis para que libere la hormona ACTH. Por su parte, esta estimula la liberación de cortisol, la hormona que prepara nuestro organismo para la reacción de miedo.



¿Cómo afecta la ansiedad?

SÍNTOMAS FISIOLÓGICOS:

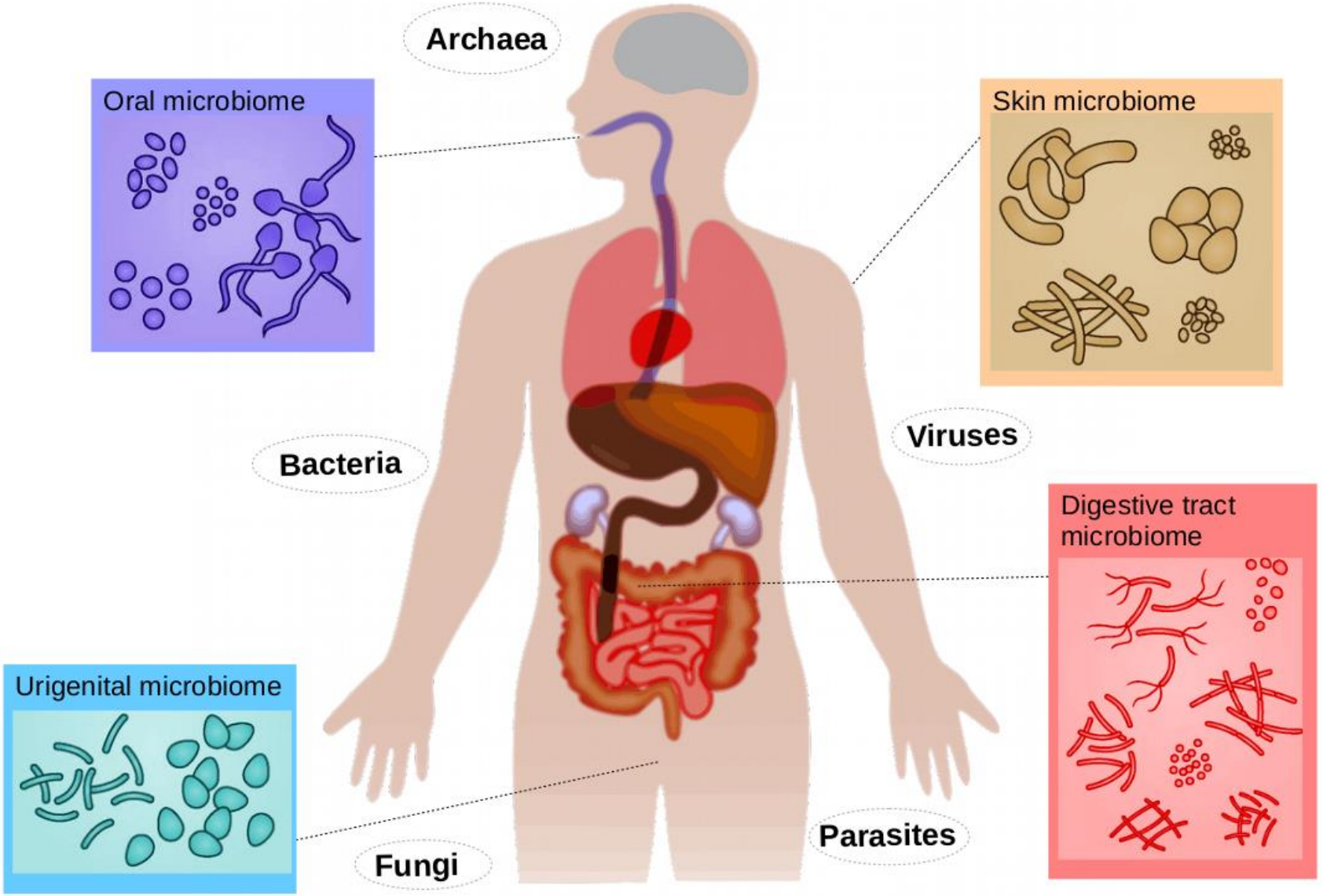
- **Aparato respiratorio** respiración rápida, superficial y torácica; frecuente sensación de sofoco opresión, ahogo.
- **Estructura muscular** cefaleas, hormigueo, tensión en los músculos, temblor, fatiga excesiva.

JOSE ANTONIO PEÑAS

¿Quién dijo que estamos solos?

Human Microbiome

https://www.dailymotion.com/video/xpe6x6?playlist=x4t2zs

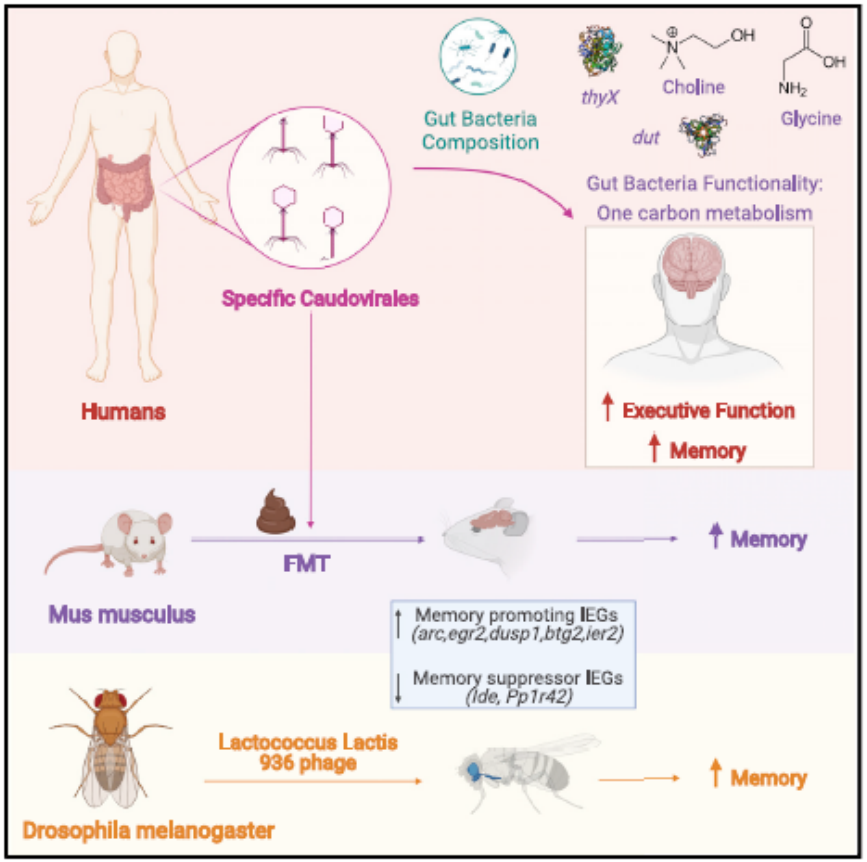


Cell Host & Microbe

Caudovirales bacteriophages are associated with improved executive function and memory in flies, mice, and humans

Cell Host & Microbe *30*, 1–17, March 9, 2022

Graphical abstract



Highlights

- Specific *Caudovirales* are linked to better executive function and memory

Authors

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Anna Castells-Nobau,
María Arnoriaga-Rodríguez, ...,
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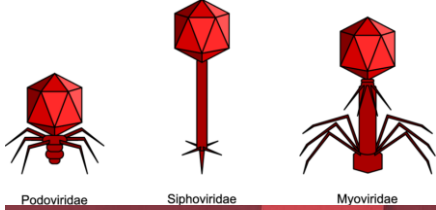
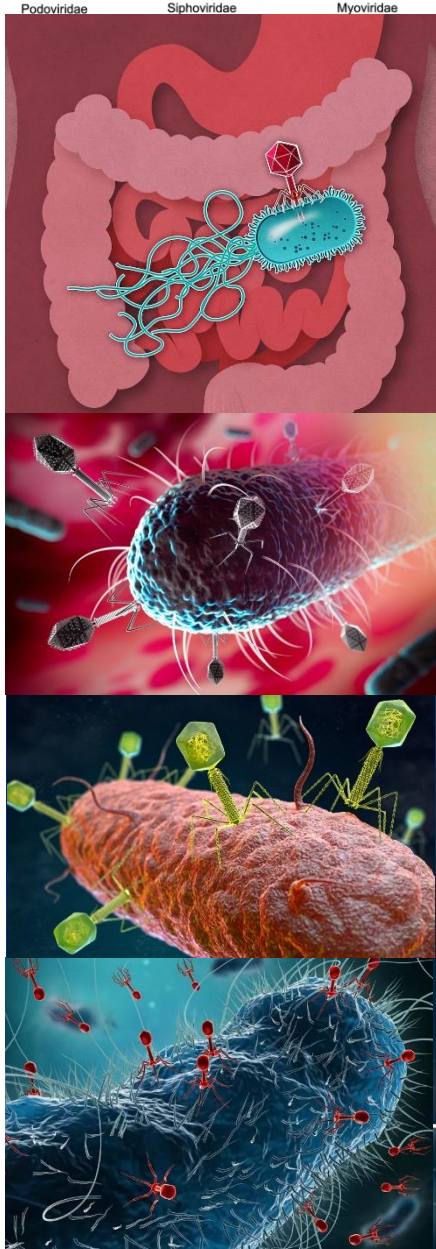
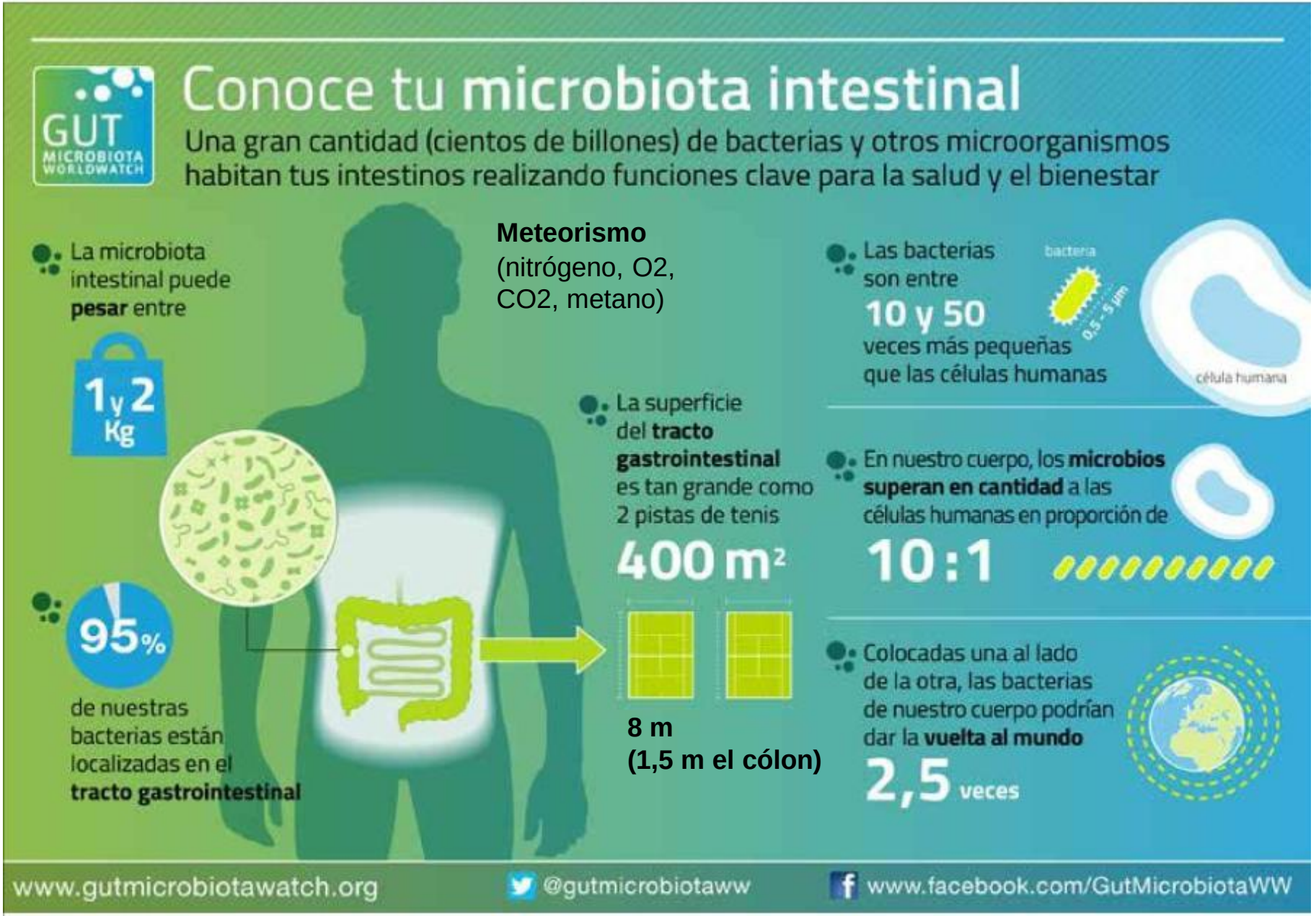
In brief

Here, Mayneris-Perxachs et al. reveal an association of the dominant bacteriophages with human host cognition in parallel to a specific bacterial composition and functionality. Microbiota transplantation and bacteriophage supplementation increased the memory of recipient mice and flies through the upregulation of memory-promoting genes. This highlights the potential of targeting bacteriophages cognitive improvement.







https://www.dailymotion.com/video/x5ucu9x?playlist=x4t2zs

WHY THE MICROBIOME Is So Vital to YOUR HEALTH

Your body is mostly microbes

The Importance of the MICROBIOME by the Numbers

90%
Up to 90% of all disease can be raced in some way back to the gut and health of the microbiome

10–100 trillion
Number of symbiotic microbial cells harbored by each person, primarily bacteria in the gut, that make up the human microbiota

>10,000
Number of different microbe species researchers have identified living in the human body

10X
There are 10 times as many outside organisms as there are human cells in the human body

100

100 to 1
The genes in our microbiome outnumber the genes in our genome by about 100 to 1

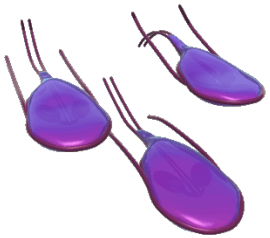
3.3 million
Number of non-redundant genes in the human gut microbiome

22,000
Approximate number genes in the human gene catalog

99.9%
Percentage individual humans are identical to one another in terms of host genome

80%–90%
Percentage individual humans are different from one another in terms of the microbiome

Journal of Cardiovascular Nursing
Vol. 29, No. 6, pp 479–481 | Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins



20 Things You Didn't Know About the Human Gut Microbiome

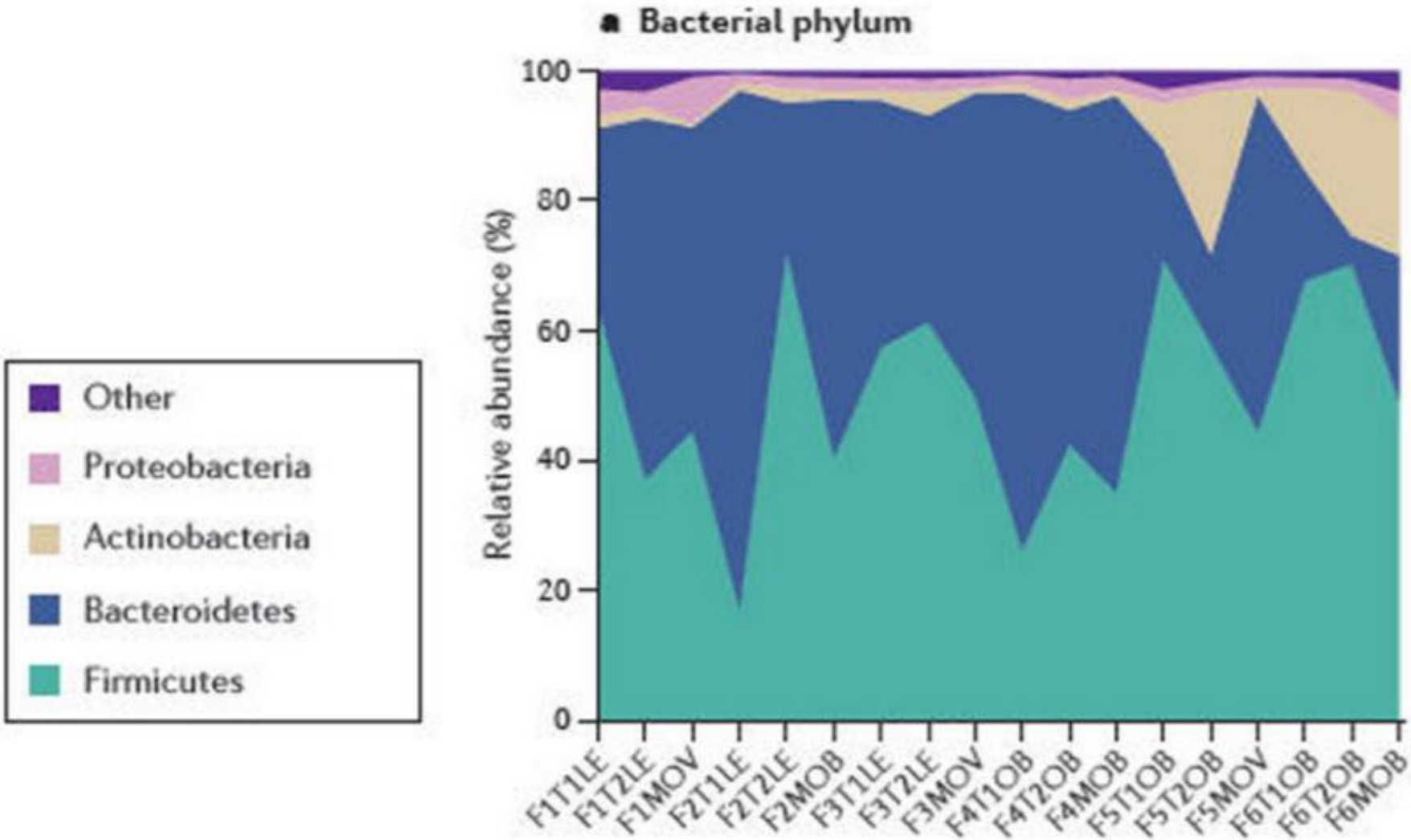
Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN

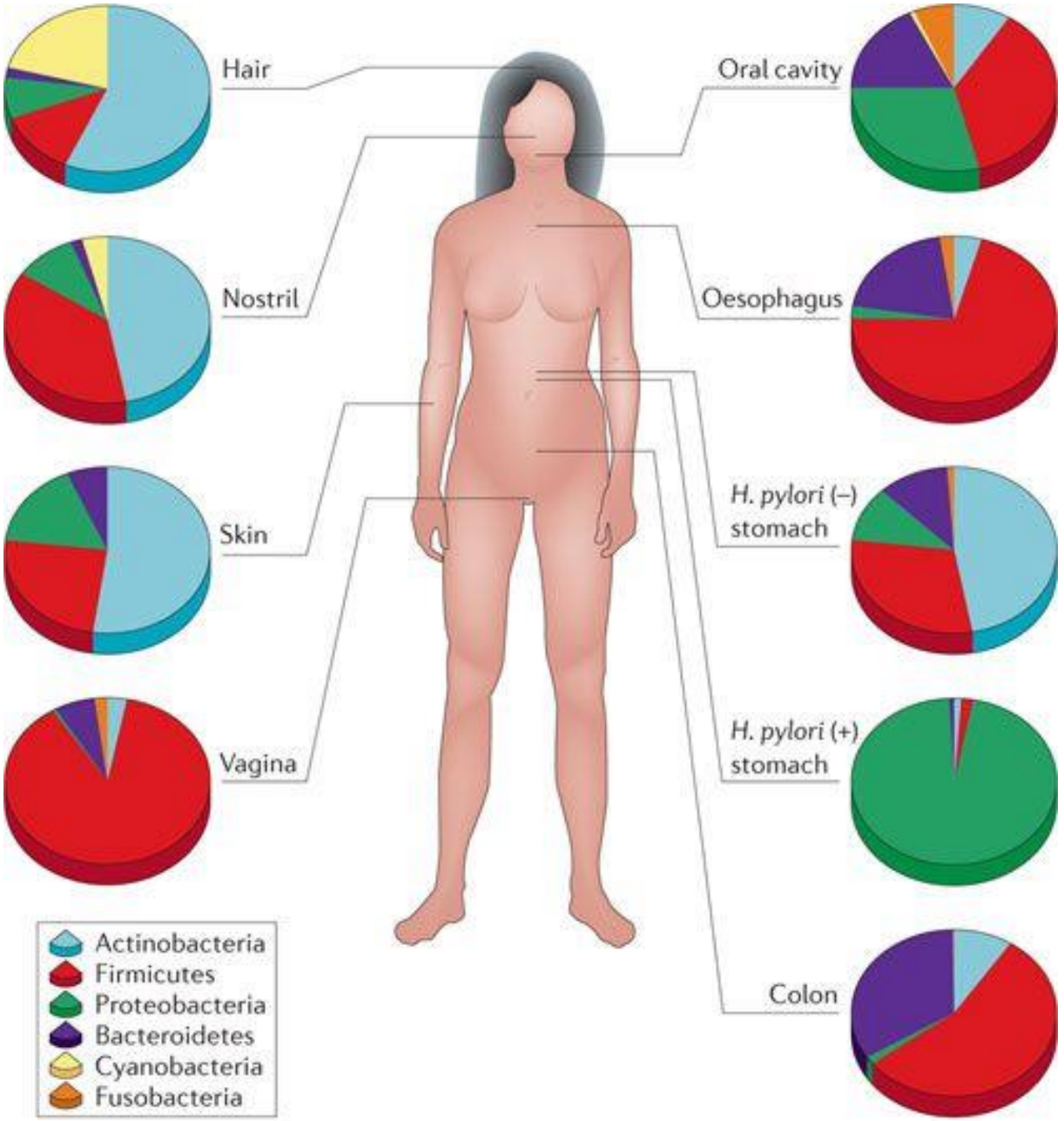
*-El **microbioma (genoma de la microbiota procariota)** se define como el material genético de todas las bacterias, virus, hongos, arqueas y eucariotas que habitan el cuerpo humano denominados colectivamente como el "segundo genoma humano" (ratio 1 celula : 10 microorganismos; 100 trillones de microbios de 10.000 especies, 2-3 kgs).* ***SIMBIOSIS. Proyecto microbioma humano 2007-2015.***

-La microbiota intestinal se considera un órgano separado, con actividad metabólica e inmunológica separada del resto del cuerpo (investigación: taxonomía de microorganismos y la genómica funcional). Otras microbiotas: vagina, piel, boca, nariz, oídos y cuero cabelludo. Todas tienen en común 4 familias de bacterias: Firmicutes, Actinobacteria, Proteobacteria y Bacteroidetes ***(composición única y personal).***

Table 1. Predominating Phyla of Specific Human Habitats

Body Habitat	Predominating Phyla
Mouth	*Firmicutes* (e.g., *Streptococcus*) > *Proteobacteria* (e.g., *Haemophilus*), *Bacteroidetes* (e.g., *Prevotella*)
Gut	*Bacteroidetes* (e.g., *Bacteroides*), *Firmicutes* (e.g., *Streptococcus*)
Skin	*Actinobacteria* (e.g., *Propionibacterium*) > *Firmicutes* (e.g., *Staphylococcus*)
Vagina	*Firmicutes* (e.g., *Lactobacillus*)


a Bacterial phylum
Relative abundance (%)
100
80
60
40
20
0
Other
Proteobacteria
Actinobacteria
Bacteroidetes
Firmicutes
F1T1LE
F1T2LE
F1MOV
F2T1LE
F2T2LE
F2MOB
F3T1LE
F3T2LE
F3MOV
F4T1OB
F4T2OB
F4MOB
F5T1OB
F5T2OB
F5MOV
F6T1OB
F6T2OB
F6MOB



The Human Microbiome: at the interface of health and disease

Ilseung Cho[1,2] and **Martin J. Blaser**[1,2,3,4]
[1]Department of Medicine, NYU Langone Medical Center, New York, NY 10016, USA

Nat Rev Genet. ; 13(4): 260–270. doi:10.1038/nrg3182. *2012*
Nature Reviews | Genetics

FIGURA 1. Esquema de los territorios colonizados por la microbiota autóctona, con indicación de los microorganismos más abundantes y la densidad total en cada localización.

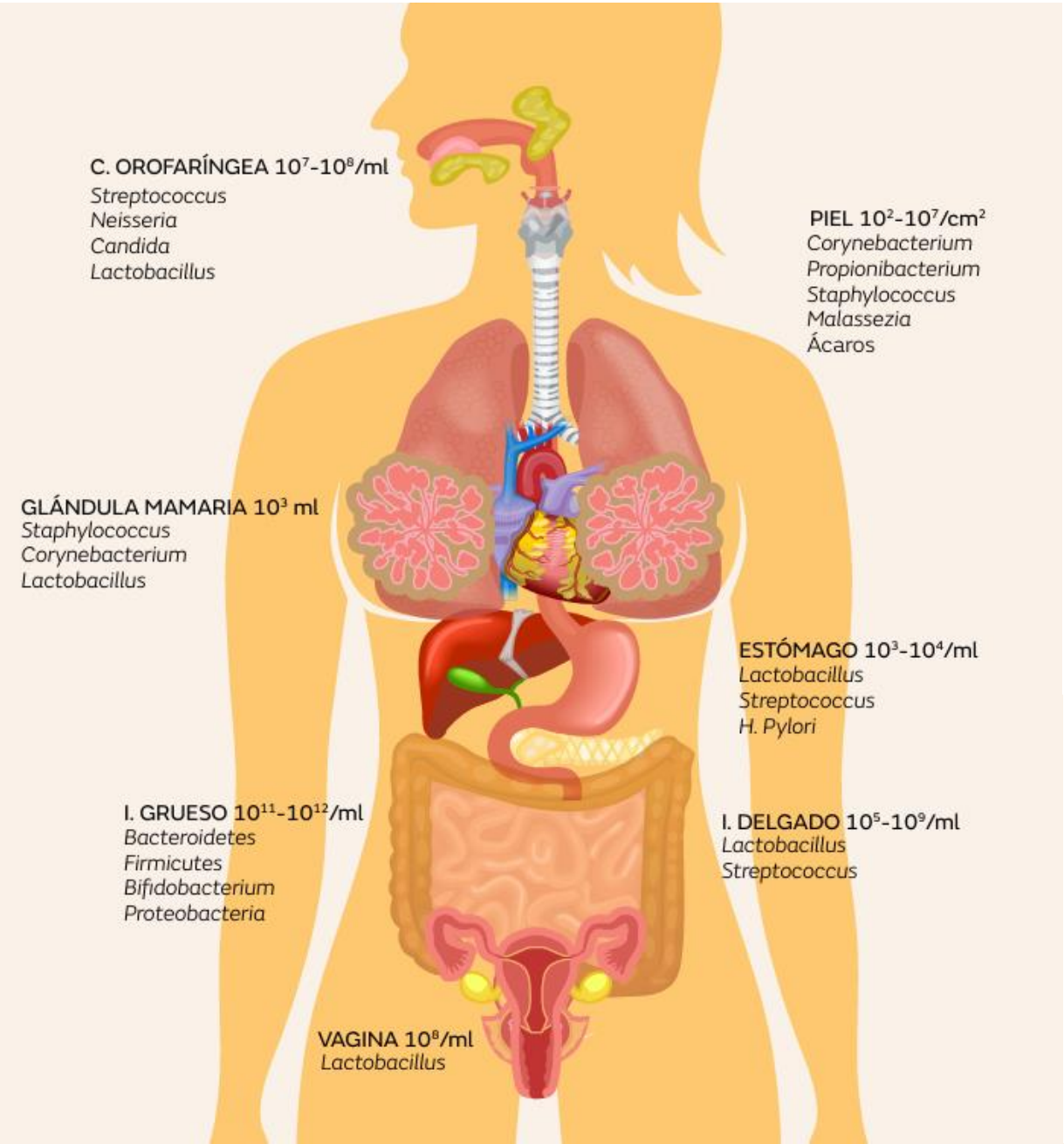


TABLA I. Diversidad taxonómica de los microorganismos que conforman la microbiota autóctona

DOMINIO	REINO	FILO	CLASE	EJEMPLO
Archaea	Archaea	A.II. Euryarcheota	Methanobacteria	Metanógenos intestinales
Bacteria	Bacteria	B.XII. Proteobacteria	Gammaproteo-bacteria	*Escherichia* (intestino grueso)
			Epsilonproteo-bacteria	*Helicobacter* (estómago)
		B.XIII. Firmicutes	Clostridia	*Lachnospira, Faecalibacterium, Roseburia* (intestino grueso)
			Bacilli	*Lactobacillus* (vagina, intestino delgado), *Staphylococcus* (piel), *Streptococcus* (boca)
		B.XIV. Actinobac-teria	Actinobacteria	*Bifidobacterium* (intestino grueso), *Propionibacterium* (piel, intestino grueso), *Corynebacte-rium* (piel), *Gardnerella* (vagina)
		B. XX. Bacteroidetes	Bacteroidetes	*Bacteroides, Prevotella* (intesti-no grueso)
		B. XXII. Verrucomi-crobia	Verrucomicro-biae	*Akkermansia* (intestino grueso)
Eukaryota	Protista	Protozoa	Rhizopoda	*Amebas comensales* (boca, intestino)
			Mastigophora	*Giardia* (duodeno)
	Fungi	Ascomycota	Saccharomy-cetes	*Candida* (vagina, boca, intesti-no grueso)
		Basidiomycota	Exobasidiomy-cetes	*Malassezia* (piel)
	Animalia	Arthropoda	Arachnida	*Demodex* (ácaros de la piel)

MICROBIOTA VAGINAL

- Enfermedades vaginales: vaginosis bacteriana *(Gardnerella vaginalis)*, candidiasis vulvovaginal *(Candida albicans)* y Tricomoniasis *(Trichomonas vaginalis)*
- Disbiosis en estados fisiológicos: ciclo menstrual, menopausia.

MICROBIOTA MAMARIA

- Mastitis: aguda, subaguda, subclínica y granulomatosa.

MICROBIOTA ORAL

- Enfermedades orales: caries dental, gingivitis, periodontitis, halitosis.

MICROBIOTA DE LA PIEL

- Enfermedades de la piel: dermatitis atópica, psoriasis, acné vulgar, rosácea, úlceras.

MICROBIOTA RESPIRATORIA

- Enfermedades respiratorias: patologías orolaringeas y otitis, asma, fibrosis quística, infección por virus respiratorio sincitial, neumonías.

MICROBIOTA TRACTO GENITOURINARIO

- Enfermedades urológicas: infecciones urinarias, disfunción neurogénica de la vejiga, incontinencia urinaria.
- Patología del tracto genital: infertilidad, abortos, endometriosis, prostatitis.

BMJ Open

Efficacy of probiotics in the management of halitosis: a systematic review and meta-analysis

Nengwen Huang , Jinjin Li , Xianghe Qiao, Yongzhi Wu, Yunkun Liu, Chenzhou Wu, Longjiang Li

Huang N, *et al*. *BMJ Open* 2022;**12**:e060753.

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► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/

ABSTRACT

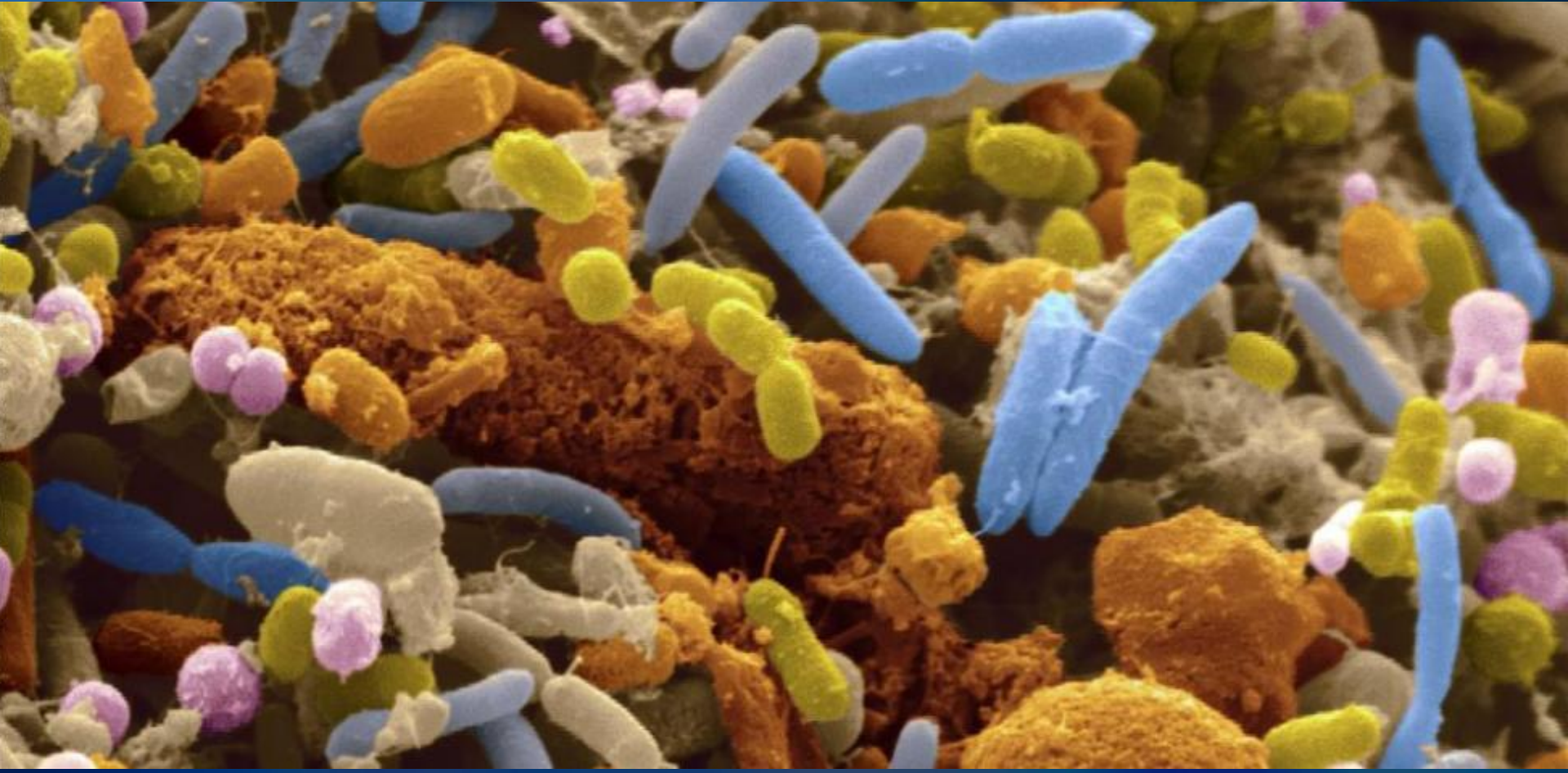
Background Halitosis is defined as a foul odour emitted from the oral cavity. Many interventions have been used to control halitosis from mouthwashes to chewing gums. Probiotics have been reported as an alternative method to alleviate halitosis.

Objective The present study aimed to investigate the effect of probiotics on halitosis from a time perspective.

Design and methods This is a meta-analysis study performed in indexed databases up to February 2021. Randomised controlled trials that compared the effects of probiotics and placebo on primary outcomes (organoleptic

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study included larger randomised controlled trials involved in halitosis and probiotics.
⇒ The results were rationally analysed from the follow-up time perspective.
⇒ Subgroup analysis was done to identify the sources of heterogeneity based on the component of volatile sulfur compounds.
⇒ The included studies had limited patients.
⇒ Some studies reported the outcomes with different forms, increasing the heterogeneity of the results.



Microbiota sexual

Henry A. Nasrallah, MD
Editor-in-Chief

doi: 10.12788/cp.0235

Exchange of microbiota via sexual contact may increase the risk of dysbiosis and psychiatric disorders

To comment on this editorial or other topics of interest:
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Sexual activity alters the microbiome, with potential psychiatric implications

Evidence is strong that sexual partners transmit microbiota (bacteria, viruses, fungi, protozoa, and archaea) to each other. While microbial flora are abundant in the gastrointestinal tract, they are also present in the vagina, penis, urethra, mouth, and skin.[1] For better or worse, sexual contact of all types means that participants will acquire each other's microbiota.

The 39 trillion microbiota in the body (which exceed the 30 trillion cells in the body) are commensal and influence both the larger brain in the skull and the smaller enteric brain in the gut. The microbiota and their microbiome genes (1,000 times larger than the human genome) have been linked to depression, anxiety, psychosis, and autism.[2-4] They produce 90% of the body's serotonin, as well as catecholamines (norepinephrine, epinephrine, dopamine), make hormones (eg, cortisol), and modulate the immune system. Microbiota have several important functions, including food digestion, synthesis of vitamins,autoimmunity,hypothalamic-pituitary-adrenal axis regulation, and CNS modulation.

Consequences of dysbiosis

Everyone should be concerned about maintaining a healthy diversity of microbiota in their body, with a predominance of beneficial bacteria such as *Lactobacillus* and *Bacteroides*, and avoiding acquiring pathogenic bacteria such as *Gardnerella*, *Prevotella*, and *Atopobium*. Sexual activity involving a partner with unhealthy microbiota may increase the risk of dysbiosis, defined as a reduction in microbiota diversity, including a loss of beneficial bacteria and a rise in harmful bacteria.

Dysbiosis is associated with multiple symptoms, including[5]:

- brain "fog," irritability, mood changes, and anxiety
- bloating, loss of intestinal permeability, and insufficient reclamation of nutrients
- congestion of certain organs, such as the liver, gallbladder, and pancreas
- production of antigen-antibody complexes in response to chemicals in partially digested food
- aggravation of inflammatory disorders such as migraine, arthritis, and autoimmune disorders.

Apart from intimate sexual contact, simply sharing a household with someone leads to sharing of gut microflora. Persons who live together, whether genetically related or not, have similar microbiota. Compared with people

La actividad sexual que implica una pareja con microbiota no saludable puede aumentar el riesgo de **disbiosis**, definido como una reducción en la diversidad de la microbiota, incluyendo una pérdida de bacterias beneficiosas y un aumento de bacterias dañinas:

-"niebla" cerebral, irritabilidad, estado de ánimo cambios y ansiedad. T. Bipolar: más en relaciones extramatrimoniales y con múltiples parejas.
-hinchazón, pérdida de permeabilidad intestinal y recuperación insuficiente de nutrientes.
-congestión de ciertos órganos, como el hígado, la vesícula biliar y el páncreas.
-producción de complejos antígeno-anticuerpo en respuesta a sustancias químicas en alimentos parcialmente digeridos.
-agravamiento de trastornos inflamatorios como migraña, artritis y trastornos autoinmunes y gingivitis

Las personas que viven juntas, ya sea genéticamente relacionados o no, tienen una microbiota similar.

Una consecuencia de adquirir microbiota patógena en la vagina es la **vaginosis bacteriana (VB),** que no es una infección sino un desequilibrio ecológico en la composición de la microbiota vaginal. La VB es causada por una disminución significativa de los Lactobacillus vaginales beneficiosos y un marcado aumento en los taxones no Lactobacillus (especialmente Gardnerella y Atopobium). Puede durar al menos 1 semana después de la relación sexual: flujo con olor a pescado (blanquecino), alcalino, bacterias anaeróbicas (Prevotella, Gardnerella y Atopobium), aumento en la tasa de enfermedad pélvica inflamatoria, embarazo ectópico, endometriosis, parto prematuro e infertilidad.

Las bacterias patógenas se pueden cultivar a partir del glande, el surco coronal y el prepucio, así como de la piel del pene, semen, uretra y orina.

Variations in Vaginal, Penile, and Oral Microbiota After Sexual Intercourse: A Case Report

frontiers in Medicine

CASE REPORT
published: 07 August 2019
doi: 10.3389/fmed.2019.00178

*Miguel Carda-Diéguez[1], Nívia Cárdenas[2], Marina Aparicio[2], David Beltrán[3], Juan M. Rodríguez[2] and Alex Mira[1,4]**

[1] Department of Health and Genomics, Center for Advanced Research in Public Health, FISABIO, Valencia, Spain, [2] Department of Nutrition and Food Science, Complutense University of Madrid, Madrid, Spain, [3] Centro de Diagnóstico Médico, Ayuntamiento de Madrid, Madrid, Spain, [4] Network of Epidemiology and Public Health, CIBERESP, Madrid, Spain

Background: Bacterial vaginosis is the most common infection in women and it has been proved that dysbiosis of vaginal microbiota can promote the infectious status. This case report shows the effect of oral and vaginal sex over the microbiota of a heterosexual couple who reported repeated problems of vaginal and oral infections after sexual intercourse.

Case Presentation: A woman (32) reported to have vaginal infections and gingivitis after she had started a relationship with a man (34) and associated them with unprotected sex. No treatments successfully removed the problem and it repeated every time they had sexual encounters. Vaginal, penile and oral swabs were collected before and after sexual encounters in order to analyze changes in the respective microbiotas. DNA was extracted from all samples and the bacterial 16S rRNA gene was sequenced using Illumina MiSeq.

Conclusions: *Lactobacillus* occupied the great majority of the vaginal microbiota in all scenarios except after unprotected sex, which caused a bacterial dysbiosis that lasted at least for a week. Similarly, the penile microbiota changed significantly after unprotected sexual relationships. Interestingly, both oral and vaginal sex increased the abundance of *Lactobacillus* in the male oral and penile microbiota, respectively. In conclusion, unprotected sexual intercourse influenced the genital microbiota in the couple studied and future studies with larger sample sizes should study if sex may be a factor promoting vaginal infection through dysbiosis and hampered protection by the resident microbiota.

Keywords: microbiota, vagina, penile, oral, oral sex, bacterial vaginosis, *Lactobacillus*

SCIENTIFIC REPORTS
nature research
www.nature.com/scientificreports/
SCIENTIFIC REPORTS | (2019) 9:19749 |

Sexual practices have a significant impact on the vaginal microbiota of women who have sex with women

Erica L. Plummer[1,2,10*], Lenka A. Vodstrcil[1,2,10], Christopher K. Fairley[1,2], Sepehr N. Tabrizi[3,4,5], Suzanne M. Garland[3,4,5], Matthew G. Law[6], Jane S. Hocking[7], Katherine A. Fethers[2], Dieter M. Bulach[8,9], Gerald L. Murray[3,4,5,11] & Catriona S. Bradshaw[1,2,7,11]

Women-who-have-sex-with-women (WSW) are at increased risk of bacterial vaginosis (BV). We investigated the impact of practices and past BV on the vaginal microbiota within a two-year longitudinal cohort of Australian WSW. Self-collected vaginal swabs were used to characterise the vaginal microbiota using 16S-rRNA gene sequencing. Hierarchical clustering defined community state types (CSTs). Bacterial diversity was calculated using the Shannon diversity index and instability of the vaginal microbiota was assessed by change of CST and Bray-Curtis dissimilarity. Sex with a new partner increased the bacterial diversity (adjusted-coefficient = 0.41, 95%CI: 0.21,0.60, $p < 0.001$) and instability of the vaginal microbiota, in terms of both change of CST (adjusted-odds-ratio = 2.65, 95%CI: 1.34,5.22, $p = 0.005$) and increased Bray-Curtis dissimilarity (adjusted-coefficient = 0.21, 95%CI: 0.11,0.31, $p < 0.001$). Women reporting sex with a new partner were more likely than women reporting no new partner to have a vaginal microbiota characterised by *Gardnerella vaginalis* (adjusted-relative-risk-ratio[aRRR] = 3.45, 95%CI: 1.42,8.41, $p = 0.006$) or anaerobic BV-associated bacteria (aRRR = 3.62, 95%CI: 1.43,9.14, $p = 0.007$) relative to a *Lactobacillus crispatus* dominated microbiota. Sex with a new partner altered the vaginal microbiota of WSW by increasing the diversity and abundance of BV-associated bacteria. These findings highlight the influence of practices on the development of a non-optimal vaginal microbiota and provide microbiological support for the sexual exchange of bacteria between women.

Las mujeres lesbianas que tienen muchas parejas sexuales tienen un mayor riesgo de vaginosis bacteriana (VB).

Se investigó la microbiota vaginal de 100 mujeres australianas durante 2 años y se relacionó con sus prácticas sexuales (hisopos vaginales): El sexo con un nueva pareja aumentó la diversidad bacteriana e inestabilizó su microbiota vaginal (Gardnerella vaginalis y bacterias anaeróbicas asociadas) en comparación con las que tenían una pareja estable, alterando el equilibrio de lactobacillus.

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

JID 2020:221 (1 February)

Gardnerella vaginalis Clade Distribution Is Associated With Behavioral Practices and Nugent Score in Women Who Have Sex With Women

Erica L. Plummer,[1,2] Lenka A. Vodstrcil,[1,2] Gerald L. Murray,[3,4,5] Christopher K. Fairley,[1,2] Jennifer A. Danielewski,[3,4] Suzanne M. Garland,[3,4,5] Eric P. F. Chow,[1,2] Dieter M. Bulach,[6,7] Katherine A. Fethers,[2] Jane S. Hocking,[8] and Catriona S. Bradshaw[1,2]

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Background. *Gardnerella vaginalis* is detected in women with and without bacterial vaginosis (BV). Identification of 4 *G. vaginalis* clades raised the possibility that pathogenic and commensal clades exist. We investigated the association of behavioral practices and Nugent Score with *G. vaginalis* clade distribution in women who have sex with women (WSW).

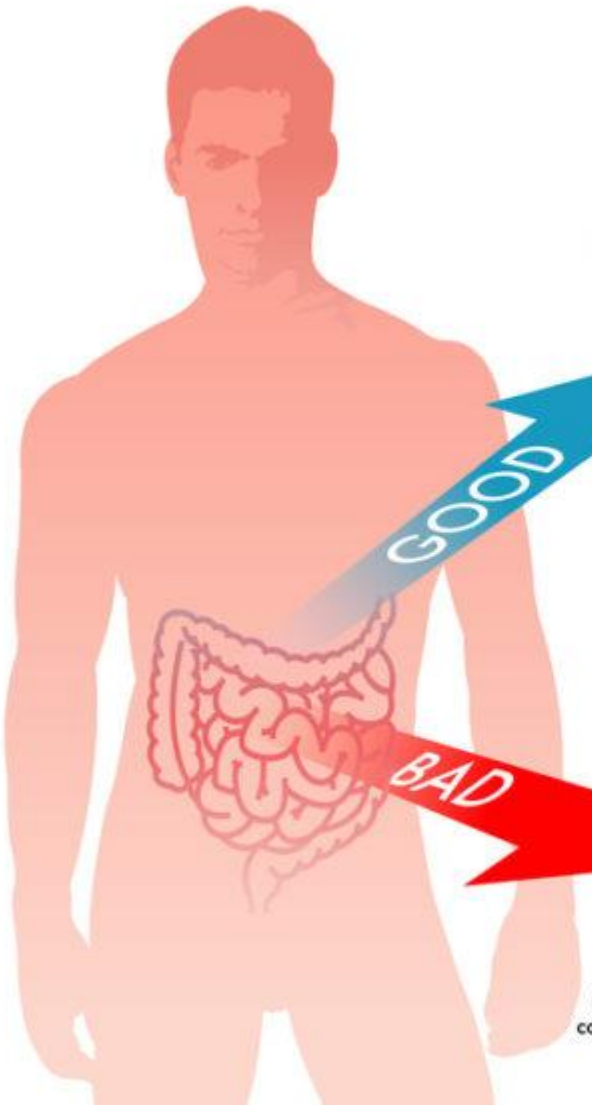
Methods. Longitudinal self-collected vaginal specimens were analyzed using established *G. vaginalis* species-specific and clade-typing polymerase chain reaction assays. Logistic regression assessed factors associated with detection of *G. vaginalis* clades, and multinomial regression assessed factors associated with number of clades.

Results. Clades 1, 2, and 3 and multiclade communities (<2 clades) were associated with Nugent-BV. Clade 1 (odds ratio [OR], 3.36; 95% confidence interval [CI], 1.65–6.84) and multiclade communities (relative risk ratio [RRR], 9.51; 95% CI, 4.36–20.73) were also associated with *Lactobacillus*-deficient vaginal microbiota. Clade 4 was neither associated with Nugent-BV nor *Lactobacillus*-deficient microbiota (OR, 1.49; 95% CI, 0.67–3.33). Specific clades were associated with differing behavioral practices. Clade 1 was associated with increasing number of recent sexual partners and smoking, whereas clade 2 was associated with penile-vaginal sex and sharing of sex toys with female partners.

Conclusions. Our results suggest that *G. vaginalis* clades have varying levels of pathogenicity in WSW, with acquisition occurring through sexual activity. These findings suggest that partner treatment may be an appropriate strategy to improve BV cure.

Keywords. bacterial vaginosis; *Gardnerella vaginalis*; sexual practices; women who have sex with women.

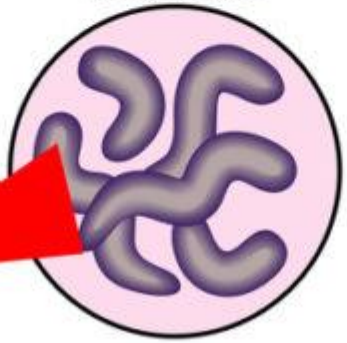
Good and Bad Bacterial Flora



BIFIDOBACTERIA
The various strains help to regulate levels of other bacteria in the gut, modulate immune responses to invading pathogens, prevent tumour formation and produce vitamins.

ESCHERICHIA COLI
Several types inhabit the human gut. They are involved in the production of vitamin K2 (essential for blood clotting) and help to keep bad bacteria in check.
But some strains can lead to illness.

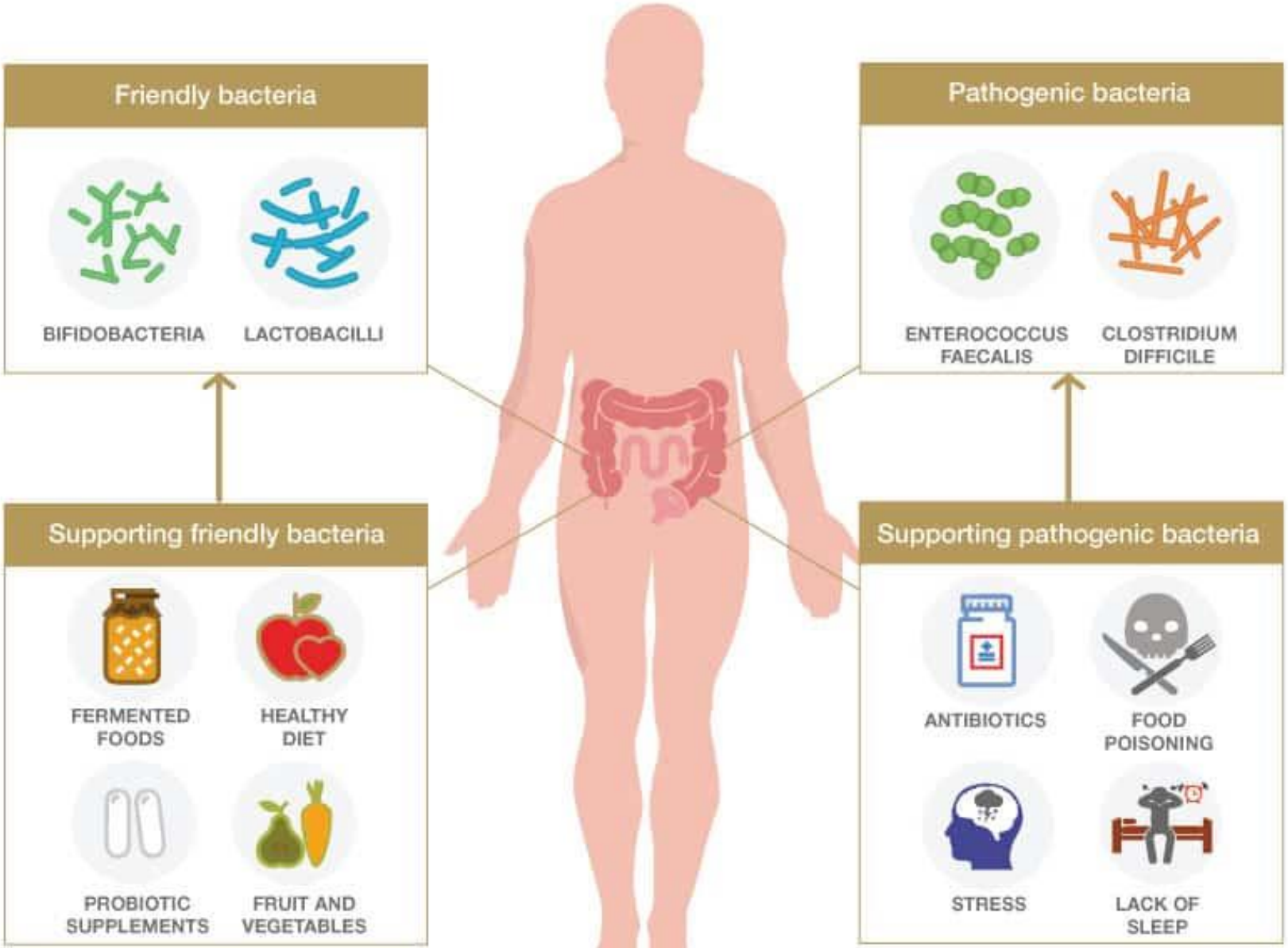
LACTOBACILLI
Beneficial varieties produce vitamins and nutrients, boost immunity and protect against carcinogens.



CAMPYLOBACTER
C Jejuni and C coli are the strains most commonly associated with human disease. Infection usually occurs throught the ingestion of contaminated food.

ENTEROCOCCUS FAECALIS
A common cause of post-surgical infections.

CLOSTRIDIUM DIFFICILE
Most harmfull following a course of antibiotics when it is able to proliferate.


Friendly bacteria
BIFIDOBACTERIA
LACTOBACILLI
Pathogenic bacteria
ENTEROCOCCUS FAECALIS
CLOSTRIDIUM DIFFICILE
Supporting friendly bacteria
FERMENTED FOODS
HEALTHY DIET
PROBIOTIC SUPPLEMENTS
FRUIT AND VEGETABLES
Supporting pathogenic bacteria
ANTIBIOTICS
FOOD POISONING
STRESS
LACK OF SLEEP

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Dietary ethanol ingestion by free-ranging spider monkeys (*Ateles geoffroyi*)

Christina J. Campbell[1], Aleksey Maro[2], Victoria Weaver[1] and Robert Dudley[2]

[1]Anthropology, California State University, Northridge, CA, USA
[2]Integrative Biology, University of California, Berkeley, CA, USA

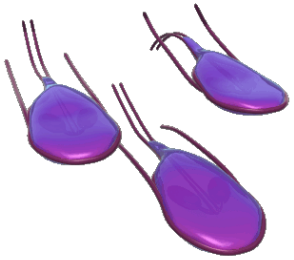
AM, 0000-0003-1183-4

Research

Cite this article: Campbell CJ, Maro A, Weaver V, Dudley R. 2022 Dietary ethanol ingestion by free-ranging spider monkeys (*Ateles geoffroyi*). *R. Soc. Open Sci.* **9**: 211729.

Ethanol within ripe and over-ripe fruit is produced naturally through the metabolic activity of fermentative yeasts. As a consequence, frugivorous animals may chronically consume ethanol as part of their routine diet, although direct measurements of such exposure are lacking. Here, we present data on ethanol concentrations within fruits of *Spondias mombin* (Anacardiaceae) that are eaten by black-handed spider monkeys (*Ateles geoffroyi*) on Barro Colorado Island, Panama. Of collected fruits that were partially consumed and then dropped by foraging monkeys, pulp-ethanol content was typically in the range of 1–2%; the percentage of pulp for consumed fruits was not significantly correlated with the ethanol concentration of the pulp remaining within each fruit. Urine samples from foraging spider monkeys were also evaluated for the ethanol metabolites ethyl glucuronide and ethyl sulfate; five of six samples tested positive for both compounds. In aggregate, these data indicate natural exposure to fruit-associated ethanol in a wild primate species.

Journal of Cardiovascular Nursing
Vol. 29, No. 6, pp 479–481 | Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins



20 Things You Didn't Know About the Human Gut Microbiome

Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN

-Hasta 2005 (Metagenómica) no se pudo medir la microbiota intestinal debido a que son bacterias anaeróbicas mayoritariamente (no crecen a través de cultivos). Ciencia en pañales. Proyecto microbioma humano (2007-2015) (American gut project & National Institutes of Health, USA)

-El microbioma se desarrolla durante la etapa fetal (el meconio no es estéril) y está influido por el tipo de parto (vaginal vs. cesárea) y el tipo de alimentación infantil (lactancia materna vs. leche de fórmula). Hacia los 2-3 años la microbiota es similar a la adulta.

-Los antibióticos durante la etapa temprana (infancia) alteran los patrones de la microbiota intestinal (mayor probabilidad de obesidad, anormalidades metabólicas, y/o enfermedades autoinmunes (ganado con antibióticos).

- La microbiota intestinal "normal" en personas sanas incluye cepas de patógenos como la Escherichia coli y los enterococos.

https://www.dailymotion.com/video/x7gc9v?playlist=x4t2zs

doi: 10.1093/nutrit/nuw069 2017.
Nutrition Reviews® Vol. 75(4):225–240

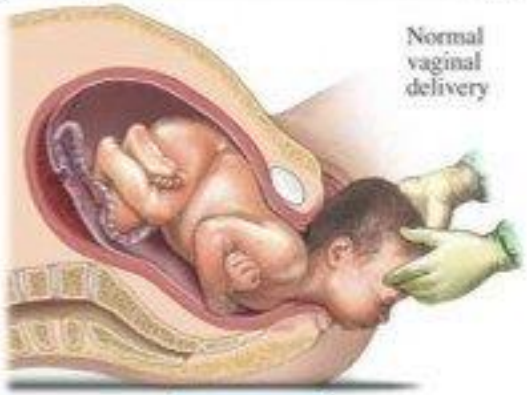
Feature Article

Intervention strategies for cesarean section–induced alterations in the microbiota-gut-brain axis

Angela Moya-Pérez, Pauline Luczynski, Ingrid B. Renes, Shugui Wang, Yuliya Borre, C. Anthony Ryan, Jan Knol, Catherine Stanton, Timothy G. Dinan, and John F. Cryan

Microbial colonization of the gastrointestinal tract is an essential process that modulates host physiology and immunity. Recently, researchers have begun to understand how and when these microorganisms colonize the gut and the early-life factors that impact their natural ecological establishment. The vertical transmission of maternal microbes to the offspring is a critical factor for host immune and metabolic development. Increasing evidence also points to a role in the wiring of the gut-brain axis. This process may be altered by various factors such as mode of delivery, gestational age at birth, the use of antibiotics in early life, infant feeding, and hygiene practices. In fact, these early exposures that impact the intestinal microbiota have been associated with the development of diseases such as obesity, type 1 diabetes, asthma, allergies, and even neurodevelopmental disorders. The present review summarizes the impact of cesarean birth on the gut microbiome and the health status of the developing infant and discusses possible preventative and restorative strategies to compensate for early-life microbial perturbations.

Vaginal Delivery



Introduced to Vaginal Microbes: Lactobacillus

Normal Introduction of Gut Microbes

Normal Development of the Immune System
- Production of specific cytokines for proper immune system development

Richardson; 2013

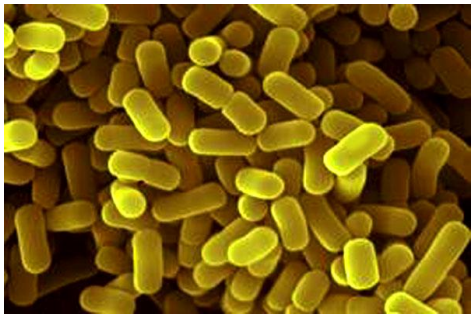
VS.

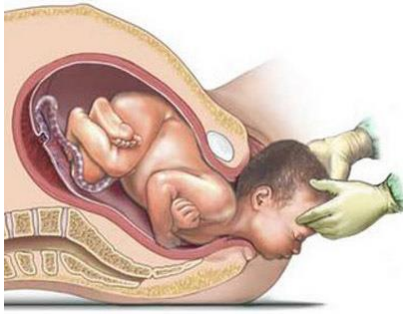
Cesarean Delivery

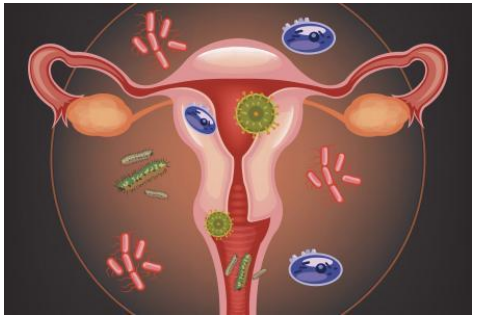
Introduced to Skin Flora: Staphylococcus

Abnormal Microbial Introduction

Disrupted Intestinal Microbial Colonization
- Increase risk for Atopic Diseases, Asthma, Allergic Rhinitis, and Celiac Disease
- Association: Delayed Onset of Lactation
  - Lack Breast Milk Support for Gut Flora







Obtención de microbiota intestinal

RECIEN NACIDO

Intestino estéril

- ¿ADN bacteriano materno en liquido amniótico?

Parto

- Provenientes

Microbiota intestinal y vaginal

Colonización

L. acidophilus, L. casei, L. fermentum, L. gasseri, L. johnsonii, L. paracasei, L. plantarum, L. reuteri, L. rhamnosus, L. salivarius,

Lactobacilos

Estafilococos
Enterococos
Estreptococos

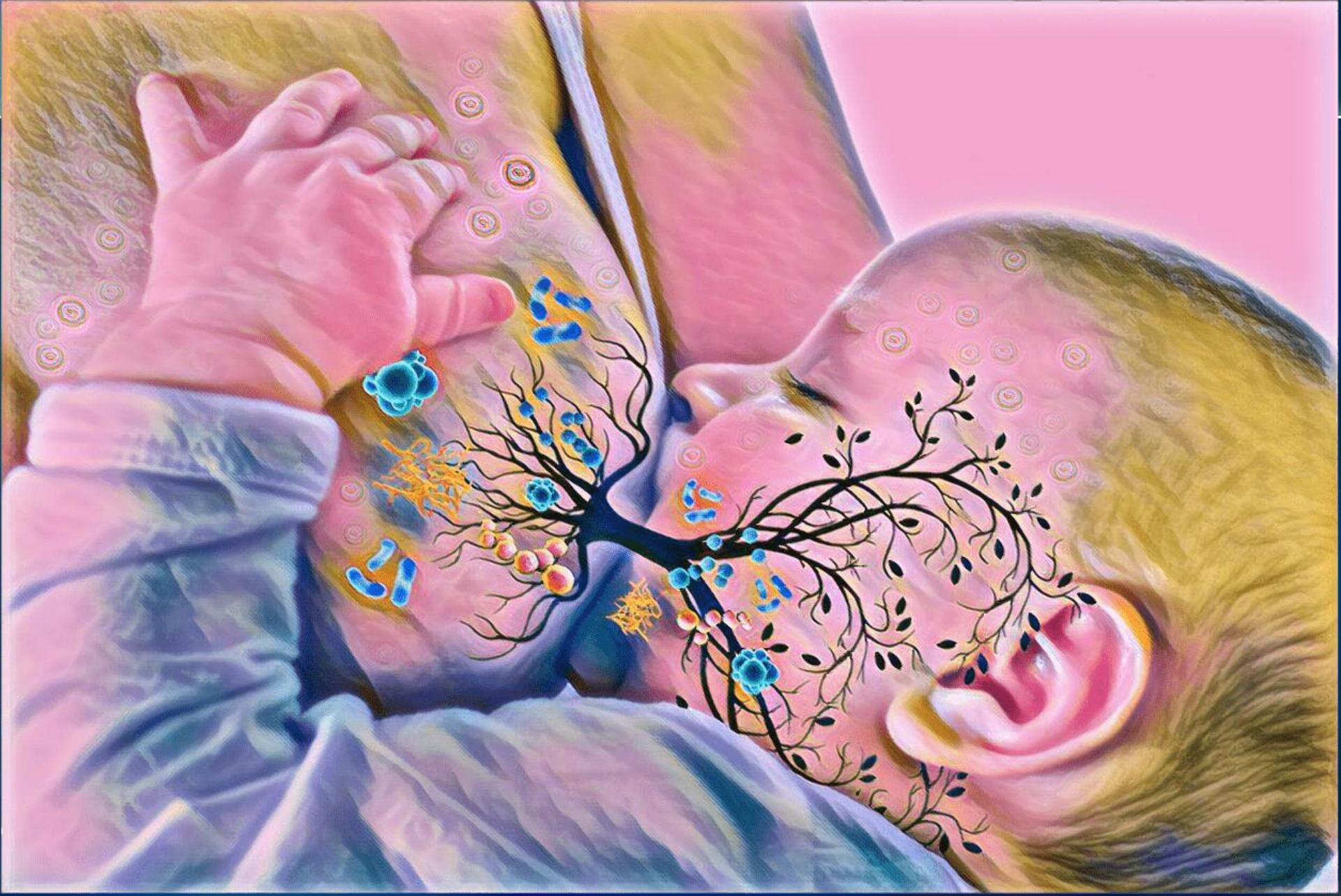
104 UFC/ml

Leche materna

Microbiota intestinal

- Principal factor en la iniciación, desarrollo y composición

Hernández Hernández A. Pediatr Integral 2015



Selma-Royo *et al. Microbiome Res Rep* 2022;1:19
DOI: 10.20517/mrr.2022.05

Microbiome Research Reports

Review

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Human milk microbiota: what did we learn in the last 20 years?

Marta Selma-Royo, Joaquim Calvo-Lerma, Christine Bäuerl, Maria Esteban-Torres, Raul Cabrera-Rubio, Maria Carmen Collado

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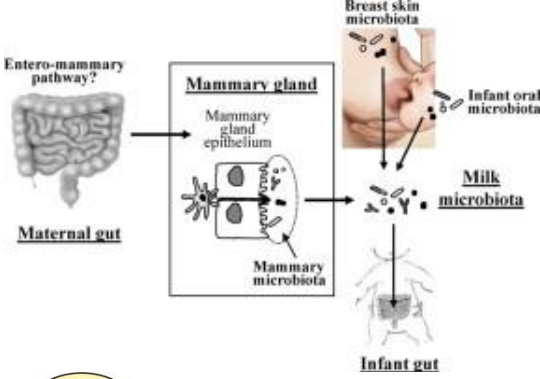
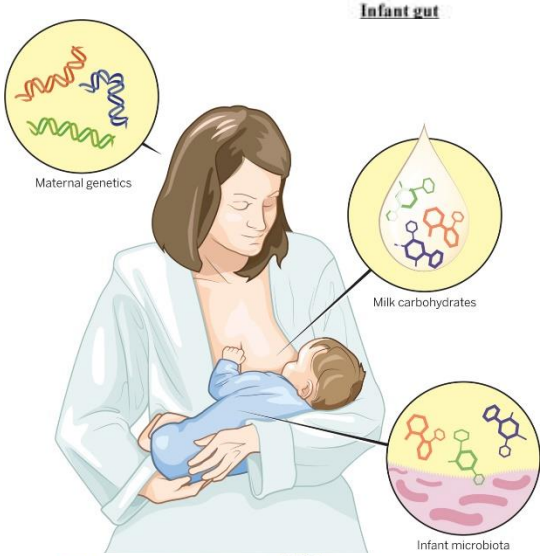
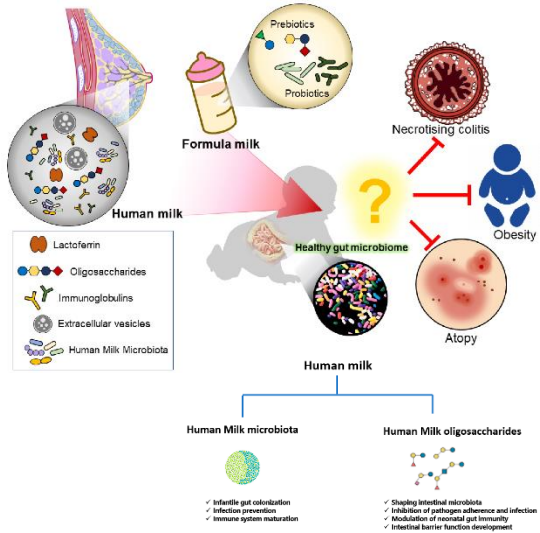
Abstract

Human milk (HM) is the gold standard for infant nutrition during the first months of life. Beyond its nutritional components, its complex bioactive composition includes microorganisms, their metabolites, and oligosaccharides, which also contribute to gut colonization and immune system maturation. There is growing evidence of the beneficial effects of bacteria present in HM. However, current research presents limited data on the presence and functions of other organisms. The potential biological impacts on maternal and infant health outcomes, the factors contributing to milk microbes' variations, and the potential functions in the infant's gut remain unclear. This review provides a global overview of milk microbiota, what the actual knowledge is, and what the gaps and challenges are for the next years.

Keywords: Human milk, microbiota, infant health







nutrients

Review

Lactobacillus Bacteria in Breast Milk

Katarzyna Łubiech * and Magdalena Twarużek

Department of Physiology and Toxicology, Faculty of Biological Sciences, Kazimierz Wielki University, Chodkiewicza 30 St., 85-064 Bydgoszcz, Poland; twarmag@ukw.edu.pl
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Received: 11 November 2020; Accepted: 8 December 2020; Published: 10 December 2020

Abstract: Breast milk is an optimal food for infants and toddlers. The composition of breast milk adapts to the needs of the developing organism, satisfying nutritional needs at an early stage of growth and development. The results of research to date have shown that breast milk is the best food for a child, containing not only nutrients but also biologically active substances that aid in the optimal, proper growth and development of infants. Among the many components of breast milk, an important element is the probiotic microflora, including bacteria of the genus *Lactobacillus* spp. These organisms exert a multidirectional, health-promoting effect on the body of children who consume breast milk. The number of lactic acid bacteria, including *Lactobacillus*, colonizing the breast milk environment and their species diversity varies and depends on many factors, both maternal and environmental. Breast milk, as a recommended food for infants, is an important source of probiotic microflora. The aim of this study was to present the current understanding of probiotic bacteria of the genus *Lactobacillus* present in breast milk.

Keywords: breast milk; probiotic microflora; *Lactobacillus* spp.; infant nutrition; breastfeeding


CANAL+
EL PARTO
3:37

doi: 10.1093/nutrit/nuw069 2017.
Nutrition Reviews® Vol. 75(4):225–240

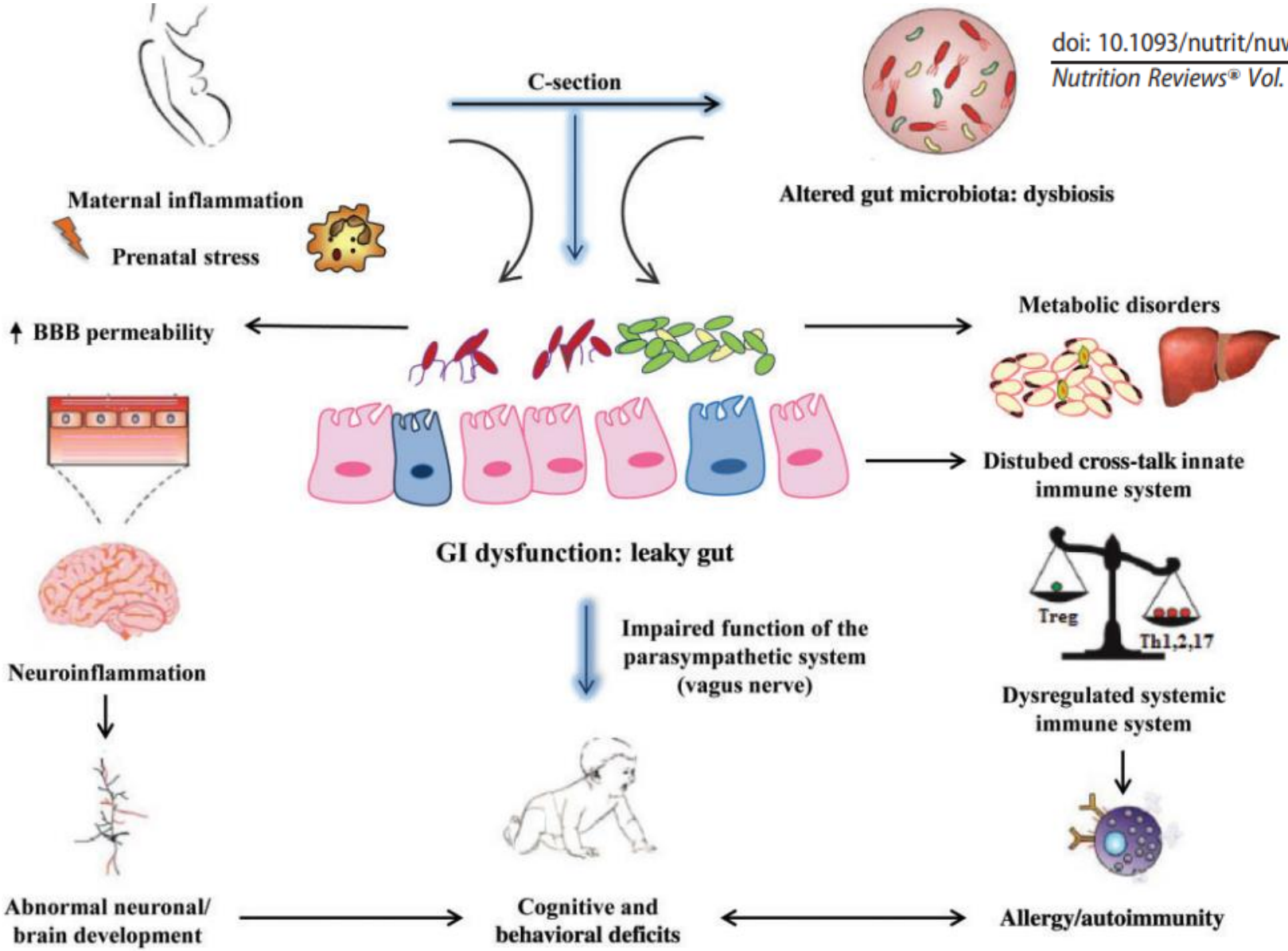

Figure 1 **Cesarean section can alter colonization of the newborn intestine, which is a critical event influencing many developmental and physiological processes and, thereby, the functioning of the immune and neuroendocrine systems, with long-lasting effects on health.** It is thought that an unhealthy microbiota can promote the increased translocation of pathogenic bacterial components from the intestinal mucosa to the systemic circulation, where they activate innate immunity characterized by production of proinflammatory cytokines, resulting in metabolic inflammation and abnormal gut function. *Abbreviation:* BBB, blood-brain barrier.

doi: 10.1093/nutrit/nuw069 2017.
Nutrition Reviews® Vol. 75(4):225–240

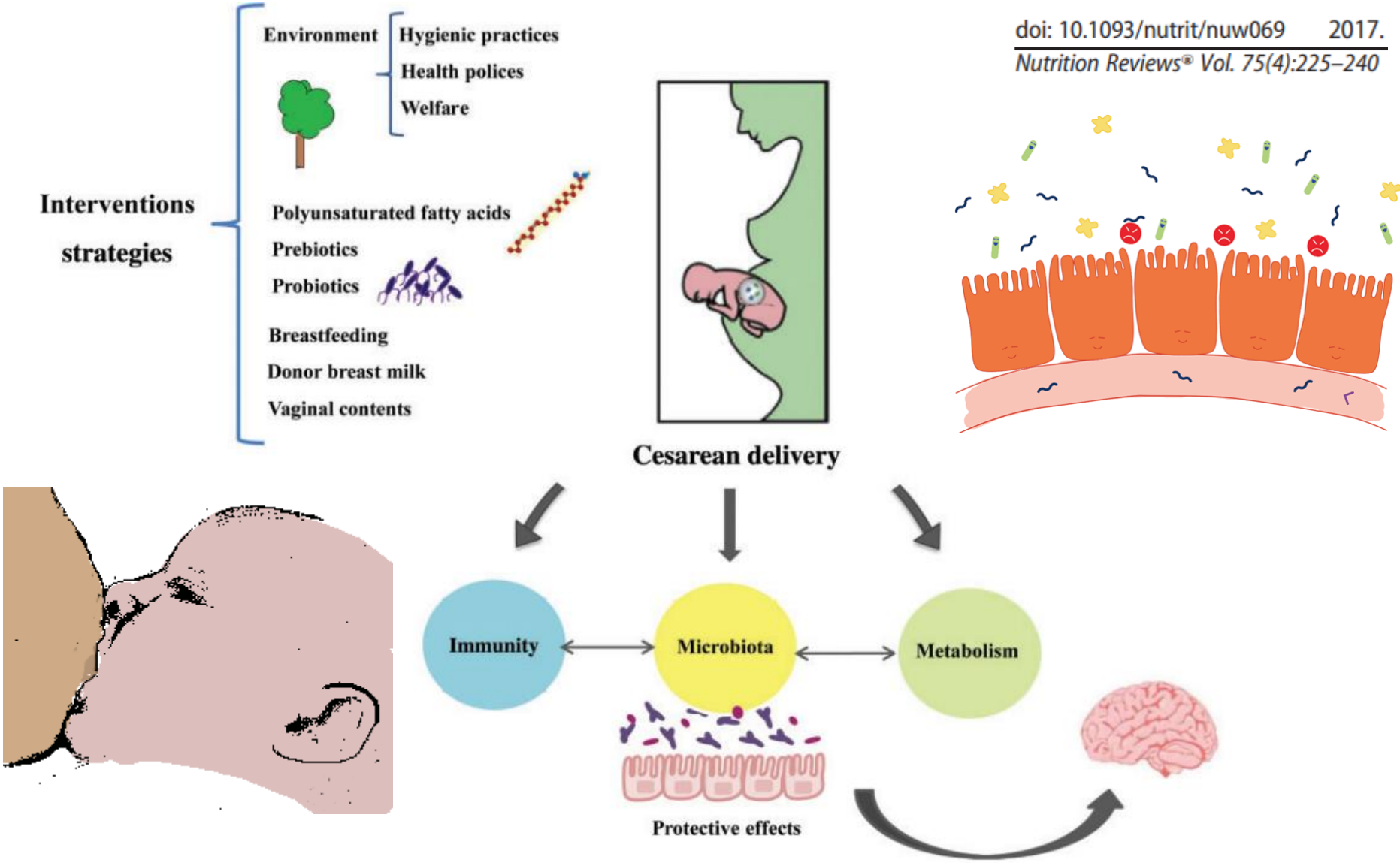

Figure 2 **Schematic representation of the main strategic points of intervention to reverse the effects of cesarean section delivery.** This can be done by improving the environment through different hygienic habits and health practices. Alternatively, the intervention could be focused on the mother herself by using probiotics and/or prebiotics and/or polyunsaturated fatty acids during pregnancy. Finally, the intervention could focus on the newborn with "seeding" approaches: breastfeeding instead of formula feeding or the use of infant formulas enriched and improved with probiotics/prebiotics. This figure summarizes the current modulating therapies to improve the composition of the microbiota and neurodevelopmental health of the infant.

The Composition and Concordance of *Lactobacillus* Populations of Infant Gut and the Corresponding Breast-Milk and Maternal Gut

Xuyao Zhang[1], Saiyidan Mushajiang[1], Baolong Luo[1], Fengwei Tian[2], Yongqing Ni[1] and Wenli Yan[1]**

ORIGINAL RESEARCH
published: 21 December 2020
doi: 10.3389/fmicb.2020.597911

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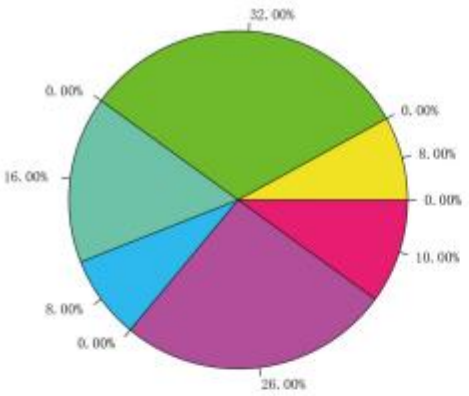
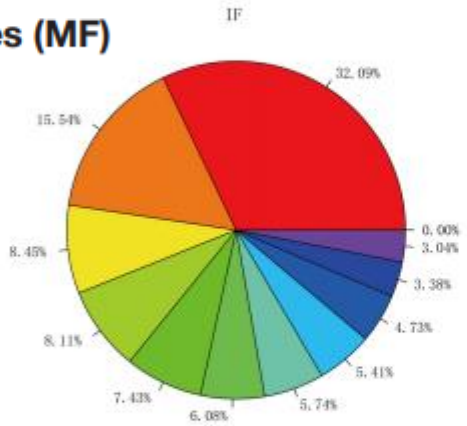
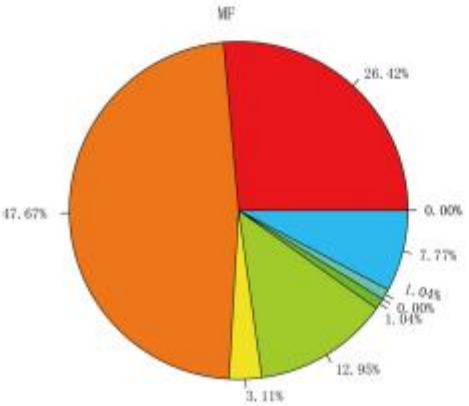


Breast milks (BM)

Maternal feces (MF)





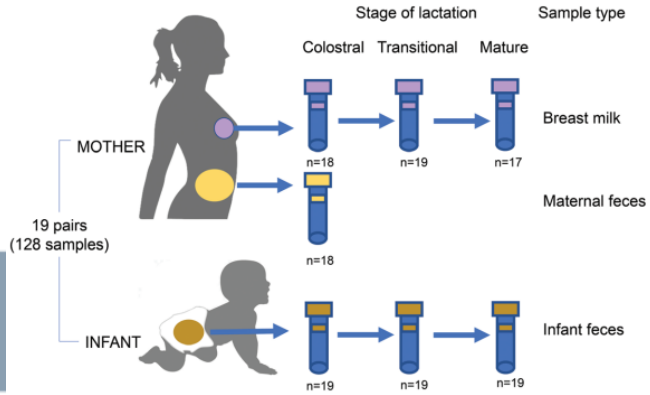
Infant feces (IF)

- *Lactobacillus mucosae*
- *Lactobacillus ruminis*
- *Lactobacillus crispatus*
- *Lactobacillus salivarius*
- *Lactobacillus gasseri*
- *Lactobacillus fermentum*
- *Lactobacillus paracasei*
- *Lactobacillus oris*
- *Lactobacillus plantarum*
- *Lactobacillus rhamnosus*
- *Lactobacillus delbrueckii*
- *Lactobacillus brevis*
- *Lactobacillus helveticus*

TABLE 2 | Average relative abundance of Illumina reads attributed to the main phyla, to the orders *Lactobacillales*, and the genera *Lactobacillus*.

Phylum/order/genus	Breast milks (BM)	Maternal feces (MF)	Infant feces (IF)
Firmicutes	40.00%	57.66%	60.06%
Bacilli	37.54%	24.84%	39.57%
Lactobacillales	29.56%	21.87%	38.61%
Lactobacillaceae	5.59%	7.09%	14.34%
Lactobacillus	5.56%	7.07%	14.34%
Streptococcaceae	19.27%	11.93%	23.34%
Enterococcaceae	2.48%	1.23%	0.24%
Actinobacteria	2.75%	6.02%	9.17%
Bacteroidetes	4.03%	8.71%	6.53%
Proteobacteria	45.79%	20.25%	20.22%

Food & Function



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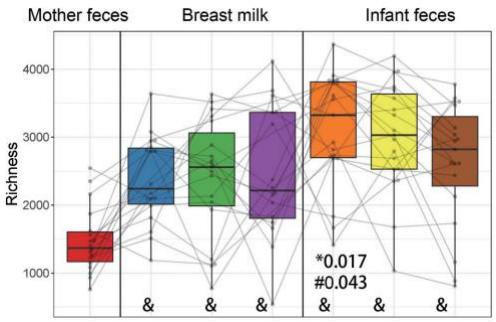
Cite this: *Food Funct.*, 2022, **13**, 304

Lactation-dependent vertical transmission of natural probiotics from the mother to the infant gut through breast milk†

Ce Qi,[a] Jingbo Zhou,[a] Huayu Tu,[a] Rundan Tu,[a] Hong Chang,[b] Jie Chen,[c] Duo Li,[a] Jin Sun *[a] and Renqiang Yu*[d]



The transmission of certain bacteria from the mother's gut to the infant's gut *via* breast milk (BM) is critical for the offspring's immune system development. Dysbiosis of the BM microbiota can be caused by a variety of reasons, which can be influenced by probiotics delivered *via* the enteromammary route. The goal of this study was to investigate the bacteria that can be transmitted from the mother to the infant's intestine during various lactation periods in 19 mother–child dyads. Bacterial transmission is most common during the colostrum phase when bacteria with certain amplicon sequence variants (ASVs) enter the newborn intestine and inhabit it permanently. We have established that anaerobic gut-associated bacteria, such as *Faecalibacterium*, *Blautia* and *Lachnoclostridium*, transfer from the mother to the infant's gut with lactation dependence using the idea of weighted transfer ratios. *Streptococcus salivarius*, *Bifidobacterium longum*, and *Lactobacillus gasseri* are transferred from the maternal gut to the BM, as well as from the BM to the newborn gut, depending on different ASVs. These findings suggest that isolation of key microorganisms from breast milk could be utilized to modify the microbiota of BM or newborns by giving the mother a probiotic or adding it to artificial milk to promote neonatal health.

Received 18th September 2021,
Accepted 16th November 2021

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applied sciences

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Appl. Sci. 2021, 11, 7247.

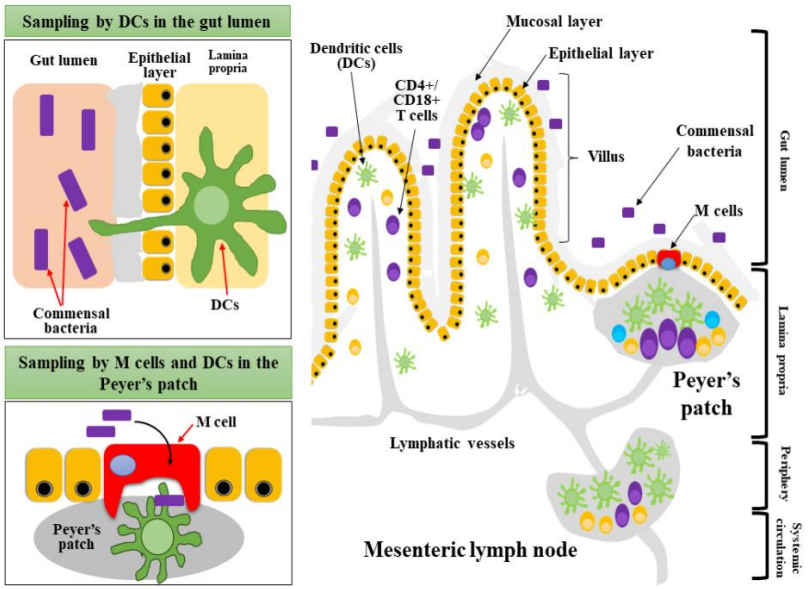
Review

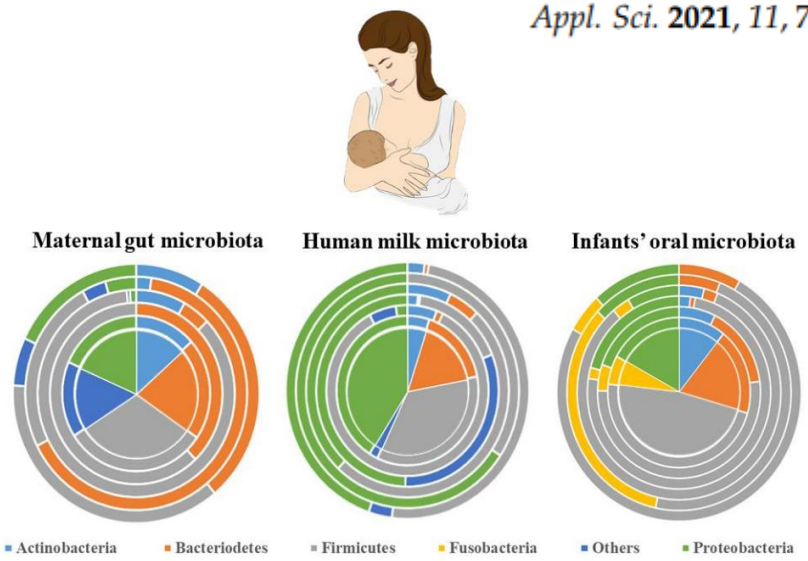
An Insight into Probiotics Bio-Route: Translocation from the Mother's Gut to the Mammary Gland

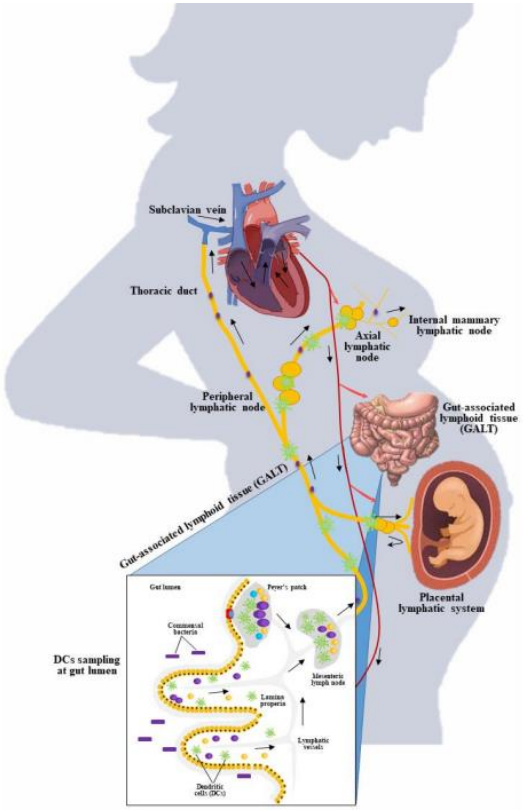
Shanmugaprakasham Selvamani [1,2], Daniel Joe Dailin [1,2], Vijai Kumar Gupta [3], Mohd Wahid [4], Ho Chin Keat [1], Khairun Hani Natasya [1], Roslinda Abd Malek [1], Shafiul Haque [4,5], R. Z. Sayyed [6], Bassam Abomoelak [7], Dalia Sukmawati [8], Theodoros Varzakas [9] and Hesham Ali El Enshasy [1,2,10,*]

Abstract: Human breast milk (HBM) is unique in its composition as it is adapted to fulfil the newborns' nutritional requirement and helps in improving the health of newborns. Besides various nutrients, the human milk also contains diverse group of microbiotas. The human milk microbiota has a remarkable impact on the growth and development of a newborn. Additionally, the human milk microbiota enhances the colonization of microbes in the gut of infants. Debates about the origin of HBM microbial flora remain premature and contradictory in some cases. Recent data suggest that the maternal gut microbiota has a major impact on microbial composition, areolar skin, and from the infant's oral cavity. The current review investigates the possible route of microbial transfer from the maternal gut to mammary gland and suggests that it might occur through the entero-mammary pathway. It involves precise selection of probiotic microorganisms from the gut, as the human gut hosts trillions of microorganisms involved in gut homeostasis and other metabolic pathways. Gastrointestinal lymphatic vessels, macrophages, and dendritic cells are shown to play a significant role in the microbial transmission. Furthermore, the role of microbial factors in the development of neonatal immunity and translocation of secretory IgA (SIgA) cells from the intestinal lumen to GALT and finally to mammary glands via entero-mammary link are discussed.

Keywords: breast milk; microbiome; probiotics; lactic acid bacteria; entero-mammary pathway







Journal of Functional Foods 87 (2021) 104719

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Journal of Functional Foods

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

Recent advances of intestinal microbiota transmission from mother to infant

Lan Yang, Hafiz Arbab Sakandar, Zhihong Sun, Heping Zhang *

Key Laboratory of Dairy Biotechnology and Engineering, Ministry of Education, Inner Mongolia Agricultural University, Hohhot 010018, China
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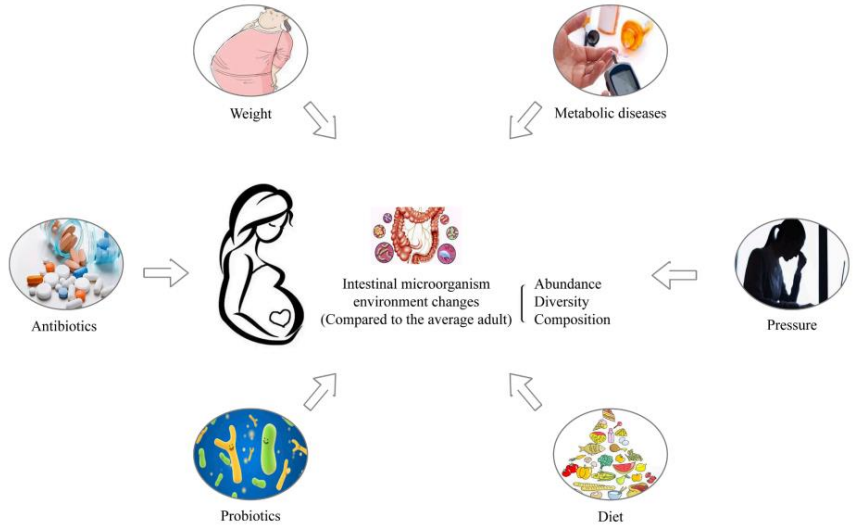
ARTICLE INFO

Keywords:
Mother
Infant
Intestinal microbiota
Transmission

ABSTRACT

The intestinal microbiota of infants plays an important role in early life and affects health throughout lifespan. The mother is closely associated with the infant microbiota, by helping to establish it through her own gut microbiota, intrauterine and birth canal environments, and feeding. In this study, the characteristics, influencing factors, and effects of pregnant women on offspring, the establishment and development of intestinal microbiota in infants, and the significance of mother-to-infant transmission were reviewed, to provide new research impetus on the establishment of intestinal microbiota in infants.



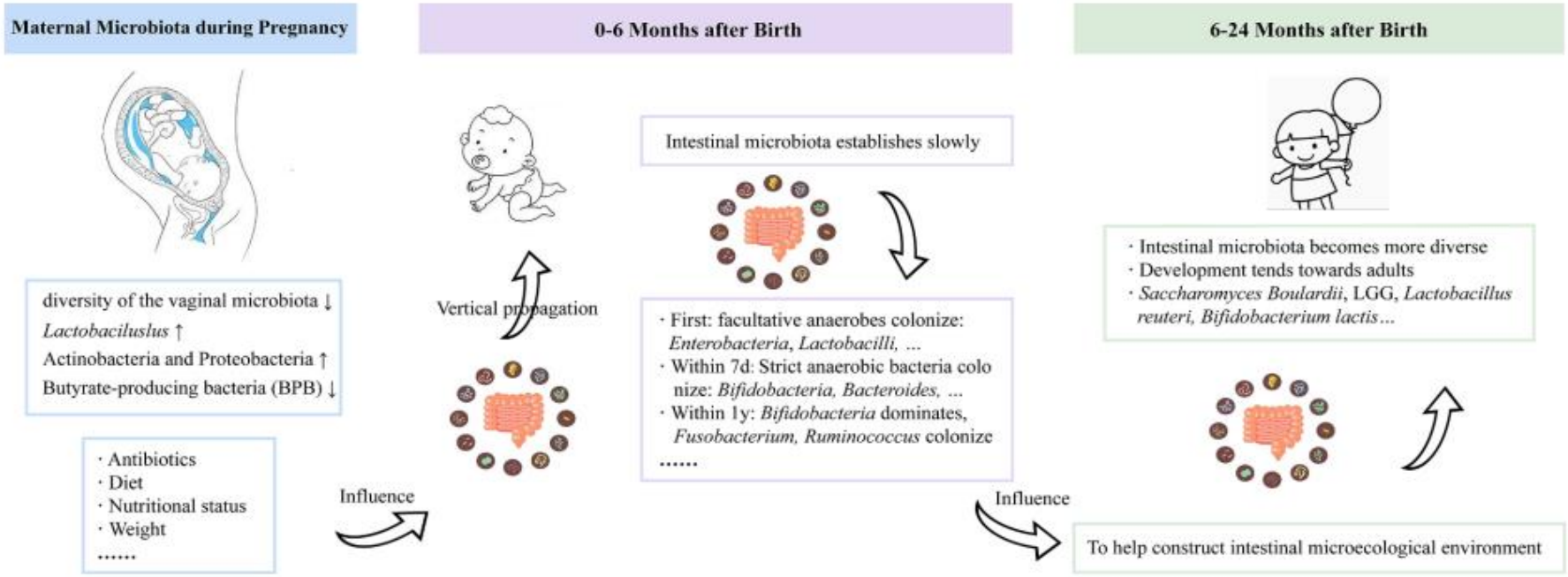


Fig. 2. Development of infant intestinal microbiota during the first 1000 days of life.

Tomar antibióticos demasiado pronto podría alterar lo cognitivo y emocional

María Cardoso

Barcelona. Sábado, 24 de Julio 2021. 22:24
Actualizado: Lunes, 26 de Julio 2021. 16:45
Tiempo de lectura: 2 minutos

La exposición a antibióticos en una etapa temprana de la vida podría alterar el desarrollo del cerebro humano en zonas responsables de las funciones cognitivas y emocionales. Así queda de manifiesto en un estudio llevado a cabo en el Centro de Biotecnología y Medicina Avanzadas en Rutgers publicado en la revista *iScience*.

Brain, Behavior, and Immunity 56 (2016) 140–155

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

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

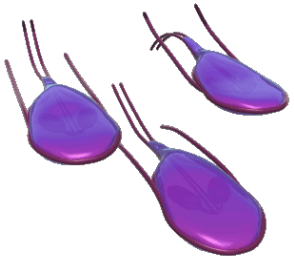
Full-length Article

Cognitive impairment by antibiotic-induced gut dysbiosis: Analysis of gut microbiota-brain communication

Esther E. Fröhlich [a,*], Aitak Farzi [a], Raphaela Mayerhofer [a], Florian Reichmann [a], Angela Jačan [a], Bernhard Wagner [b], Erwin Zinser [b], Natalie Bordag [c], Christoph Magnes [d], Eleonore Fröhlich [e], Karl Kashofer [f], Gregor Gorkiewicz [f,g,h], Peter Holzer [a,*]

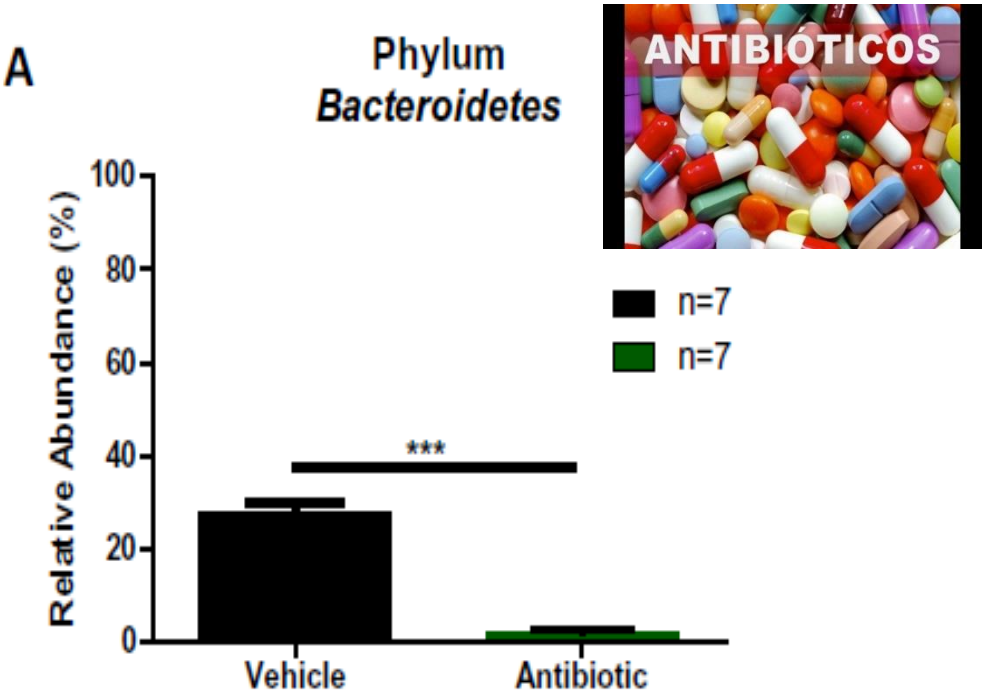
Emerging evidence indicates that disruption of the gut microbial community (dysbiosis) impairs mental health. Germ-free mice and antibiotic-induced gut dysbiosis are two approaches to establish causality in gut microbiota-brain relationships. However, both models have limitations, as germ-free mice display alterations in blood-brain barrier and brain ultrastructure and antibiotics may act directly on the brain. We hypothesized that the concerns related to antibiotic-induced gut dysbiosis can only adequately be addressed if the effect of intragastric treatment of adult mice with multiple antibiotics on (i) gut microbial community, (ii) metabolite profile in the colon, (iii) circulating metabolites, (iv) expression of neuronal signaling molecules in distinct brain areas and (v) cognitive behavior is systematically investigated. Of the antibiotics used (ampicillin, bacitracin, meropenem, neomycin, vancomycin), ampicillin had some oral bioavailability but did not enter the brain. 16S rDNA sequencing confirmed antibiotic-induced microbial community disruption, and metabolomics revealed that gut dysbiosis was associated with depletion of bacteria-derived metabolites in the colon and alterations of lipid species and converted microbe-derived molecules in the plasma. Importantly, novel object recognition, but not spatial, memory was impaired in antibiotic-treated mice. This cognitive deficit was associated with brain region-specific changes in the expression of cognition-relevant signaling molecules, notably brain-derived neurotrophic factor, N-methyl-D-aspartate receptor subunit 2B, serotonin transporter and neuropeptide Y system. We conclude that circulating metabolites and the cerebral neuropeptide Y system play an important role in the cognitive impairment and dysregulation of cerebral signaling molecules due to antibiotic-induced gut dysbiosis.

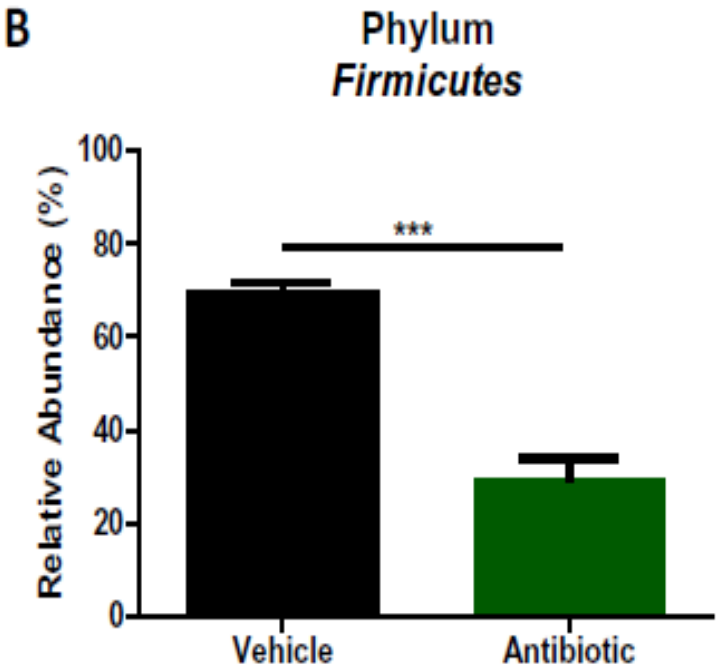
Journal of Cardiovascular Nursing
Vol. 29, No. 6, pp 479–481 | Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins



20 Things You Didn't Know About the Human Gut Microbiome

Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN





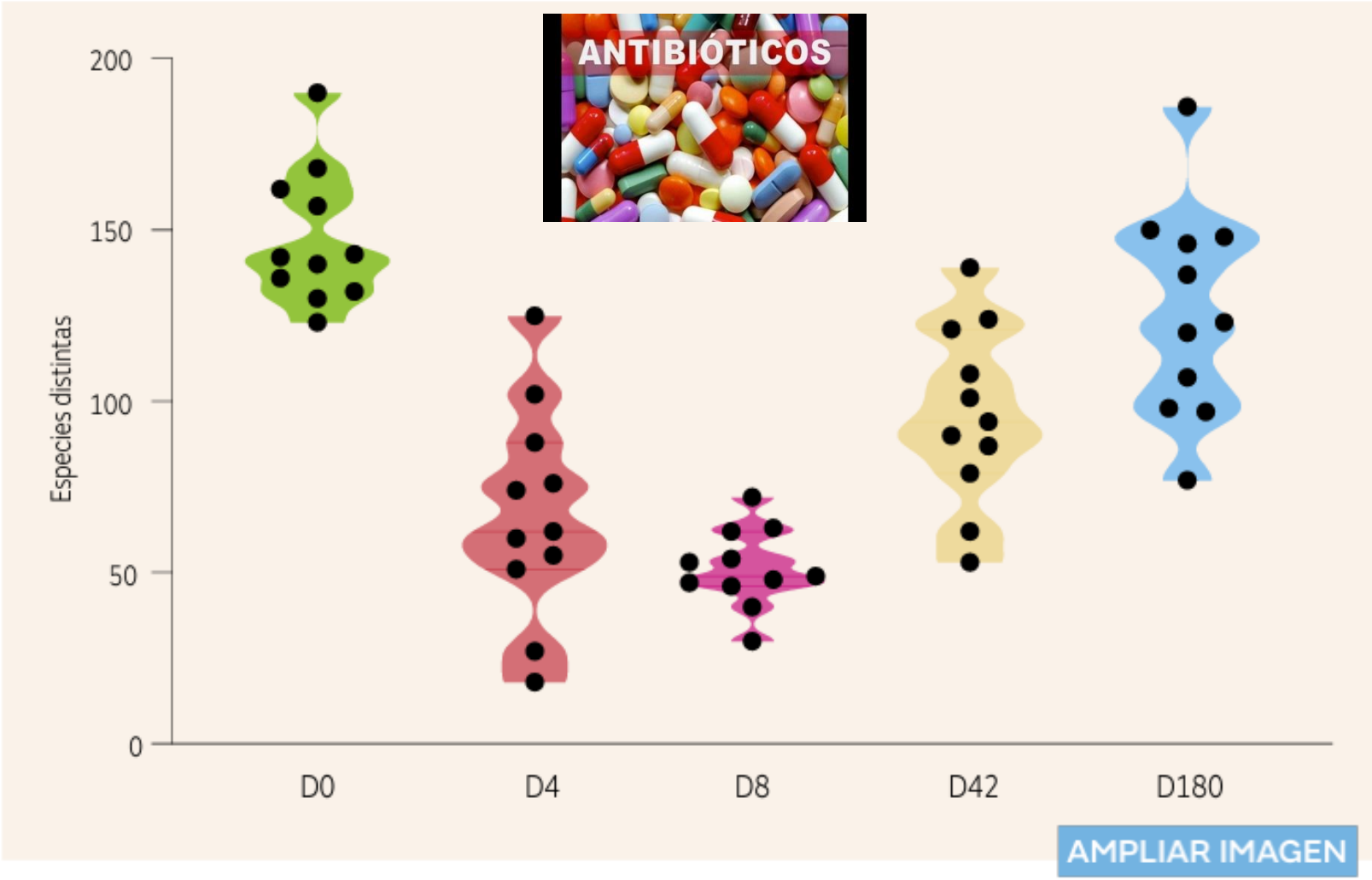


FIGURA 2. El número de especies bacterianas distintas en muestras fecales de voluntarios sanos cayó drásticamente después de 4 días de tratamiento antibiótico (D0 a D4), y la recuperación fue lenta a lo largo de un período de 180 días. Hubo grandes cambios en la abundancia de bacterias por sobrecrecimiento de oportunistas y pérdida definitiva de algunas especies fermentadoras[26].

Science of the Total Environment 822 (2022) 153628

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

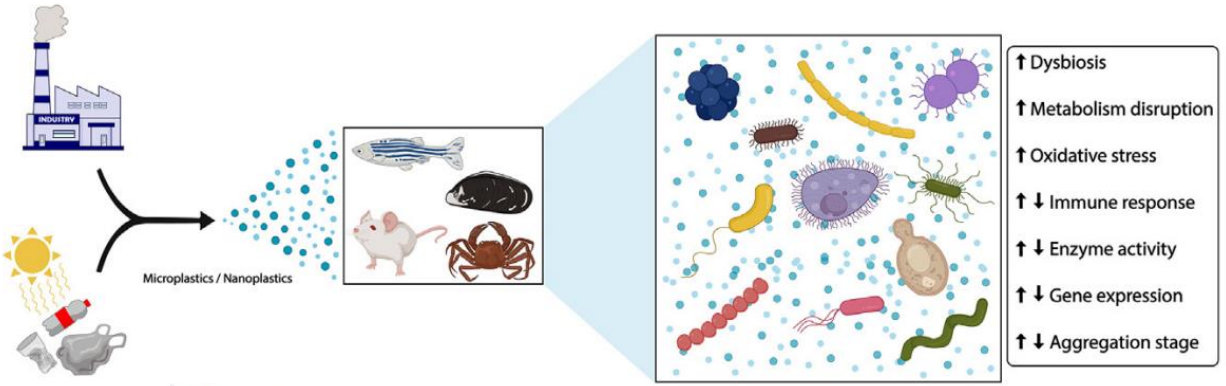
Review

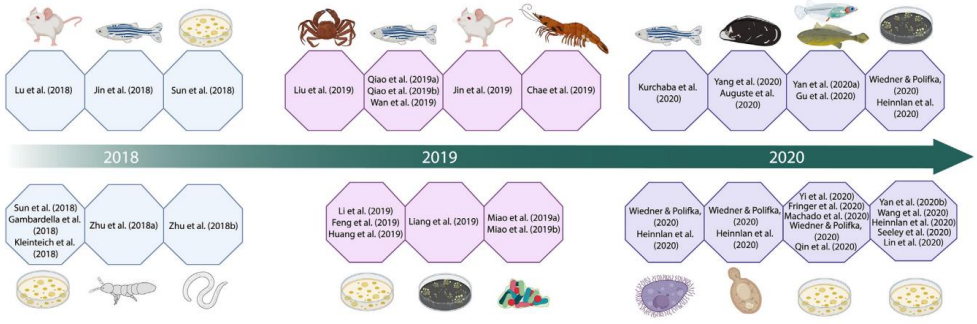
Microbiome: A forgotten target of environmental micro(nano)plastics?

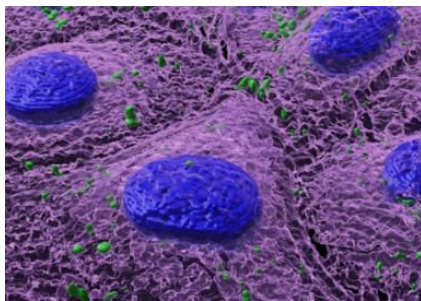
Andressa Liberal Santos [a], Cândido Carvalho Rodrigues [a], Miguel Oliveira [b], Thiago Lopes Rocha [a,*]

[a] Laboratory of Environmental Biotechnology and Ecotoxicology, Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, Goiás, Brazil
[b] Department of Biology & CESAM, University of Aveiro, 3810-193 Aveiro, Portugal

- Micro(nano)plastics can interact with microorganisms.
- Micro(nano)plastics can affect health through effects on the microbiota.
- Micro(nano)plastics can affect ecosystems through effects on environmental microorganisms.
- Microbiome disruption as an emerging biomarker in toxicology and ecotoxicology







Science Bulletin 65 (2020) 1966–1969

Contents lists available at ScienceDirect

Science Bulletin

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

Perspective

Insights into nanoplastics effects on human health

Mariana Teles [a,1], Joan Carles Balasch [a,1], Miguel Oliveira [b], Jordi Sardans [c,d], Josep Peñuelas [c,d,*]

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[b] Centre for Environmental and Marine Studies, Department of Biology, University of Aveiro, Aveiro 3810-193, Portugal
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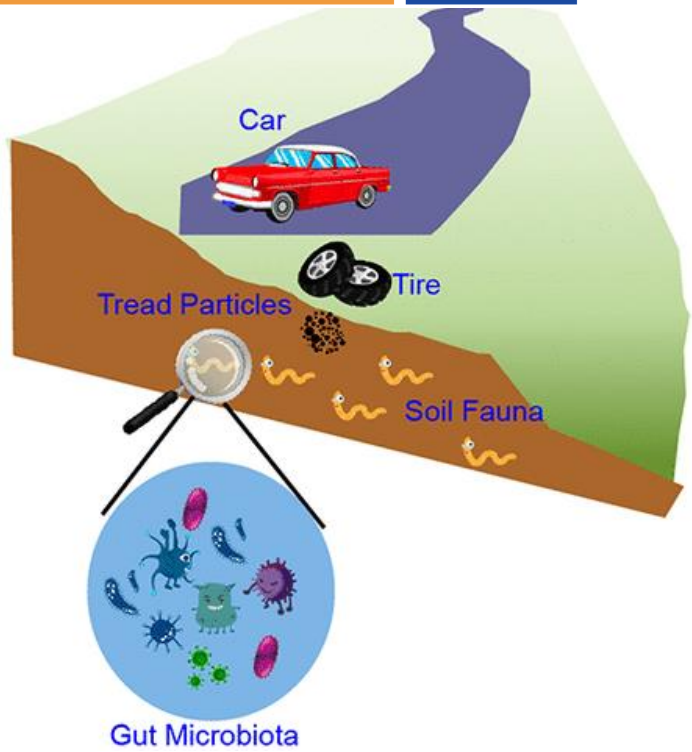
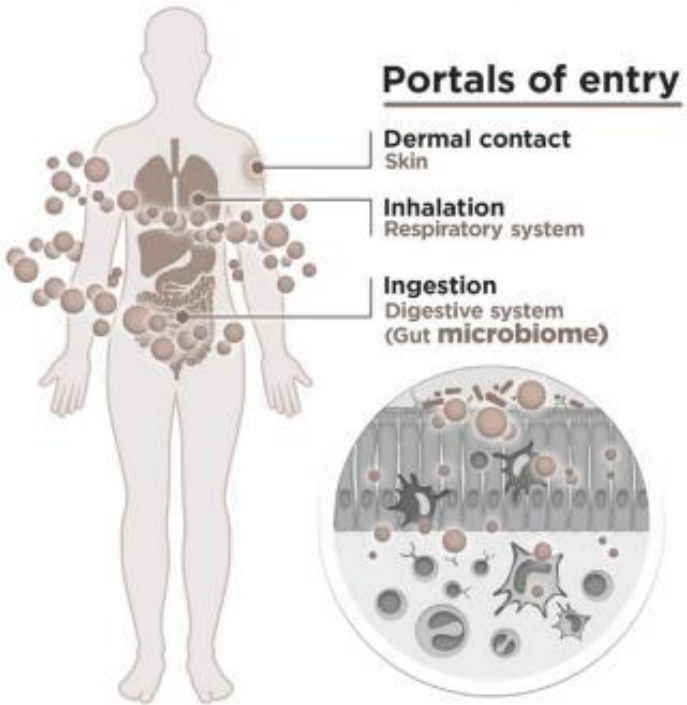
[d] Centre de Recerca Ecològica i Aplicacions Forestals (CREAF), Cerdanyola del Vallès, Catalonia E-08193, Spain

Dysbiosis in the Gut Microbiota of Soil Fauna Explains the Toxicity of Tire Tread Particles

Jing Ding,○ Dong Zhu,○ Hong-Tao Wang, Simon Bo Lassen, Qing-Lin Chen, Gang Li, Min Lv, and Yong-Guan Zhu*

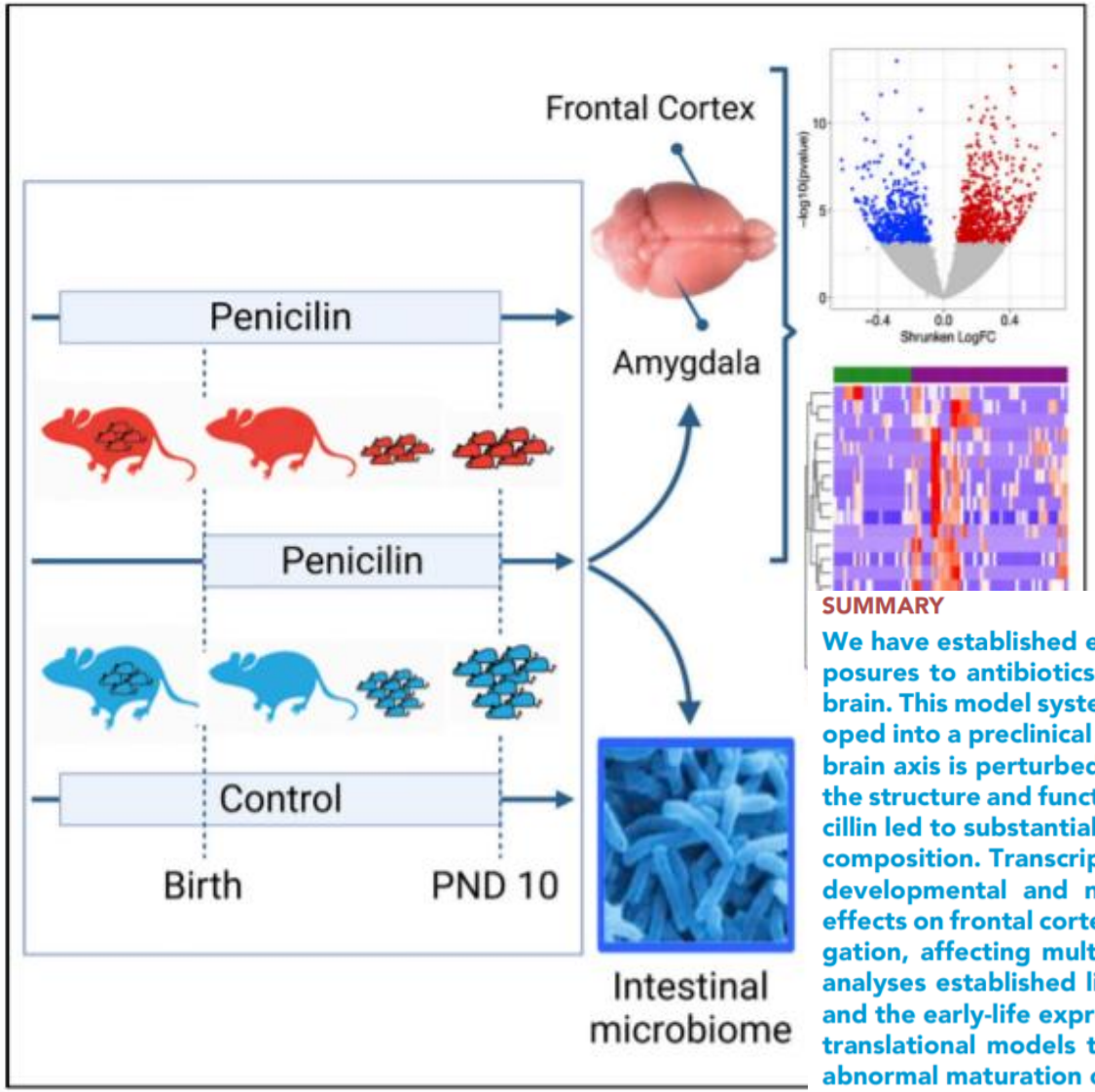
Cite This: Environ. Sci. Technol. 2020, 54, 7450–7460 Read Online





Effects of early-life penicillin exposure on the gut microbiome and frontal cortex and amygdala gene expression

iScience *24*, 102797, July 23, 2021



Angelina Volkova, Kelly Ruggles, Anjelique Schulfer, Zhan Gao, Stephen D. Ginsberg, Martin J. Blaser

ginsberg@nki.rfmh.org (S.D.G.)
martin.blaser@cabm.rutgers.edu (M.J.B.)

Highlights

Low-dose antibiotic exposure perturbs the infant gut mouse microbiome to PND10

SUMMARY

We have established experimental systems to assess the effects of early-life exposures to antibiotics on the intestinal microbiota and gene expression in the brain. This model system is highly relevant to human exposure and may be developed into a preclinical model of neurodevelopmental disorders in which the gut–brain axis is perturbed, leading to organizational effects that permanently alter the structure and function of the brain. Exposing newborn mice to low-dose penicillin led to substantial changes in intestinal microbiota population structure and composition. Transcriptomic alterations implicate pathways perturbed in neurodevelopmental and neuropsychiatric disorders. There also were substantial effects on frontal cortex and amygdala gene expression by bioinformatic interrogation, affecting multiple pathways underlying neurodevelopment. Informatic analyses established linkages between specific intestinal microbial populations and the early-life expression of particular affected genes. These studies provide translational models to explore intestinal microbiome roles in the normal and abnormal maturation of the vulnerable central nervous system.

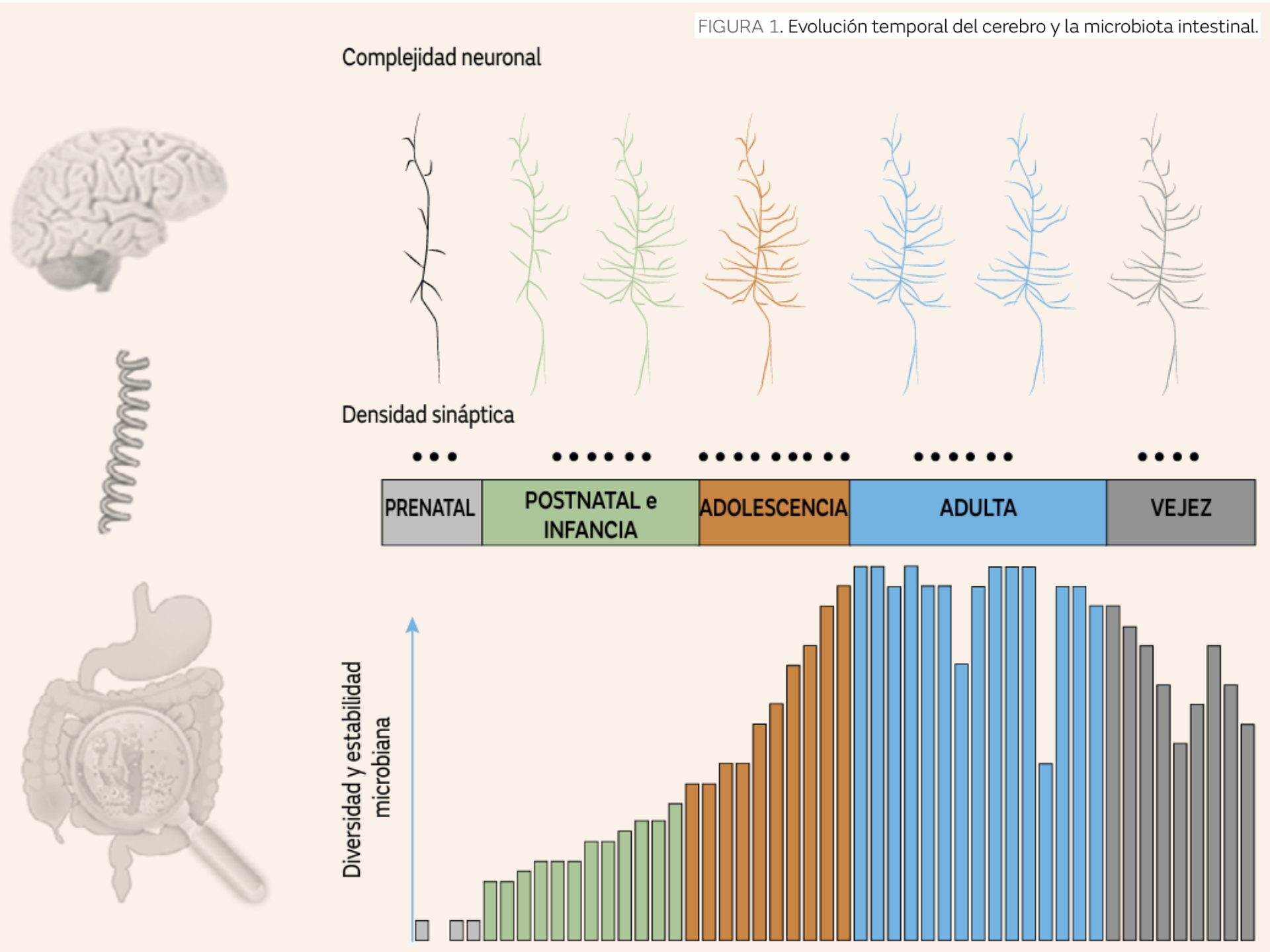
La microbiota intestinal potencia el desarrollo cerebral

Pablo Javier Piacente hace 3 meses

Una investigación liderada por la Universidad de Alberta, en Canadá, ha verificado que las características de la microbiota intestinal inciden directamente en el desarrollo cerebral de los bebés varones. La diferencia la hacen los bacteroidetes, un tipo de bacteria que genera metabolitos llamados esfingolípidos: los mismos son fundamentales para la formación y estructura de las neuronas en el cerebro.

Los científicos sostienen que luego de realizar un estudio en el que participaron 400 bebés se pudieron obtener evidencias significativas: los niños con una microbiota intestinal que incluía una importante proporción de bacteroidetes mostraron, al pasar un año, **habilidades cognitivas y de lenguaje notablemente mejoradas**. La investigación, publicada en la revista Gut Microbes, concluye que las bacterias intestinales influyen en el desarrollo de las funciones cerebrales.

FIGURA 1. Evolución temporal del cerebro y la microbiota intestinal.



The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

Leading Edge
Review

Cell *167*, November 3, 2016

Neurodevelopment is a complex process governed by both intrinsic and extrinsic signals. While historically studied by researching the brain, inputs from the periphery impact many neurological conditions. Indeed, emerging data suggest communication between the gut and the brain in anxiety, depression, cognition, and autism spectrum disorder (ASD). The development of a healthy, functional brain depends on key pre- and post-natal events that integrate environmental cues, such as molecular signals from the gut. These cues largely originate from the microbiome, the consortium of symbiotic bacteria that reside within all animals. Research over the past few years reveals that the gut microbiome plays a role in basic neurogenerative processes such as the formation of the blood-brain barrier, myelination, neurogenesis, and microglia maturation and also modulates many aspects of animal behavior. Herein, we discuss the biological intersection of neurodevelopment and the microbiome and explore the hypothesis that gut bacteria are integral contributors to development and function of the nervous system and to the balance between mental health and disease.

The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

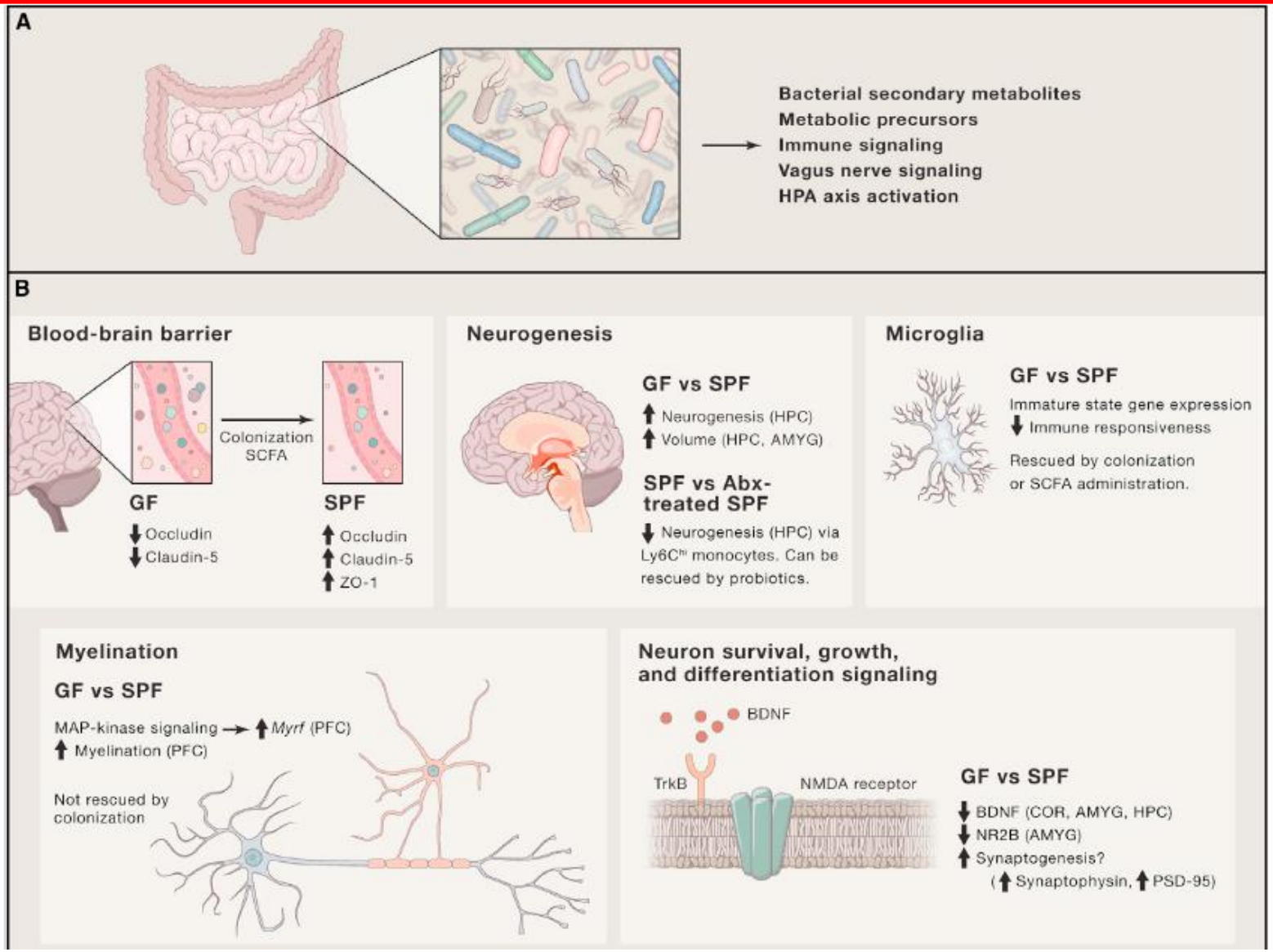


Figure 1. Intersections of Gut Microorganisms and Basic Developmental Processes

Basic developmental processes driven directly or indirectly by gut microbes and their products.

(A) Gut microorganisms relay messages to the brain via various direct and indirect mechanisms.

(B) Basic neurodevelopmental processes are modulated as a result of colonization of GF animals or depletion of gut bacteria by antibiotics. Specifically, the following processes are modulates: blood-brain barrier (BBB) formation and integrity (Braniste et al., 2014), neurogenesis (Möhle et al., 2016; Ogbonnaya et al., 2015), microglia maturation and ramification (Erny et al., 2015; Matcovitch-Natan et al., 2016), myelination (Gacias et al., 2016; Hoban et al., 2016) and expression of neurotrophins (Bercik et al., 2011a, 2011b; Desbonnet et al., 2015), neurotransmitters (Bercik et al., 2011a; O'Mahony et al., 2015), and their respective receptors.

GUT MICROBES
2021, VOL. 13, NO. 1, e1930875 (17 pages)
https://doi.org/10.1080/19490976.2021.1930875

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RESEARCH PAPER

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Bacteroides-dominant gut microbiome of late infancy is associated with enhanced neurodevelopment

Sukhpreet K. Tamana[a*], Hein M. Tun[b,a*], Theodore Konya[c], Radha S. Chari[d], Catherine J. Field[e], David S. Guttman[f], Allan B. Becker[g], Theo J. Moraes[h], Stuart E. Turvey[i], Padmaja Subbarao[h], Malcolm R. Sears[j], Jacqueline Pei[k], James A. Scott[c], Piush J. Mandhane[a], and Anita L. Kozyrskyj[a]

[a]Department of Pediatrics, University of Alberta, Edmonton, AB, Canada; [b]HKU-Pasteur Research Pole, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China; [c]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; [d]Department of Obstetrics and Gynecology, University of Alberta, Edmonton, AB, Canada; [e]Department of Agricultural, Food & Nutritional Science, University of Alberta, Edmonton, AB, Canada; [f]Centre for the Analysis of Genome Evolution and Function, University of Toronto, Toronto, ON, Canada; [g]Department of Pediatrics & Child Health, Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, MB, Canada; [h]Department of Pediatrics, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada; [i]Department of Pediatrics, Child & Family Research Institute, BC Children's Hospital, University of British Columbia, Vancouver, BC, Canada; [j]Department of Medicine, McMaster University, Hamilton, ON, Canada; [k]Department of Educational Psychology, University of Alberta, Edmonton, AB, Canada

ABSTRACT

Dysbiosis of gut microbiota has been retrospectively linked to autism spectrum disorders but the temporal association between gut microbiota and early neurodevelopment in healthy infants is largely unknown. We undertook this study to determine associations between gut microbiota at two critical periods during infancy and neurodevelopment in a general population birth cohort.

Here, we analyzed data from 405 infants (199 females) from the CHILD (Canadian Healthy Infant Longitudinal Development) Cohort Study. Neurodevelopmental outcomes were objectively assessed using the Bayley Scale of Infant Development (BSID-III) at 1 and 2 years of age. Microbiota profiling with 16S rRNA gene sequencing was conducted on fecal samples obtained at a mean age of 4 and 12 months.

Using clustering methods, we identified three groups of infants based on relative abundance of gut microbiota at 12 months: *Proteobacteria*-dominant cluster (22.4% higher abundance at 12 months), *Firmicutes*-dominant cluster (46.0% higher abundance at 12 months) and Bacteroidetes-dominant cluster (31.6% higher abundance at 12 months). Relative to the *Proteobacteria*-dominant cluster, the *Bacteroidetes*-dominant cluster was associated with higher scores for cognitive (4.8 points; FDRp = .02), language (4.2 points; FDRp≤0.001), and motor (3.1 points; FDRp = .03) development at age 2 in models adjusted for covariates. When stratified by sex, only male infants with a *Bacteroidetes*-dominant microbiota had more favorable cognitive (5.9 points, FDRp = .06) and language (7.9 points; FDRp≤0.001) development. Genus *Bacteroides* abundance in gut microbiota was positively correlated with cognitive and language scores at age 2. Fully adjusted linear mixed model analysis revealed a positive association between *Bacteroidetes*-dominant cluster and change in cognitive and language performance from 1 to 2 years, predominantly among males. No associations were evident between 4-month microbiota clusters and BSID-II scores. Noteworthy is that enhanced sphingolipid synthesis and metabolism, and antagonism or competition between *Bacteroides* and *Streptococcus* were characteristic of a *Bacteroidetes*-dominant gut microbiota.

This study found strong evidence of positive associations between Bacteroidetes gut microbiota in late infancy and subsequent neurodevelopment, most prominently among males but not females.

ARTICLE HISTORY
Received 4 December 2020
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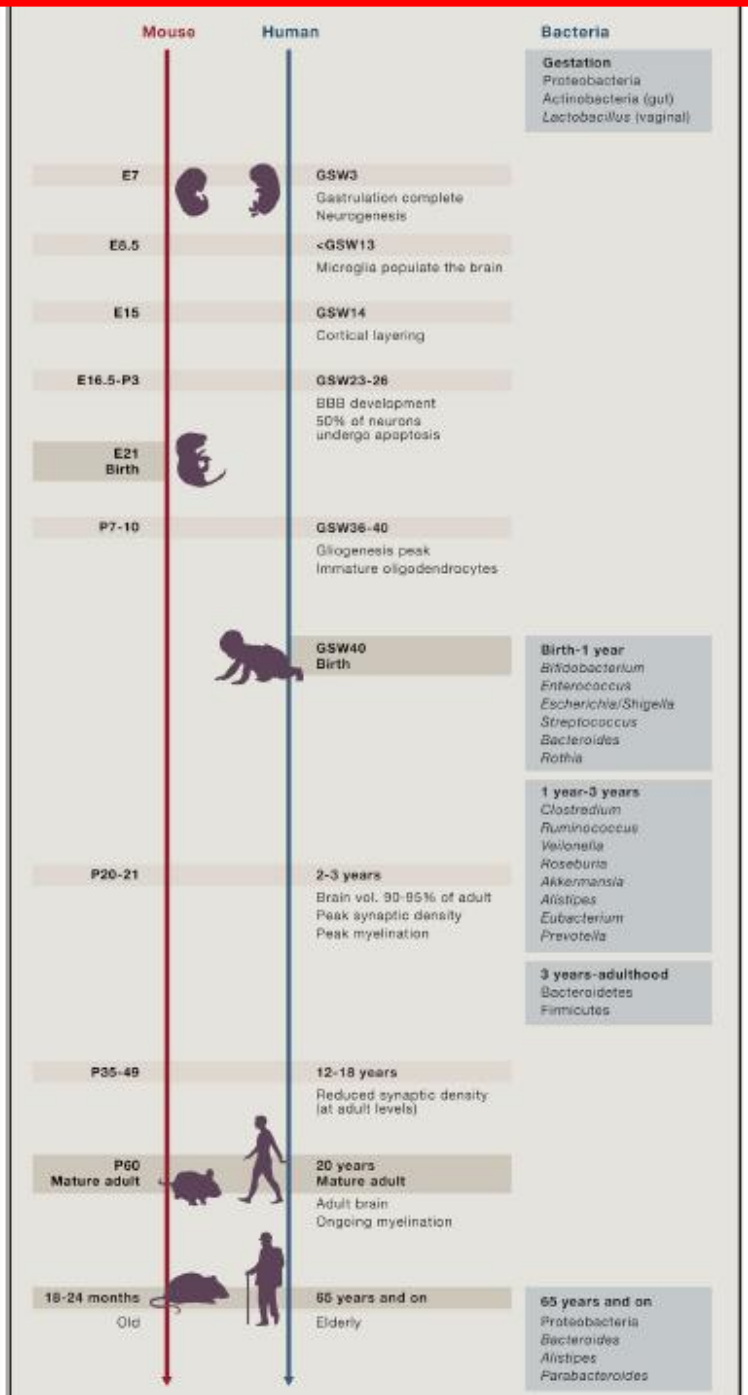
KEYWORDS
Infant; gut microbiota; neurodevelopment; cognition; bacteroidetes; early colonization; birth cohort

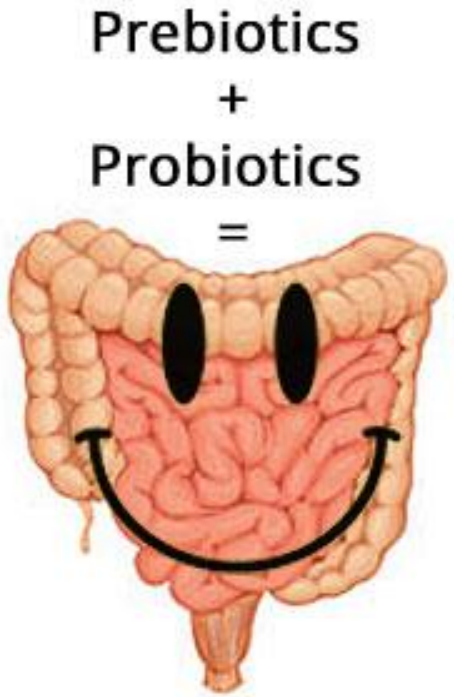


The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

Figure 2. Major Events in Mammalian Brain Development

Developmental trajectories and key neurodevelopmental events in mice and humans (adapted from Knuesel et al., 2014; Pressler and Auvin, 2013; Semple et al., 2013). E, embryonic age; P, postnatal age; GSW, gestational week. Bacterial taxa on the right panel are the dominant ones at each life stage (Bäckhed et al., 2015; Lloyd-Price et al., 2016; Nuriel-Ohayon et al., 2016).



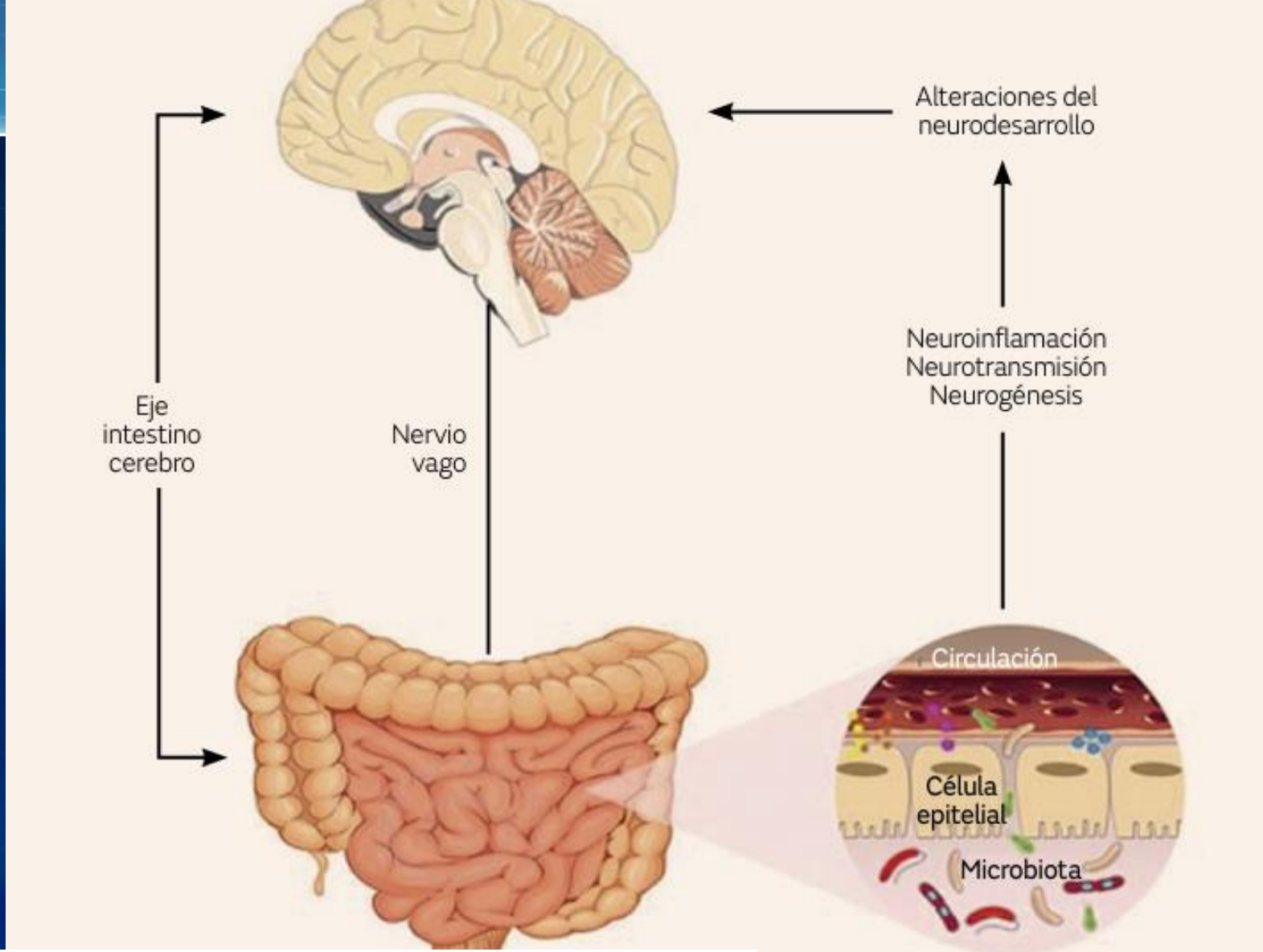


FIGURA 1. Eje intestino-cerebro. Existen varios mecanismos a través de los cuales la disbiosis intestinal puede afectar la función cerebral; estos incluyen el aumento de la permeabilidad intestinal, la producción de citocinas/quimiocinas proinflamatorias, y la síntesis de compuestos tóxicos, neuropéptidos y sus respectivos precursores. La modificación de la permeabilidad permite el paso de todas estas moléculas a la circulación sanguínea y la barrera hematoencefálica. En consecuencia, se genera una posible afectación en procesos de neurogénesis, neurotransmisión y neuroinflamación, lo que originaría alteraciones en el neurodesarrollo (extraída de Richarte et al. 2018[13]).

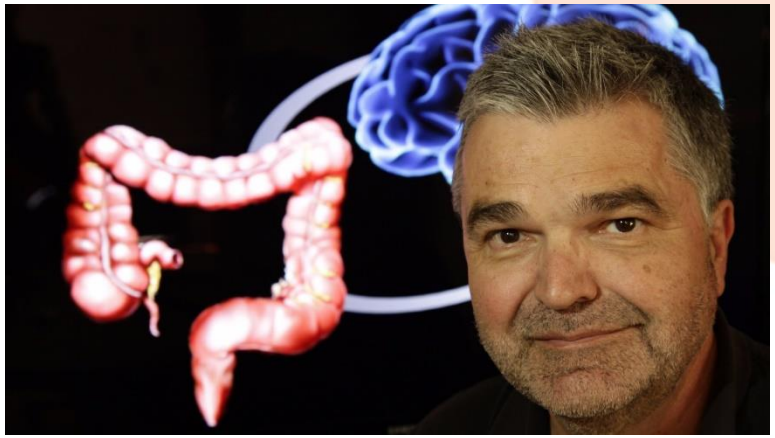
Volume 125 Number 3 March 2015

REVIEW SERIES: ENTERIC NERVOUS SYSTEM

Series Editor: Rodger Liddle

Gut/brain axis and the microbiota

Emeran A. Mayer,[1,2,3,4] Kirsten Tillisch,[1,2,5] and Arpana Gupta[1,2]



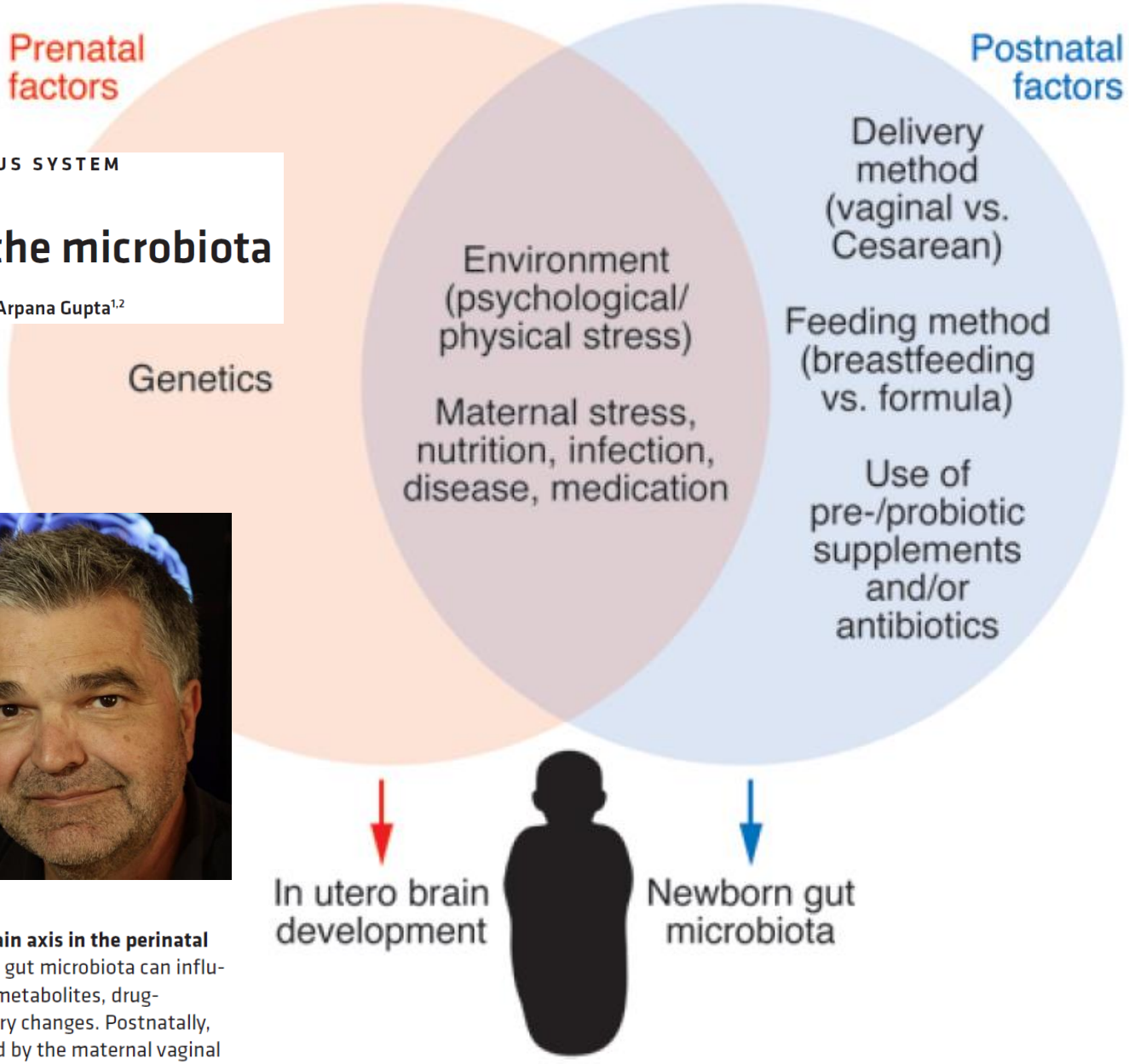


Figure 2. Influences on the gut microbiota/brain axis in the perinatal period. Multiple factors affecting the maternal gut microbiota can influence brain development in utero via microbial metabolites, drug-derived chemical metabolites, and inflammatory changes. Postnatally, the newborn's microbiota is strongly influenced by the maternal vaginal or skin-derived microbiota (depending on the mode of delivery) during birth and by various nutritional factors (breast vs. infant formula feeding).

- *Mientras que los fetos pueden nacer casi desprovistos de bacterias en el útero, el proceso de parto natural asegura que un bebé se expone a la inoculación de una gran complejo de microorganismos.*

- *En circunstancias normales, esta exposición ocurre en el canal de parto de la madre (**lactobacillus**). Sin embargo, durante la cesárea los fetos no son expuestos a la microbiota vaginal pero si a la microbiota de la piel (**Staphylococcus**). Los bebés nacidos por vía vaginal, tienen una mayor abundancia relativa de **Bacteroidetes** y una menor abundancia de Firmicutes que los niños nacidos a través de cesárea.*

- *En los primeros 2-3 años de vida, se da una progresión de la la microbiota intestinal hacia una microbiota de tipo adulto. Cuando se inicia la dieta sólida aumenta la familia de Bacteroidetes.*

- *El género **Bifidobacterium** es numéricamente dominante a lo largo el primer año debido a **la lactancia materna** (con colonización más lenta de los niños alimentados con biberón). Importante no usar antibióticos durante la primera infancia (3 primeros meses) y especialmente en niños prematuros*

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Vol. 29, No. 6, pp 479–481 | Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins

20 Things You Didn't Know About the Human Gut Microbiome

Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN

-Las bacterias intestinales están involucradas en la obtención de energía de los alimentos, funciones metabólicas, inmunológicas y la fabricación de neurotransmisores (5-HT), enzimas y vitaminaS (K2, antihemorrágica).

-El microbioma intestinal de los occidentales que viven en ciudades es menos diverso que el de los que viven en zonas rurales (mayor exposición a las bacterias del suelo y las de los animales). Niños criados con mascotas (perros) tienen menos probabilidad de alergias e infecciones de vías respiratorias (lametones de perros). (Hipótesis de la higiene)

-La microbiota intestinal difiere en obesos vs. delgados y aquellos con la aterosclerosis, diabetes y el síndrome metabólico, pero se sabe poco del sentido de estas diferencias.

Infant pacifier sanitization and risk of challenge-proven food allergy: A cohort study

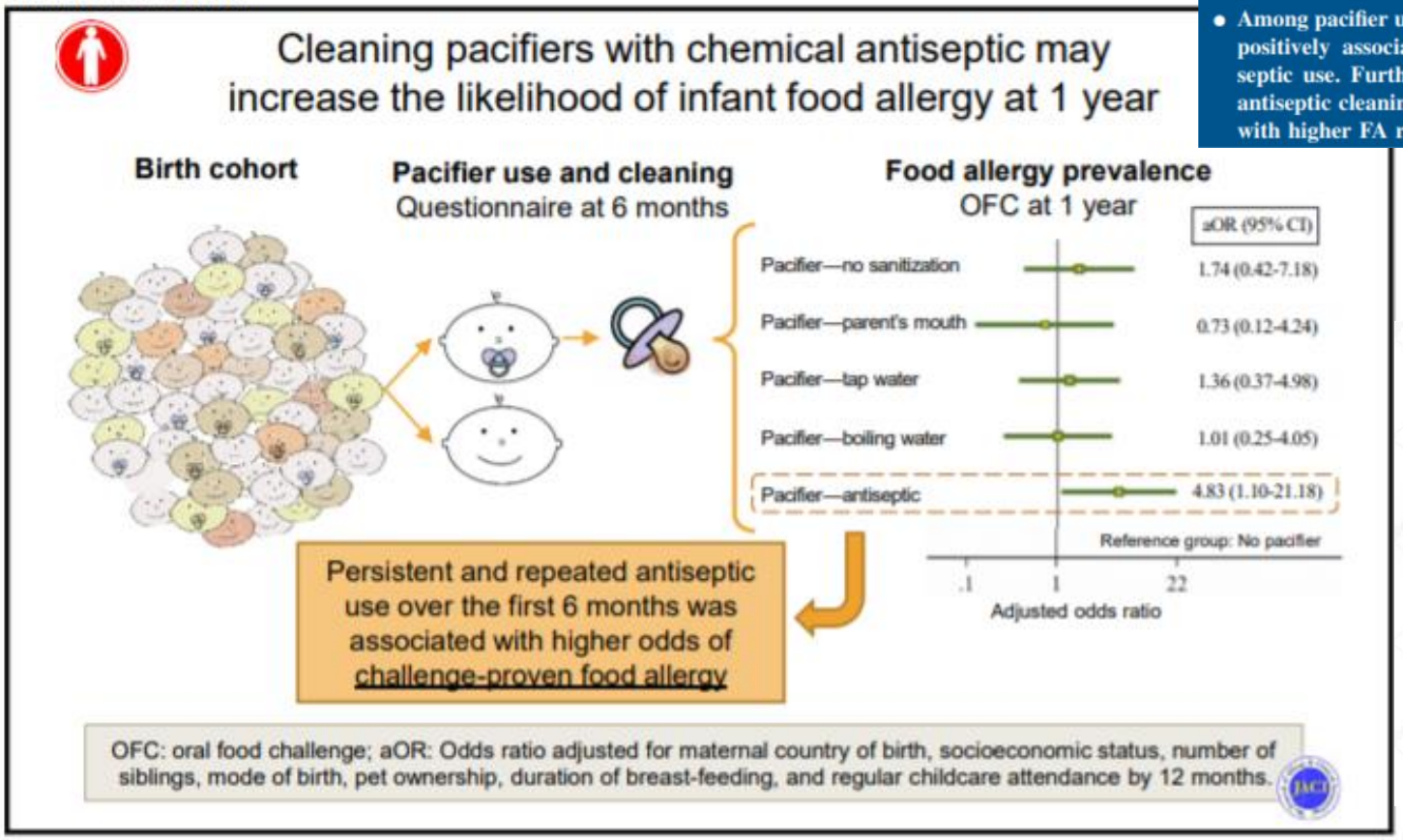
J ALLERGY CLIN IMMUNOL
MAY 2021

Victoria X. Soriano, BSc,[a,b] Jennifer J. Koplin, PhD,[a,b] Mike Forrester, MD,[c,d,e] Rachel L. Peters, PhD,[a,b] Martin O'Hely, PhD,[c,f] Shyamali C. Dharmage, PhD,[g] Rosemary Wright, MPH,[h] Sarath Ranganathan, MD, PhD,[b,f] David Burgner, PhD,[b,f] Kristie Thompson, BSc,[i] Terence Dwyer, MD,[j,k] Peter Vuillerman, PhD,[c,d,f] Anne-Louise Ponsonby, MBBS, PhD,[f,g,l] and the BIS Investigator Group

Parkville, Geelong, Canberra, and Brisbane, Australia; and Oxford, United Kingdom

- Pacifiers sanitized with antiseptic agents at 6 months were a risk factor for subsequent challenge-proven FA in 1-year-old infants.
- Among pacifier users, antiseptic cleaning at 6 months was positively associated with FA, compared with no antiseptic use. Furthermore, persistent and repeated use of antiseptic cleaning over the first 6 months was associated with higher FA risk ($P = .029$).

GRAPHICAL ABSTRACT



MINI REVIEW
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frontiers in Pediatrics

The Prebiotic and Probiotic Properties of Human Milk: Implications for Infant Immune Development and Pediatric Asthma

Shirin Moossavi[1,2,3,4], *Kozeta Miliku*[2,3,5], *Shadi Sepehri*[2], *Ehsan Khafipour*[1,2,6] *and Meghan B. Azad*[2,3,5*]

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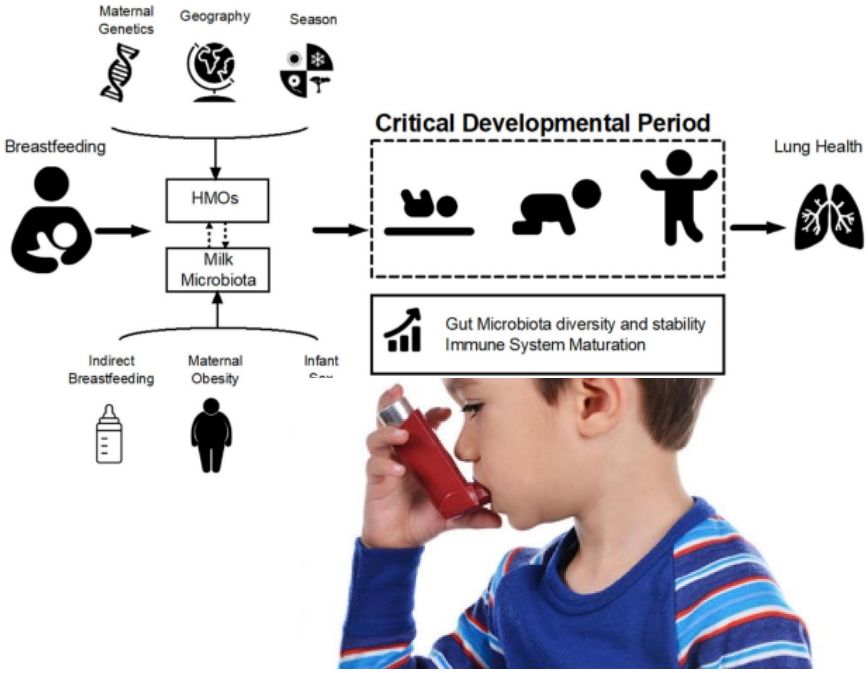
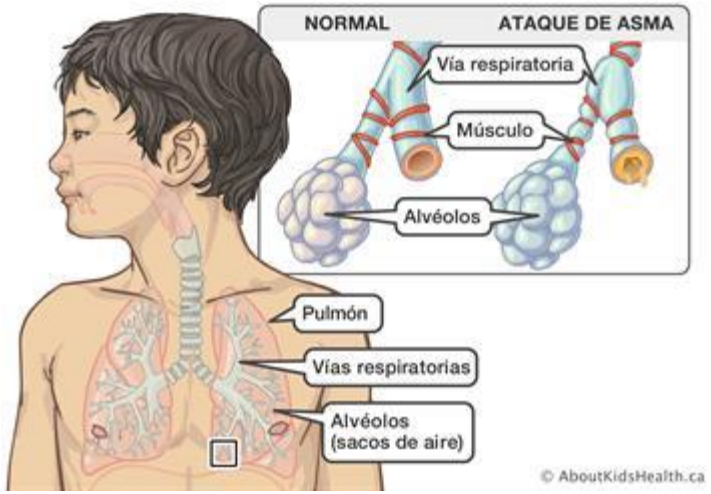
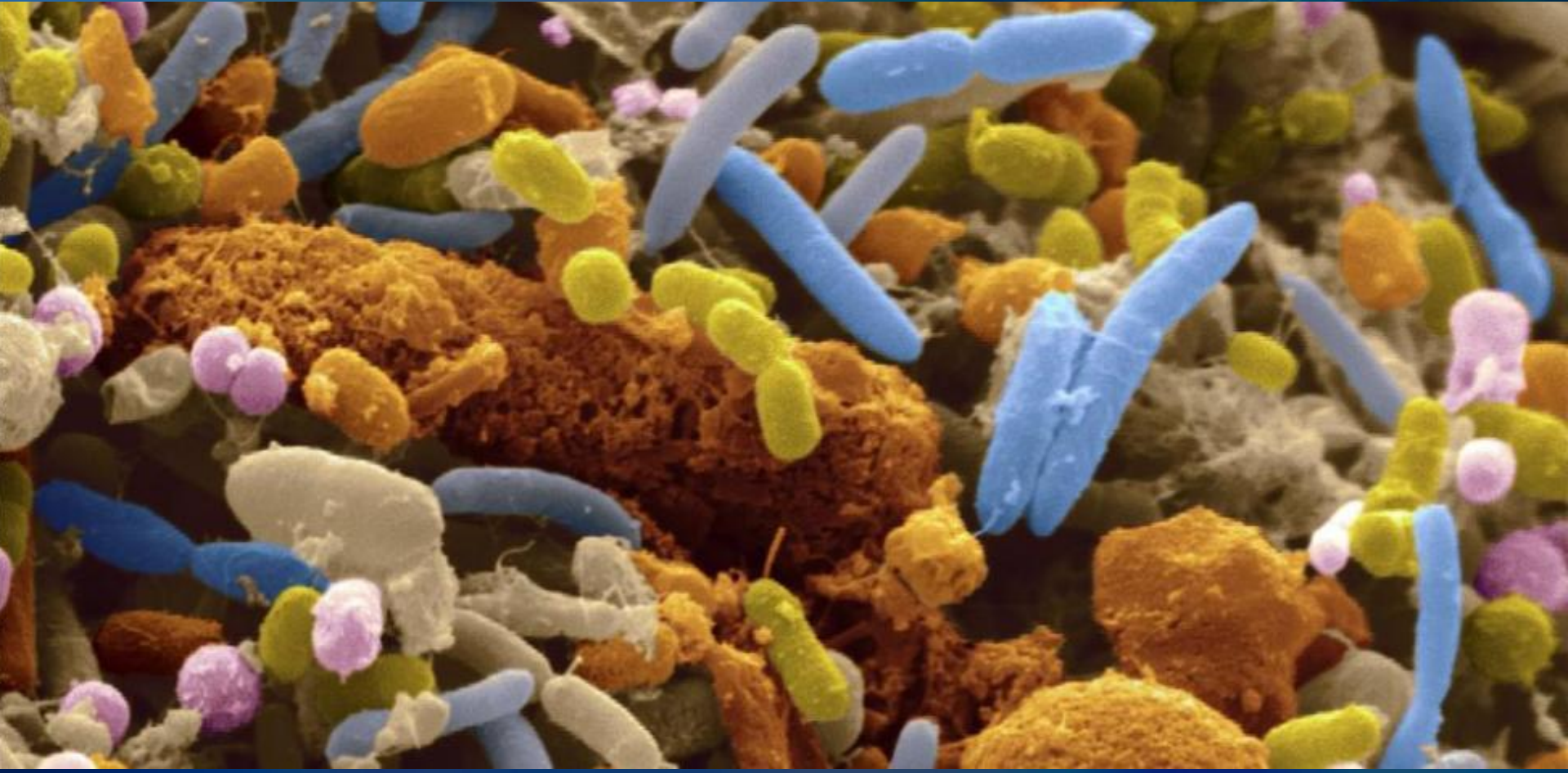


The incidence of pediatric asthma has increased substantially in recent decades, reaching a worldwide prevalence of 14%. This rapid increase may be attributed to the loss of "Old Friend" microbes from the human microbiota resulting in a less diverse and "dysbiotic" gut microbiota, which fails to optimally stimulate immune development during infancy. This hypothesis is supported by observations that the gut microbiota is different in infants who develop asthma later in life compared to those who remain healthy. Thus, early life exposures that influence gut microbiota play a crucial role in asthma development. Breastfeeding is one such exposure; it is generally considered protective against pediatric asthma, although conflicting results have been reported, potentially due to variations in milk composition between individuals and across populations. Human milk oligosaccharides (HMOs) and milk microbiota are two major milk components that influence the infant gut microbiota and hence, development of the immune system. Among their many immunomodulatory functions, HMOs exert a selective pressure within the infant gut microbial niche, preferentially promoting the proliferation of specific bacteria including *Bifidobacteria*. Milk is also a source of viable bacteria originating from the maternal gut and infant oral cavity. As such, breastmilk has prebiotic and probiotic properties that can modulate two of the main forces controlling the gut microbial community assembly, i.e., dispersal and selection. Here, we review the latest evidence, mechanisms and hypotheses for the synergistic and/or additive effects of milk microbiota and HMOs in protecting against pediatric asthma.

Keywords: human milk, microbiota, human milk oligosaccharides, immune development, asthma, pediatrics, probiotic, prebiotic





Breve Historia de los probióticos

Fermented beverages of pre- and proto-historic China

Patrick E. McGovern*†, Juzhong Zhang‡, Jigen Tang§, Zhiqing Zhang¶, Gretchen R. Hall*, Robert A. Moreau‖, Alberto Nuñez‖, Eric D. Butrym, Michael P. Richards††, Chen-shan Wang*, Guangsheng Cheng‡‡, Zhijun Zhao§, and Changsui Wang‡**

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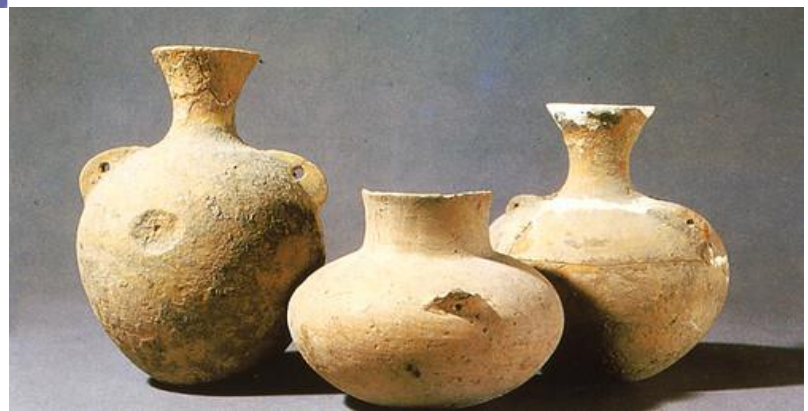
Communicated by Ofer Bar-Yosef, Harvard University, Cambridge, MA, November 16, 2004 (received for review September 30, 2003)

7000 a.C

Chemical analyses of ancient organics absorbed into pottery jars from the early Neolithic village of Jiahu in Henan province in China have revealed that a mixed fermented beverage of rice, honey, and fruit (hawthorn fruit and/or grape) was being produced as early as the seventh millennium before Christ (B.C.). This prehistoric drink paved the way for unique cereal beverages of the proto-historic second millennium B.C., remarkably preserved as liquids inside sealed bronze vessels of the Shang and Western Zhou Dynasties. These findings provide direct evidence for fermented beverages in ancient Chinese culture, which were of considerable social, religious, and medical significance, and help elucidate their earliest descriptions in the Shang Dynasty oracle inscriptions.

archaeological chemistry | Neolithic period | Shang Dynasty | alcohol | saccharification

A much earlier history for fermented beverages in China has long been hypothesized based on the similar shapes and styles of Neolithic pottery vessels to the magnificent Shang Dynasty bronze vessels (8), which were used to present, store, serve, drink, and ritually present fermented beverages during that period. By using a combined chemical, archaeobotanical, and archaeological approach, we present evidence here that ancient Chinese fermented beverage production does indeed extend back nearly nine millennia. Moreover, our analyses of unique liquid samples from tightly lidded bronze vessels, dated to the Shang/Western Zhou Dynasties (*ca.* 1250–1000 B.C.), reveal that refinements in beverage production took place over the ensuing 5,000 years, including the development of a special saccharification (amylolysis) fermentation system (5, 9) in which fungi break down the polysaccharides in rice and millet.



Maixner et al., 2021, Current Biology *31*, 5149–5162

Current Biology

CellPress
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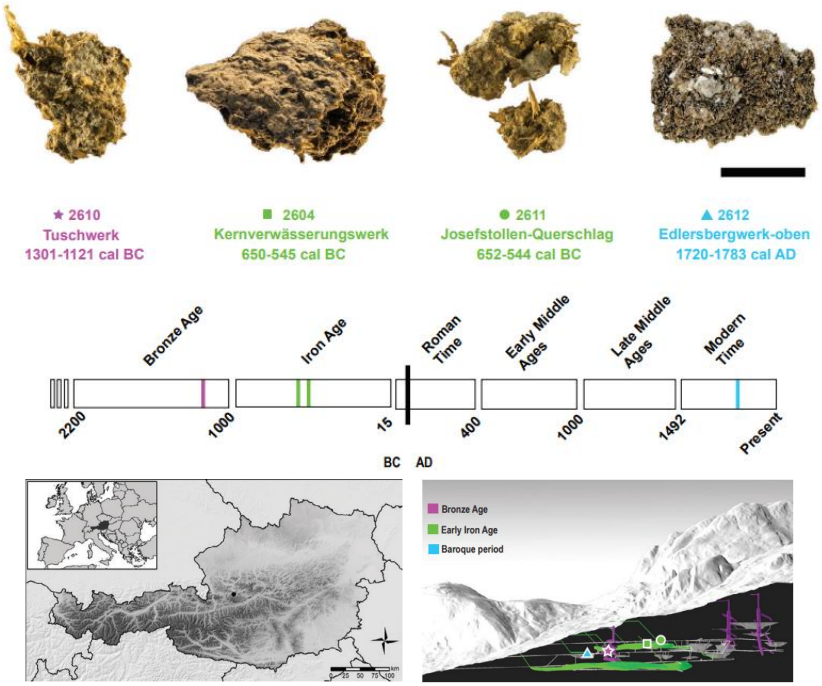
Article

Hallstatt miners consumed blue cheese and beer during the Iron Age and retained a non-Westernized gut microbiome until the Baroque period

Frank Maixner,[1,12,13,16,17,*] Mohamed S. Sarhan,[1,12,16] Kun D. Huang,[2,3,16] Adrian Tett,[2,4] Alexander Schoenafinger,[1,5,12] Stefania Zingale,[1,12] Aitor Blanco-Míguez,[2] Paolo Manghi,[2] Jan Cemper-Kiesslich,[6] Wilfried Rosendahl,[7,8] Ulrike Kusebauch,[9] Seamus R. Morrone,[9] Michael R. Hoopmann,[9] Omar Rota-Stabelli,[10] Thomas Rattei,[4] Robert L. Moritz,[9] Klaus Oeggl,[5] Nicola Segata,[2,14,16] Albert Zink,[1,16] Hans Reschreiter,[11,16] and Kerstin Kowarik[11,15,16,*]



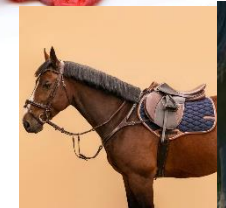
Highlights

- Gut microbiome and diet of European salt miners determined using paleofeces
- Until the Baroque, the microbiome resembled that of modern non-Westernized people
- Food-fermenting fungi in Iron Age feces indicates blue cheese and beer consumption

SUMMARY

We subjected human paleofeces dating from the Bronze Age to the Baroque period (18th century AD) to in-depth microscopic, metagenomic, and proteomic analyses. The paleofeces were preserved in the underground salt mines of the UNESCO World Heritage site of Hallstatt in Austria. This allowed us to reconstruct the diet of the former population and gain insights into their ancient gut microbiome composition. Our dietary survey identified bran and glumes of different cereals as some of the most prevalent plant fragments. This highly fibrous, carbohydrate-rich diet was supplemented with proteins from broad beans and occasionally with fruits, nuts, or animal food products. Due to these traditional dietary habits, all ancient miners up to the Baroque period have gut microbiome structures akin to modern non-Westernized individuals whose diets are also mainly composed of unprocessed foods and fresh fruits and vegetables. This may indicate a shift in the gut community composition of modern Westernized populations due to quite recent dietary and lifestyle changes. When we extended our microbial survey to fungi present in the paleofeces, in one of the Iron Age samples, we observed a high abundance of *Penicillium roqueforti* and *Saccharomyces cerevisiae* DNA. Genome-wide analysis indicates that both fungi were involved in food fermentation and provides the first molecular evidence for blue cheese and beer consumption in Iron Age Europe.

TARTARIA es el nombre por el que se conocía en Europa, desde la Edad Media hasta el siglo XIX, a una gran extensión de tierra del centro y noreste de Asia que iba desde el mar Caspio y los montes Urales hasta el océano Pacífico y que estaba habitada por varios pueblos túrquicos y mongoles, a los que genéricamente llamaba «tártaros» (Siberia, Extremo Oriente ruso, Turquestán, Mongolia, Manchuria y, parte del Tíbet). Desplazamientos rápidos gracias a su dieta probiótica: carne de caballo curada debajo de la montura (ácido láctico del sudor) y yogur de leche de yegua.



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Research

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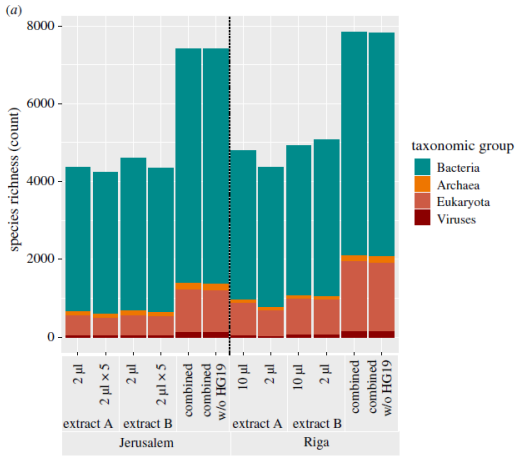
Accepted: 22 July 2020

One contribution of 14 to a theme issue 'Insights into health and disease from ancient biomolecules'.



Estimating molecular preservation of the intestinal microbiome via metagenomic analyses of latrine sediments from two medieval cities

Susanna Sabin[1,2], Hui-Yuan Yeh[3], Aleks Pluskowski[4], Christa Clamer[5], Piers D. Mitchell[6] and Kirsten I. Bos[1]

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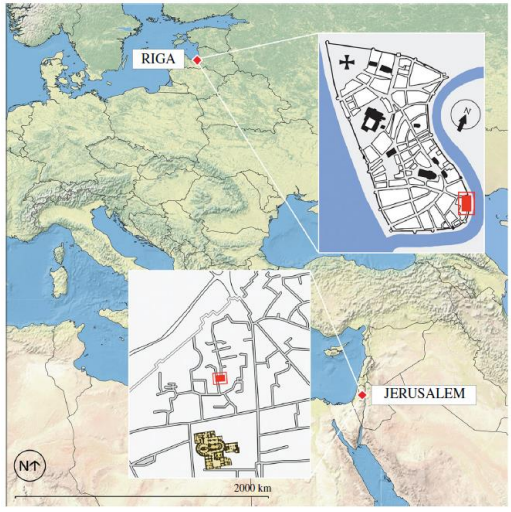
Ancient latrine sediments, which contain the concentrated collective biological waste of past whole human communities, have the potential to be excellent proxies for human gastrointestinal health on the population level. A rich body of literature explores their use to detect the presence of gut-associated eukaryotic parasites through microscopy, immunoassays and genetics. Despite this interest, a lack of studies have explored the whole genetic content of ancient latrine sediments through consideration not only of gut-associated parasites, but also of core community gut microbiome signals that remain from the group that used the latrine. Here, we present a metagenomic analysis of bulk sediment from medieval latrines in Riga (Latvia) and Jerusalem. Our analyses reveal survival of microbial DNA representative of intestinal flora as well as numerous parasites. These data are compared against parasite taxon identifications obtained via microscopy and ELISA techniques. Together, these findings provide a first glimpse into the rich prokaryotic and eukaryotic intestinal flora of pre-industrial agricultural populations, which may give a better context for interpreting the health of modern microbiomes.

This article is part of the theme issue 'Insights into health and disease from ancient biomolecules'.



frontiers in
PUBLIC HEALTH

PERSPECTIVE ARTICLE
published: 13 November 2013
doi: 10.3389/fpubh.2013.00052

Recycling Metchnikoff: probiotics, the intestinal microbiome and the quest for long life

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Probiotics: 100 years (1907-2007) after Elie Metchnikoff's Observation

Kingsley C. Anukam [1,2•] **PhD, MHPM and Gregor Reid** [1,2,3] **PhD, MBA, ARM, CCM**
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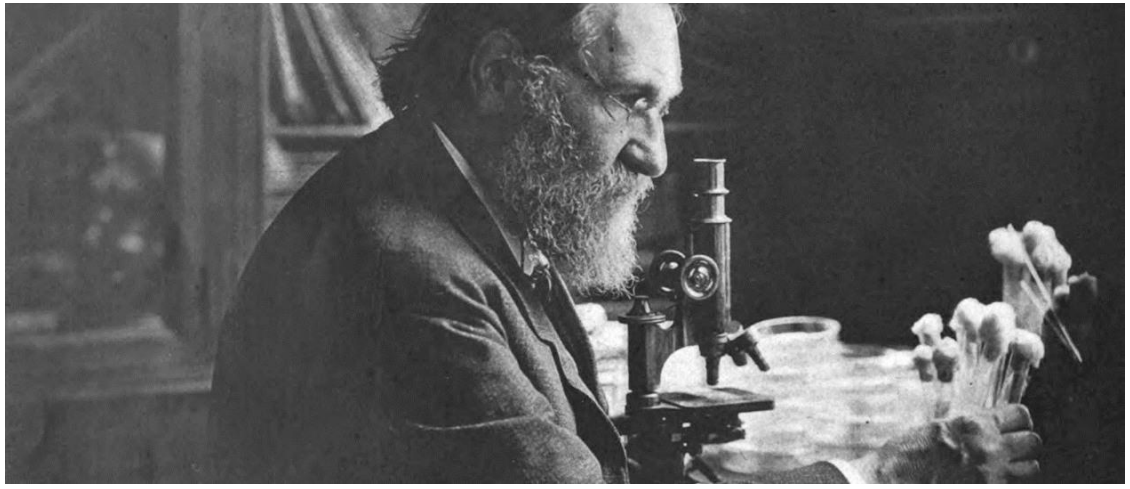
Over a century ago, Elie Metchnikoff theorized that health could be enhanced and senility delayed by manipulating the intestinal microbiome with host-friendly bacteria found in yogurt. His theory flourished for a time, then drifted to the fringe of medical practice before re-emerging in the mid-1990s as a concept worthy of mainstream medical attention. Metchnikoff also predicted the existence of bacterial translocation and anticipated theories linking chronic inflammation with the pathogenesis of atherosclerosis and other disorders of the aged.

Bacterias ácido-lácticas (BAC)

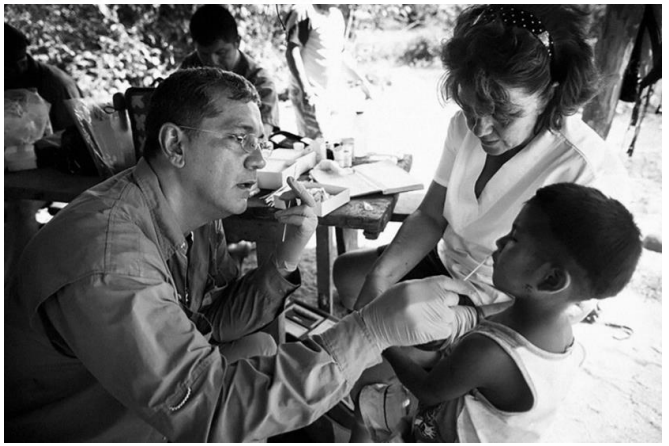


Cell

A Microbial Anthropologist in the Jungle

Cell *167*, October 20, 2016

Maria Gloria Dominguez-Bello



RESEARCH ARTICLE

MICROBIAL ECOLOGY

The microbiome of uncontacted Amerindians

Jose C. Clemente,[1,2]* Erica C. Pehrsson,[3]* Martin J. Blaser,[4,5] Kuldip Sandhu,[5]† Zhan Gao,[5] Bin Wang,[3] Magda Magris,[6] Glida Hidalgo,[6] Monica Contreras,[7] Óscar Noya-Alarcón,[6] Orlana Lander,[8] Jeremy McDonald,[9] Mike Cox,[9] Jens Walter,[10]‡ Phaik Lyn Oh,[10] Jean F. Ruiz,[11] Selena Rodriguez,[11] Nan Shen,[1] Se Jin Song,[12] Jessica Metcalf,[12] Rob Knight,[12,13]§ Gautam Dantas,[3,14] M. Gloria Dominguez-Bello[5,7,11]¶

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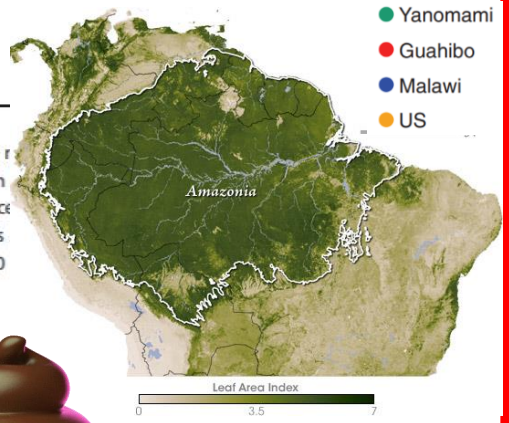

Most studies of the human microbiome have focused on westernized people with life-style practices that decrease microbial survival and transmission, or on traditional societies that are currently in transition to westernization. We characterize the fecal, oral, and skin bacterial microbiome and resistome of members of an isolated Yanomami Amerindian village with no documented previous contact with Western people. These Yanomami harbor a microbiome with the highest diversity of bacteria and genetic functions ever reported in a human group. Despite their isolation, presumably for >11,000 years since their ancestors arrived in South America, and no known exposure to antibiotics, they harbor bacteria that carry functional antibiotic resistance (AR) genes, including those that confer resistance to synthetic antibiotics and are syntenic with mobilization elements. These results suggest that westernization significantly affects human microbiome diversity and that functional AR genes appear to be a feature of the human microbiome even in the absence of exposure to commercial antibiotics. AR genes are likely poised for mobilization and enrichment upon exposure to pharmacological levels of antibiotics. Our findings emphasize the need for extensive characterization of the function of the microbiome and resistome in remote nonwesternized populations before globalization of modern practices affects potentially beneficial bacteria harbored in the human body.

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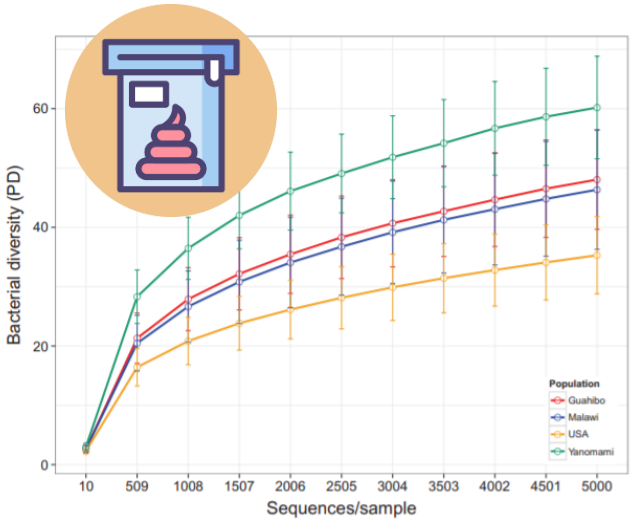

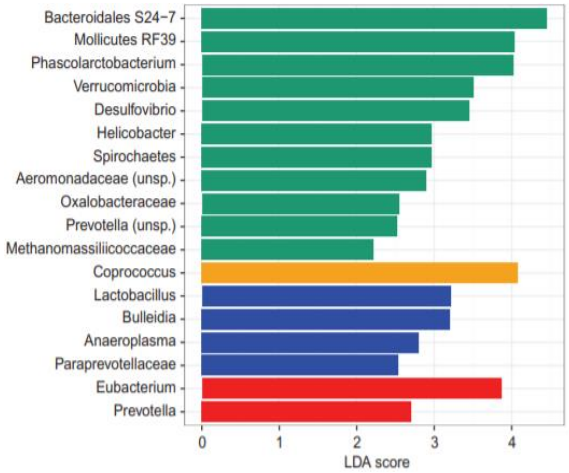

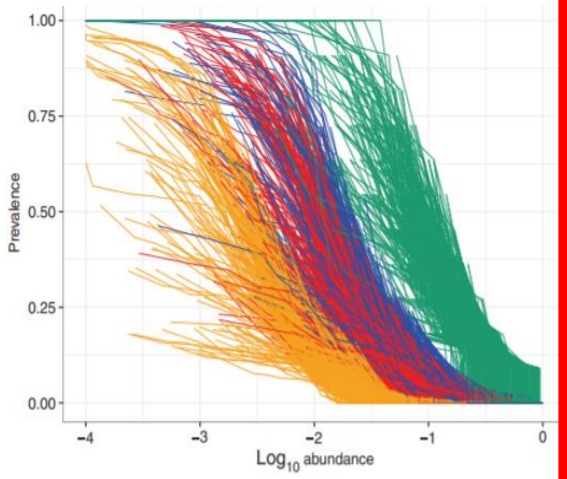

Muere el hombre más sucio del mundo poco después de bañarse por primera vez desde hace más de medio siglo

20MINUTOS / NOTICIA / 26.10.2022 - 10:40H

- Amou Haji, de 94 años, no quería ducharse por miedo a enfermarse.

Journal of Cardiovascular Nursing
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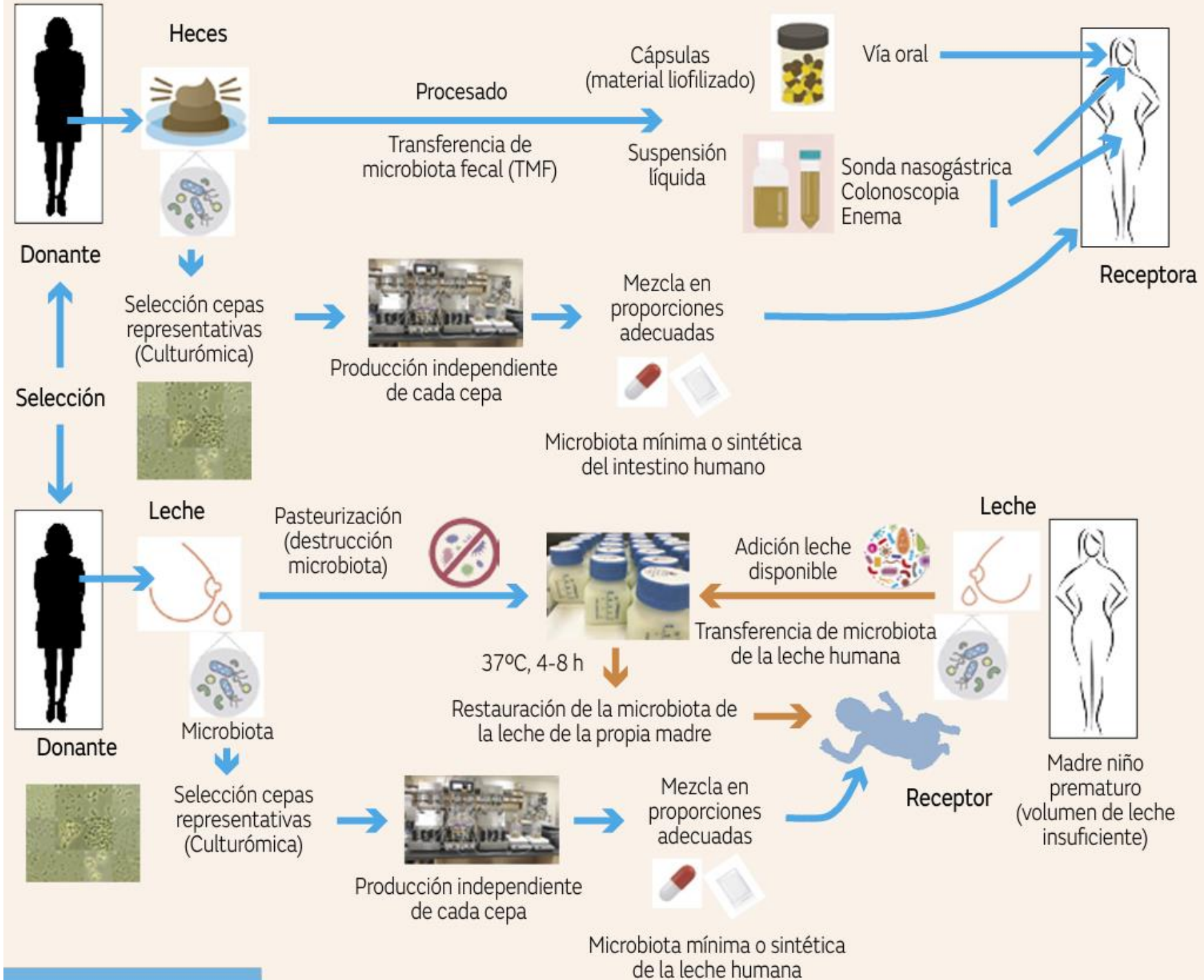
20 Things You Didn't Know About the Human Gut Microbiome

Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN

-Trasplante fecal (1000 años, antigua China) fue publicado por vez primera como terapia en 1958. Es un proceso por el que una muestra fecal de una persona sana se trasplanta (mediante enema, colonoscopia o sonda nasogástrica) a una persona enferma (colonizada por la Clostridium difficile resistente a los antibióticos). Http://www.openbiome.org/

-Trasplantes fecales de personas sanas delgadas mejoran la sensibilidad a la insulina de personas con el síndrome metabólico. En diabetes tipo II la microbiota está alterada y es proinflamatoria (mejora con trasplante fecal).

-Dieta: mayor influencia sobre la microbiota intestinal. Alimentos procesados pueden dañar el revestimiento intestinal y producir una inflamación de bajo grado que contribuyen a diabetes y enfermedades cardiovasculares.
Prebióticos: Alimentos fermentados y con fibra soluble e insoluble promocionan la fermentación de una microbiota sana.


Heces
Donante
Procesado
Transferencia de microbiota fecal (TMF)
Cápsulas (material liofilizado)
Suspensión líquida
Vía oral
Sonda nasogástrica
Colonoscopia
Enema
Receptora
Selección
Selección cepas representativas (Culturómica)
Producción independiente de cada cepa
Mezcla en proporciones adecuadas
Microbiota mínima o sintética del intestino humano
Leche
Donante
Pasteurización (destrucción microbiota)
Adición leche disponible
Leche
Transferencia de microbiota de la leche humana
37ºC, 4-8 h
Restauración de la microbiota de la leche de la propia madre
Microbiota
Receptor
Madre niño prematuro (volumen de leche insuficiente)
Selección cepas representativas (Culturómica)
Producción independiente de cada cepa
Mezcla en proporciones adecuadas
Microbiota mínima o sintética de la leche humana

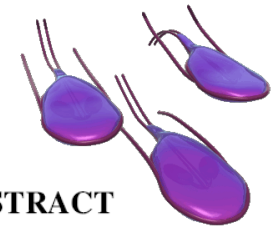
3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

Un banco de heces para combatir una bacteria resistente

El hospital de Bellvitge de Barcelona crea un banco de microbiota fecal para realizar trasplantes en pacientes con infecciones complejas por 'Clostridium difficile'

TRASPLANTES FECALES

Fecal Microbiota Transplantation: Just a Fancy Trend?



*Yvan Vandenplas, †Denis Pierard, and *Elisabeth De Greef

ABSTRACT

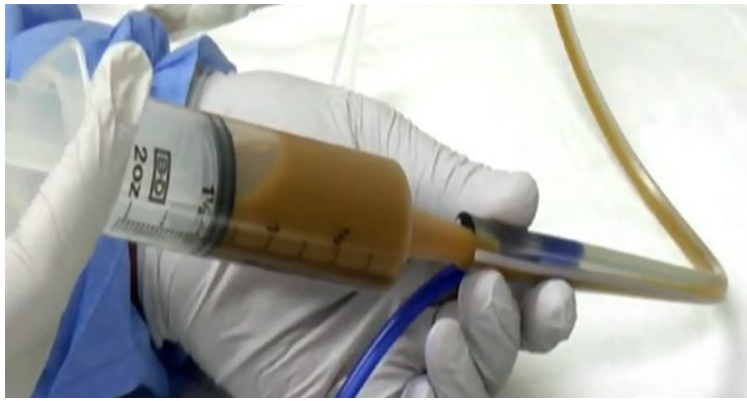
The risks and advantages of the administration of fecal material of healthy people to patients are heavily debated. In adults, recurrent *Clostridium difficile* has become an accepted indication. In addition to all of the possible indications, many other questions need to be answered before pediatric indications and recommendations can be established. Optimal donor selection, fresh versus frozen stools versus capsules containing only microbiota, volume, and route of administration are just a few examples of the areas with missing data to allow in formulating recommendations for fecal microbiota or fecal material administration in children. A careful but not-too-complex regulation is the first priority in order to minimize the risk of administration of fecal slurry from unselected donors at home without medical supervision.

Key Words: *Clostridium difficile*, fecal substance administration, fecal transplant, inflammatory bowel disease, microbial replacement therapy, microbiota

(*JPGN* 2015;61: 4–7)

Bedouins have been giving camel feces to human with dysentery for centuries.

The first publication in recent literature dates back from 1958 in a patient with recurrent *C difficile* in whom the fecal microbiota transplantation (FMT) was given by enema (3). In 2007, it was shown that FMT from a human to germ-free piglets produced a donor-like microbial community with minimal individual variation (4). Two years later, a case series was reported of 15 patients with recurrent *C difficile*–associated diarrhea, of which 11 were cured (5). The first randomized controlled trial was published in 2013 and showed that duodenal infusion of donor feces in patients with recurrent *C difficile* was more than twice as effective in resolving symptoms as antibiotics alone (6). One should not forget that a couple of years earlier a trial with duodenal administration of probiotics in patients with pancreatitis was stopped prematurely, however, because the intervention group was doing much worse than the control group (7).



U.S. FOOD & DRUG ADMINISTRATION

FDA NEWS RELEASE

REBYOTA® (fecal microbiota, live-jslm) suspension, for rectal use

FDA Approves First Fecal Microbiota Product

Rebyota Approved for the Prevention of Recurrence of Clostridioides difficile Infection in Adults

November 30, 2022

Today, the U.S. Food and Drug Administration approved Rebyota, the first fecal microbiota product approved by the agency. Rebyota is approved for the prevention of recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older. It is for use after an individual has completed antibiotic treatment for recurrent CDI.

"Today's approval of Rebyota is an advance in caring for patients who have recurrent *C. difficile* infection," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research. "Recurrent CDI impacts an individual's quality of life and can also potentially be life-threatening. As the first FDA-approved fecal microbiota product, today's action represents an important milestone, as it provides an additional approved option to prevent recurrent CDI."

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20 Things You Didn't Know About the Human Gut Microbiome

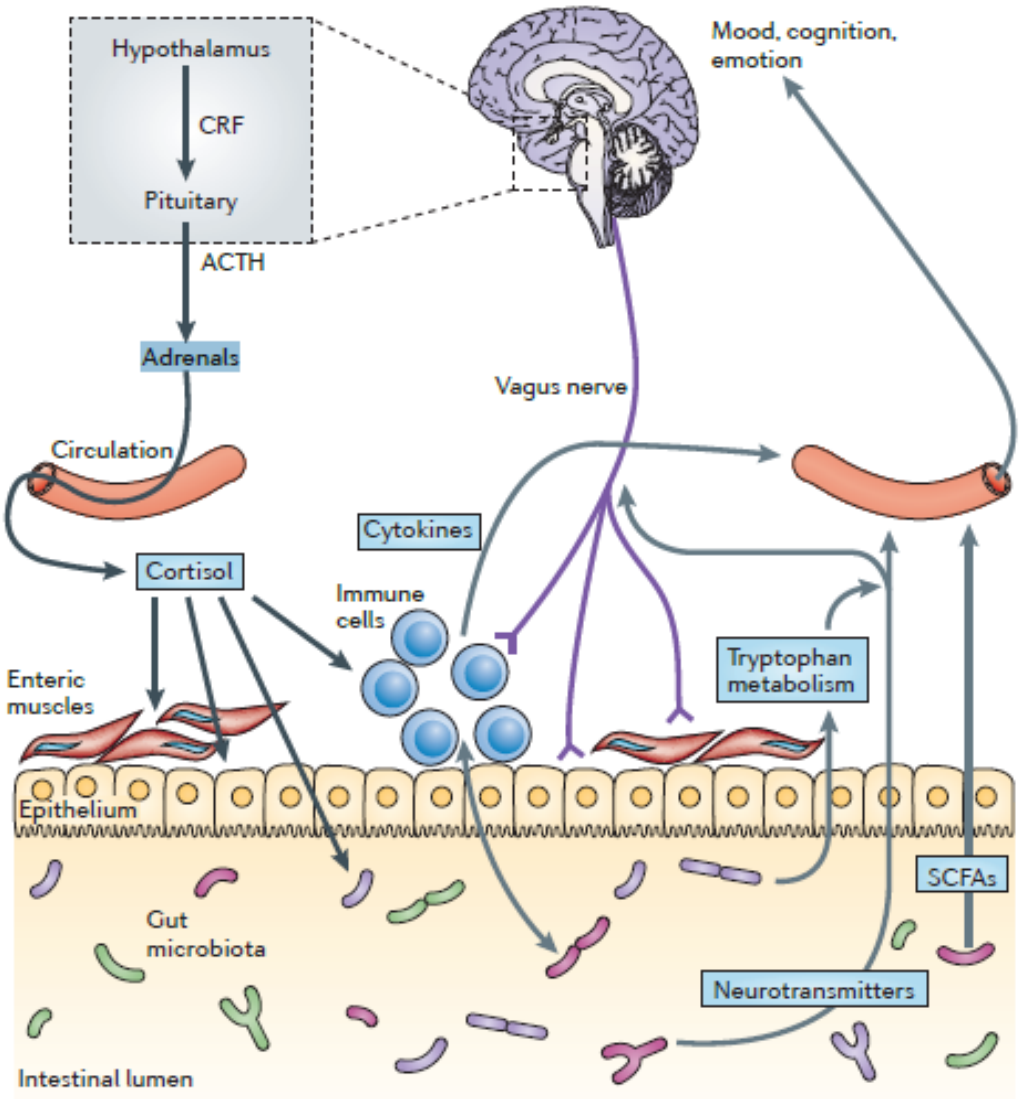
Erin P. Ferranti, PhD, MPH, RN; Sandra B. Dunbar, PhD, RN, FAHA, FAAN; Anne L. Dunlop, MD, MPH; Elizabeth J. Corwin, PhD, RN, FAAN

-Probióticos: Bacterias vivas. Controversia (no se conoce la eficacia de la mayoría de los probióticos de uso comercial, no hay fórmulas estándar o dosificaciones, y algunas fórmulas probióticas incluyen bacterias que pueden ser beneficiosas para algunos problemas pero no otros). La mayoría de especialistas en probióticos no los toman, prefieren prebióticos (dieta variada rica en vegetales frutas con abundante fibra insoluble, alimento para las bacterias y su reproducción).

*-El **envejecimiento** se asocia a una disminución en la diversidad de la microbiota intestinal que correlaciona con el estado nutricional y con las enfermedades inflamatorias.*

-La aterosclerosis está asociada con una microbiota intestinal específica rica en óxido-N-trimetilamina (procedente de componentes de la carne roja como la colina, fosfatidilcolina y la L-carnitina). Nueva área de investigación.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)



Vías involucradas en la comunicación bidireccional entre la microbiota intestinal y el cerebro: *endocrina (cortisol), inmune (citoquinas) y neural (nervio vago y sistema nervioso entérico).*

Cerebro → Microbiota:

Estrés: cortisol → afecta a las células inmunes (secreción de citoquinas) → alteración de la permeabilidad intestinal y la función de la barrera, y cambio la composición de la microbiota intestinal.

Microbiota → cerebro:

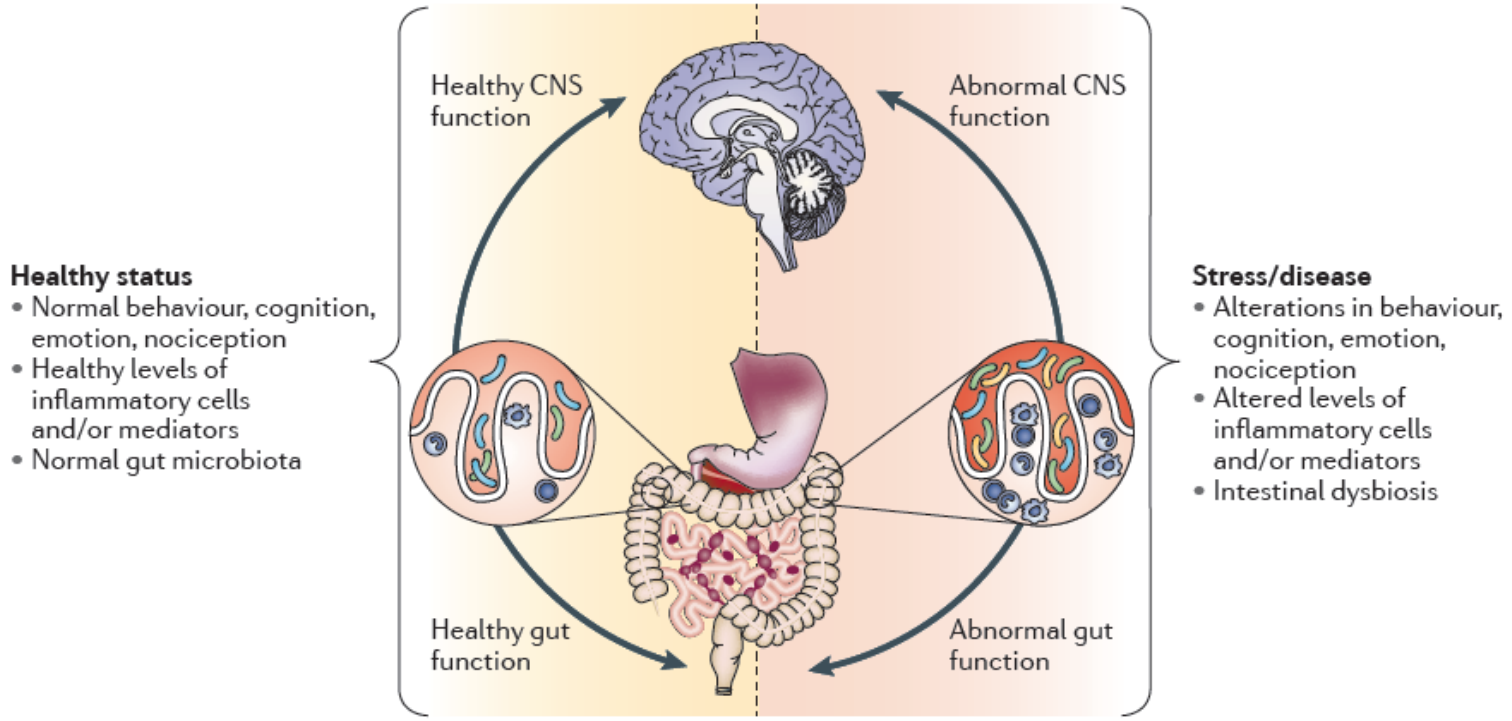
- La microbiota y los agentes probióticos pueden alterar los niveles de citoquinas, lo que afecta a la función cerebral.

- El nervio vago y los niveles de triptófano están fuertemente implicados en la transmisión de la influencia de la microbiota intestinal al cerebro. El 80% de las fibras nerviosas del vago son sensoriales: transmisión de información sobre el estado de los órganos del cuerpo al SNC.

Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

- *La microbiota intestinal estable es esencial para un buen funcionamiento intestinal, y contribuye al funcionamiento apropiado a lo largo del eje intestino-cerebro y, por tanto, al estado saludable de la persona (lado izquierdo).*
- *La disbiosis intestinal puede influir negativamente en el funcionamiento intestinal, dando lugar a una señalización inapropiada del eje intestino-cerebro, asociado a consecuencias para las funciones del SNC que dan lugar a estados de enfermedad (lado derecho)*



3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

Brain, Behavior, and Immunity 38 (2014) 1–12

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Brain, Behavior, and Immunity

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

Invited Review

The role of microbiome in central nervous system disorders

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Neuro-psychiatric disorders

ABSTRACT

Mammals live in a co-evolutionary association with the plethora of microorganisms that reside at a variety of tissue microenvironments. The microbiome represents the collective genomes of these co-existing microorganisms, which is shaped by host factors such as genetics and nutrients but in turn is able to influence host biology in health and disease. Niche-specific microbiome, prominently the gut microbiome, has the capacity to effect both local and distal sites within the host. The gut microbiome has played a crucial role in the bidirectional gut–brain axis that integrates the gut and central nervous system (CNS) activities, and thus the concept of microbiome–gut–brain axis is emerging. Studies are revealing how diverse forms of neuro-immune and neuro-psychiatric disorders are correlated with or modulated by variations of microbiome, microbiota-derived products and exogenous antibiotics and probiotics. The microbiome poises the peripheral immune homeostasis and predisposes host susceptibility to CNS autoimmune diseases such as multiple sclerosis. Neural, endocrine and metabolic mechanisms are also critical mediators of the microbiome–CNS signaling, which are more involved in neuro-psychiatric disorders such as autism, depression, anxiety, stress. Research on the role of microbiome in CNS disorders deepens our academic knowledge about host-microbiome commensalism in central regulation and in practicality, holds conceivable promise for developing novel prognostic and therapeutic avenues for CNS disorders.

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Eje microbiota-intestino-cerebro (SNE)

Review

Trends in Neurosciences May 2013, Vol. 36, No. 5

Cell PRESS

Gut–brain axis: how the microbiome influences anxiety and depression

Jane A. Foster and Karen-Anne McVey Neufeld

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Within the first few days of life, humans are colonized by commensal intestinal microbiota. Here, we review recent findings showing that microbiota are important in normal healthy brain function. We also discuss the relation between stress and microbiota, and how alterations in microbiota influence stress-related behaviors. New studies show that bacteria, including commensal, probiotic, and pathogenic bacteria, in the gastrointestinal (GI) tract can activate neural pathways and central nervous system (CNS) signaling systems. Ongoing and future animal and clinical studies aimed at understanding the microbiota–gut–brain axis may provide novel approaches for prevention and treatment of mental illness, including anxiety and depression.

Overview of the microbiome

Early postnatal life in mammals represents a period of bacterial colonization. Resident or commensal microbiota colonize the mammalian gut shortly after birth and remain there throughout life. In humans, the lower intestine contains 10^{14}–10^{15} bacteria, that is, there are 10–100 times more bacteria in the gut than eukaryotic cells in the human body (10^{13}) [1,7,8]. The presence of commensal microbiota is critical to immune function, nutrient processing, and other aspects of host physiology [9–13]. As we discuss here, microbiota are also important in the function of the CNS.

To understand effectively the role of commensal microbiota in health and disease, we must be able to describe the complex ecology of the microbiome. Recently developed

Article

https://doi.org/10.1038/s41467-022-34504-1

The gut microbiota and depressive symptoms across ethnic groups

nature COMMUNICATIONS

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nature communications

Jos A. Bosch[1,2] ✉, Max Nieuwdorp[3], Aeilko H. Zwinderman[4], Mélanie Deschasaux[4,5], Djawad Radjabzadeh[6], Robert Kraaij[6], Mark Davids[3], Susanne R. de Rooij[4,8] & Anja Lok[7,8]

The gut microbiome is thought to play a role in depressive disorders, which makes it an attractive target for interventions. Both the microbiome and depressive symptom levels vary substantially across ethnic groups. Thus, any intervention for depression targeting the microbiome requires understanding of microbiome-depression associations across ethnicities. Analysing data from the HELIUS cohort, we characterize the gut microbiota and its associations with depressive symptoms in 6 ethnic groups (Dutch, South-Asian Surinamese, African Surinamese, Ghanaian, Turkish, Moroccan; $N = 3211$), living in the same urban area. Diversity of the gut microbiota, both within (α-diversity) and between individuals (β-diversity), predicts depressive symptom levels, taking into account demographic, behavioural, and medical differences. These associations do not differ between ethnic groups. Further, β-diversity explains 29%–18% of the ethnic differences in depressive symptoms. Bacterial genera associated with depressive symptoms belong to mulitple families, prominently including the families *Christensenellaceae, Lachnospiraceae*, and *Ruminococcaceae*. In summary, the results show that the gut microbiota are linked to depressive symptom levels and that this association generalizes across ethnic groups. Moreover, the results suggest that ethnic differences in the gut microbiota may partly explain parallel disparities in depression.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

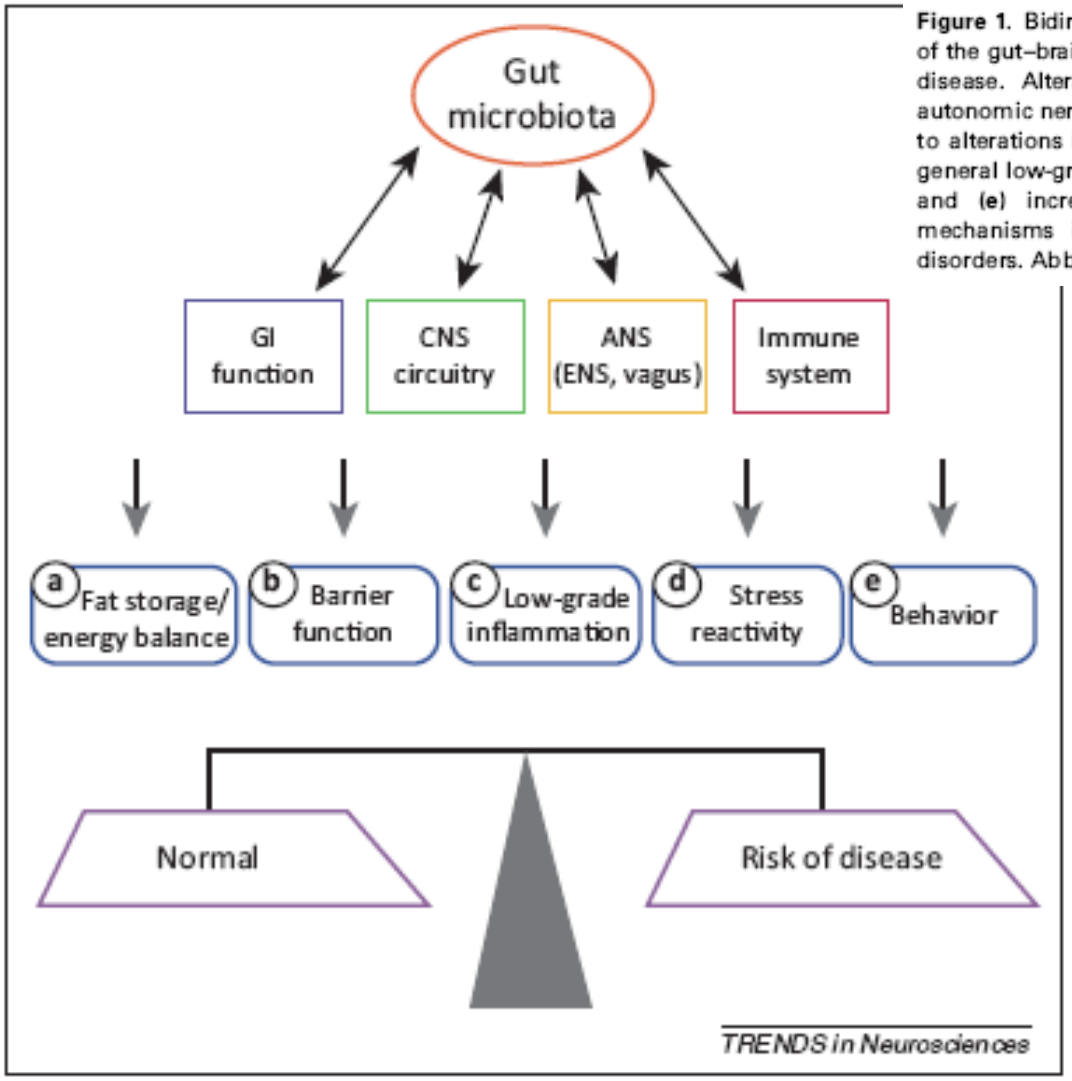

Figure 1. Bidirectional communication between gut microbiota and components of the gut–brain axis influence normal homeostasis and may contribute to risk of disease. Alterations in gastrointestinal (GI), central nervous system (CNS), autonomic nervous system (ANS), and immune systems by microbiota may lead to alterations in **(a)** fat storage and energy balance; **(b)** GI barrier function; **(c)** general low-grade inflammation (GI and systemic); **(d)** increased stress reactivity; and **(e)** increased anxiety and depressive-like behaviors. Each of these mechanisms is implicated in the pathophysiology of mood and anxiety disorders. Abbreviation: ENS, enteric nervous system.

Review

Cell PRESS

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Jane A. Foster and Karen-Anne McVey Neufeld

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Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

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Journal of Psychiatric Research

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

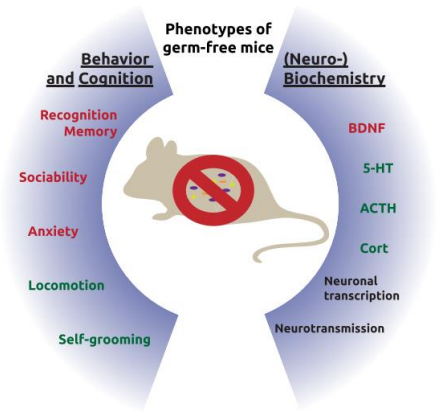
Review

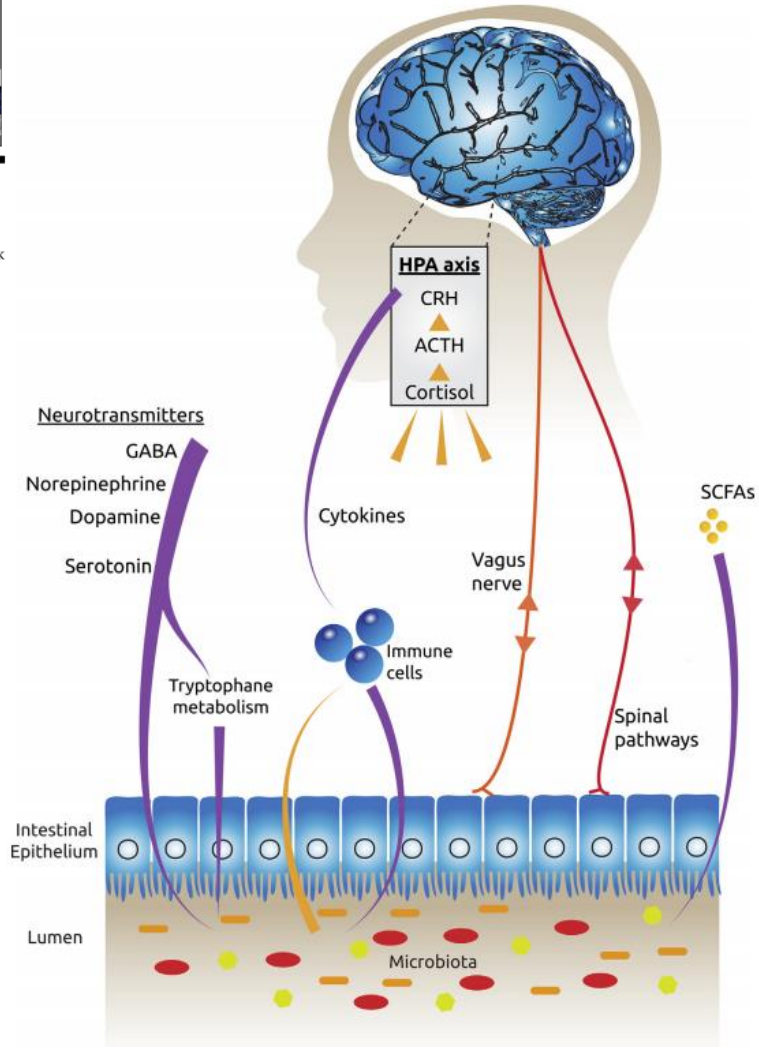
Journal of Psychiatric Research 63 (2015) 1–9

Collective unconscious: How gut microbes shape human behavior

Timothy G. Dinan [a, b, *], Roman M. Stilling [a, d], Catherine Stanton [a, b, c], John F. Cryan [a, d]

The human gut harbors a dynamic and complex microbial ecosystem, consisting of approximately 1 kg of bacteria in the average adult, approximately the weight of the human brain. The evolutionary formation of a complex gut microbiota in mammals has played an important role in enabling brain development and perhaps sophisticated social interaction. Genes within the human gut microbiota, termed the microbiome, significantly outnumber human genes in the body, and are capable of producing a myriad of neuroactive compounds. Gut microbes are part of the unconscious system regulating behavior. Recent investigations indicate that these microbes majorly impact on cognitive function and fundamental behavior patterns, such as social interaction and stress management. In the absence of microbes, underlying neurochemistry is profoundly altered. Studies of gut microbes may play an important role in advancing understanding of disorders of cognitive functioning and social interaction, such as autism.





Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

INMUNOLOGÍA

Microbiota intestinal y depresión

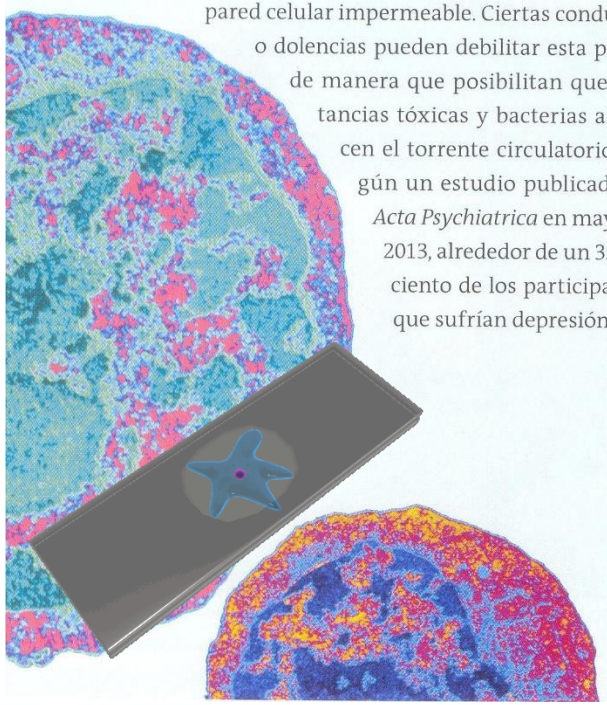
Los microorganismos fugados del tracto digestivo pueden alterar el estado de ánimo

Abundan cada vez más indicios de que el cerebro y el tracto digestivo se encuentran crucialmente vinculados, y de que la dieta y las bacterias intestinales pueden influir en nuestra conducta, pensamiento y estado anímico. En una investigación reciente se han hallado pruebas de translocación bacteriana o «permeabilidad intestinal» en personas con depresión.

El sistema digestivo se encuentra revestido por una pared celular impermeable. Ciertas conductas o dolencias pueden debilitar esta pared, de manera que posibilitan que sustancias tóxicas y bacterias alcancen el torrente circulatorio. Según un estudio publicado en *Acta Psychiatrica* en mayo de 2013, alrededor de un 35 por ciento de los participantes que sufrían depresión presentaban también signos de permeabilidad intestinal, situación que se había detectado previamente a través de un análisis de sangre.

Se ignora todavía la relación entre permeabilidad y depresión, aunque trabajos anteriores ofrecen algunas pistas. Las bacterias desplazadas pueden activar respuestas autoinmunitarias e inflamación, que se sabe están asociadas con la aparición de depresión, decaimiento y cansancio. Michael Maes, autor del artículo e investigador en psiquiatría con afiliaciones en Australia y Tailandia, asegura: «un intestino permeable puede aumentar la inflamación en pacientes deprimidos». De no recibir tratamiento, ello podría exacerbar su sintomatología. En la actualidad, si los cambios en la dieta y la modificación de la conducta no resultan eficaces, la permeabilidad intestinal se trata con una combinación de glutamato, N-acetilcisteína y zinc, sustancias que poseen, se cree, propiedades antiinflamatorias o antioxidantes.

—Tori Rodriguez

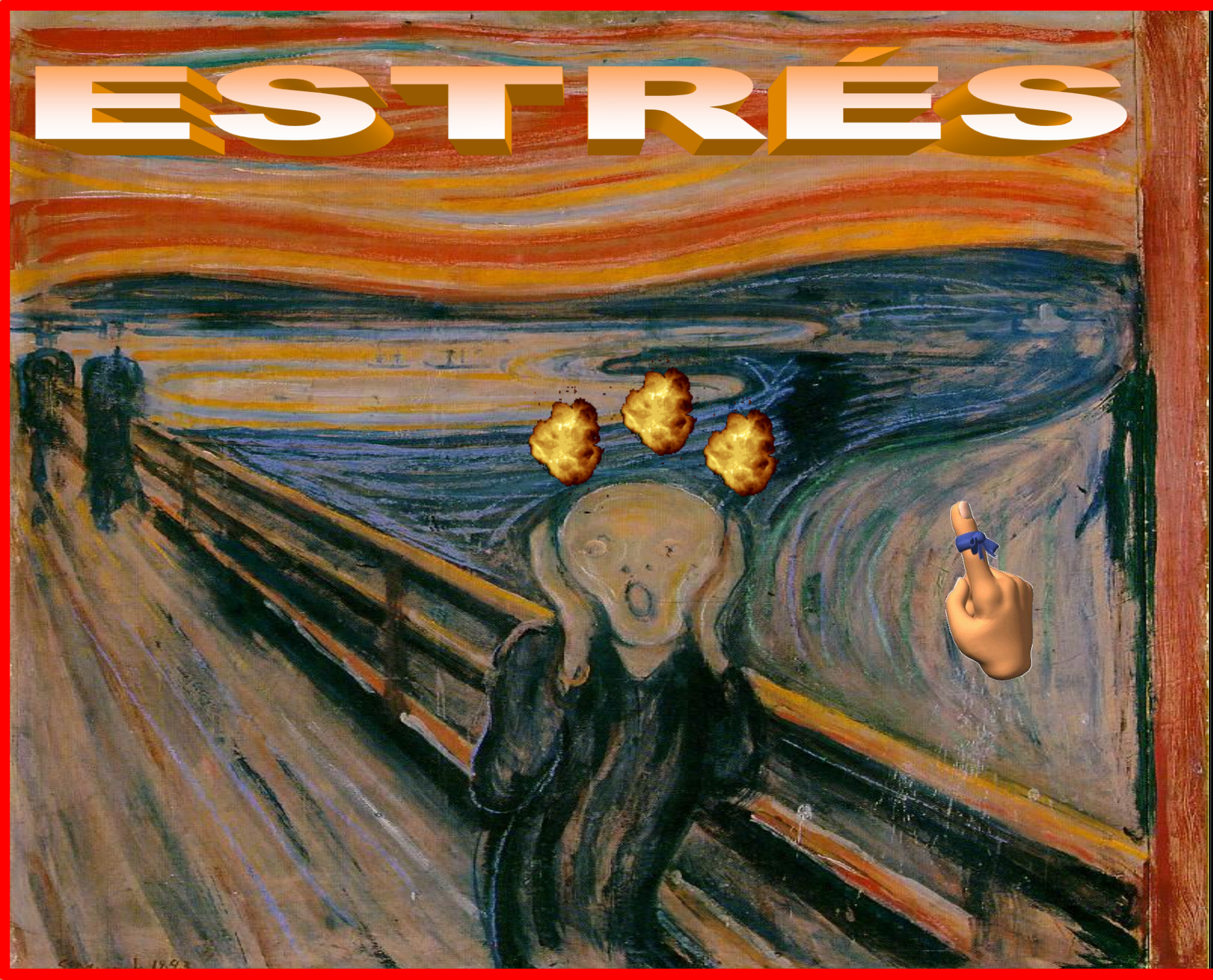


Causas de permeabilidad intestinal

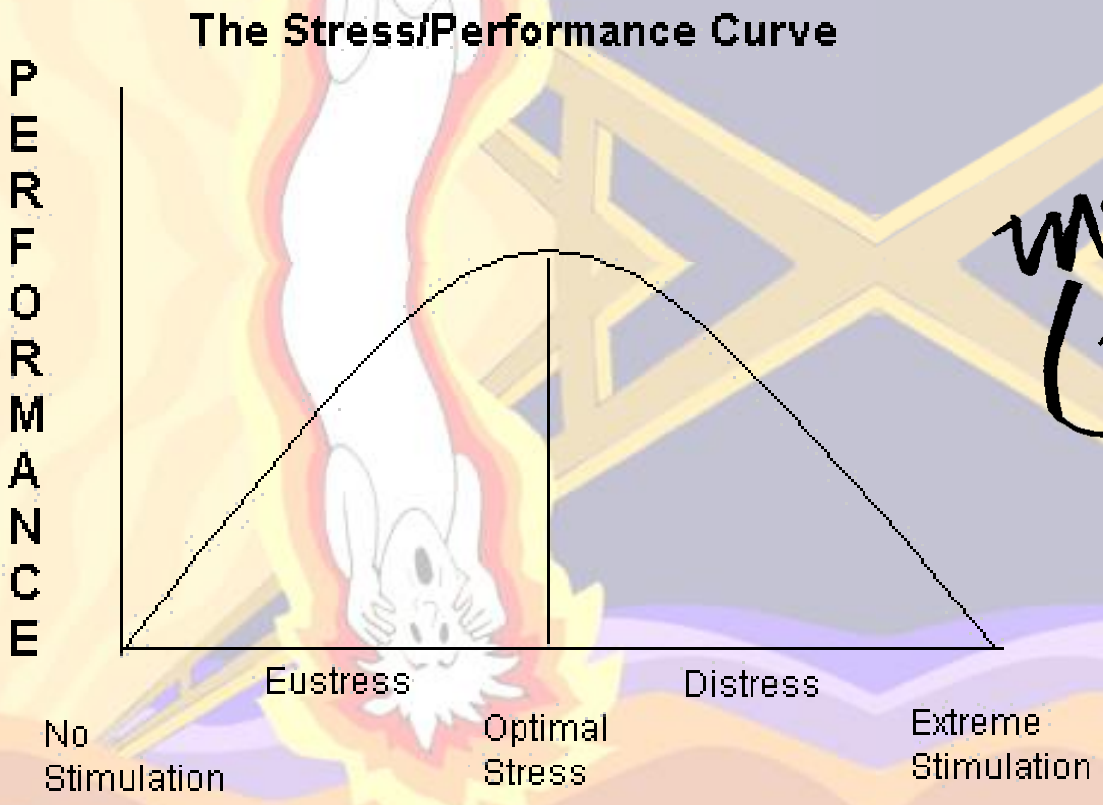
- Uso habitual de analgésicos
- Uso habitual de antibióticos
- Infecciones (como el VIH)
- Enfermedades autoinmunitarias
- Abuso del alcohol
- Enfermedad inflamatoria intestinal
- Hipersensibilidad al gluten
- Alergias alimentarias graves
- Tratamientos por radiación
- Trastornos inflamatorios
- Estrés psicológico
- Agotamiento

Eje microbiota-intestino-cerebro (SNE)

ESTRÉS



Curva de estrés-rendimiento



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Psychoneuroendocrinology (2012) 37, 1369—1378

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

REVIEW

Regulation of the stress response by the gut microbiota: Implications for psychoneuroendocrinology

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Received 1 February 2012; received in revised form 7 March 2012; accepted 7 March 2012

KEYWORDS
Brain—gut axis;
Microbiota;
HPA;
Probiotics;
Germ-free;
Stress;
Novel psychotropics

Summary There is now an expanding volume of evidence to support the view that commensal organisms within the gut play a role in early programming and later responsivity of the stress system. The gut is inhabited by 10^{13}—10^{14} micro-organisms, which is ten times the number of cells in the human body and contains 150 times as many genes as our genome. It has long been recognised that gut pathogens such as *Escherichia coli*, if they enter the gut can activate the HPA. However, animals raised in a germ-free environment show exaggerated HPA responses to psychological stress, which normalises with monocolonisation by certain bacterial species including *Bifidobacterium infantis*. Moreover, increased evidence suggests that animals treated with probiotics have a blunted HPA response. Stress induces increased permeability of the gut allowing bacteria and bacterial antigens to cross the epithelial barrier and activate a mucosal immune response, which in turn alters the composition of the microbiome and leads to enhanced HPA drive. Increasing data from patients with irritable bowel syndrome and major depression indicate that in these syndromes alteration of the HPA may be induced by increased gut permeability. In the case of irritable bowel syndrome the increased permeability can respond to probiotic therapy. Detailed prospective studies in patients with mood disorders examining the gut microbiota, immune parameters and HPA activity are required to throw further light on this emerging area. It is however clear that the gut microbiota must be taken into account when considering the factors regulating the HPA.
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Eje microbiota-intestino-cerebro (SNE)

Review

Trends in Neurosciences May 2013, Vol. 36, No. 5

Gut–brain axis: how the microbiome influences anxiety and depression

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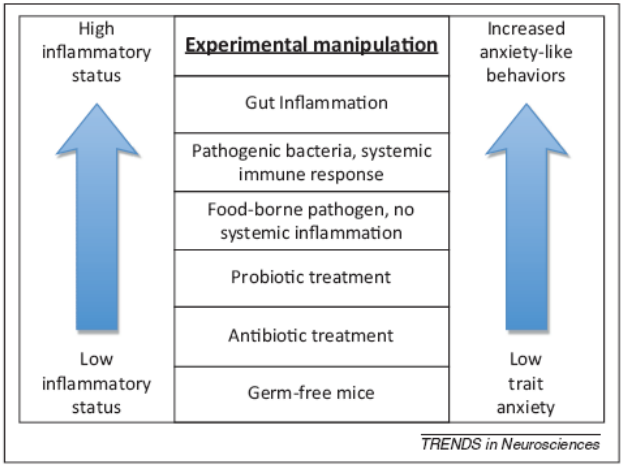


- *La dieta afecta al microbioma y a los sistemas de neurotransmisión y por lo tanto cómo se siente, (capacidad para manejar el estrés y sus niveles de energía).*
- *Cambios en la dieta durante el siglo pasado (agricultura industrial, uso de pesticidas y herbicidas degradación de los nutrientes en los alimentos) están detrás de la depresión y ansiedad*
- *La inflamación intestinal de bajo grado y el estrés oxidativo afecta a los neurotransmisores* ***dopamina, norepinefrina y serotonina****, que controlan el estado de ánimo.*
- *La salud intestinal deficiente contribuye a los problemas del estado de ánimo, y altas cantidades de estrés también causa daños en el intestino y el equilibrio hormonal.*

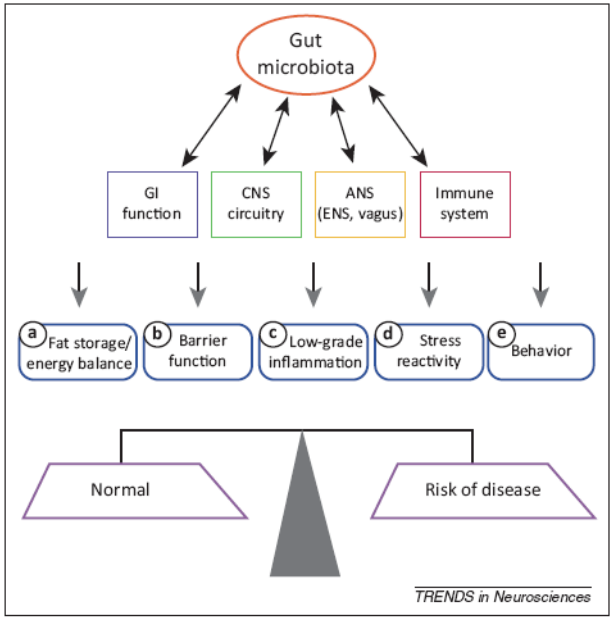
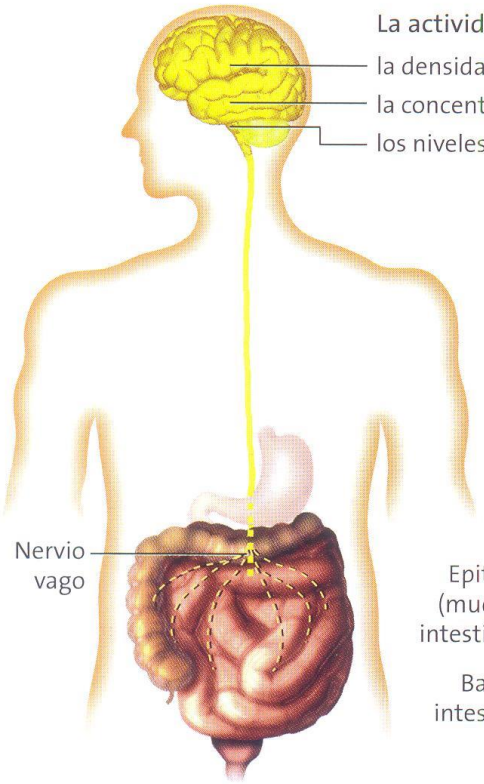
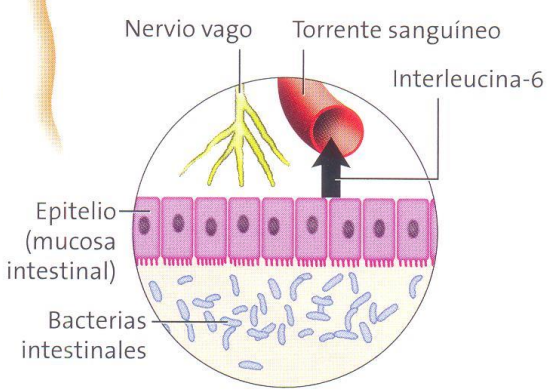
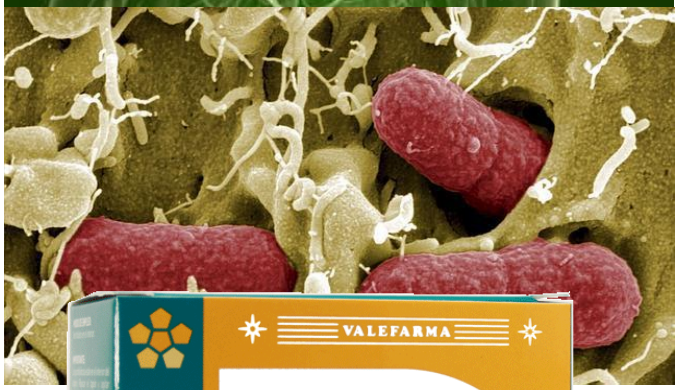


Figure 1. Bidirectional communication between gut microbiota and components of the gut–brain axis influence normal homeostasis and may contribute to risk of disease. Alterations in gastrointestinal (GI), central nervous system (CNS), autonomic nervous system (ANS), and immune systems by microbiota may lead to alterations in **(a)** fat storage and energy balance; **(b)** GI barrier function; **(c)** general low-grade inflammation (GI and systemic); **(d)** increased stress reactivity; and **(e)** increased anxiety and depressive-like behaviors. Each of these mechanisms is implicated in the pathophysiology of mood and anxiety disorders. Abbreviation: ENS, enteric nervous system.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO







EL NERVIO COMO INTERMEDIARIO

La experimentación con animales ha revelado que las bacterias intestinales transmiten señales al cerebro a través del nervio vago. Los aditivos probióticos alimentarios modifican la concentración de los factores de crecimiento, los mensajeros cerebrales y sus receptores, así como la concentración sanguínea de la interleucina 6.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

REVIEW

Regulation of the stress response by the gut microbiota: Implications for psychoneuroendocrinology

Timothy G. Dinan*, John F. Cryan

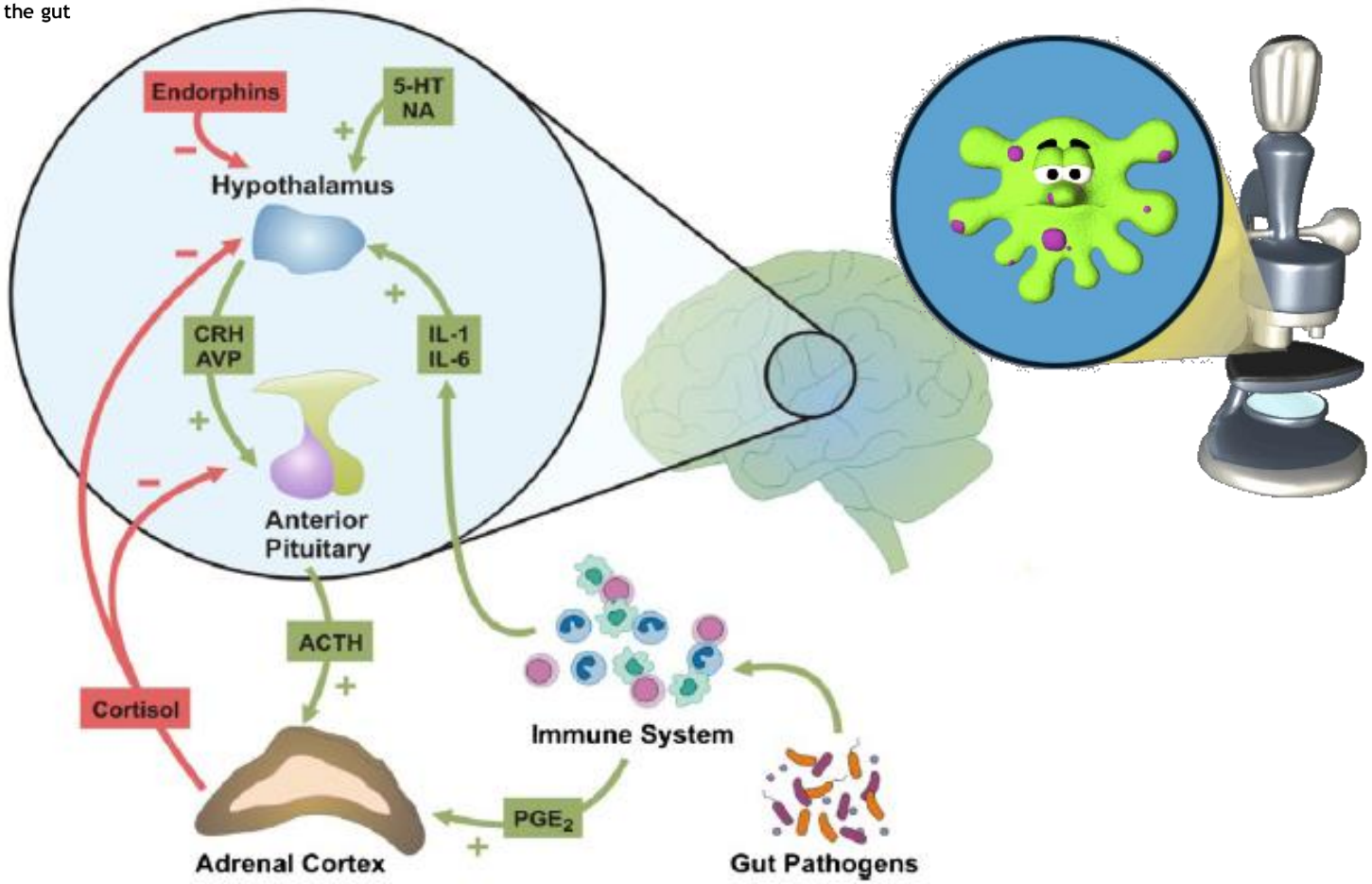


Figure 1 At a hypothalamic level classic neurotransmitters and cytokines regulate corticotrophin releasing hormone (CRH) and vasopressin (AVP) release into the portal vasculature. A series of negative feedback loops controls the forward drive. The adrenal cortex can be directly activated by PGE2 from the immune system stimulated by gut pathogens.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

REVIEW

Regulation of the stress response by the gut microbiota: Implications for psychoneuroendocrinology

Timothy G. Dinan*, John F. Cryan

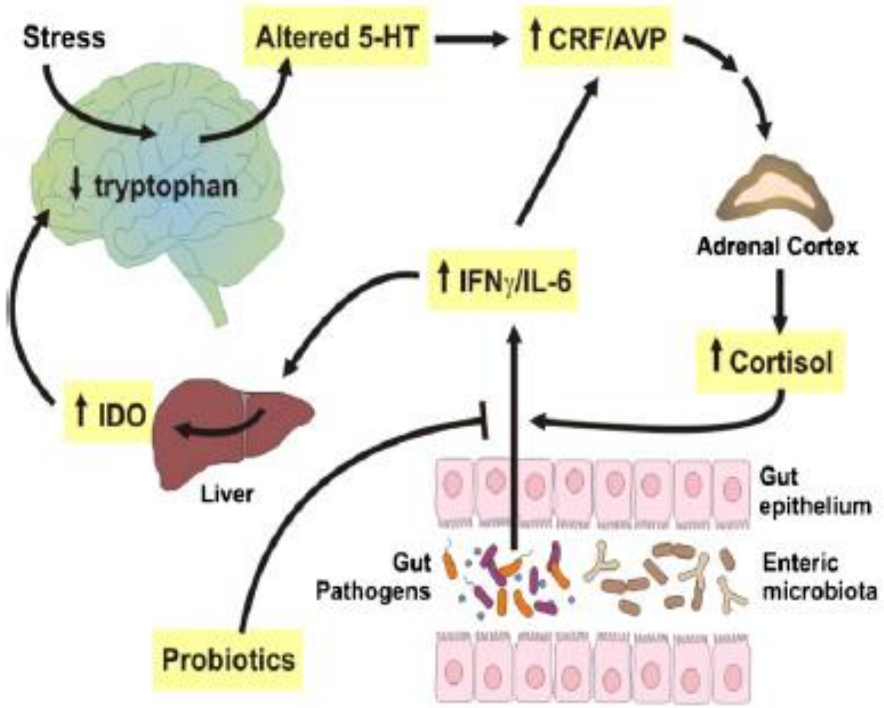


Figure 2 Stress can alter barrier function in the gut increasing gut 'leakiness' and leading to an increase in pro-inflammatory cytokines which in turn can alter indoleamine 2,3-dioxygenase (IDO) activity. This leads to altered tryptophan availability. Pro-inflammatory cytokines such as IL-1 and IL-6 together with 5-HT influence the release of CRF and AVP from the paraventricular nucleus of the hypothalamus. Certain probiotic bacteria can alter gut barrier function and via the vagus may impact on key central neurotransmitter systems.

Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

Contents lists available at ScienceDirect

Neurobiology of Stress

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

Neurobiology of Stress 7 (2017) 124–136

Stress & the gut-brain axis: Regulation by the microbiome

Jane A. Foster [a], Linda Rinaman [b, *], John F. Cryan [c, d]

[a] Department of Psychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada
[b] Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA, United States
[c] APC Microbiome Institute, University College Cork, Cork, Ireland
[d] Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

The importance of the gut–brain axis in regulating stress-related responses has long been appreciated. More recently, the microbiota has emerged as a key player in the control of this axis, especially during conditions of stress provoked by real or perceived homeostatic challenge. Diet is one of the most important modifying factors of the microbiota-gut-brain axis. The routes of communication between the microbiota and brain are slowly being unravelled, and include the vagus nerve, gut hormone signaling, the immune system, tryptophan metabolism, and microbial metabolites such as short chain fatty acids. The importance of the early life gut microbiota in shaping later health outcomes also is emerging. Results from preclinical studies indicate that alterations of the early microbial composition by way of antibiotic exposure, lack of breastfeeding, birth by Caesarean section, infection, stress exposure, and other environmental influences - coupled with the influence of host genetics - can result in long-term modulation of stress-related physiology and behaviour. The gut microbiota has been implicated in a variety of stress-related conditions including anxiety, depression and irritable bowel syndrome, although this is largely based on animal studies or correlative analysis in patient populations. Additional research in humans is sorely needed to reveal the relative impact and causal contribution of the microbiome to stress-related disorders. In this regard, the concept of psychobiotics is being developed and refined to encompass methods of targeting the microbiota in order to positively impact mental health outcomes. At the 2016 Neurobiology of Stress Workshop in Newport Beach, CA, a group of experts presented the symposium "The Microbiome: Development, Stress, and Disease". This report summarizes and builds upon some of the key concepts in that symposium within the context of how microbiota might influence the neurobiology of stress.

Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

Neurobiology of Stress 4 (2016) 23–33

Contents lists available at ScienceDirect

Neurobiology of Stress

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

The microbiome: A key regulator of stress and neuroinflammation

Kieran Rea [a], Timothy G. Dinan [a, b], John F. Cryan [a, c, *]

There is a growing emphasis on the relationship between the complexity and diversity of the microorganisms that inhabit our gut (human gastrointestinal microbiota) and health/disease, including brain health and disorders of the central nervous system. The microbiota-gut-brain axis is a dynamic matrix of tissues and organs including the brain, glands, gut, immune cells and gastrointestinal microbiota that communicate in a complex multidirectional manner to maintain homeostasis. Changes in this environment can lead to a broad spectrum of physiological and behavioural effects including hypothalamic-pituitary-adrenal (HPA) axis activation, and altered activity of neurotransmitter systems and immune function. While an appropriate, co-ordinated physiological response, such as an immune or stress response are necessary for survival, a dysfunctional response can be detrimental to the host contributing to the development of a number of CNS disorders.

In this review, the involvement of the gastrointestinal microbiota in stress-mediated and immune-mediated modulation of neuroendocrine, immune and neurotransmitter systems and the consequential behaviour is considered. We also focus on the mechanisms by which commensal gut microbiota can regulate neuroinflammation and further aim to exploit our understanding of their role in stress-related disorders as a consequence of neuroinflammatory processes.

Eje microbiota-intestino-cerebro (SNE)

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

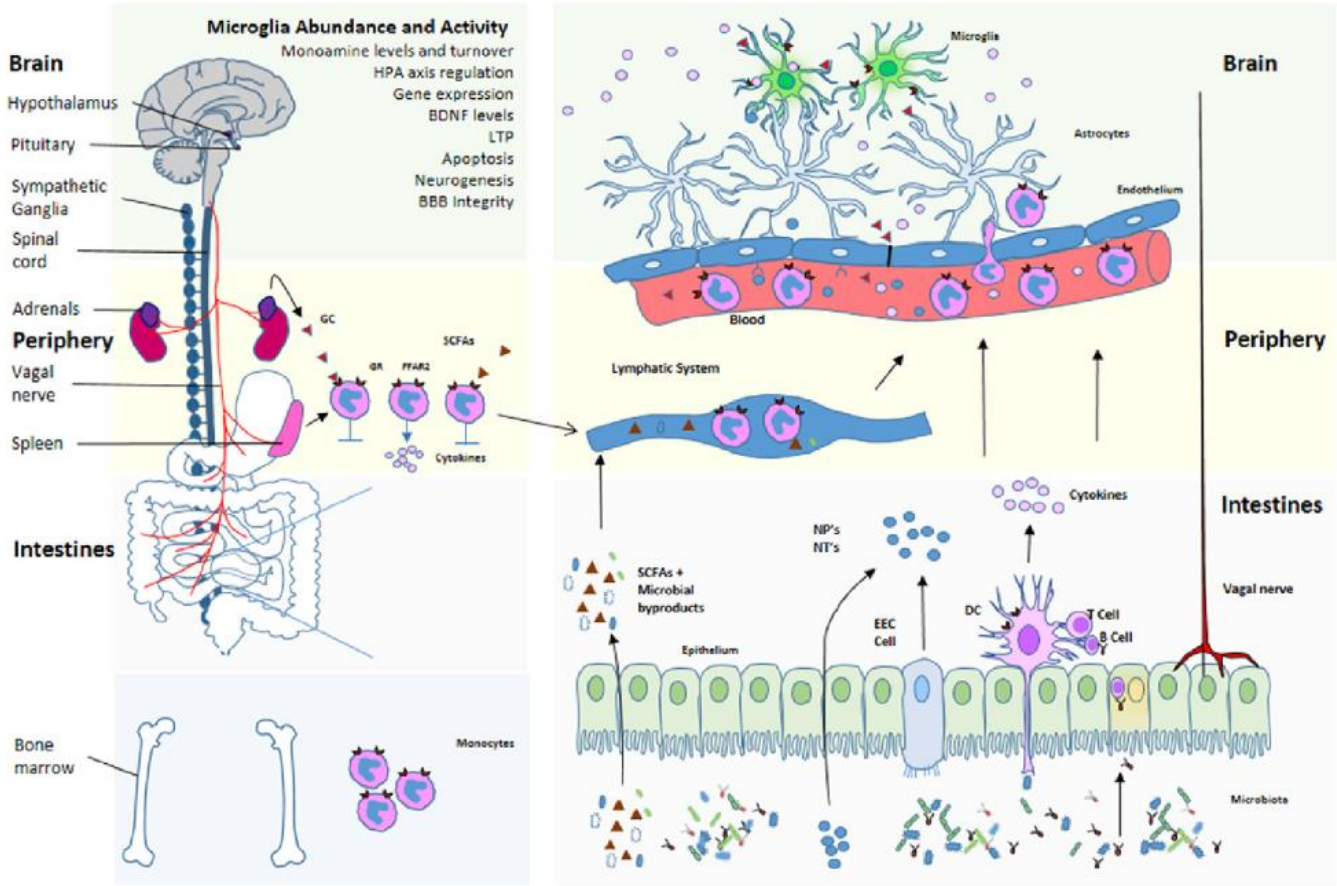


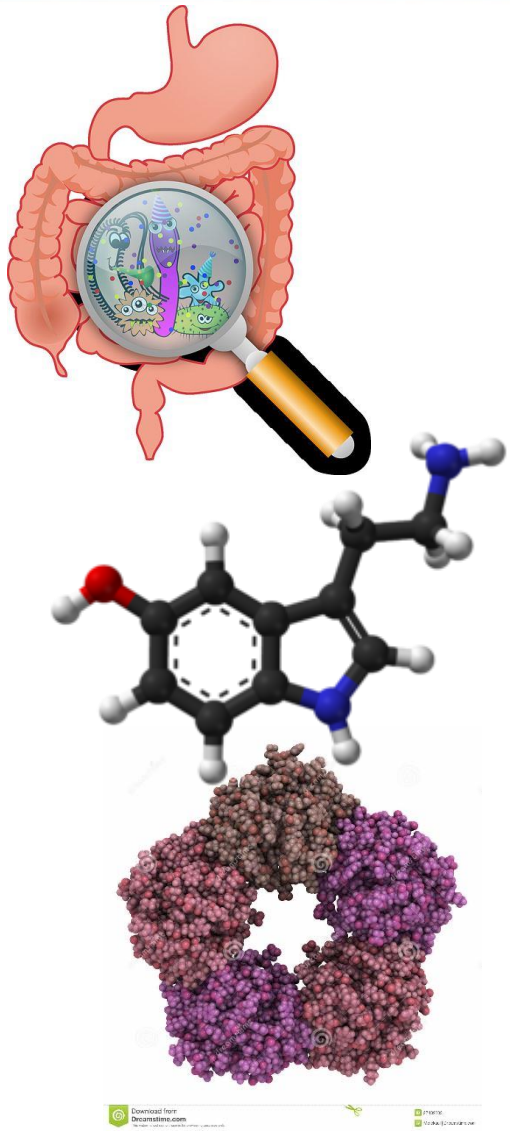
Fig. 1. Schematic for microbiota regulation of neuroinflammation and HPA axis activity. Communication within the microbiota-gut-brain axis involves the complex co-ordination of a number of factors and systems. The microbiota can govern events in the periphery and CNS by various means of communication including vagal nerve activation, cytokine production, neuropeptide and neurotransmitter release, SCFA release and microbial by-products, and by utilising the lymphatic and systemic circulation. Once these signals penetrate the blood brain barrier and reach the brain, they can influence the maturation and activation state of the microglia. Once activated, microglia play a key role in immune surveillance, synaptic pruning and clearance of debris. They also facilitate a number of everyday functions in the brain, including the regulation of HPA axis activation state. The release of glucocorticoids (cortisol) as a consequence of HPA axis activation can in turn regulate the activation state of brain microglia, as well as influence cytokine release and trafficking of monocytes from the periphery to the brain. HPA Hypothalamic-Pituitary-Adrenal; BDNF Brain derived neurotrophic factor; LTP Long term potentiation; BBB Blood-brain barrier; GC Glucocorticoids; GR Glucocorticoid receptor; FFAR Free fatty acid receptor; SCFA Short chain fatty acid; NP Neuropeptide; NT Neurotransmitter; DC Dendritic cell; EEC Enteroendocrine cell.

3. LAS EMOCIONES: SISTEMA N. ENTÉRICO (SNE)

Los microbios gobiernan el ánimo

Los hallazgos más recientes demuestran, además de la existencia de comunicaciones intensas entre el intestino y el cerebro, la influencia de la flora intestinal en el estado de ánimo, es decir, del número incontable de microorganismos del intestino que, entre otras funciones, contribuyen a la descomposición de los alimentos. En este sentido, la flora intestinal varía en su composición de una persona a otra: es tan única como la huella digital. A pesar de que apenas se conoce cuál es su influencia sobre el cerebro, se sabe que las bacterias intestinales potencian la liberación de sustancias activadoras de la inflamación, como la proteína C reactiva (PCR). Esta reduce los niveles de serotonina (la «hormona de la felicidad»), lo que explicaría por qué los pacientes con enfermedades intestinales crónicas suelen encontrarse deprimidos durante las fases inflamatorias. La industria alimentaria promueve alimentos probióticos que regulan la flora intestinal y, en teoría, mejoran la sensación de bienestar. De hecho, los productos probióticos poseen una función positiva en el tratamiento del síndrome del intestino irritable y de las enfermedades inflamatorias intestinales crónicas. En este sentido, se ha comprobado que los lactobacilos y las bifidobacterias de la alimentación influyen en el estado de ánimo, así como en la percepción del estrés.

(«Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus *R0052 and* Bifidobacterium longum *R0175) in rats and human subjects». M. Messaoudi et al. en* The British Journal of Nutrition, *vol. 105, págs. 755-764, 2011.)*



Eje microbiota-intestino-cerebro (SNE)

THE LANCET

Leucopenia: **Disminución del número de leucocitos en la sangre, por debajo de 4 000 por milímetro cúbico.**

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CORRESPONDENCE | VOLUME 395, ISSUE 10229, P1033-1034, MARCH 28, 2020

PDF [55 KB]

COVID-19: consider cytokine storm syndromes and immunosuppression

Puja Mehta • Daniel F McAuley • Michael Brown • Emilie Sanchez • Rachel S Tattersall • Jessica J Manson • et al.

Show all authors

Published: March 16, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)30628-0

Journal Pre-proof

Cytokine Storm in COVID-19 and Treatment

Qing Ye MD , Bili Wang MS , Jianhua Mao MD

PII: S0163-4453(20)30165-1
DOI: https://doi.org/10.1016/j.jinf.
Reference: YJINF 4511

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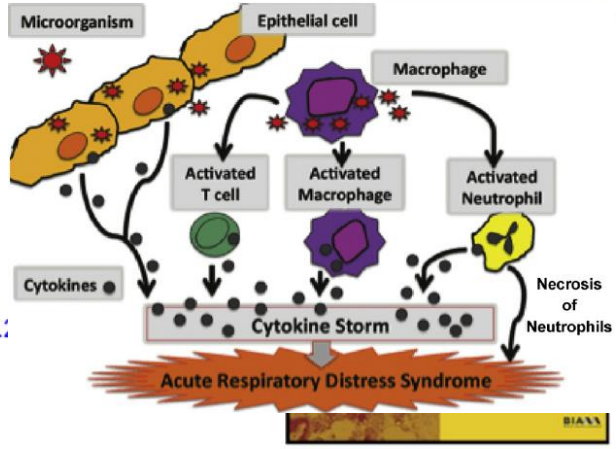
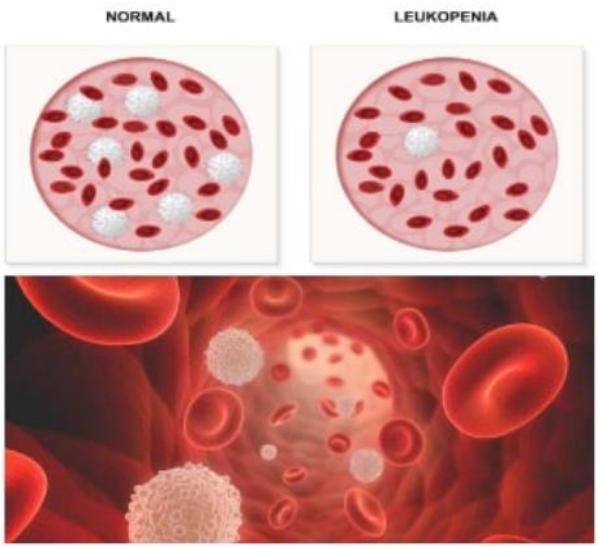




Coronavirus

Radiografía del coronavirus en residencias de ancianos: más de 17.000 fallecidos a falta de test generalizados

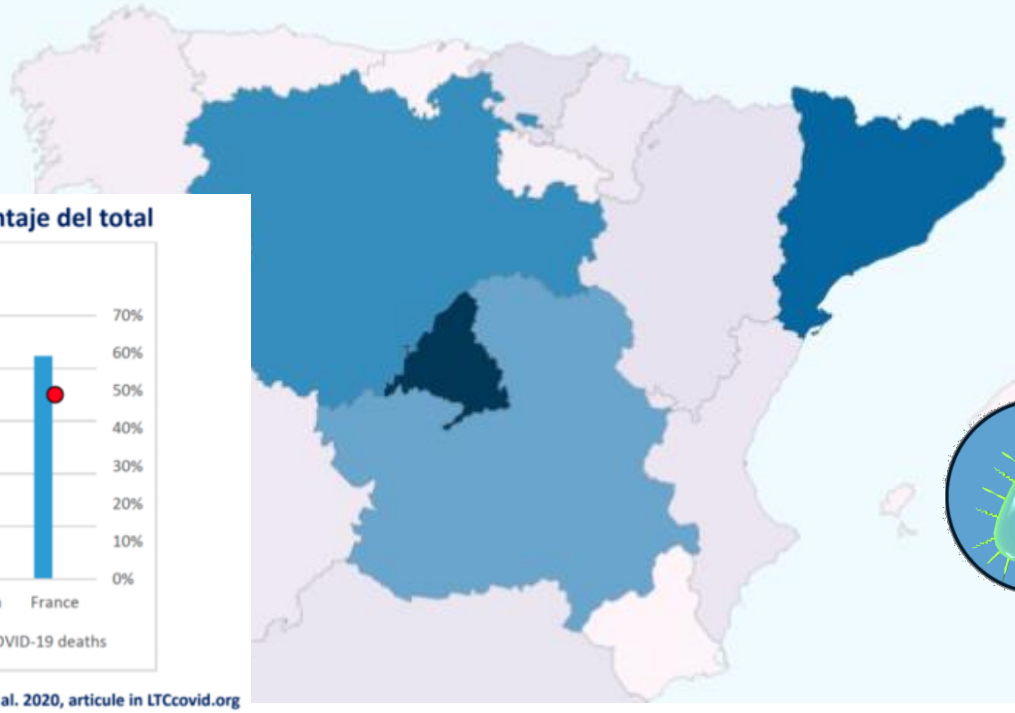
- Madrid, Cataluña y las dos Castillas son las regiones donde más defunciones ha habido desde el comienzo de la crisis
- Coronavirus: última hora en directo | Así evoluciona la curva del coronavirus en España | Así varía en las CC.AA.
- Mapa de España | Mapa mundial | ¿Qué es el coronavirus? | La situación en las UCIs

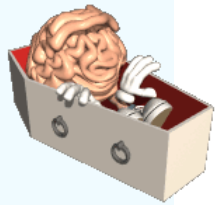
Fallecimientos con coronavirus en residencias por comunidades autónomas

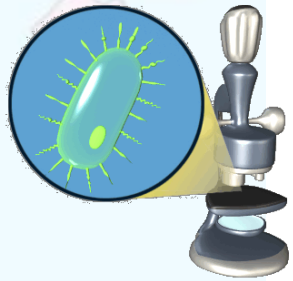
En España hay 17.017 ancianos que han muerto en residencias con COVID-19 o síntomas compatibles con la enfermedad

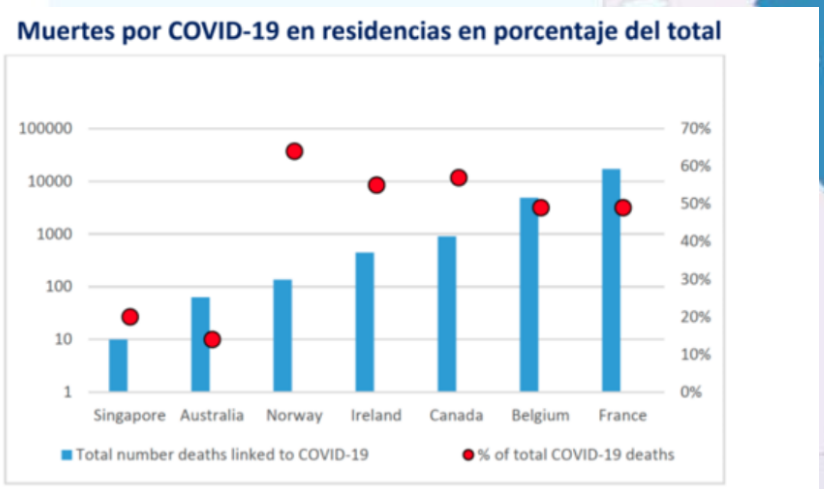
0 3.600

España: 17.000 de los 25.500 fallecidos por COVID-19 son mayores de 65 años en gerorresidencias
(cifras oficiales: 68%)

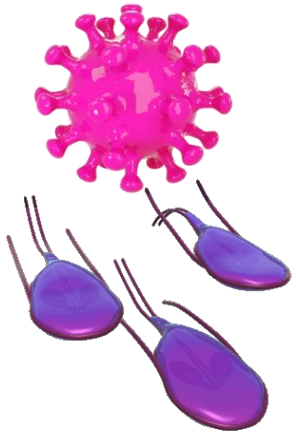








Comas-Herrera et al. 2020, articule in LTCcovid.org

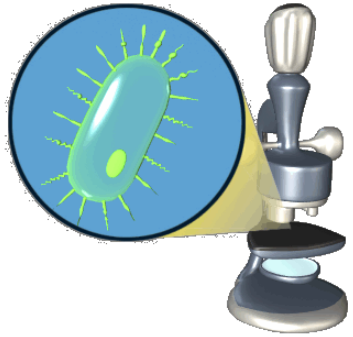


Directo

La última hora de la crisis del coronavirus

OPINIÓN

¿Podrían haberse reducido las muertes por Covid en residencias de anciano con una microbiota sana?

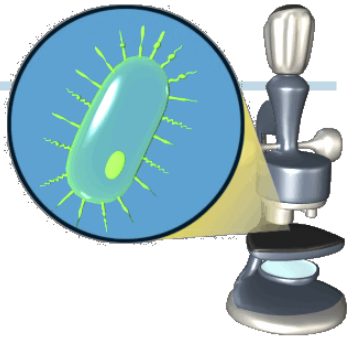


FRANCISCO GUARNER

FRANCISCO GUARNER, INVESTIGADOR VALL D'HEBRON INSTITUT DE RECERCA (VHIR)

27/04/2020 15:45 | Actualizado a 27/04/2020 16:21

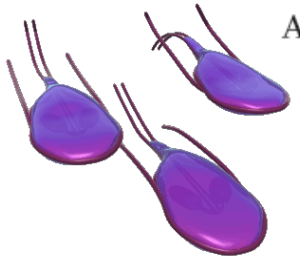
Focus Article



The role of the microbiota in ageing: current state and perspectives

Denise B. Lynch,[1,2†] Ian B. Jeffery[1,2†] and Paul W. O'Toole[1,2*]

Since the application of high-throughput technologies to investigate complex microbial communities, alterations in the human gut microbiota have been associated with an increasing number of diseases and conditions. This field of research has developed into an area of intense study which is quite different to the microbial investigations that have preceded it in terms of both the broadness of the area of research and the complexity of the analyses. In this review, we discuss gut microbiota changes observed in ageing in the context of the physiological changes that accompany senescence, examine what correlations can be established or inferred, and we discuss what key questions remain to be answered in the field. © 2015 The Authors. *WIREs Systems Biology and Medicine* published by Wiley Periodicals, Inc.

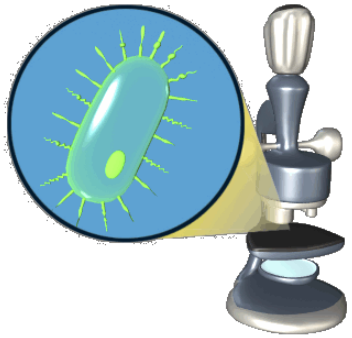


How to cite this article:
WIREs Syst Biol Med 2015, 7:131–138. doi: 10.1002/wsbm.1293

La microbiota intestinal es muy estable en la vida adulta, pero hay una serie de etapas y condiciones de vida durante el cual la microbiota cambia en su composición.

-El primero de ellos es la fase temprana establecimiento de la microbiota. Una vez plenamente establecida, la microbiota es relativamente estable desde la infancia hasta la edad adulta (desde los 3 a.)

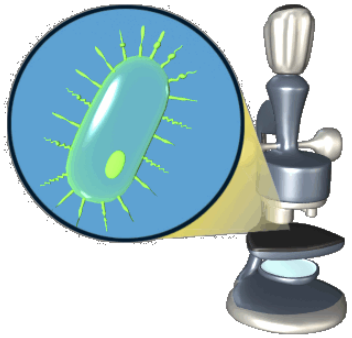
*-Durante el **envejecimiento**, hay un cambio de la composición de la microbiota que está asociada con deterioro de la salud y cambios en la dieta.*



-Ratones libres de gérmenes pueden sobrevivir sin una microbiota, sin embargo sufren de problemas de comportamiento y una serie de problemas morfológicos e inmunológicos debidos a la alteración del metabolismo, el desarrollo, y la fisiología, incluyendo el desarrollo de órganos (morfogénesis).

The Microbiota and Microbiome in Aging: Potential Implications in Health and Age-Related Diseases

Heidi J. Zapata, MD, PhD, and Vincent J. Quagliarello, MD



Advances in bacterial deoxyribonucleic acid sequencing allow for characterization of the human commensal bacterial community (microbiota) and its corresponding genome (microbiome). Surveys of healthy adults reveal that a signature composite of bacteria characterizes each unique body habitat (e.g., gut, skin, oral cavity, vagina). A myriad of clinical changes, including a basal proinflammatory state (inflamm-aging), that directly interface with the microbiota of older adults and enhance susceptibility to disease accompany aging. Studies in older adults demonstrate that the gut microbiota correlates with diet, location of residence (e.g., community dwelling, long-term care settings), and basal level of inflammation. Links exist between the microbiota and a variety of clinical problems plaguing older adults, including physical frailty, *Clostridium difficile* colitis, vulvovaginal atrophy, colorectal carcinoma, and atherosclerotic disease. Manipulation of the microbiota and microbiome of older adults holds promise as an innovative strategy to influence the development of comorbidities associated with aging. **J Am Geriatr Soc 63:776–781, 2015.**

Key words: microbiome; older adults; infection

microbes (e.g., bacterial microorganisms) cannot be cultured using conventional methods.[1,2] In 1977, it was proposed that the 16S ribosomal ribonucleic acid (RNA) subunit can classify bacteria, including commensal microbial flora.[3] This small RNA subunit is evolutionarily conserved in prokaryotes, but it contains nine hypervariable regions (V1–V9) useful for phylogenetic analysis. Ongoing advances in next-generation sequencing of 16S ribosomal RNA genes and whole-genome shotgun sequencing allow for large-scale analysis and characterization of the human bacterial community (the microbiota); the genome of the microbiota is referred to as the microbiome.[4,5] It is estimated that there are approximately 100 trillion bacteria associated with humans that outnumber human cells by a factor of 10.[6] Therefore, this second prokaryotic genome of microbes supplements the primary eukaryotic genome of humans.[7] This represents a paradigm shift for medicine in which our relationship with microbes is now viewed as a complex symbiosis instead of a potential source of clinical infectious disease. The purpose of this review is to highlight the role of the microbiota and microbiome in health and disease and its potential clinical relevance to older adults.

- *Los estudios en adultos mayores demuestran que la microbiota intestinal se correlaciona con la dieta, el lugar de residencia (casa vs. centros geriátricos a largo plazo).*

- *Existen vínculos entre la microbiota intestinal y problemas clínicos de los adultos mayores:* ***fragilidad física, colitis por Clostridium difficile, neumonía, infecciones urinarias, atrofia vulvovaginal, carcinoma colorrectal, aterosclerosis y neurodegeneración.***

- *La manipulación de la microbiota de los adultos mayores es una estretegia prometedora e innovadora para influir el desarrollo de comorbilidades asociadas con envejecimiento.*

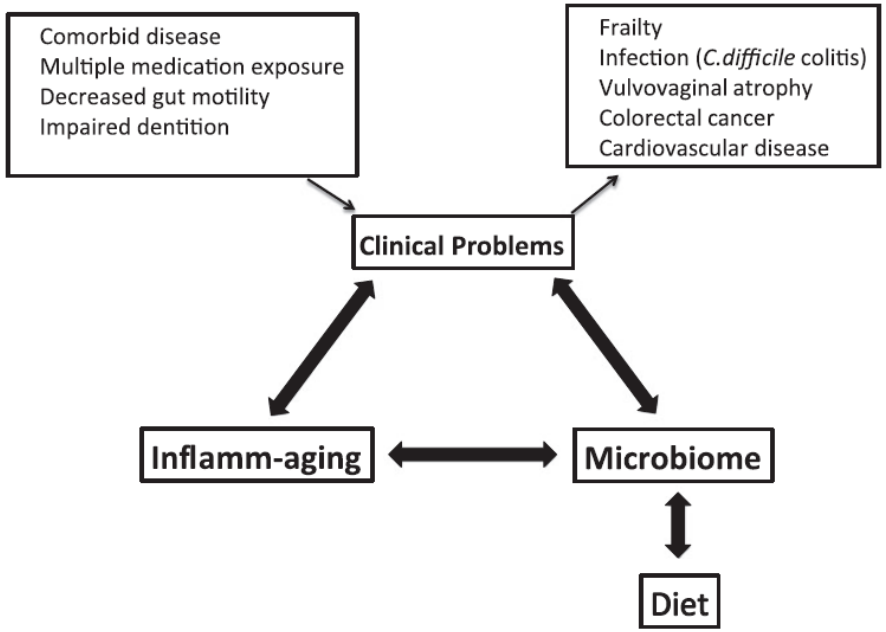


Figure 1. Association between the microbiome and clinical problems affecting older adults.

GERIATRIC BIOSCIENCES

The Microbiota and Microbiome in Aging: Potential Implications in Health and Age-Related Diseases

Heidi J. Zapata, MD, PhD, and Vincent J. Quagliarello, MD

Advances in bacterial deoxyribonucleic acid sequencing allow for characterization of the human commensal bacterial community (microbiota) and its corresponding genome (microbiome). Surveys of healthy adults reveal that a signature composite of bacteria characterizes each unique body habitat (e.g., gut, skin, oral cavity, vagina). A myriad of clinical changes, including a basal proinflammatory state (inflamm-aging), that directly interface with the microbiota of older adults and enhance susceptibility to disease accompany aging. Studies in older adults demonstrate that the gut microbiota correlates with diet, location of residence (e.g., community dwelling, long-term care settings), and basal level of inflammation. Links exist between the microbiota and a variety of clinical problems plaguing older adults, including physical frailty, *Clostridium difficile* colitis, vulvovaginal atrophy, colorectal carcinoma, and atherosclerotic disease. Manipulation of the microbiota and microbiome of older adults holds promise as an innovative strategy to influence the development of comorbidities associated with aging. J Am Geriatr Soc 63:776–781, 2015.

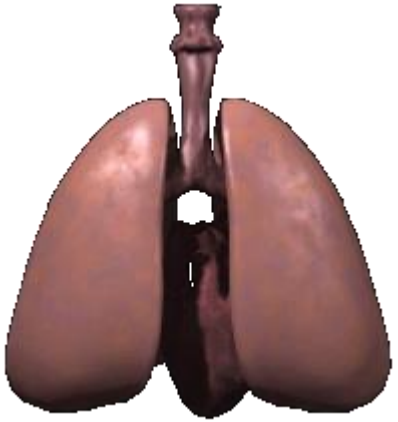
Key words: microbiome; older adults; infection

microbes (e.g., bacterial microorganisms) cannot be cultured using conventional methods.[1,2] In 1977, it was proposed that the 16S ribosomal ribonucleic acid (RNA) subunit can classify bacteria, including commensal microbial flora.[3] This small RNA subunit is evolutionarily conserved in prokaryotes, but it contains nine hypervariable regions (V1–V9) useful for phylogenetic analysis. Ongoing advances in next-generation sequencing of 16S ribosomal RNA genes and whole-genome shotgun sequencing allow for large-scale analysis and characterization of the human bacterial community (the microbiota); the genome of the microbiota is referred to as the microbiome.[4,5] It is estimated that there are approximately 100 trillion bacteria associated with humans that outnumber human cells by a factor of 10.[6] Therefore, this second prokaryotic genome of microbes supplements the primary eukaryotic genome of humans.[7] This represents a paradigm shift for medicine in which our relationship with microbes is now viewed as a complex symbiosis instead of a potential source of clinical infectious disease. The purpose of this review is to highlight the role of the microbiota and microbiome in health and disease and its potential clinical relevance to older adults.

- *Los adultos mayores (≥ 65 años) tienen una alta prevalencia de patologías de forma concomitante a la polifarmacia (incluyendo **antibióticos:** > prob. de colitis por clostridium difficile posterior a la antibioterapia (transplantes fecales).*

- *El envejecimiento del tracto alimentario está sujeto a una variedad de cambios: deterioro de la dentición y función salivar, menos peristaltismo (estreñimiento), divertículos en colon y cambios dietéticos → cambios en la microbiota intestinal (> susceptibilidad de enfermedades infecciosas): **"inflamm-aging" (altas concentraciones de citoquinas proinflamatorias y > respuesta inmune a los patógenos).** La Probiota intestinal regula el sistema inmunitario.*

- ***>** Probabilidad de infección por citomegalovirus, niveles altos de lipopolisacáridos en sangre y de subproductos microbianos en orina.*



Composition, variability, and temporal stability of the intestinal microbiota of the elderly

4586–4591 | PNAS | March 15, 2011 | vol. 108 | suppl. 1

Marcus J. Claesson[a,b], Siobhán Cusack[a], Orla O'Sullivan[c], Rachel Greene-Diniz[a], Heleen de Weerd[d], Edel Flannery[e], Julian R. Marchesi[b,f], Daniel Falush[g], Timothy Dinan[b,h], Gerald Fitzgerald[a,b], Catherine Stanton[b,c], Douwe van Sinderen[a,b], Michael O'Connor[i,j], Norma Harnedy[i,j], Kieran O'Connor[j,k,l], Colm Henry[k,l], Denis O'Mahony[i,j,m], Anthony P. Fitzgerald[e,n], Fergus Shanahan[b,m], Cillian Twomey[i,j,m], Colin Hill[a,b], R. Paul Ross[b,c], and Paul W. O'Toole[a,b,1]

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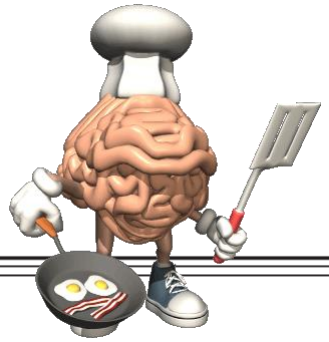
- *El consorcio **ELDERMET** (2007) caracterizó la microbiota intestinal de adultos mayores.*
- *En 2011, estudiaron muestras fecales de 161 adultos irlandeses mayores de 65 años (un subgrupo de 26 sujetos se vuelve a muestrear 3 meses después). 9 sujetos más jóvenes sirvieron como controles.*
- *La especie Bacteroidetes fue dominante en el 57% de los adultos mayores en comparación con 40% para el filo Firmicutes.*
- *Por el contrario, Firmicutes estaba más presente en las muestras fecales de los más jovenes (51%) en comparación con la especie Bacteroidetes (41%).*
- *La exposición a antibióticos se asoció con mayores niveles de Bacteroidetes y menores niveles de Firmicutes, Actinobacterias y Proteobacterias.*

ARTICLE



doi:10.1038/nature11319

Gut microbiota composition correlates with diet and health in the elderly

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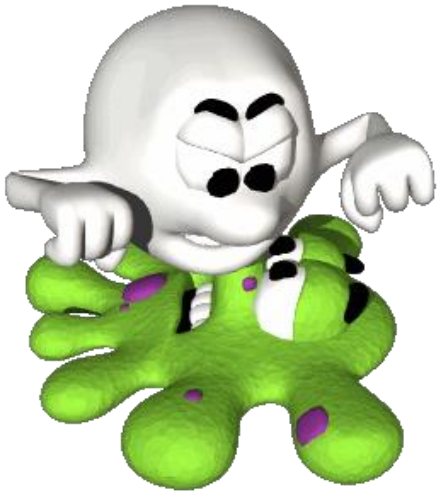
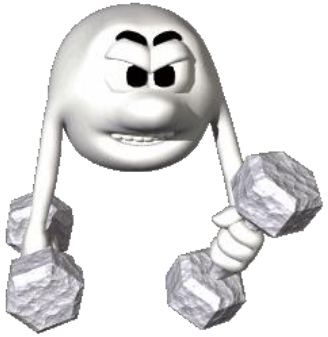
Alterations in intestinal microbiota composition are associated with several chronic conditions, including obesity and inflammatory diseases. The microbiota of older people displays greater inter-individual variation than that of younger adults. Here we show that the faecal microbiota composition from 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.

- *¿**Afecta el estado inmunológico del individuo a la microbiota, o afecta la microbiota al estado inmunológico del individuo**? Ambas…*
- *ANCIANOS: > presencia de Moléculas proinflamatorias. Modulación de la microbiota por la dieta: Problemas para masticar, tragar, pérdida de los dientes, de olfato y el gusto (desnutrición) junto con incremento de consumo de azúcar y grasas saturadas y la ingesta de menos fibra.*
- *La producción **de butirato y otros ácidos grasos de cadena corta** (AGCC) por parte de algunas bacterias mantiene la función de barrera del epitelio mucoso, evitando que bacterias potencialmente dañinas pasen al torrente sanguíneo.*
- *La **microbiota disbiótica** aumenta la probabilidad de enfermedad celíaca, enfermedad inflamatoria del intestino, diabetes tipo I, la artritis reumatoide, cáncer colorrectal, gástrico, cánceres de próstata y los trastornos cardiovasculares y metabólicos.*
- *> número de **Genotoxinas**, compuestos cancerígenos producidos por la dieta, cascadas inflamatorias locales y sistémicas que resultan en inflamación crónica de bajo grado que daña los tejidos y órganos afectados.*
- *Esta barrera epitelial controla la microbiota a través de la producción de antimicrobianos y secretores de IgA (sIgA), y permite el paso de los fagocitos y linfocitos si se rompe dicha barrera.*





frontiers in
MICROBIOLOGY

REVIEW ARTICLE
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Diet and the development of the human intestinal microbiome

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The important role of the gut microbiome in maintaining human health has necessitated a better understanding of the temporal dynamics of intestinal microbial communities as well as the host and environmental factors driving these dynamics. Genetics, mode of birth, infant feeding patterns, antibiotic usage, sanitary living conditions and long term dietary habits contribute to shaping the composition of the gut microbiome. This review focuses primarily on diet, as it is one of the most pivotal factors in the development of the human gut microbiome from infancy to the elderly. The infant gut microbiota is characterized by a high degree of instability, only reaching a state similar to that of adults by 2–3 years of age; consistent with the establishment of a varied solid food diet. The diet-related factors influencing the development of the infant gut microbiome include whether the child is breast or formula-fed as well as how and when solid foods are introduced. In contrast to the infant gut, the adult gut microbiome is resilient to large shifts in community structure. Several studies have shown that dietary changes induce transient fluctuations in the adult microbiome, sometimes in as little as 24 h; however, the microbial community rapidly returns to its stable state. Current knowledge of how long-term dietary habits shape the gut microbiome is limited by the lack of long-term feeding studies coupled with temporal gut microbiota characterization. However, long-term weight loss studies have been shown to alter the ratio of the Bacteroidetes and Firmicutes, the two major bacterial phyla residing in the human gastrointestinal tract. With aging, diet-related factors such as malnutrition are associated with microbiome shifts, although the cause and effect relationship between these factors has not been established. Increased pharmaceutical usage is also more prevalent in the elderly and can contribute to reduced gut microbiota stability and diversity. Foods containing prebiotic oligosaccharide components that nurture beneficial commensals in the gut community and probiotic supplements are being explored as interventions to manipulate the gut microbiome, potentially improving health status.

Keywords: enterotype, gut microbiome, aging, dietary patterns, colonization

- *Microbiota intestinal de 178 adultos mayores de ascendencia irlandesa entre 64-102 años de edad estratificados por su* ***dieta, tipo de residencia y dependencia****.*
- *13 adultos jóvenes (edad media 36 años): grupo de control.*
- *Personas en residencias geriátricas a largo plazo tuvieron una mayor proporción del filo Bacteroidetes en su intestino (>filo firmicutes en casa). Microbiota más diversa en dietas ricas en fibra y pobres en grasa con menores niveles de marcadores inflamatorios intestinales y menor fragilidad y dependencia (índice de Barthel AVD, Escala de Depresión y MMSE).*
- *La residencia y la dieta se asocian con la microbiota intestinal en mayores y correlacionan con la inflamación sistémica y el deterioro funcional.*

Table 2. Correlation of Microbiota, Diet, Inflammation, and Frailty in Older Adults

Association	Long-Term Care (>6 Weeks)	Rehabilitation Care (<6 Weeks)	Day Hospital	Community Dwellers
DG				
1: low fat/high fiber	DG3, DG4 predominate	Variable[a]	DG1, DG2 predominate	DG1, DG2 predominate
2: moderate fat/high fiber				
3: moderate fat/low fiber				
4: high fat/low fiber				
Inflammatory markers (tumor necrosis factor-α, IL-6, IL-8, C-reactive protein)	Highest	Intermediate[b]	Intermediate[b]	Lowest
Functional status and frailty	Impaired function and frailty predominate	Intermediate[c]	Intermediate[c]	Normal function predominate
Microbiota Predominating phyla	*Bacteroidetes* predominate	Variable[d]	Variable[d]	*Firmicutes* predominate

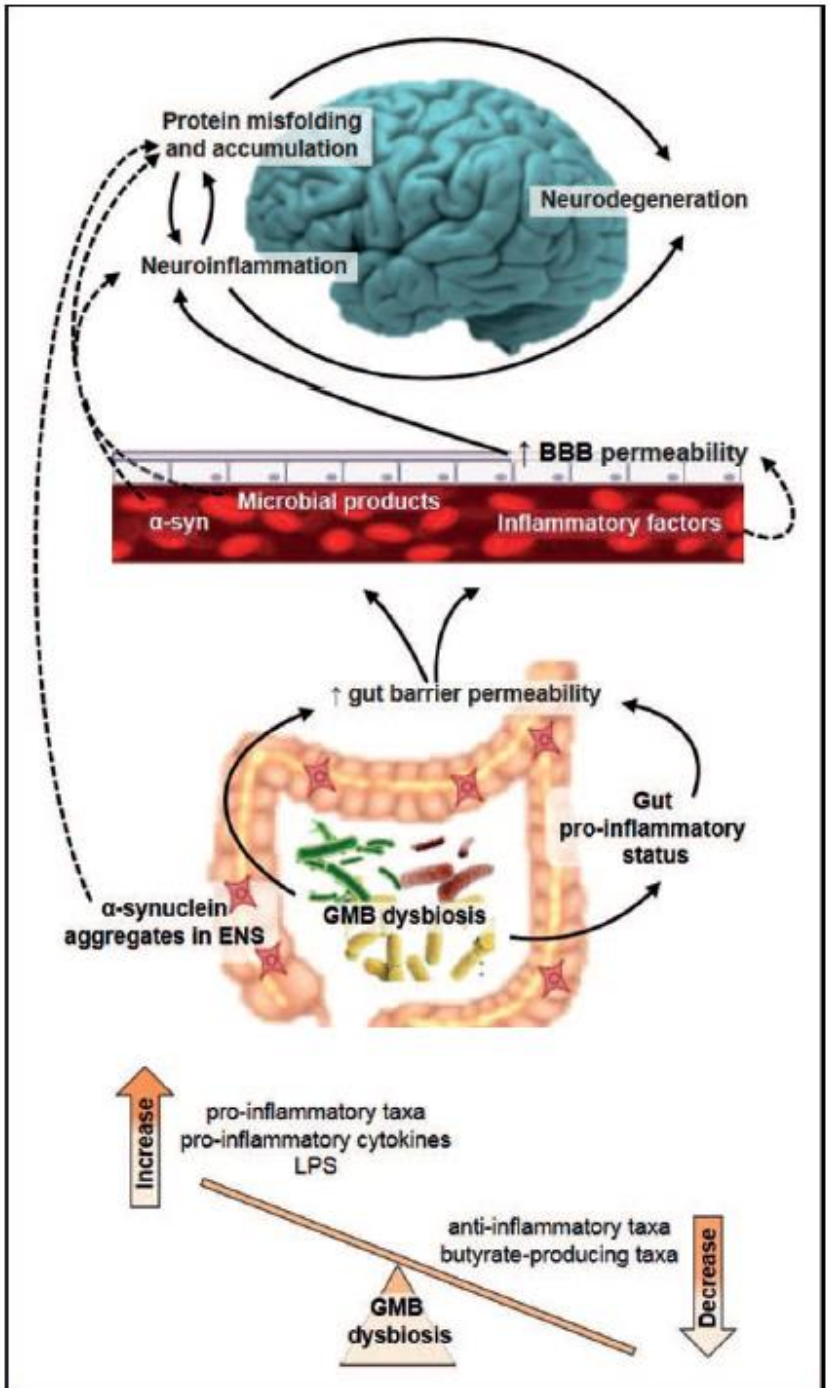


Figure 1. Environmental Factors and the Bidirectional Interaction with Host Organ Systems Shape the Intestinal Microbiome

Studies over the past decade have revealed that many environmental factors, including diet, antibiotic exposure, energy intake (EI), and exercise, can dramatically influence the intestinal microbiome (both membership and functional capacity). In addition to environment, further research has revealed a bidirectional interaction between host organ systems and the intestinal microbiome in shaping host metabolic outcomes.

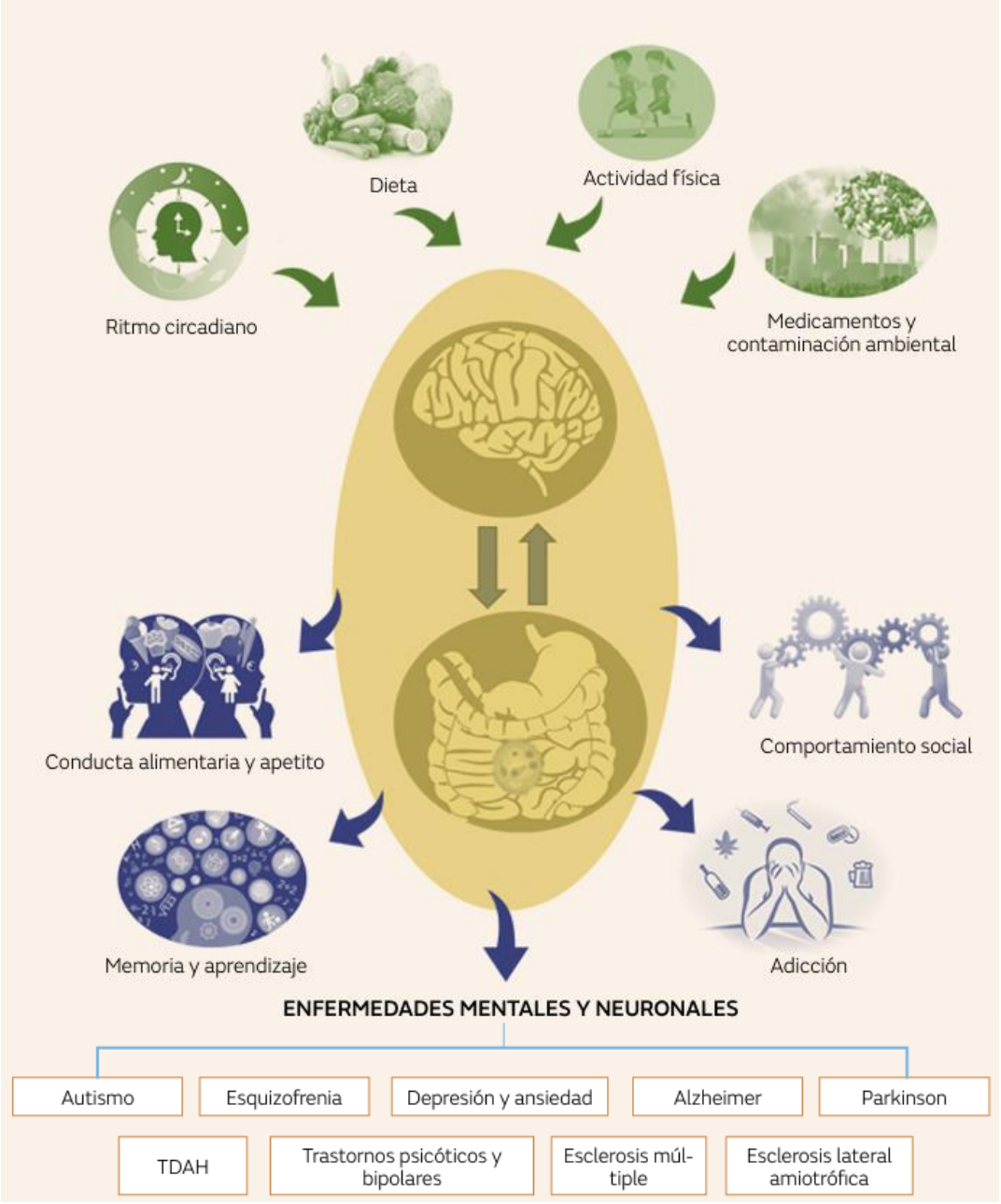
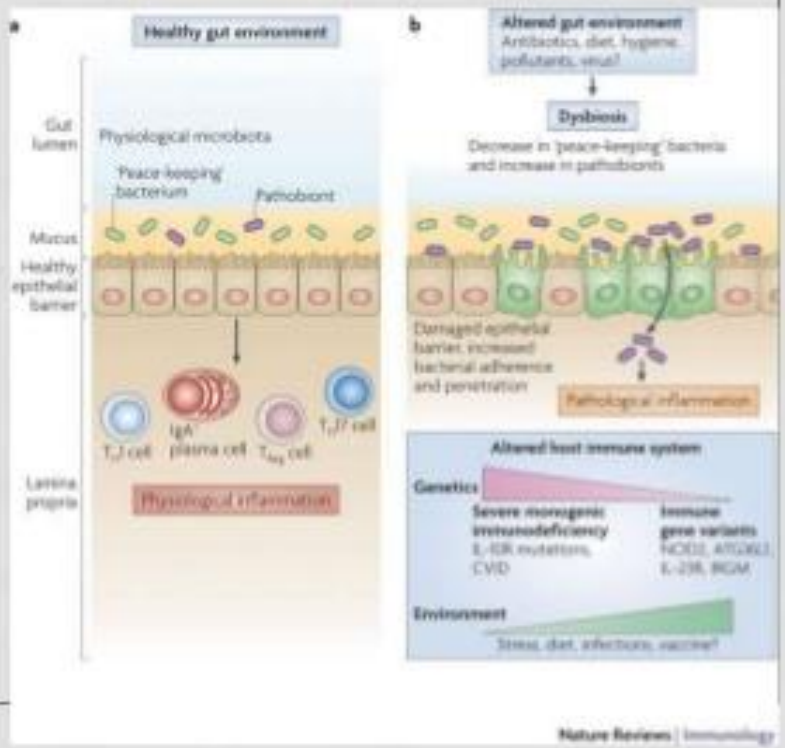


FIGURA 2. Factores que afectan al eje microbiota-intestino-cerebro. Comportamiento y enfermedades mentales y neuronales que se pueden ver afectados por cambios en dicho eje.

ENFERMEDADES RELACIONADAS CON LA MICROBIOTA

- DESEQUILIBRIO EN LA MICROBIOTA (DISBIOSIS) PUEDE CAUSAR VARIAS ENFERMEDADES



- OBESIDAD
- DIABETES
- ENFERMEDAD DEL INTESTINO IRRITABLE
- COLITIS
- ENFERMEDAD DE CROHN
- AUTISMO

Cáncer cólon
Esquizofrenia
Alzheimer
Parkinson
Aterosclerosis
Atrofia vaginal
Alergia y asma
DCL

The Human Microbiome: at the interface of health and disease

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DOCUMENTO DE CONSENSO

sobre la MICROBIOTA y el uso de PROBIÓTICOS/PREBIÓTICOS en patologías neurológicas y psiquiátricas

ICTUS, EPILEPSIA, CEFALEAS, DOLOR CRÓNICO, ALZHEIMER, PARKINSON, ESCLEROSIS MÚLTIPLE, ELA, ENF. AUTOINMUNES, AUTISMO, TDAH, TRAST. BIPOLAR, DEPRESIÓN, PSICOSIS, TEPT

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Association between the vaginal microbiota, menopause status and signs of vulvovaginal atrophy

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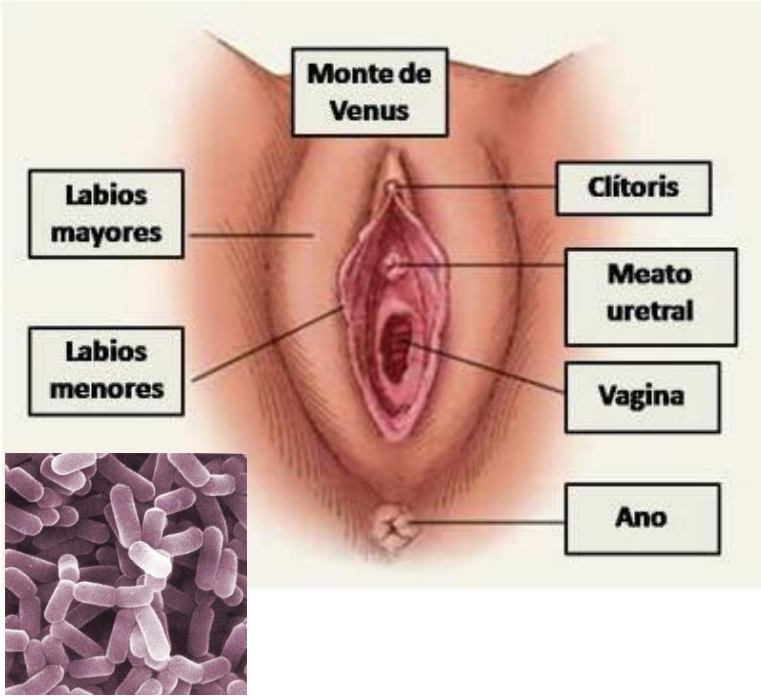
Abstract

Objectives—The vaginal microbiota help protect the female genital tract from disease. We sought to describe the composition of the vaginal microbiota between pre-, peri- and postmenopausal women and to explore the association between the microbiota and vulvovaginal atrophy (VVA).

Methods—87 women (age 35–60) were classified as premenopausal (n=30), perimenopausal (n=29) or postmenopausal (n=28) according to STRAW guidelines. Mid-vagina bacterial community composition was characterized by 16S rRNA gene analysis.

Results—Bacterial communities clustered into six community state types (CSTs), of which four were dominated by *Lactobacillus crispatus, L. gasseri, L. iners*, or *L. jensenii*; and two (CST-IV-A and IV-B) had low relative abundance of *Lactobacillus*. CST IV-A was characterized by *Streptococcus* and *Prevotella*, whereas CST IV-B by *Atopobium*. There was a significant association between menopause stage and CST (p-value=0.004) and VVA and CST (p-value=0.002). Perimenopausal women were more likely to be classified as CST IV-A or the *L. gasseri* CST, whereas postmenopausal women were mostly CST IV-A. CSTs dominated by *L. crispatus* and *L. iners* were more prevalent in premenopausal women. Nineteen participants had



Otras patologías relacionadas con la microbiota:

atrofia vulvovaginal *(sequedad vaginal, dolor y dispareunia): baja abundancia de Lactobacillus* ***(ingesta oral).***

Cell Host Microbe. 2014 March 12; 15(3): 317–328. doi:10.1016/j.chom.2014.02.007.

Microbes, Microbiota and Colon Cancer

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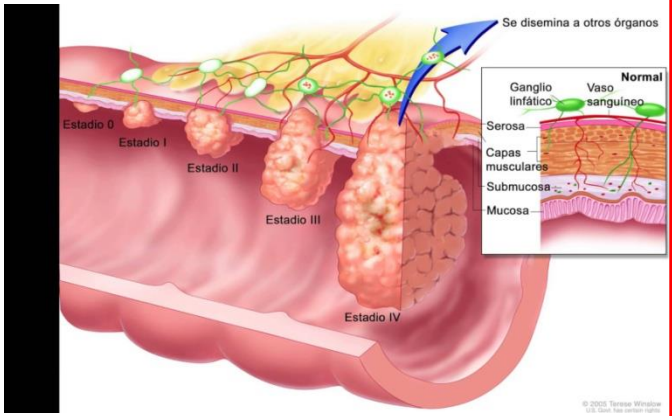
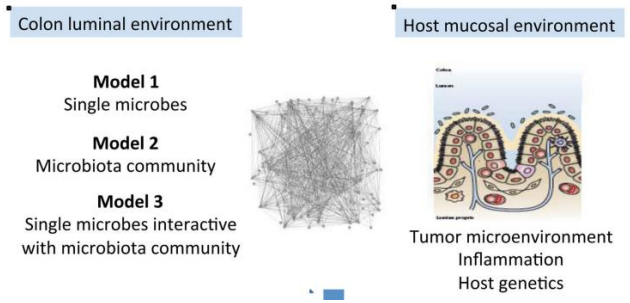
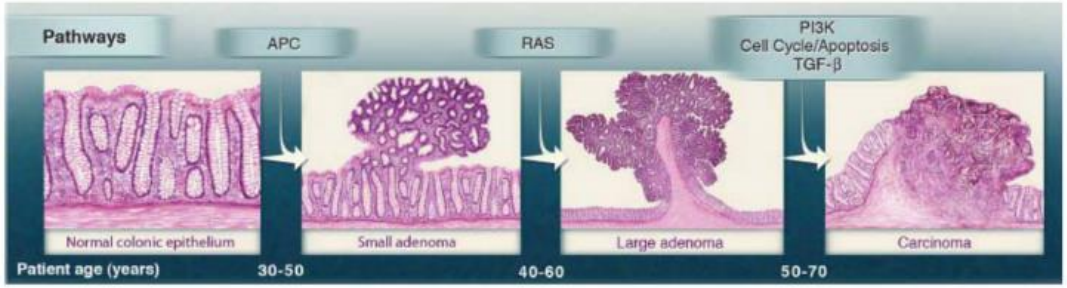
- *Microbiota intestinal y cáncer de cólon (más especies de Fusobacterium menores niveles de las bacterias productoras de butirato y mayores niveles de patógenos oportunistas (ambiente proinflamatorio que promueve el tumor)*

Summary

Colorectal cancer (CRC) presents a considerable disease burden worldwide. The human colon is also an anatomical location with the largest number of microbes. It is natural therefore to anticipate a role for microbes, particularly bacteria, in colorectal carcinogenesis. The increasing accessibility of microbial meta'omics is fueling a surge in our understanding of the role that microbes and the microbiota play in CRC. In this review, we will discuss recent insights into contributions of the microbiota to CRC and explore conceptual frameworks for evaluating the role of microbes in cancer causation. We also highlight new findings on candidate CRC-potentiating species and current knowledge gaps. Finally, we explore the roles of microbial metabolism as it relates to bile acids, xenobiotics, and diet in the etiology and therapeutics of CRC.







RESEARCH ARTICLE

Irritable Bowel Syndrome Is Associated with an Increased Risk of Dementia: A Nationwide Population-Based Study

Chien-Hua Chen[1,2,3], Cheng-Li Lin[4,5], Chia-Hung Kao[6,7]*

Purpose

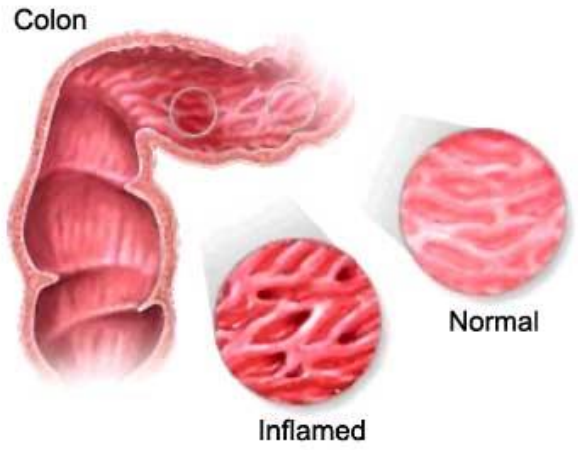
Abnormal interaction in the brain–gut axis has emerged as one of the relevant pathophysiological mechanisms for the development of irritable bowel syndrome (IBS). Moreover, the brain–gut axis has recently been demonstrated to be crucial for the maintenance of cognitive performance. Therefore, we assessed the risk of dementia following diagnosis of IBS.

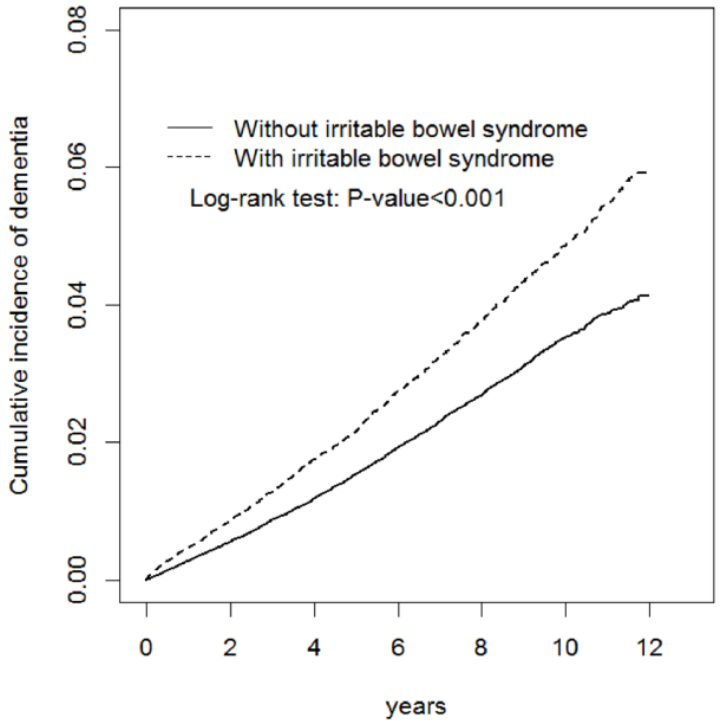
Methods

Using the Taiwan National Health Insurance Research Database (NHIRD) to obtain medical claims data from 2000 to 2011, we employed a random sampling method to enroll32 298 adult patients with IBS and frequency-matched them according to sex, age, and baseline year with 129 192 patients without IBS.

Results

The patients with IBS exhibited an increased risk of dementia [adjusted hazard ratio (aHR) = 1.26, 95% confidence interval (CI) = 1.17–1.35]after adjustment for age, sex, diabetes, hypertension, stroke, coronary artery disease (CAD), head injury, depression, and epilepsy, and the overall incidence of dementia for the cohorts with and without IBS was 4.86 and 3.41 per 1000 person-years, respectively. IBS was associated with an increased risk of dementia in patients older than 50 years in both male and female, and in those with comorbidity or without comorbidity. After adjustment for age, sex, and comorbidity, patients with IBS were also more likely to develop either non- Alzheimer's disease (AD) dementia (aHR = 1.24, 95% CI = 1.15–1.33) or AD (aHR = 1.76, 95% CI = 1.28–2.43).





Human oral, gut, and plaque microbiota in patients with atherosclerosis

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Edited by Todd R. Klaenhammer, North Carolina State University, Raleigh, NC, and approved September 17, 2010 (received for review August 2, 2010)

- *Asociación entre **infección periodontal y riesgo cardiovascular**. Las mismas bacterias presentes en la boca se han encontrado en la placa ateroscerótica.*
- *Vínculo entre el metabolismo de la microflora intestinal y la enfermedad cardiovascular:*
- *El N-óxido-trimetliamina **(OTMA),** un metabolito proaterosclerótico de la fosfatidilcolina en el intestino está implicado en la enfermedad cardiovascular (niveles mayores).*

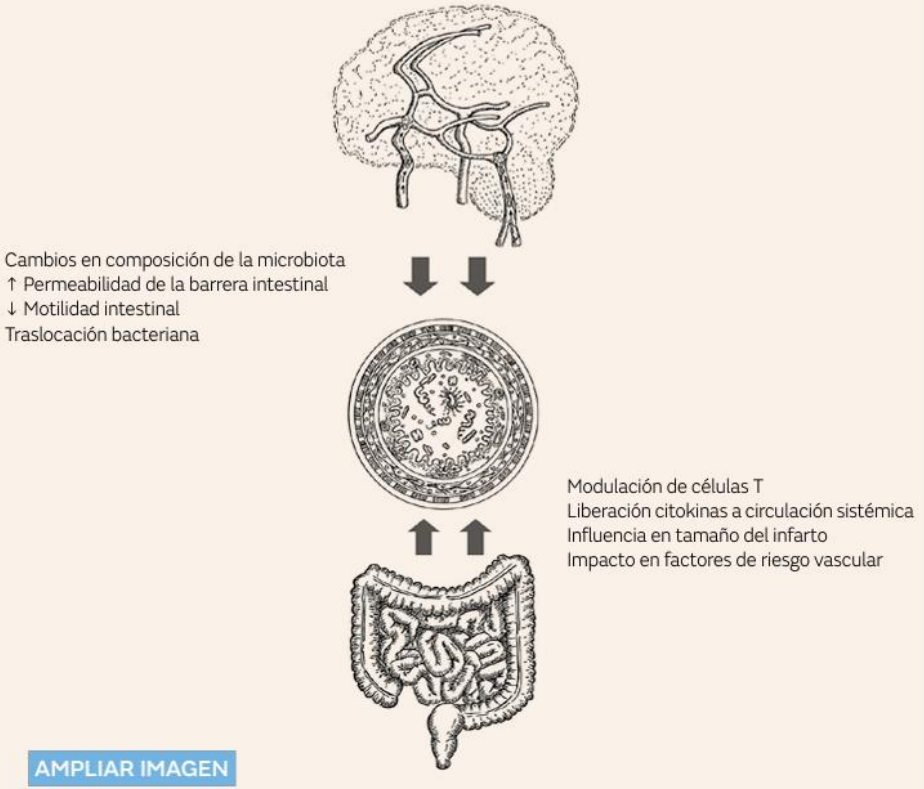

FIGURA 2. Relación del eje intestino-cerebro con la patología vascular cerebral. En el contexto de un ictus se producen cambios en la composición de la microbiota, con disminución de la motilidad, aumento de la permeabilidad de la barrera intestinal y fenómenos de traslocación bacteriana aumentando el riesgo de infecciones postictus. Los cambios en la composición de la microbiota generan expansión de células T con efectos pro o antiinflamatorios que pasan a la circulación sistémica y modulan cambios a nivel inflamatorio que influyen en el tamaño del área infartada.

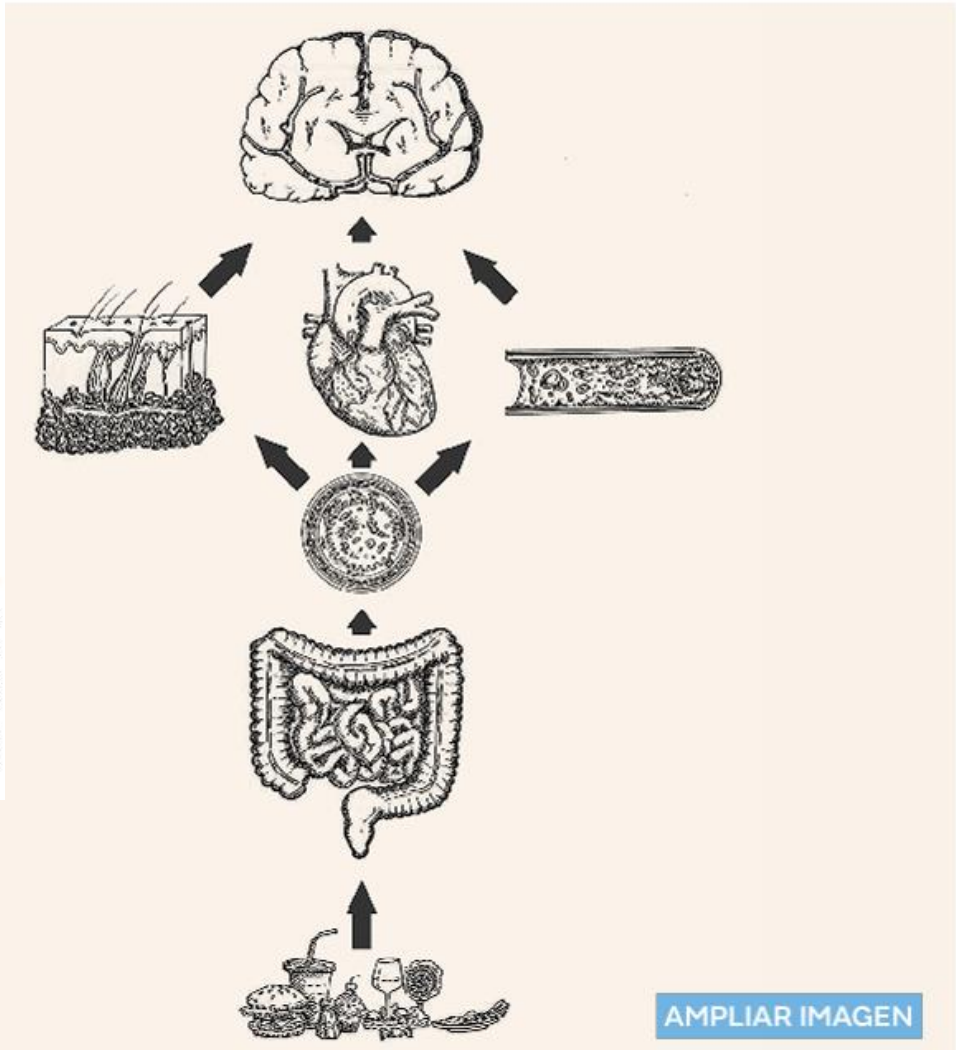

FIGURA 1. Influencia de la alimentación en la composición de la microbiota y su implicación directa con los principales factores de riesgo vascular, y en el desarrollo y progresión de fenómenos inflamatorios asociados con la arteriosclerosis.

EXPERT REVIEWS

The intricate association between gut microbiota and development of Type 1, Type 2 and Type 3 diabetes

Expert Rev. Clin. Immunol. 9(11), 1031–1041 (2013)

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It has been proposed that changes in the composition of gut microbiota contribute to the development of diabetes Types 1, 2 and 3 (the latter known as Alzheimer's disease). The onset of these diseases is affected by complex interactions of genetic and several environmental factors. Alterations in gut microbiota in combination with specific diets can result in increased intestinal permeability leading via a continuous state of low-grade inflammation to the development of insulin resistance. Since a change in composition of gut microbiota is also suggested to be the underlying factor for the development of obesity, it is obvious to link gut microbiota with the pathogenesis of diabetes. In addition, insulin resistance in the brain has been recently associated with Alzheimer's disease. These new paradigms in combination with data from studies with prebiotics and probiotics may lead to a novel way to control and even prevent diabetes in general.

Box 1. Gut microbiota that can maintain and restore gut barrier integrity.

- *Streptococcus thermophilus*
- *Lactobacillus acidophilus*
- *Lactobacillus plantarum*
- *Lactobacillus rhamnosus* OLL2838
- *Lactobacillus rhamnosus* GG
- *Bifidobacterium infantis* Y1

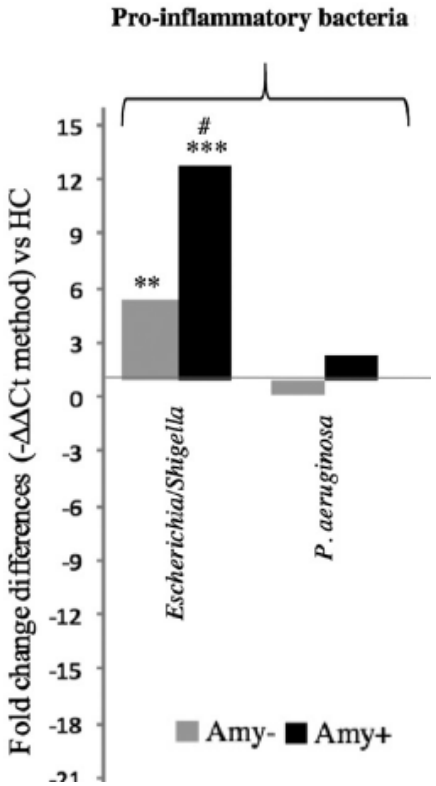
- An altered composition of gut microbiota may result in mucosal and systemic inflammation at least in part due to disrupted gut barrier function.
- In this inflamed state with aberrant antigen exposure, autoreactive T cells can be activated leading to pancreas-specific autoimmune responses, such as Type 1 diabetes.
- Inflammation is an important factor in the development of Type 2 diabetes. In addition, gut microbiota contributes to the development of obesity which consequently may result in insulin resistance.
- Alzheimer's disease associated with insulin resistance in the brain is also referred to as Type 3 diabetes.
- Gut microbiota management by administration of prebiotics and/or probiotics as well as lifestyle changes could become novel ways for possible prevention and amelioration of diabetes in general.

Neurobiology of Aging 49 (2017) 60–68

Association of brain amyloidosis with pro-inflammatory gut bacterial taxa and peripheral inflammation markers in cognitively impaired elderly

Annamaria Cattaneo [a,b,*], Nadia Cattane [a], Samantha Galluzzi [c], Stefania Provasi [a],

The pathway leading from amyloid-β deposition to cognitive impairment is believed to be a cornerstone of the pathogenesis of Alzheimer's disease (AD). However, what drives amyloid buildup in sporadic nongenetic cases of AD is still unknown. AD brains feature an inflammatory reaction around amyloid plaques, and a specific subset of the gut microbiota (GMB) may promote brain inflammation. We investigated the possible role of the GMB in AD pathogenesis by studying the association of brain amyloidosis with (1) GMB taxa with pro- and anti-inflammatory activity; and (2) peripheral inflammation in cognitively impaired patients. We measured the stool abundance of selected bacterial GMB taxa (*Escherichia/Shigella*, *Pseudomonas aeruginosa*, *Eubacterium rectale*, *Eubacterium hallii*, *Faecalibacterium prausnitzii*, and *Bacteroides fragilis*) and the blood expression levels of cytokines (pro-inflammatory cytokines: CXCL2, CXCL10, interleukin [IL]-1β, IL-6, IL-18, IL-8, inflammasome complex (NLRP3), tumor necrosis factor-alpha [TNF-α]; anti-inflammatory cytokines: IL-4, IL-10, IL-13) in cognitively impaired patients with ($n = 40$, Amy+) and with no brain amyloidosis ($n = 33$, Amy−) and also in a group of controls ($n = 10$, no brain amyloidosis and no cognitive impairment). Amy+ patients showed higher levels of pro-inflammatory cytokines (IL-6, CXCL2, NLRP3, and IL-1β) compared with both controls and with Amy− patients. A reduction of the anti-inflammatory cytokine IL-10 was observed in Amy+ versus Amy−. Amy+ showed lower abundance of *E. rectale* and higher abundance of *Escherichia/Shigella* compared with both healthy controls (fold change, FC = −9.6, $p < 0.001$ and FC = +12.8, $p < 0.001$, respectively) and to Amy− (FC = −7.7, $p < 0.001$ and FC = +7.4, $p = 0.003$). A positive correlation was observed between pro-inflammatory cytokines IL-1β, NLRP3, and CXCL2 with abundance of the inflammatory bacteria taxon *Escherichia/Shigella* (rho = 0.60, $p < 0.001$; rho = 0.57, $p < 0.001$; and rho = 0.30, $p = 0.007$, respectively) and a negative correlation with the anti-inflammatory *E. rectale* (rho = −0.48, $p < 0.001$; rho = −0.25, $p = 0.024$; rho = −0.49, $p < 0.001$). Our data indicate that an increase in the abundance of a pro-inflammatory GMB taxon, *Escherichia/Shigella*, and a reduction in the abundance of an anti-inflammatory taxon, *E. rectale*, are possibly associated with a peripheral inflammatory state in patients with cognitive impairment and brain amyloidosis. A possible causal relation between GMB-related inflammation and amyloidosis deserves further investigation.



REVIEW

Microbiota and neurodegenerative diseases

Moira Marizzoni[a], *Stefania Provasi*[b], *Annamaria Cattaneo*[b,c], *and Giovanni B. Frisoni*[a,d]

December 2017

Purpose of review

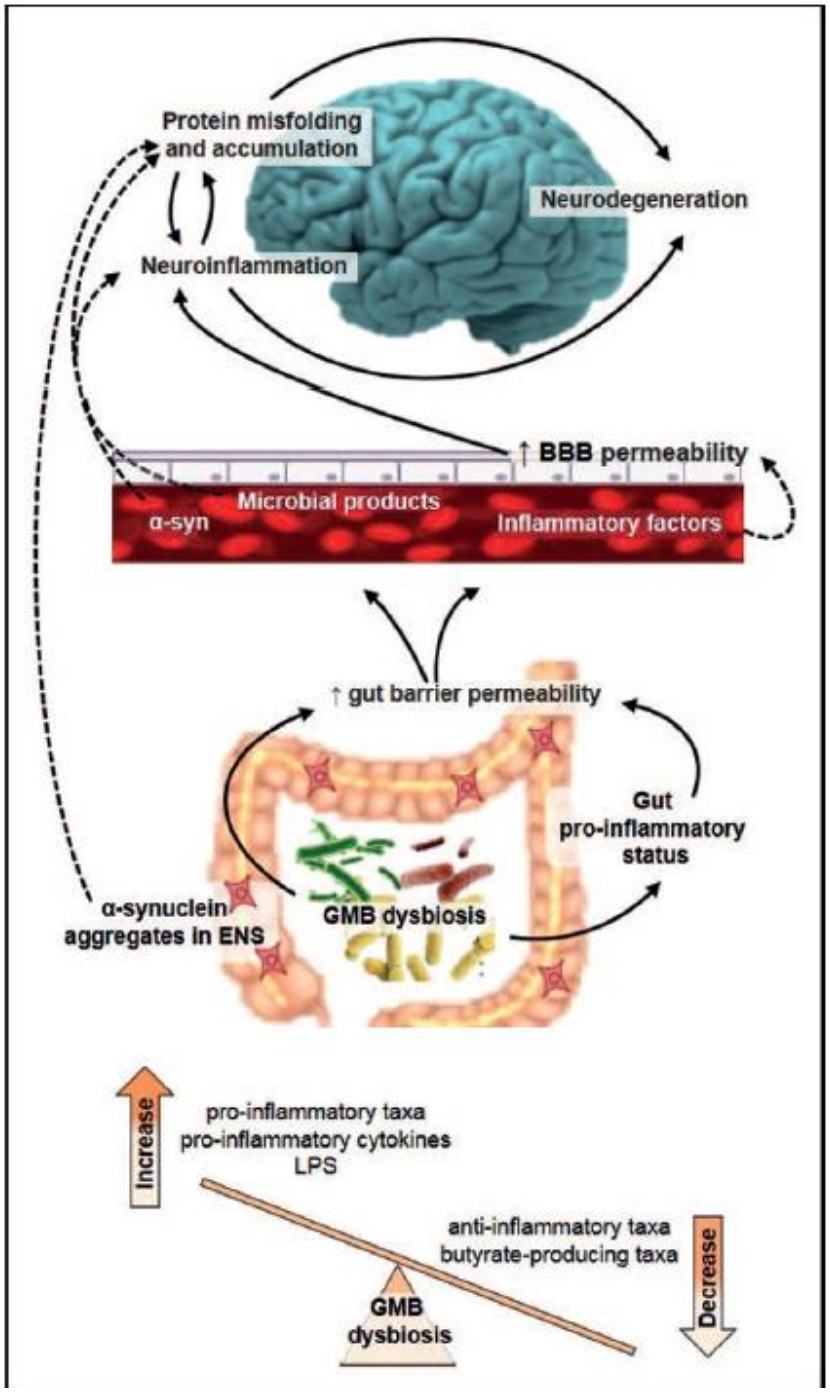
Despite the extensive research carried out in the past decades, the current pathophysiological notions of neurodegenerative disease as well as effective treatments to reduce their progression are largely unknown. Alterations of the human microbiota, the plethora of different microscopic organisms that our body hosts, have been linked to neurodegenerative disease risk, onset and progression. This review summarizes the current knowledge on the possible role of microbiota in neurodegenerative disorders and briefly discusses strategies to restore microbiota homeostasis.

Recent findings

Preclinical evidences and human cross-sectional studies posit the gut microbiota as a key actor in the Parkinson's disease onset and progression, reporting the presence of a specific gut microbiota profile in association with the modulation of disease and symptoms. Gut microbiota alterations have been correlated with brain disease and peripheral inflammation also in Alzheimer's patients.

Summary

The interaction between the microbiota and the host is promising to answer clinical questions that have so far escaped clarification with the current pathophysiological notions of health and disease. However, human longitudinal studies starting in the earlier disease phases are needed to understand the causative relation between microbiota and the hallmarks of these neurodegenerative disorders and to develop innovative treatments aimed at preventing or slowing brain damages.



CURRENT OPINION

Figure 1. Environmental Factors and the Bidirectional Interaction with Host Organ Systems Shape the Intestinal Microbiome

Studies over the past decade have revealed that many environmental factors, including diet, antibiotic exposure, energy intake (EI), and exercise, can dramatically influence the intestinal microbiome (both membership and functional capacity). In addition to environment, further research has revealed a bidirectional interaction between host organ systems and the intestinal microbiome in shaping host metabolic outcomes.


ENVEJECIMIENTO Y
FEMINIZACION DE LOS
VARONES
DIETA-ADIPOCITOS-AROMATASA

frontiers in
CELLULAR NEUROSCIENCE

OPINION ARTICLE
published: 17 September 2013
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Alzheimer's disease and the microbiome

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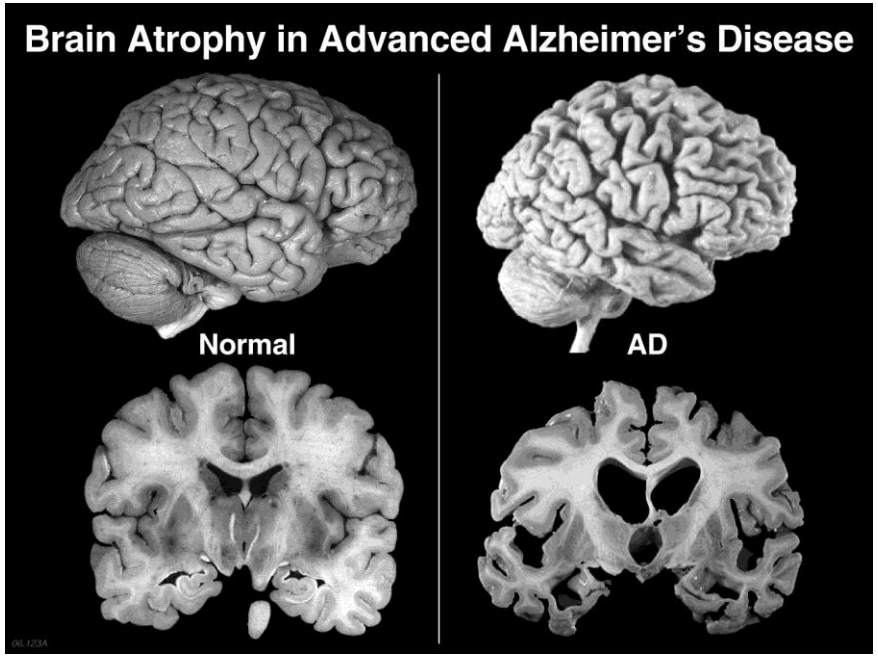
La inflamación está altamente correlacionada con el deterioro cognitivo.

Un estilo de vida anti-inflamatorio se ha demostrado que conduce a una mejor retención de la memoria, longevidad y salud del cerebro.

Ahora sabemos que hay múltiples vías neuroquímicas y neurometabólicas entre el SNC y el tracto microbioma/digestivo (segundo cerebro) que envían señales entre sí, lo que afecta la memoria, patrones de pensamiento y razonamiento.



Alzheimer's disease and gut microbiota

SCIENCE CHINA
Life Sciences

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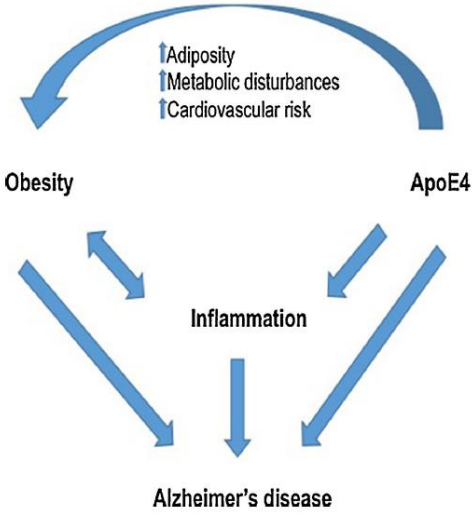
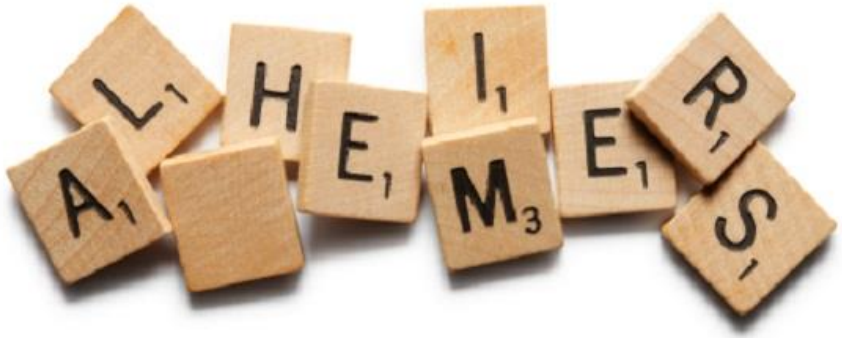
Received June 24, 2016; accepted July 10, 2016; published online August 25, 2016

Alzheimer's disease (AD) is a most common neurodegenerative disorder, which associates with impaired cognition. Gut microbiota can modulate host brain function and behavior via microbiota-gut-brain axis, including cognitive behavior. Germ-free animals, antibiotics, probiotics intervention and diet can induce alterations of gut microbiota and gut physiology and also host cognitive behavior, increasing or decreasing risks of AD. The increased permeability of intestine and blood-brain barrier induced by gut microbiota disturbance will increase the incidence of neurodegeneration disorders. Gut microbial metabolites and their effects on host neurochemical changes may increase or decrease the risk of AD. Pathogenic microbes infection will also increase the risk of AD, and meanwhile, the onset of AD support the "hygiene hypothesis". All the results suggest that AD may begin in the gut, and is closely related to the imbalance of gut microbiota. Modulation of gut microbiota through personalized diet or beneficial microbiota intervention will probably become a new treatment for AD.





European Review for Medical and Pharmacological Sciences 2019; 23: 426-430

Microbes and Alzheimer' disease: lessons from *H. pylori* and GUT microbiota

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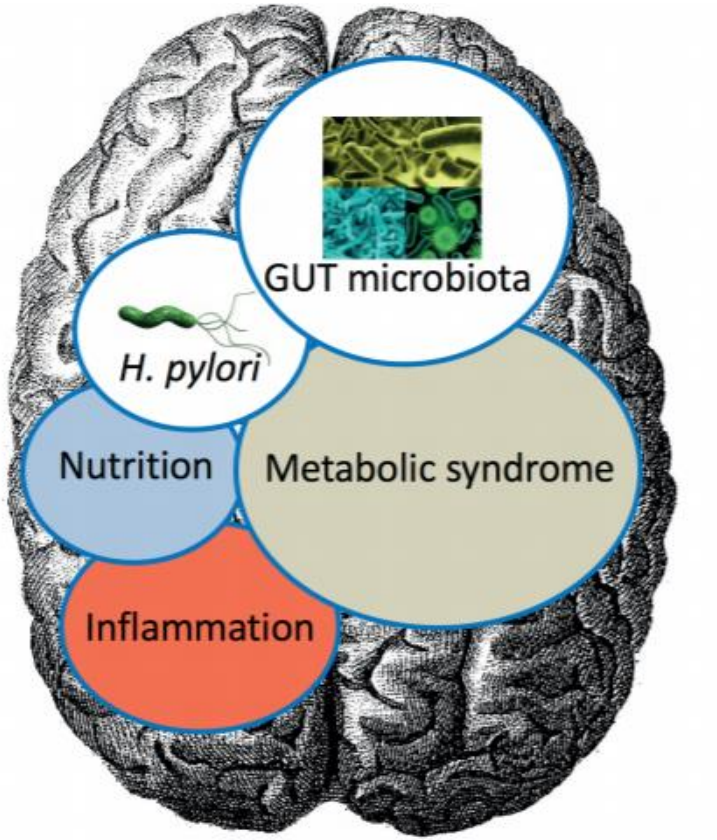
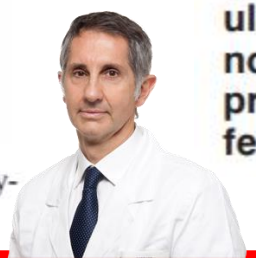


Figure 1. Main mechanisms by which *H. pylori* and dysbiosis may affect the development and evolution of AD.

Abstract. – OBJECTIVE: the role of microbes and chronic inflammation in the pathogenesis of Alzheimer' disease (AD) has been postulated by many authors. On the other hand, several studies have reported the main role of *H. pylori* infection and/or GUT microbiota alteration in promoting chronic inflammation, thus possibly influencing both occurrence and evolution of AD. In this article, we analyze the most important and recent studies performed on this field both on humans and animals and provide possible pathogenic explanations.

RESULTS: all main and most recent animal, human, epidemiological and in-silico studies, showed a role of *H. pylori* and/or dysbiosis in AD, mostly through the promotion of systemic chronic inflammation and/or by triggering molecular mimicry mechanisms. In particular, *H. pylori* infection seems to be related to a poorer cognitive performance.

CONCLUSIONS: Indeed, bacteria have been shown to affect neurodegeneration by promoting inflammation, inducing molecular mimicry mechanisms and accumulation of Aβ into the brain. These findings open the way for *H. pylori* eradicating trials and/or GUT microbiota remodulating strategies. Therefore, further studies are now needed in order to test whether antibiotics, pre and/or probiotics may exert a beneficial effect in the prevention of AD.



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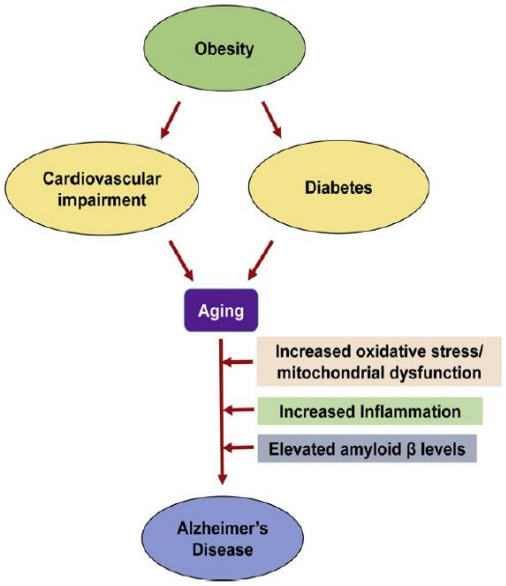


Common neurodegenerative pathways in obesity, diabetes, and Alzheimer's disease☆

Subbiah Pugazhenthi [a,b,*], Limei Qin [a], P. Hemachandra Reddy [c]

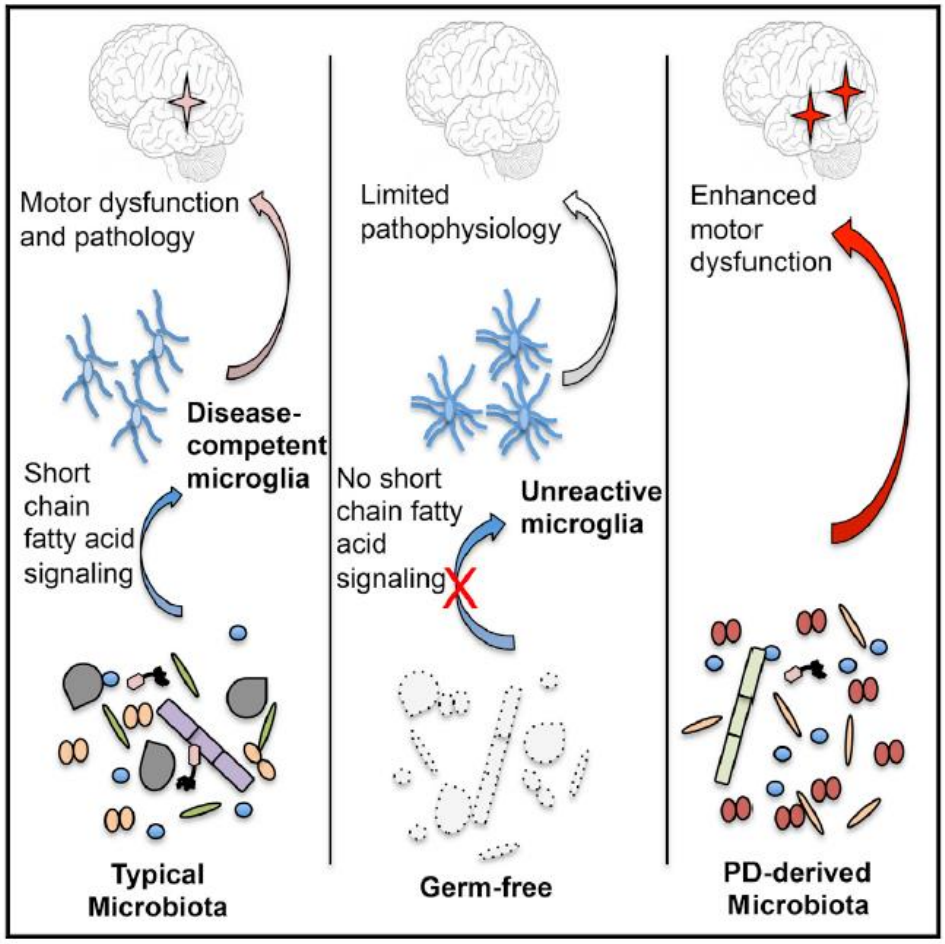
Cognitive decline in chronic diabetic patients is a less investigated topic. Diabetes and obesity are among the modifiable risk factors for Alzheimer's disease (AD), the most common form of dementia. Studies have identified several overlapping neurodegenerative mechanisms, including oxidative stress, mitochondrial dysfunction, and inflammation that are observed in these disorders. Advanced glycation end products generated by chronic hyperglycemia and their receptor RAGE provide critical links between diabetes and AD. Peripheral inflammation observed in obesity leads to insulin resistance and type 2 diabetes. Although the brain is an immune-privileged organ, cross-talks between peripheral and central inflammation have been reported. Damage to the blood brain barrier (BBB) as seen with aging can lead to infiltration of immune cells into the brain, leading to the exacerbation of central inflammation. Neuroinflammation, which has emerged as an important cause of cognitive dysfunction, could provide a central mechanism for aging-associated ailments. To further add to these injuries, adult neurogenesis that provides neuronal plasticity is also impaired in the diabetic brain. This review discusses these molecular mechanisms that link obesity, diabetes and AD. This article is part of a Special Issue entitled: Oxidative Stress and Mitochondrial Quality in Diabetes/Obesity and Critical Illness Spectrum of Diseases — edited by P. Hemachandra Reddy.

Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease

Cell *167*, 1469–1480, December 1, 2016 ©

Timothy R. Sampson,[1,*] Justine W. Debelius,[2] Taren Thron,[1] Stefan Janssen,[2] Gauri G. Shastri,[1] Zehra Esra Ilhan,[3] Collin Challis,[1] Catherine E. Schretter,[1] Sandra Rocha,[4] Viviana Gradinaru,[1] Marie-Francoise Chesselet,[5] Ali Keshavarzian,[6] Kathleen M. Shannon,[7,9] Rosa Krajmalnik-Brown,[3] Pernilla Wittung-Stafshede,[4] Rob Knight,[2,8] and Sarkis K. Mazmanian[1,10,*]

The intestinal microbiota influence neurodevelopment, modulate behavior, and contribute to neurological disorders. However, a functional link between gut bacteria and neurodegenerative diseases remains unexplored. Synucleinopathies are characterized by aggregation of the protein α-synuclein (αSyn), often resulting in motor dysfunction as exemplified by Parkinson's disease (PD). Using mice that overexpress αSyn, we report herein that gut microbiota are required for motor deficits, microglia activation, and αSyn pathology. Antibiotic treatment ameliorates, while microbial re-colonization promotes, pathophysiology in adult animals, suggesting that postnatal signaling between the gut and the brain modulates disease. Indeed, oral administration of specific microbial metabolites to germ-free mice promotes neuroinflammation and motor symptoms. Remarkably, colonization of αSyn-overexpressing mice with microbiota from PD-affected patients enhances physical impairments compared to microbiota transplants from healthy human donors. These findings reveal that gut bacteria regulate movement disorders in mice and suggest that alterations in the human microbiome represent a risk factor for PD.



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The vermiform appendix impacts the risk of developing Parkinson's disease

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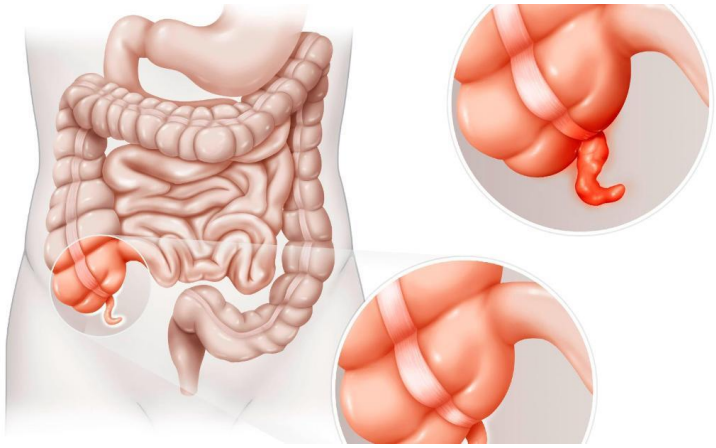

Abstract

The pathogenesis of Parkinson's disease (PD) involves the accumulation of aggregated α-synuclein, which has been suggested to begin in the gastrointestinal tract. Here, we determined the capacity of the appendix to modify PD risk and influence pathogenesis. In two independent epidemiological datasets, involving more than 1.6 million individuals and over 91 million person-years, we observed that removal of the appendix decades before PD onset was associated with a lower risk for PD, particularly for individuals living in rural areas, and delayed the age of PD onset. We also found that the healthy human appendix contained intraneuronal α-synuclein aggregates and an abundance of PD pathology–associated α-synuclein truncation products that are known to accumulate in Lewy bodies, the pathological hallmark of PD. Lysates of human appendix tissue induced the rapid cleavage and oligomerization of full-length recombinant α-

Human gut microbiota: the links with dementia development

REVIEW

Rashad Alkasir[1], Jing Li[1], Xudong Li[2], Miao Jin[2], Baoli Zhu[1,3]✉

Protein Cell 2017, 8(2):90–102
DOI 10.1007/s13238-016-0338-6

ABSTRACT

Dementia is a comprehensive category of brain diseases that is great enough to affect a person's daily functioning. The most common type of dementia is Alzheimer's disease, which makes most of cases. New researches indicate that gastrointestinal tract microbiota are directly linked to dementia pathogenesis through triggering metabolic diseases and low-grade inflammation progress. A novel strategy is proposed for the management of these disorders and as an adjuvant for psychiatric treatment of dementia and other related diseases through modulation of the microbiota (e.g. with the use of probiotics).

Table 1. The gut bacteria and their metabolites on the nervous system

Gut microbiota	Metabolites product	Effects on the nervous system function	References
Lactobacillus, Bifidobacterium	GABA	Inhibitory neurotransmitter, metabolic disorders can lead to anxiety and depression	(Barrett et al., 2012)
Streptococcus, Escherichia, enterococci, Enterococcus, Lactococcus, Lactobacillus	Serotonin	Neurotransmitters, regulate emotions	(Shishov et al., 2009; Özogul, 2011)
Bacillus	Norepinephrine	Neurotransmitters involved in motor, cognitive, memory, emotion and other central nervous and endocrine control	(Tsavkelova et al., 2000; Shishov et al., 2009)
Lactobacillus, Bacillus	Acetylcholine	Acting on neurotransmitters in the central and peripheral nervous systems, and cognitive function, particularly closely related to learning and memory	(Marquardt and Spitznagel 1959; Kawashima et al., 2007)
Lactobacillus, Lactococcus, Streptococcus, Enterococcus	Histamine	Regulating neurotransmitter; sleep and cognitive function related	(Landete et al. 2008; Thomas et al., 2012)
Clostridium, C. sporogenes	Indole-3-propionic acid (IPA)	Antioxidants, protect neurons	(Jellet et al., 1980; Bendheim et al., 2002)
Bacteroides, Bifidobacterium, Propionibacterium, Eubacterium, Lactobacillus, Clostridium, Roseburia, Prevotella	Short-chain fatty acids (SCFA)	Carbohydrates (starch, cellulose, etc.), the main products of fermentation, to provide energy for the host, regulate endothelial cell function, promote the synthesis and secretion of neurotransmitters and hormones, reduce inflammation	(Russell et al., 2013)
Blue-green algae (*Cyanobacteria*)	BMAA	Neurotoxicity, neuronal damage, and misfolded proteins related	(Bradley and Mash, 2009)
Gram-negative bacteria	Endotoxin	Induced inflammation, release large amounts of inflammatory cytokines (TNF-α, IL-6 and IL-8, etc.), obesity, IR, diabetes and is closely related to the occurrence of AD	(Levi et al., 2003; Wang and Quinn, 2010)
Escherichia, Bacillus, Lactococcus, Lactobacillus, Streptococcus	Dopamine	System activity, Parkinson's disease, AD, and depression-related	(Tsavkelova et al., 2000; Shishov et al., 2009; Özogul, 2011)
Spore-forming microbes, *Candida, Streptococcus, Enterococcus* spp.	Promote 5-HT biosynthesis	Increase the motility of the gut	(Yano et al., 2015)

NOTE: GABA: gamma-aminobutyric acid; BMAA: beta-N- methylamino -L- alanine; 5-HT: 5-hydroxytryptamine; AD: Alzheimer's disease; IR: insulin resistance.

Human gut microbiota: the links with dementia development

Rashad Alkasir[1], Jing Li[1], Xudong Li[2], Miao Jin[2], Baoli Zhu[1,3]

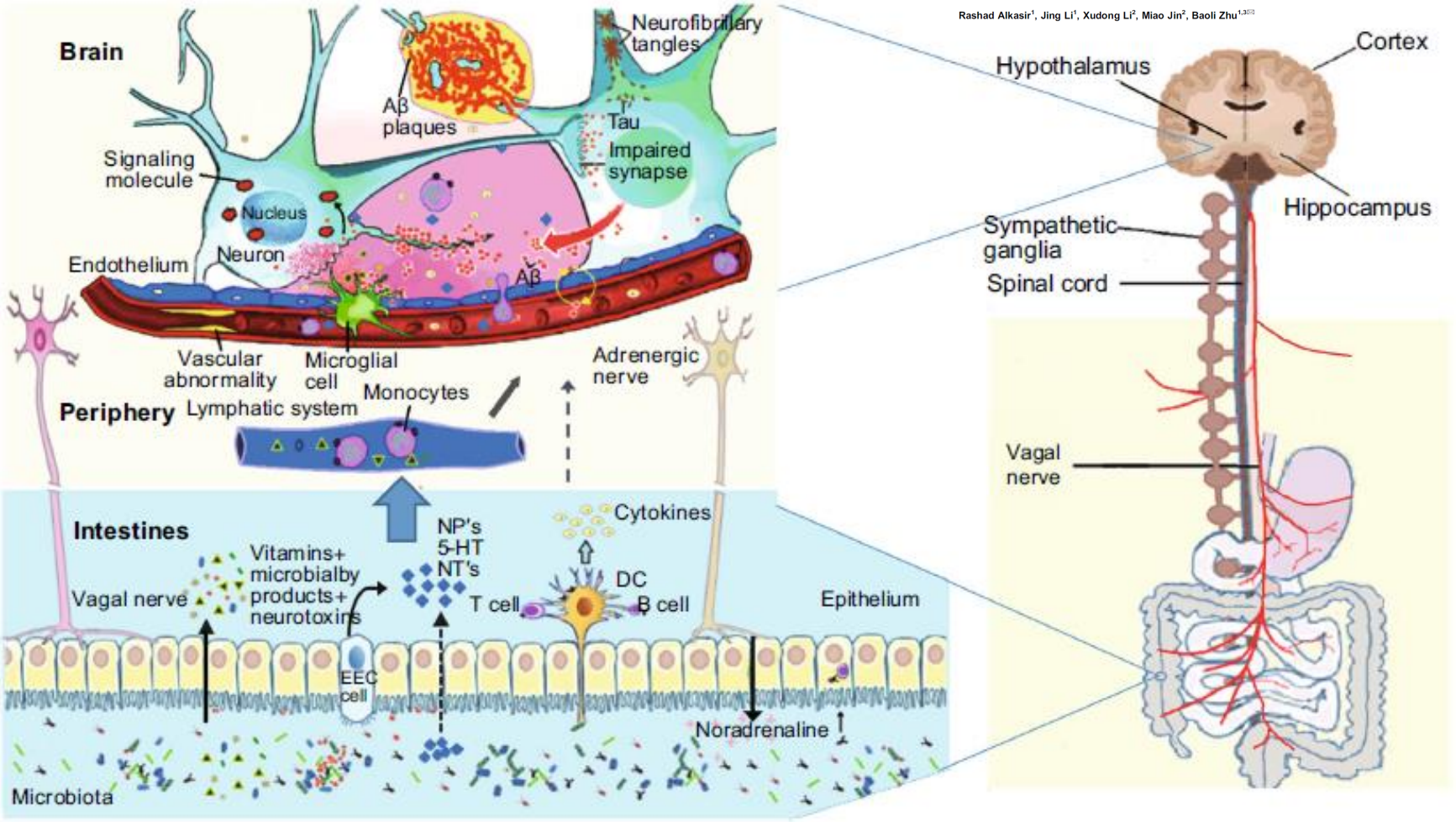

Figure 1. Schematic of some key players in the pathogenesis of AD. The gut microbiota regulation of neuro-inflammation and the hypothalamic–pituitary–adrenal (HPA) axis activity and may lead to AD. The bacterial products that gain access to the brain through the bloodstream and the area postrema, via cytokine release from mucosal immune cells, through the release of gut hormones such as 5-HT from EEC cells, or via afferent neural pathways, including the vagal nerve. NP: Neuropeptide; NT: Neurotransmitter; 5-HT: 5-hydroxytryptamine; DC: Dendritic cell; EEC: Enteroendocrine cell; Aβ: amyloid beta protein; AD: Alzheimer's disease.

Human gut microbiota: the links with dementia development

Rashad Alkasir[1], Jing Li[1], Xudong Li[2], Miao Jin[2], Baoli Zhu[1,3]✉

Table 2. Some methods that using to delay the process of neurodegeneration

Products	Description	Components	Foods contain them
Probiotic	Live microorganisms confer a health benefit and boost the host immunity	· *Lactobacillus acidophilus* · *Lactobacillus casei* · *Lactobacillus reuteri* · *Lactobacillus plantarum* · *Lactobacillus rhamnosus* · *Bifidobacterium animalis* · *Bifidobacterium infantis* · *Bifidobacterium lactis* · *Bifidobacterium longum*	Yogurt, Soy yogurt fermented dairy products Kombucha[a], Kimchi[b] Miso[c], Sauerkraut[d]
Prebiotic	Chemical substances, nondigestible foods that make their way through our digestive system and help good bacteria grow and flourish. Prebiotics help feed and keep beneficial bacteria healthy	Mostly come from carbohydrate fibers called oligosaccharides	Bananas, Onions, Garlic, Leeks, Asparagus, Whole wheat, Barley, Rye, Inulin[e]
NSAIDs	A drug class that groups together drugs: provide analgesic (pain-killing) and antipyretic (fever-reducing) effects, and, in higher doses, anti-inflammatory effects	Aspirin, indomethacin, ibuprofen, ketoprofen, diclofenac, piroxicam, celecoxib, nimesulid	Apples, Avocados, Blueberries, Broccoli, Cauliflower, Cherries, Chili peppers, Cucumbers, Dates, Eggplant, Figs…
GSPE[f]	An industrial derivative of whole grape seeds used as a dietary supplement with widespread health benefits	Catechin, gallic acid, epicatechin, proanthocyanidin dimers, larger oligomers	Grape seeds

Riiser *Allergy Asthma Clin Immunol* (2015) 11:35
DOI 10.1186/s13223-015-0102-0

ALLERGY, ASTHMA & CLINICAL IMMUNOLOGY

REVIEW Open Access

The human microbiome, asthma, and allergy

Amund Riiser*

Abstract

The human microbiome can be defined as the microorganisms that reside within and on our bodies and how they interact with the environment. Recent research suggests that numerous mutually beneficial interactions occur between a human and their microbiome, including those that are essential for good health. Modern microbiological detection techniques have contributed to new knowledge about microorganisms in their human environment. These findings reveal that the microbiomes of the lung and gut contribute to the pathogenesis of asthma and allergy. For example, evidence indicates that the microbiome of the gut regulates the activities of helper T cell subsets (Th1 and Th2) that affect the development of immune tolerance. Moreover, recent studies demonstrate differences between the lung microbiomes of healthy and asthmatic subjects. The hygiene and biodiversity hypotheses explain how exposure to microorganisms is associated with asthma and allergy. Although those living in developed countries are exposed to fewer and less diverse microorganisms compared with the inhabitants of developing countries, they are experiencing an increase in the incidence of asthma and allergies. Detailed analyses of the human microbiome, as are being conducted under the auspices of the Human Microbiome Project initiated in 2007, promise to contribute insights into the mechanisms and factors that cause asthma and allergy that may lead to the development of strategies to prevent and treat these diseases.

Keywords: Asthma, Allergy, Microbiome

Clinical & Experimental Immunology
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Clinical and Experimental Immunology
STELLAR REVIEW

The 'hygiene hypothesis' for autoimmune and allergic diseases: an update

H. Okada, C. Kuhn, H. Feillet and J.-F. Bach
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Accepted for publication 21 January 2010
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Summary

According to the 'hygiene hypothesis', the decreasing incidence of infections in western countries and more recently in developing countries is at the origin of the increasing incidence of both autoimmune and allergic diseases. The hygiene hypothesis is based upon epidemiological data, particularly migration studies, showing that subjects migrating from a low-incidence to a high-incidence country acquire the immune disorders with a high incidence at the first generation. However, these data and others showing a correlation between high disease incidence and high socio-economic level do not prove a causal link between infections and immune disorders. Proof of principle of the hygiene hypothesis is brought by animal models and to a lesser degree by intervention trials in humans. Underlying mechanisms are multiple and complex. They include decreased consumption of homeostatic factors and immunoregulation, involving various regulatory T cell subsets and Toll-like receptor stimulation. These mechanisms could originate, to some extent, from changes in microbiota caused by changes in lifestyle, particularly in inflammatory bowel diseases. Taken together, these data open new therapeutic perspectives in the prevention of autoimmune and allergic diseases.

-Una dieta antiinflamatoria ayuda a prevenir la susceptibilidad al síndrome de intestino permeable y ayuda a eliminar la flema o mucosidad en los pulmones o en los conductos nasales, lo que hace que sea más fácil respirar.

- Ciertas bacterias beneficiosas tienen efecto antiinflamatorio, lo que reduce la gravedad de las reacciones alérgicas, alergias a los alimentos, asma o infecciones de las vías respiratorias.

https://www.dailymotion.com/video/x2euked?playlist=x4t2zs

THE WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY, 2018
https://doi.org/10.1080/15622975.2018.1433878

REVIEW ARTICLE

The role of the gut microbiota in schizophrenia: Current and future perspectives

Daniela Rodrigues-Amorim[a], Tania Rivera-Baltanás[a], Benito Regueiro[b], Carlos Spuch[c], María Elena de las Heras[a], Raul Vázquez-Noguerol Méndez[a], Maria Nieto-Araujo[a], Carolina Barreiro-Villar[a], Jose Manuel Olivares[a] and Roberto Carlos Agís-Balboa[a]

[a]Psychiatric Diseases Research Group, Galicia Sur Health Research Institute. Complexo Hospitalario Universitario de Vigo (CHUVI),

ABSTRACT

Objectives: Schizophrenia is a poorly understood chronic disease. Its pathophysiology is complex, dynamic, and linked to epigenetic mechanisms and microbiota involvement. Nowadays, correlating schizophrenia with the environment makes sense owing to its multidimensional implications: temporal and spatial variability. Microbiota involvement and epigenetic mechanisms are factors that are currently being considered to better understand another dimension of schizophrenia.

Methods: This review summarises and discusses currently available information, focussing on the microbiota, epigenetic mechanisms, technological approaches aimed at performing exhaustive analyses of the microbiota, and psychotherapies, to establish future perspectives.

Results: The connection between the microbiota, epigenetic mechanisms and technological developments allows for formulating new approaches objectively oriented towards the development of alternative psychotherapies that may help treat schizophrenia.

Conclusions: In this review, the gut microbiota and epigenetic mechanisms were considered as key regulators, revealing a potential new aetiology of schizophrenia. Likewise, continuous technological advances (e.g. culturomics), aimed at the microbiota-gut–brain axis generate new evidence on this concept.

Schizophrenia Research xxx (2018) xxx–xxx

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Schizophrenia Research

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Analysis of gut microbiota diversity and auxiliary diagnosis as a biomarker in patients with schizophrenia: A cross-sectional study

Yang Shen [a,1], Jintian Xu [b,c,1], Zhiyong Li [a], Yichen Huang [a], Ye Yuan [d], Jixiang Wang [d], Meng Zhang [d], Songnian Hu [b,c,*], Ying Liang [a,**]

Esquizofrénicos n 64
Controles: n 56

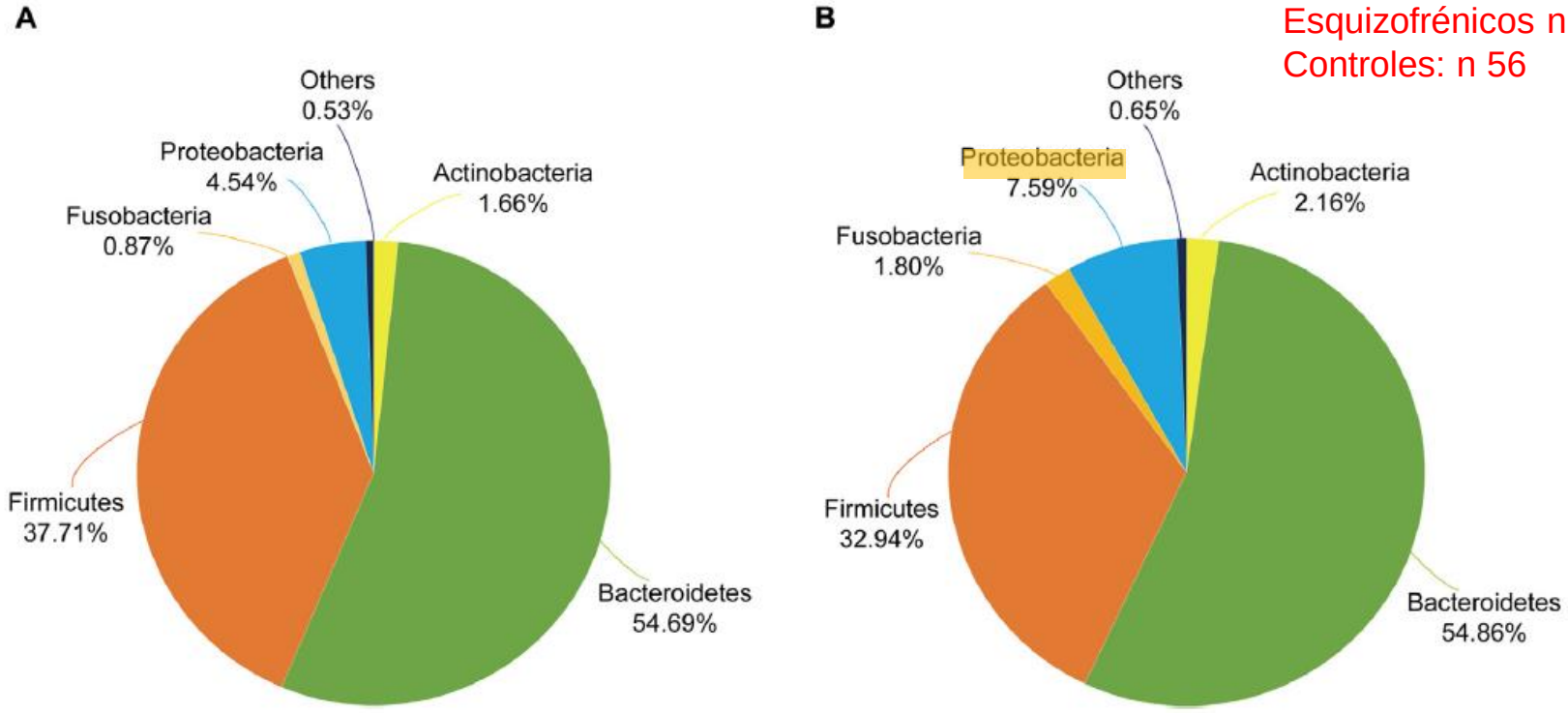

Fig. 2. Microbial composition at phylum level. (A–B) indicate the most abundant phyla detected in the healthy and schizophrenia cohorts. Compared to healthy controls, schizophrenia patients had a significantly higher abundance of *Proteobacteria*.

JORNADA DE PUERTAS ABIERTAS

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ENVEJECIMIENTO Y ANTIOXIDANTES: EL ZUMO DE GRANADA

Dr. Raúl Espert

Dpto. Psicobiología UV

Unidad de Neuropsicología, Hospital Clínico (Valencia)

Antioxidant and antiatherogenic effects of pomegranate

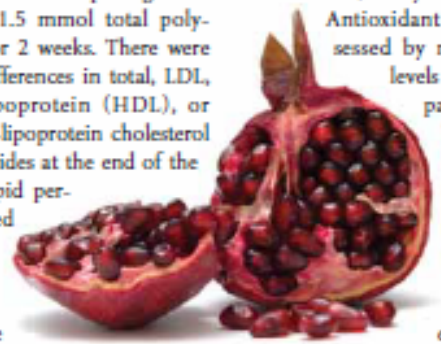
Pomegranate, or *Punica granatum*, has been used for many years as a food and medicinal agent in Asia and South America.[1] In the United States, it is typically made into a juice, or the seeds are consumed as a food. One pomegranate fruit contains about 40% of an adult's recommended daily requirement of vitamin C and is high in polyphenol compounds, which have been suggested to be involved in many diseases. Historically, pomegranate has been used as an anthelmintic and antidiarrheal agent but in recent years has grown in popularity due to its reported antioxidant properties.[1] This article summarizes the human studies that have investigated the antioxidant and antiatherogenic effects of pomegranate.

The pomegranate plant contains alkaloids, mannite, ellagic acid, and gallic acid, and the bark and rind contain various tannins.[1,2] The polyphenols in pomegranate are believed to provide the antioxidant activity and protect low-density lipoprotein (LDL) against cell-mediated oxidation directly by interaction with the lipoprotein and indirectly by accumulation in arterial macrophages. The inner and outer rinds of the fruit contain more polyphenols than the seeds and juice, and commercially prepared pomegranate juice has been found to have more rind constituents and stronger antioxidant effects than hand-processed juice.[1,2] In addition, pomegranate juice may cause antihypertensive effects by decreasing angiotensin-converting enzyme (ACE) activity.[1,3]

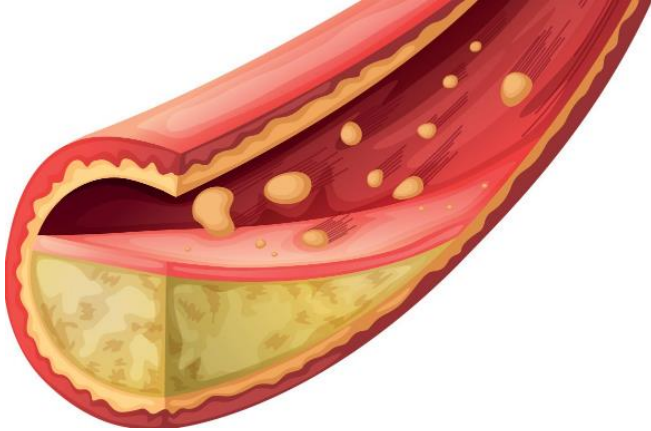
The Alternative Therapies column features short reviews of herbals and other "nutraceuticals" for which there is some scientific evidence of effectiveness. Readers are invited to send ideas for the column to AJHP at ajhp@ashp.org.

A literature search of MEDLINE (1950–May 2010) and International Pharmaceutical Abstracts (1970–May 2010) using the terms *pomegranate, pomegranates, punicaceae,* and *Punica granatum* (with limits for "human and clinical trial, all") identified 10 non-pharmacokinetic, human studies that investigated the clinical antioxidant and antiatherogenic effects of pomegranate. The reference lists of all retrieved articles were reviewed for additional pertinent citations.

Antioxidant effects. In a study by Aviram et al.,[4] 13 healthy men age 20–35 years were given 50 mL of pomegranate juice (equal to 1.5 mmol total polyphenols) daily for 2 weeks. There were no significant differences in total, LDL, high-density-lipoprotein (HDL), or very-low-density-lipoprotein cholesterol levels or triglycerides at the end of the study period. Lipid peroxides decreased significantly by 6%. Antioxidant activity and serum paraoxonase concentration increased significantly by 9% ($p < 0.05$) and 18% ($p < 0.01$), respectively. Three patients were studied for an extended time period of ≤10 weeks and given increasing amounts of pomegranate juice, 20–80 mL daily (equal to 0.54–2.16 mmol total polyphenols). After week 1, lipid peroxide levels decreased by 11% with 20 mL of pomegranate juice daily. The amount of pomegranate juice was increased to 50 mL, which resulted in a 21% decrease in lipid peroxide levels. Pomegranate juice amounts of over 50 mL daily did not result in further changes in lipid peroxide values. Platelet activation was decreased in platelet-rich plasma prepared from 11 volunteers who were given pomegranate juice for 2 weeks, demonstrated by an 11% decrease in collagen-induced platelet aggregation. Limitations of this study included its small sample size, short duration, and lack of a control group. The authors concluded that the antioxidant activity of pomegranate juice may have an important role in atherosclerosis based on its effects on platelets, oxidation, and macrophages.



Rosenblat et al.[5] investigated the effects of pomegranate juice on oxidative stress and blood glucose levels. Ten men age 35–71 years with type 2 diabetes mellitus were given 50 mL of pomegranate juice (equal to 1.5 mmol total polyphenols) daily for three months. Antioxidant activity was assessed by measuring serum levels of lipid peroxides, paraoxonase 1, thiobarbituric acid reactive substances (TBARS), and total sulfhydryl groups. Paraoxonase 1 and total sulfhydryl groups exhibit antiatherosclerotic activity; lipid peroxides and TBARS exhibit oxidative activity. Total sulfhydryl groups are also a marker for oxidative stress. Levels of lipid peroxides and TBARS decreased by 56% and 28%, respectively ($p < 0.01$ for both). Total sulfhydryl groups and paraoxonase 1 levels increased by 12% and 24%, respectively ($p < 0.01$ for both). C-peptide levels (a product of proinsulin) decreased by 23%. Total cholesterol, LDL cholesterol, glycosylated hemoglobin, and triglycerides were not affected by pomegranate consumption. Insulin and glucose levels improved, but the differences were not significant. The



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Pomegranate as a Functional Food and Nutraceutical Source

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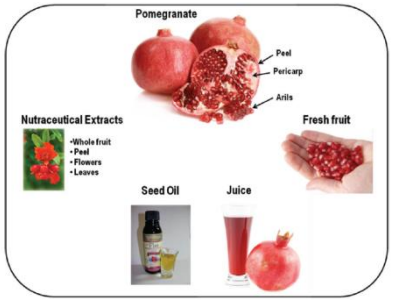

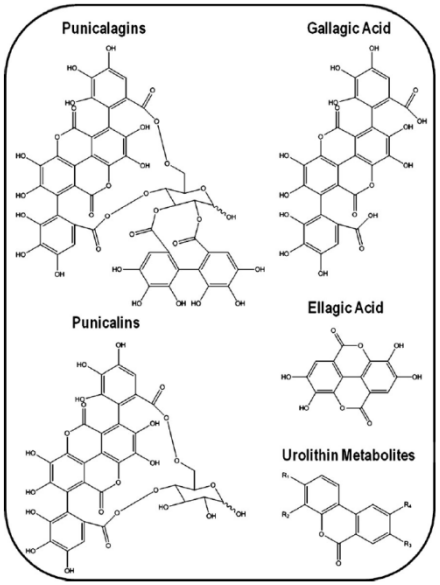

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*Corresponding author

Keywords

antioxidant, ellagitannin, urolithin, cancer, cardiovascular health, diabetes

Abstract

Pomegranate, a fruit native to the Middle East, has gained widespread popularity as a functional food and nutraceutical source. The health effects of the whole fruit, as well as its juices and extracts, have been studied in relation to a variety of chronic diseases. Promising results against cardiovascular disease, diabetes, and prostate cancer have been reported from human clinical trials. The in vitro antioxidant activity of pomegranate has been attributed to its high polyphenolic content, specifically punicalagins, punicalins, gallagic acid, and ellagic acid. These compounds are metabolized during digestion to ellagic acid and urolithins, suggesting that the bioactive compounds that provide in vivo antioxidant activity may not be the same as those present in the whole food. Anthocyanins and the unique fatty acid profile of the seed oil may also play a role in pomegranate's health effects. A more complete characterization of pomegranate components and their physiological fate may provide mechanistic insight into the potential health benefits observed in clinical trials.

Table 1 Scientific studies on the potential health effects of pomegranate products

Disease/health claim	Total studies	Human clinical trials (# study subjects)	Animal model studies	Cell culture studies
Cancer	32	1	11	20
-prostate	11	1 (46)		
-colon	6			
-breast	6			
-skin	3			
-lung	2			
-cervical	1			
-leukemia	1			
Cardiovascular disease	22	8 (10, 13, 22, 20, 45, 289, 30)	9	7
Diabetes	11	3 (22, 20, 30)	7	1
Arthritis	3	0	2	1
Antimicrobial	8	3 (60, 60, 32)	0	5
Skin care	14	2 (20, 13)	5	7
Weight control	3	0	3	0
Inflammatory bowel disease	2	0	2	0
Chronic obstructive pulmonary disease	1	1 (30)	0	0
Alzheimer's disease	1	0	1	0
Neonatal neuroprotectant	1	0	1	0
Male infertility	1	0	1	0
Erectile dysfunction	1	1 (53)	0	0
Immune function	1	0	1	0
Menopause	1	1 (351)	0	0

ELX

GRANADAS DE **ELCHE**
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La UMH y Vitalgrana presentan un estudio sobre los efectos del consumo de zumo de granada en corredores de maratón

lunes, 14 de octubre de 2013

El Servicio de Nutrición Deportiva de la Universidad Miguel Hernández (UMH) de Elche, junto a la empresa especializada en la elaboración de productos derivados de la granada Vitalgrana, presentó el pasado viernes, 11 de octubre, el estudio "Efectos del consumo de zumos de granada Vitalgrana en la resistencia y la recuperación de corredores de maratón". La presentación tuvo lugar a las 18:00 horas en el Aula Magna del edificio Altabix del campus de Elche y, a la misma, asistió el bicampeón Mundial de Maratón Abel Antón.

El estudio, dirigido por el catedrático de Nutrición y Bromatología de la UMH, Enrique Roche, se ha llevado a cabo en deportistas sanos en los que se ha estandarizado la dieta y la carga de trabajo durante 21 días, que en este caso ha consistido en la preparación para correr la media maratón de Santa Pola. Los investigadores han analizado algunos de los parámetros obtenidos de las analíticas sanguíneas y han observado que, aquellos corredores que habían consumido el zumo 100% granada de Vitalgrana de modo regular, sufrían menor daño oxidativo y presentaban una ligera disminución de los niveles de colesterol.

UNIVERSITAS Miguel Hernández

ELCHE

La UMH certifica el zumo de granada ilicitano como el mejor del mercado

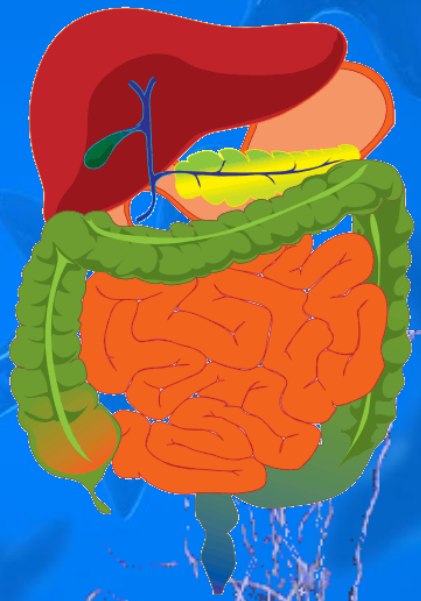
Los investigadores han analizado productos importados de Inglaterra, Alemania, Irlanda y Francia El jugo local mantiene mejor las cualidades del fruto tras el procesado térmico que el fresco

Investigarán los beneficios del zumo de granada para prevenir el Alzheimer

Catral (Alicante), 20 may (EFE).- La empresa de elaboración de zumo natural de granada Vitalgrana, radicada en Elche y con fábrica también en Catral (Alicante), impulsa una investigación sobre los beneficios del consumo de este producto en la prevención del Alzheimer, según ha anunciado su director general, Manuel Esclapez.

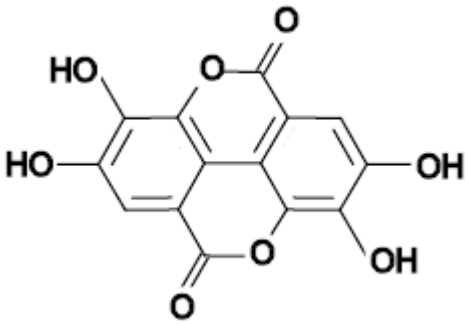
Zumo de granada 100% natural sin aditivos solo granada mollar de elche

ZUMO DE GRANADA Y UROLICINA A: EL PAPEL DE LA MICROBIOTA INTESTINAL



ACIDO ELÁGICO Y URILICINA A

El **ácido elágico** es un polifenol que protege a muchas plantas contra la luz ultravioleta, virus, bacterias y parásitos. El ácido elágico está presente en las plantas como elagitanino, que se activa bajo estrés a ácido elágico. La **urolitina A**, metabolito del ácido elágico, también promueve la regeneración mitocondrial a través de su síntesis por bacterias del colon a partir de la granada.



Según estudios en Japón, Alemania y Estados Unidos de Norteamérica, los elagitaninos de plantas cuando son comidos por mamíferos y humanos, activan sus propiedades protectoras en el cuerpo, **combatiendo inflamaciones crónicas (reuma, artritis), colesterol, radicales libres de oxígeno (peróxidos, superóxidos) y ciertos tipos de cáncer.**

Las fuentes de elagitaninos/ácido elágico son varias nueces y frutas, **en especial las granadas** y frambuesas, estando también presentes en muchos frutos rojos (granadas, fresas, frambuesas, arándanos, moras), en algunos frutos secos (nueces, pacanas y castañas) y también en kiwis y uvas.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2013

THE ABILITY OF POMEGRANATE TO AMELIORATE SYMPTOMS ASSOCIATED WITH ALZHEIMER'S DISEASE IN AGED TRANSGENIC MICE

Aseef H. Ahmed
University of Rhode Island, aahmed@une.edu

Accumulating research has demonstrated that polyphenolic compounds from natural products, such as pomegranate, may have antioxidant and neuroprotective properties in animal models of Alzheimer's disease (AD). However, the present study explores whether the administration of a pomegranate peel extract could have a rescuing effect on AD pathology in aged transgenic animal models of AD. These mice already have abundant AD pathology since amyloid beta (Aβ) deposition continues with time. Two doses of the extract or a control solution were fed daily to groups of transgenic mice (R1.40), ranging in age from 24-30 months. Treatment and behavioral assessment lasted thirty-seven days total. Mice were tested in the Morris water maze and the Y-maze for improvements in spatial, long-term and working memory functions. This was followed by the measurements of cortical amyloid precursor protein (APP) and $A\beta$ levels along with other relevant biomarkers for AD. The resulting data demonstrated a lack of change in cognitive performance in the mazes, as well as the precursor protein and other enzymes associated with the amyloidogenic pathway. However, biochemical analyses revealed an alteration in the levels and ratio of the $A\beta$ peptides that favored a diminution in AD pathogenesis. This was featured by the lowering of the more amyloidogenic $A\beta_{1-42}$ peptide and an increase in the $A\beta_{1-40}$ peptide. Further experiments revealed that this reversal could be the product of the modification of the gamma-secretase enzyme responsible for generating the more amyloidogenic form. In conclusion, pomegranate peel extract appears to contain ingredients that act as gamma-secretase modulators, which may be identified and developed as compounds for use in future drug therapy.

ACS Chemical Neuroscience

DOI: 10.1021/acschemneuro.5b00260
ACS Chem. Neurosci. 2016, 7, 26−33

Letter

pubs.acs.org/chemneuro

Pomegranate's Neuroprotective Effects against Alzheimer's Disease Are Mediated by Urolithins, Its Ellagitannin-Gut Microbial Derived Metabolites

Tao Yuan,[†] Hang Ma,[†] Weixi Liu,[†] Daniel B. Niesen,[†] Nishan Shah,[†] Rebecca Crews,[‡] Kenneth N. Rose,[†] Dhiraj A. Vattem,[‡] and Navindra P. Seeram*[,†]

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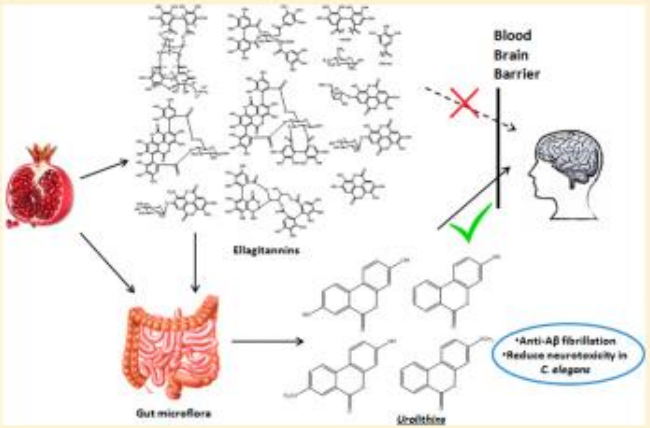
Supporting Information

ABSTRACT: Pomegranate shows neuroprotective effects against Alzheimer's disease (AD) in several reported animal studies. However, whether its constituent ellagitannins and/or their physiologically relevant gut microbiota-derived metabolites, namely, urolithins (6*H*-dibenzo[*b*,*d*]pyran-6-one derivatives), are the responsible bioactive constituents is unknown. Therefore, from a pomegranate extract (PE), previously reported by our group to have anti-AD effects in vivo, 21 constituents, which were primarily ellagitannins, were isolated and identified (by HPLC, NMR, and HRESIMS). In silico computational studies, used to predict blood-brain barrier permeability, revealed that none of the PE constituents, but the urolithins, fulfilled criteria required for penetration. Urolithins prevented β-amyloid fibrillation in vitro and methyl-urolithin B (3-methoxy-6*H*-dibenzo[*b*,*d*]pyran-6-one), but not PE or its predominant ellagitannins, had a protective effect in *Caenorhabditis elegans* post induction of amyloid β_{1-42} induced neurotoxicity and paralysis. Therefore, urolithins are the possible brain absorbable compounds which contribute to pomegranate's anti-AD effects warranting further in vivo studies on these compounds.



KEYWORDS: *Pomegranate, Alzheimer's disease, microbial metabolites, ellagitannins, urolithins, blood-brain barrier*

Clinical Nutrition xxx (2017) 1–9

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Original article

The gut microbiota metabolism of pomegranate or walnut ellagitannins yields two urolithin-metabotypes that correlate with cardiometabolic risk biomarkers: Comparison between normoweight, overweight-obesity and metabolic syndrome

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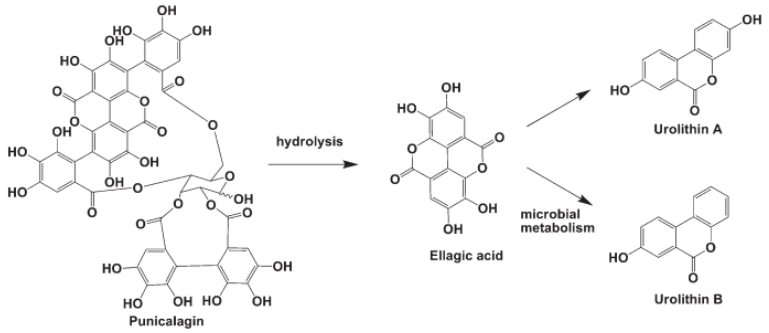

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SUMMARY

Background & aims: Urolithins are microbial metabolites produced after consumption of ellagitannin-containing foods such as pomegranates and walnuts. Parallel to isoflavone-metabolizing phenotypes, ellagitannin-metabolizing phenotypes (urolithin metabotypes A, B and 0; UM-A, UM-B and UM-0, respectively) can vary among individuals depending on their body mass index (BMI), but correlations between urolithin metabotypes (UMs) and cardiometabolic risk (CMR) factors are unexplored. We investigated the association between UMs and CMR factors in individuals with different BMI and health status.
Methods: UM was identified using UPLC-ESI-qToF-MS in individuals consuming pomegranate or nuts. The associations between basal CMR factors and the urine urolithin metabolomic signature were explored in 20 healthy normoweight individuals consuming walnuts (30 g/d), 49 healthy overweight-obese individuals ingesting pomegranate extract (450 mg/d) and 25 metabolic syndrome (MetS) patients consuming nuts (15 g-walnuts, 7.5 g-hazelnuts and 7.5 g-almonds/d).
Results: Correlations between CMR factors and urolithins were found in overweight-obese individuals. Urolithin-A (mostly present in UM-A) was positively correlated with apolipoprotein A-I ($P \leq 0.05$) and intermediate-HDL-cholesterol ($P \leq 0.05$) while urolithin-B and isourolithin-A (characteristic from UM-B) were positively correlated with total-cholesterol, LDL-cholesterol ($P \leq 0.001$), apolipoprotein B ($P \leq 0.01$), VLDL-cholesterol, IDL-cholesterol, oxidized-LDL and apolipoprotein B:apolipoprotein A-I ratio ($P \leq 0.05$). In MetS patients, urolithin-A only correlated inversely with glucose ($P \leq 0.05$). Statin-treated MetS patients with UM-A showed a lipid profile similar to that of healthy normoweight individuals while a poor response to lipid-lowering therapy was observed in MB patients.
Conclusions: UMs are potential CMR biomarkers. Overweight-obese individuals with UM-B are at increased risk of cardiometabolic disease, whereas urolithin-A production could protect against CMR factors. Further research is warranted to explore these associations in larger cohorts and whether the effect of lipid-lowering drugs or ellagitannin-consumption on CMR biomarkers depends on individuals' UM.

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Research Article

Pomegranate Juice Augments Memory and fMRI Activity in Middle-Aged and Older Adults with Mild Memory Complaints

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Despite increasing emphasis on the potential of dietary antioxidants in preventing memory loss and on diet as a precursor of neurological health, rigorous studies investigating the cognitive effects of foods and their components are rare. Recent animal studies have reported memory and other cognitive benefits of polyphenols, found abundantly in pomegranate juice. We performed a preliminary, placebo-controlled randomized trial of pomegranate juice in older subjects with age-associated memory complaints using memory testing and functional brain activation (fMRI) as outcome measures. Thirty-two subjects (28 completers) were randomly assigned to drink 8 ounces of either pomegranate juice or a flavor-matched placebo drink for 4 weeks. Subjects received memory testing, fMRI scans during cognitive tasks, and blood draws for peripheral biomarkers before and after the intervention. Investigators and subjects were all blind to group membership. After 4 weeks, only the pomegranate group showed a significant improvement in the Buschke selective reminding test of verbal memory and a significant increase in plasma trolox-equivalent antioxidant capacity (TEAC) and urolithin A-glucuronide. Furthermore, compared to the placebo group, the pomegranate group had increased fMRI activity during verbal and visual memory tasks. While preliminary, these results suggest a role for pomegranate juice in augmenting memory function through task-related increases in functional brain activity.

GRANADA

Table 1: Demographic and clinical characteristics of subjects at baseline.

Characteristic	Mean (SD)	
	Pomegranate ($n = 15$)	Placebo ($n = 13$)
Mini-mental state examination	28.0 (1.5)	27.8 (1.5)
Age, y	63.1 (8.0)	62.0 (7.8)
Female, no. (%)	11 (73.3)	10 (76.9)
TEAC baseline	1712 (299)	1927 (461)
Buschke selective reminding test		
Recall	85.0 (11.7)	86.5 (12.5)
Consistent long-term retrieval	52.8 (19.9)	55.8 (25.5)

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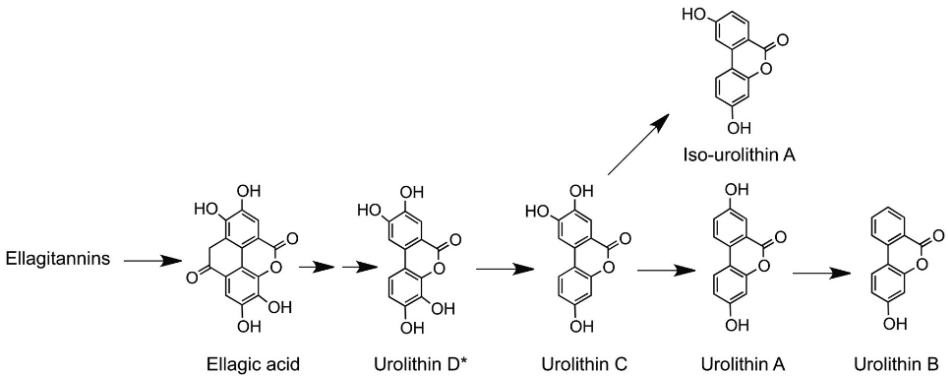


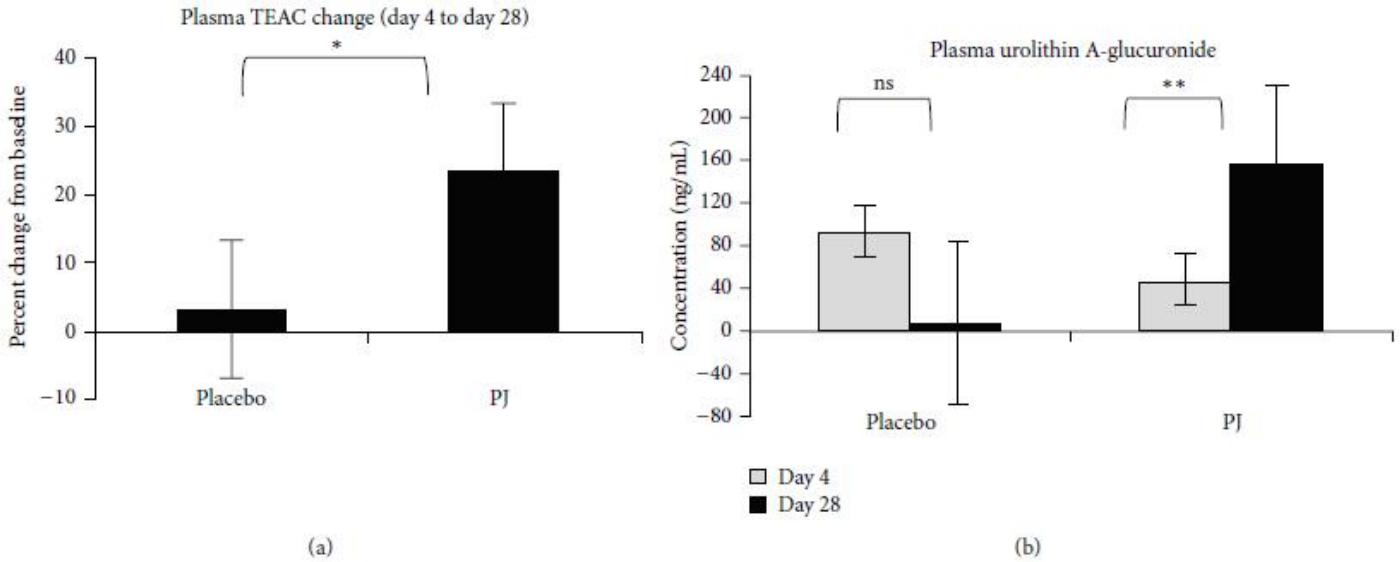


Figure 1: Metabolite results. (a) The pomegranate juice group had significantly higher change in TEAC after day 28 compared with baseline than the placebo group (*unpaired $t = 2.8$, df = 25, $p < .05$). (b) Plasma urolithin A-glucuronide significantly increased in the pomegranate juice group (**paired $t = 3.93$, df = 13, $p < .00064$), but not in the placebo group (paired $t = 1.7$, df = 11, $p > .09$).

Research Article

Pomegranate Juice Augments Memory and fMRI Activity in Middle-Aged and Older Adults with Mild Memory Complaints

TEST DE MEMORIA LIBRE Y SELECTIVAMENTE FACILITADO (FCSRT)

Free and Cued Selective Reminding Test (FCSRT)

FAutor: Buschke , 1984

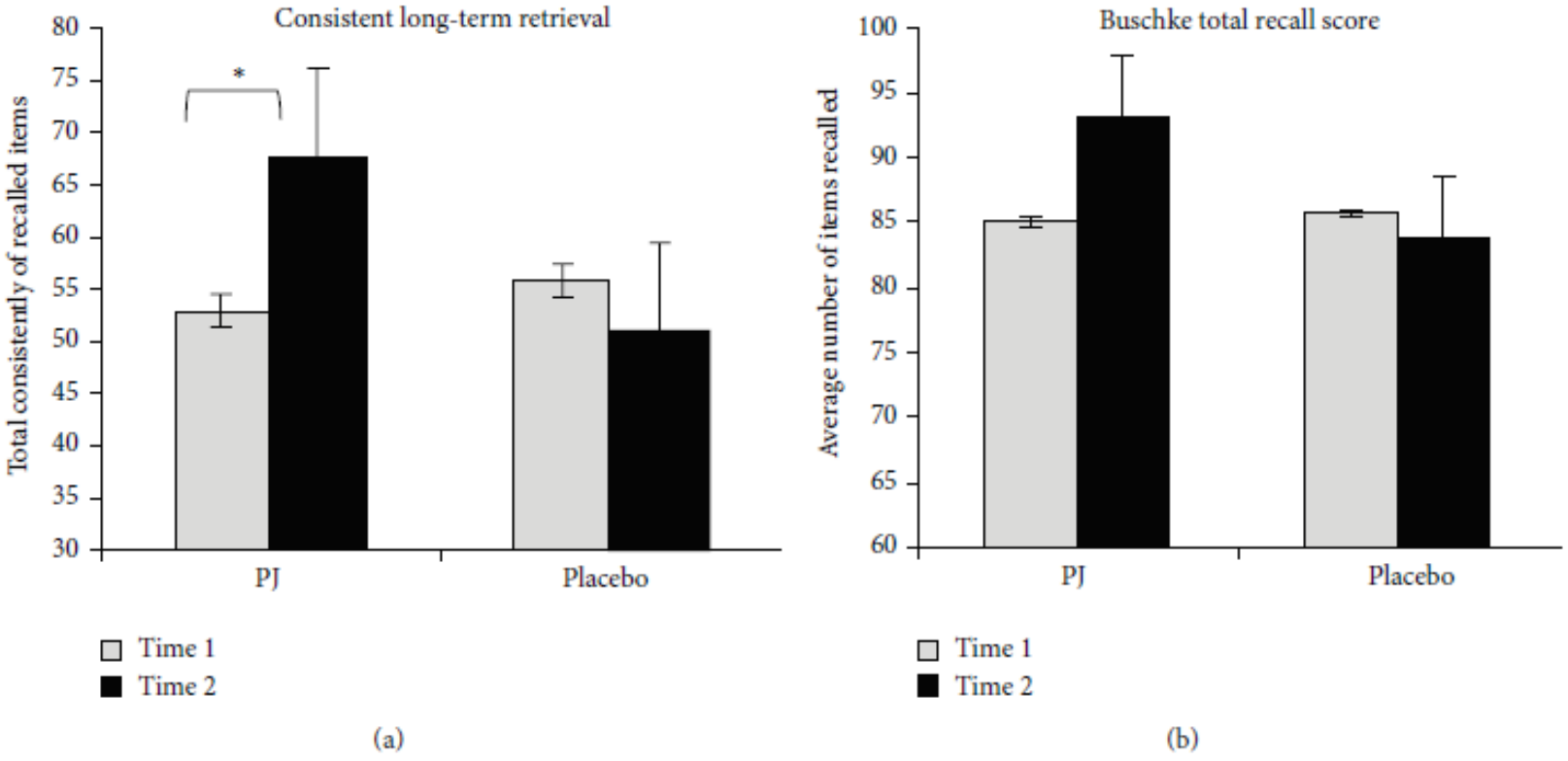
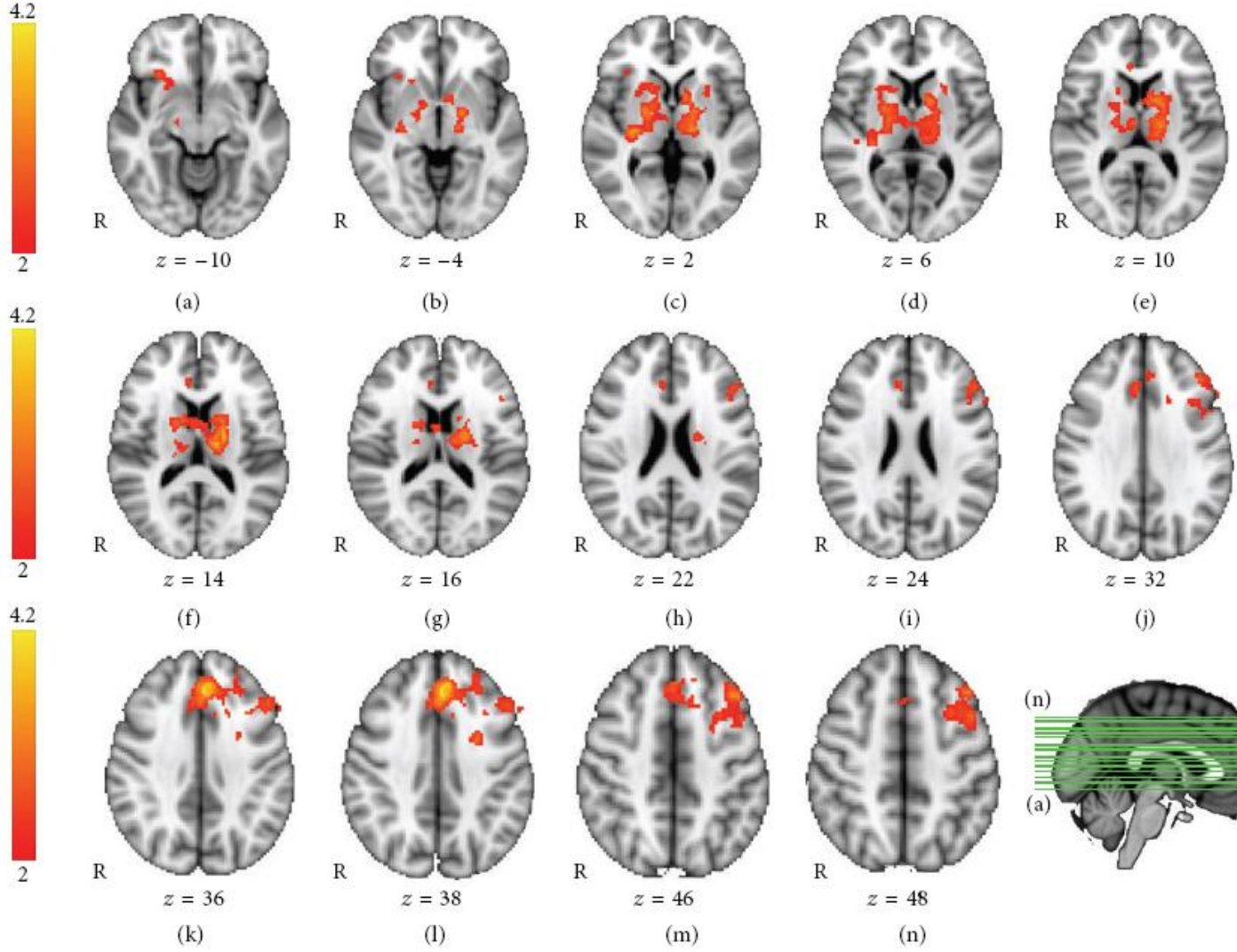
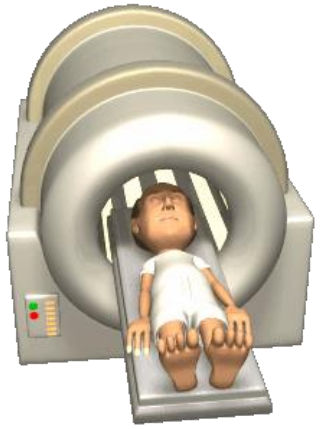


FIGURE 2: Buschke selective reminding test results. (a) On the total recall measure, the $t2$ versus $t1$ change in memory scores was significantly greater in the pomegranate juice group compared to the placebo group (mean change, number of items recalled: PJ = 7.7, placebo = –2.77; $t = 2.3$; $P = .029$). (b) Similarly, on the consistent long-term retrieval score the pomegranate juice group recalled more items compared to the placebo group (mean change, number of items consistently recalled: PJ = 15.2, placebo = –9.7; $t = 2.4$; $P = .022$).

Pomegranate Juice Augments Memory and fMRI Activity in Middle-Aged and Older Adults with Mild Memory Complaints





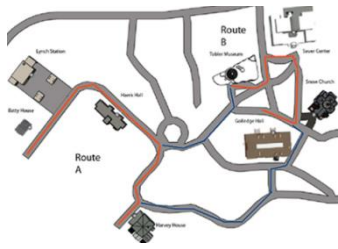


FIGURE 3: Visual memory fMRI task: between-groups $T2$ versus $T1$ ANOVA. Regions showing greater activation for $t2 > t1$, for the pomegranate juice group > placebo group (group by time interaction), were found bilaterally in the basal ganglia and thalamus, including caudate, putamen, and pallidum (ANOVA, $Z > 2.0$, $P = .05$, corrected for multiple comparisons). Additional regions significant at an uncorrected threshold ($Z > 1.7$) are listed in Table 2.

Pomegranate Juice Augments Memory and fMRI Activity in Middle-Aged and Older Adults with Mild Memory Complaints

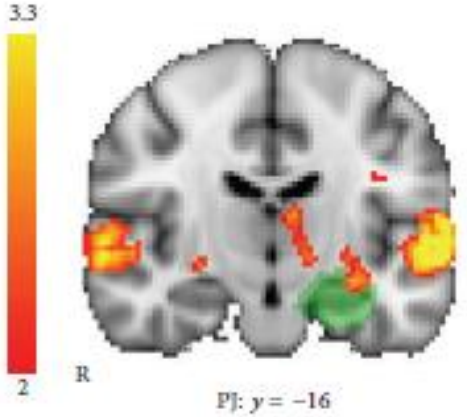


FIGURE 5: Verbal memory fMRI task: within-group activations at $t2$. Comparing the within-group results for time point $t2$, there were activation similarities and differences in the placebo group ((a): top) and the pomegranate group ((b): bottom). Only the pomegranate group recruited the hippocampus, bilaterally (group mean: placebo, $Z > 2.0, P = .05$, corrected for multiple comparisons, pomegranate, $Z > 2.0, P = .05$, corrected for multiple comparisons).

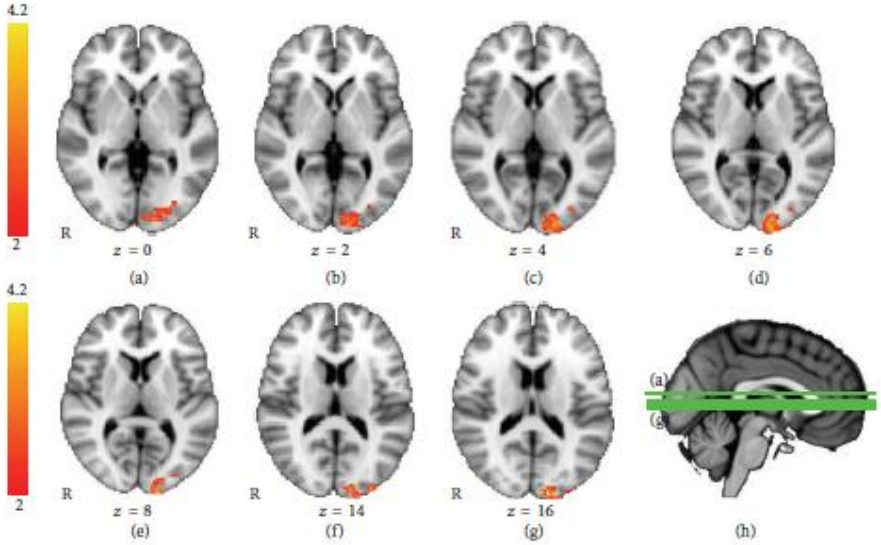


FIGURE 6: Verbal memory fMRI task: between-groups $T2$ versus $T1$ ANOVA. Regions showing greater activation for $t2 > t1$, for pomegranate group > placebo group, were found in the left hemisphere in occipital polar regions (ANOVA, $Z > 2.0, P = .05$, corrected for multiple comparisons).

Los 25 antioxidantes más eficaces

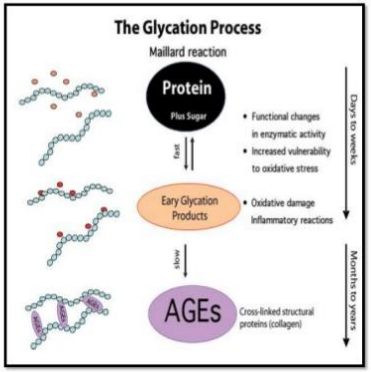
Entre las muchas sustancias que retrasan los procesos físicos de degeneración y envejecimiento celular, éstas son las más aceptadas:

ANTIOXIDANTE	DOSIS	EFECTO ANTIOXIDANTE	FUENTES ALIMENTICIAS Y OBSERVACIONES
Acido alfa-lipoico	50-200 mg	Tónico, regulador de la glucosa	Patatas.
Acido DHGLA	200-1.000 mg	Previene quistes y cáncer de ovario y mama	Semillas de borraja y onagra.
Acido linoleico	1-5 g.	Anticáncer	Aceites de semillas (girasol, soja y maíz).
Acido fólico	400-1.000 mg	Previene la anemia	Levadura de cerveza, germen de trigo, soja y otras legumbres, espárragos, nueces, espinacas, brécol.
Antocianidinas	500-3.000 mg	Mejora la circulación venosa	Arándanos, moras, mirtilos, remolacha, col lombarda.
Betacaroteno	6-40 mg	Anticáncer	Mango, naranjas, calabaza, zanahoria.
Carnitina	500-1.000 mg.	Antienvejecimiento, tónico	Leche, levadura de cerveza, carne, hígado.
Cinc	15-50 mg	Protege el corazón y la piel	Ostras, semillas de calabaza, jengibre, cordero, hígado, guisantes, leche, yema de huevo, frutos secos, pescado azul, perejil.
Coenzima Q-10	30-300 mg	Protege las arterias	Huevos, espinacas, cereales, judías secas, algunos aceites.
Curcuminoides	100-300 mg	Protegen el hígado	Cúrcuma (*Curcuma longa* y *Curcuma xantorrhiza*).
Glutatión	5-100 mg	Estimula la depuración	Alimentos crudos.
Licopeno	5-20 mg	Anticancer, protege las arterias	Tomates.
Magnesio	200-3.000 mg	Antiestrés, relajante	Salvado, almendras, levadura de cerveza, cacahuetes, nueces, tofu, soja, espinacas, arroz integral, perejil, semillas de girasol.
Manganeso	2-4 mg	Activa sistemas enzimáticos	Almendras, centeno, nueces, pasas, ruibarbo, coles de bruselas, zanahorias, brécol, arroz y trigo integral.
N-acetil-cisteína	500-2.000 mg.	Protege el hígado	Ajo, cebolla, puerro, col, nabos.
Picnogenol	5-250 mg	Antialérgico	Se extrae de la corteza del pino marítimo.
Piridoxina (B_6)	50-100 mg	Protege las neuronas	Levadura de cerveza, semillas de girasol, germen de trigo, soja, frutos secos, salmón, legumbres, arroz integral, plátanos.
Polifenoles	5-50 mg	Reducción de peso	Té, sobre todo el verde, patatas y ajos.
Quercitina	100-300 mg.	Protege las células	Cebollas, té, vino tinto y manzanas en ese orden.
Riboflavina (B_2)	10-100 mg	Antitumoral	Levadura de cerveza, hígado, almendras, germen de trigo, setas, yema de huevo, guindillas, harina de soja, arenque, perejil.
Selenio	100-400 mcg	Anticáncer	Mantequilla, pescado ahumado, germen de trigo, vinagre de sidra, pan integral, marisco, salvado, leche, arroz integral.
S.O.D.	Según prescripción	Protector celular	Se obtiene a partir de semillas germinadas.
Taurina	500-3000 mg	Tónico adaptógeno	Ostras y almejas, carnes de buey, pollo y cerdo.
Vitamina C	1 g	Tónico	Pimiento (más en el rojo), kiwi, perejil, mango, coles, berros, papaya, espinaca, fresas, naranjas, limón, pomelo.
Vitamina E	400 UI	Mejora la fertilidad	Aceite de germen de trigo, semillas de girasol, almendras, sésamo, cacahuetes, espinacas, espárragos, cereales integrales.

ADVANCED GLYCATION END PRODUCTS (AGEs)

Hyperglycemic state

Non enzymatic Glycosylation of proteins and matrix molecules



Food & Function

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Pomegranate phenolics inhibit formation of advanced glycation endproducts by scavenging reactive carbonyl species†

Weixi Liu,‡[a] Hang Ma,‡[b] Leslie Frost,[c] Tao Yuan,[b,d] Joel A. Dain*[a] and Navindra P. Seeram*[b]

Advanced Glycation Endproducts (AGEs) are a heterogeneous group of molecules produced from non-enzymatic glycation. Accumulation of AGEs *in vivo* plays an important role in the pathology of chronic human diseases including type-2 diabetes and Alzheimer's disease. Natural AGEs inhibitors such as the pomegranate (*Punica granatum*) fruit show great potential for the management of these diseases. Herein, we investigated the *in vitro* anti-glycation effects of a pomegranate fruit extract (PE), its phenolic constituents [punicalagin (PA), ellagic acid (EA) and gallic acid (GA)], and their *in vivo* derived colonic metabolites [urolithin A (UA) and urolithin B (UB)]. All of the samples showed anti-glycation activities and PE, PA, and EA were more potent inhibitors than the positive control, aminoguanidine. PE and the purified phenolics also exhibited carbonyl scavenger reactivity. Our study suggests that pomegranate may offer an attractive dietary strategy for the prevention and treatment of AGE-related diseases such as type-2 diabetes and Alzheimer's disease.

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www.rsc.org/foodfunction


ENVEJECIMIENTO Y
COMPUESTOS "AGE"
3:37

Molecular Nutrition & Food Research

2168 DOI 10.1002/mnfr.201500264 Mol. Nutr. Food Res. 2015, 59, 2168–2177

RESEARCH ARTICLE

Urolithins, gut microbiota-derived metabolites of ellagitannins, inhibit LPS-induced inflammation in RAW 264.7 murine macrophages

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[2] Institute of Physiology, Center for Physiology and Pharmacology, Medical University of Vienna, Vienna, Austria

Scope: Ellagitannin-rich food products and medicinal plant materials were shown to have beneficial effects toward intestinal inflammation. Due to the questionable bioavailability of ellagitannins their gut microbiota metabolites-urolithins have come to be regarded as potential factors responsible for biological activities observed in vivo. The aim of the study was to determine the influence of the three most abundant bioavailable ellagitannin gut microbiota metabolites-urolithins A, B, and C on inflammatory responses in RAW 264.7 murine macrophages, which are involved in the pathogenesis of intestine inflammation.

Methods and results: Urolithins A, B, and C decreased NO production via inhibition of the iNOS protein and mRNA expression. They decreased the expression of IL-1β, TNF-α, and IL-6 mRNA in LPS challenged RAW 264.7 murine macrophages. A clear inhibition of NF-κB p65 nuclear translocation and p50 DNA-binding activity was associated with the observed anti-inflammatory activities of urolithins. Among the tested compounds urolithin A had the strongest anti-inflammatory activity.

Conclusion: The anti-inflammatory effects of urolithins at concentrations that are physiologically relevant for gut tissues (≥40 μM), as revealed in this study, support the data from in vivo studies showing the beneficial effects of ellagitannin-rich products toward intestinal inflammation.

Keywords:
Ellagitannins / Inflammatory bowel disease / Inflammation / Macrophages / Urolithins

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Research Article

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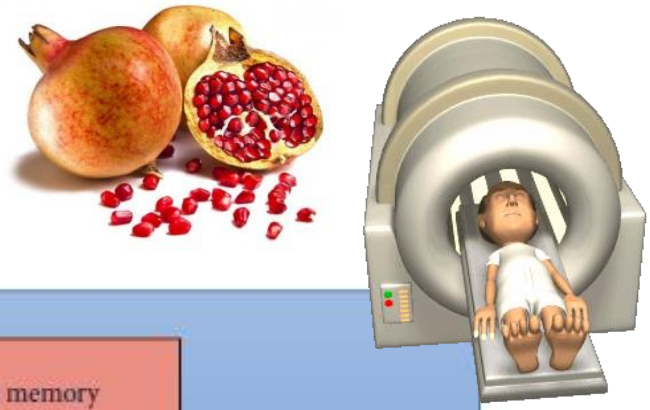

FIGURE 8: Summary of study results. Our data suggest that the antioxidant properties of pomegranate produce increased task related cerebral blood flow, with lateralized effects for verbal versus visual memory challenge, which in turn increased cerebral blood flow facilitates memory performance. Metabolic measures confirm the increase in polyphenols among the experimental group.

The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

Leading Edge
Review

Cell *167*, November 3, 2016

Neurodevelopment is a complex process governed by both intrinsic and extrinsic signals. While historically studied by researching the brain, inputs from the periphery impact many neurological conditions. Indeed, emerging data suggest communication between the gut and the brain in anxiety, depression, cognition, and autism spectrum disorder (ASD). The development of a healthy, functional brain depends on key pre- and post-natal events that integrate environmental cues, such as molecular signals from the gut. These cues largely originate from the microbiome, the consortium of symbiotic bacteria that reside within all animals. Research over the past few years reveals that the gut microbiome plays a role in basic neurogenerative processes such as the formation of the blood-brain barrier, myelination, neurogenesis, and microglia maturation and also modulates many aspects of animal behavior. Herein, we discuss the biological intersection of neurodevelopment and the microbiome and explore the hypothesis that gut bacteria are integral contributors to development and function of the nervous system and to the balance between mental health and disease.

The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
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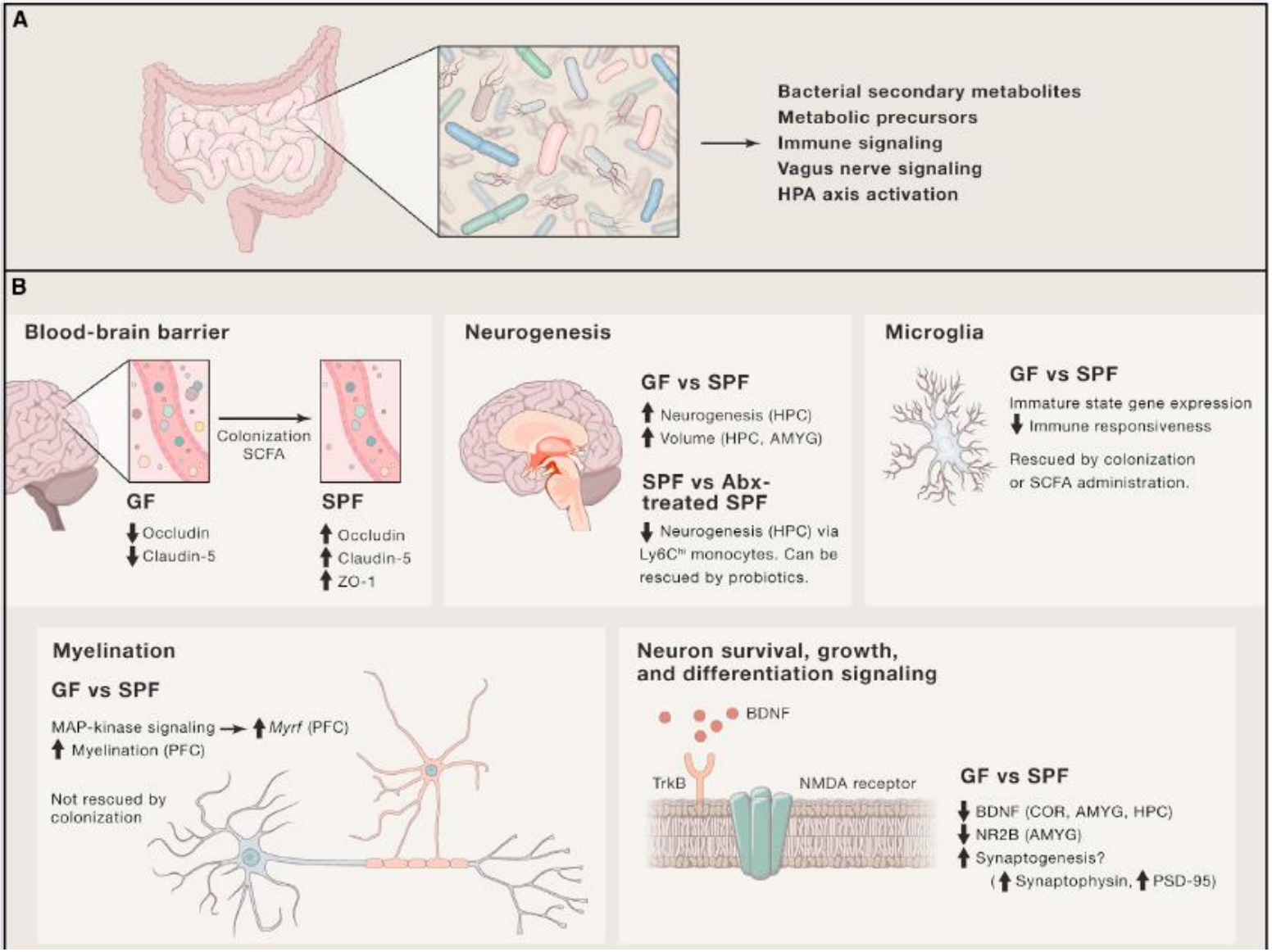

Figure 1. Intersections of Gut Microorganisms and Basic Developmental Processes

Basic developmental processes driven directly or indirectly by gut microbes and their products.

(A) Gut microorganisms relay messages to the brain via various direct and indirect mechanisms.

(B) Basic neurodevelopmental processes are modulated as a result of colonization of GF animals or depletion of gut bacteria by antibiotics. Specifically, the following processes are modulates: blood-brain barrier (BBB) formation and integrity (Braniste et al., 2014), neurogenesis (Möhle et al., 2016; Ogbonnaya et al., 2015), microglia maturation and ramification (Erny et al., 2015; Matcovitch-Natan et al., 2016), myelination (Gacias et al., 2016; Hoban et al., 2016) and expression of neurotrophins (Bercik et al., 2011a, 2011b; Desbonnet et al., 2015), neurotransmitters (Bercik et al., 2011a; O'Mahony et al., 2015), and their respective receptors.

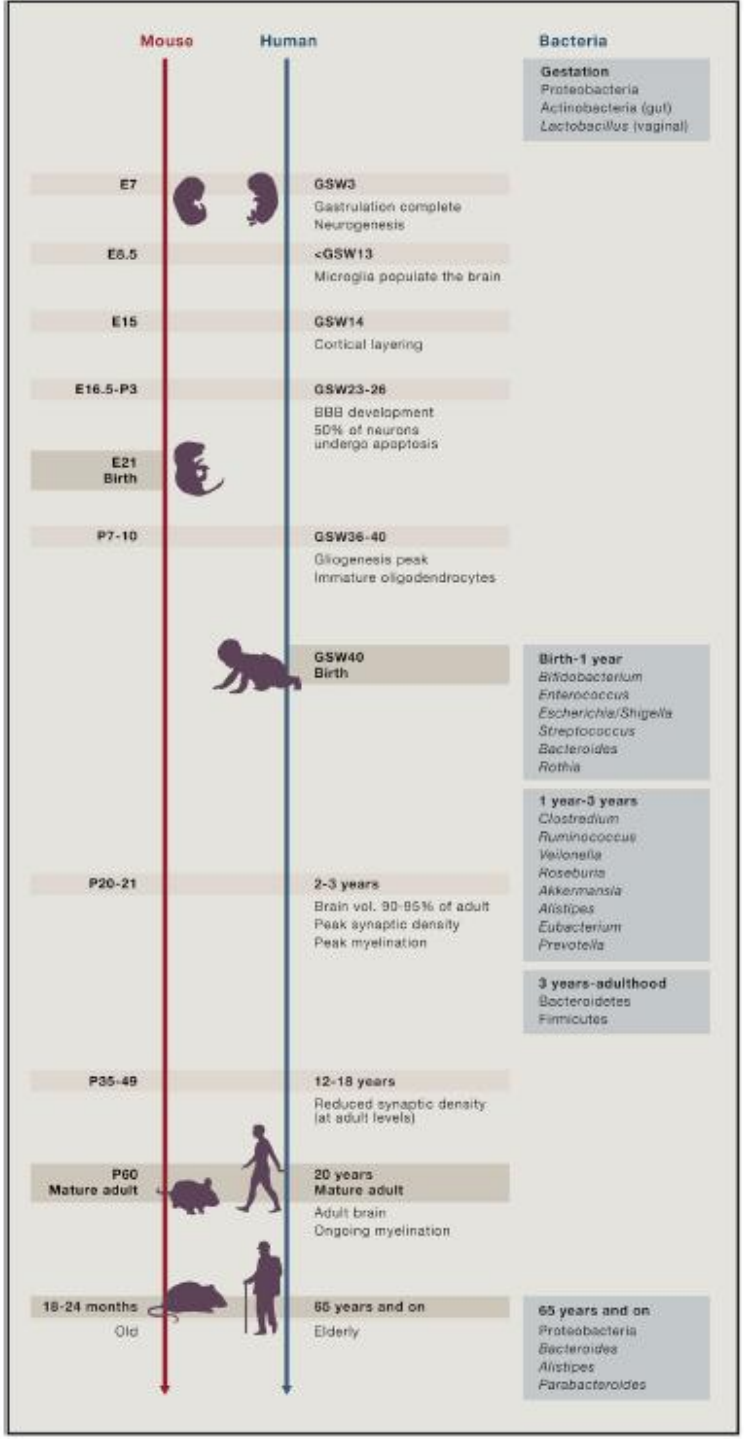

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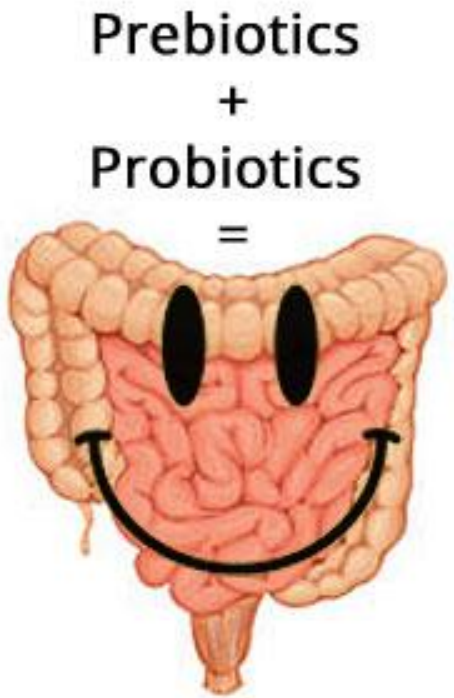
Figure 2. Major Events in Mammalian Brain Development

Developmental trajectories and key neurodevelopmental events in mice and humans (adapted from Knuesel et al., 2014; Pressler and Auvin, 2013; Semple et al., 2013). E, embryonic age; P, postnatal age; GSW, gestational week. Bacterial taxa on the right panel are the dominant ones at each life stage (Bäckhed et al., 2015; Lloyd-Price et al., 2016; Nuriel-Ohayon et al., 2016).



LA REVOLUCIÓN DE LOS PSICOBIÓTICOS

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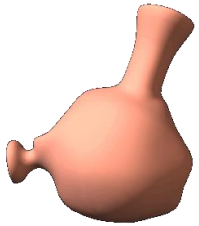

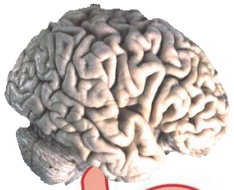

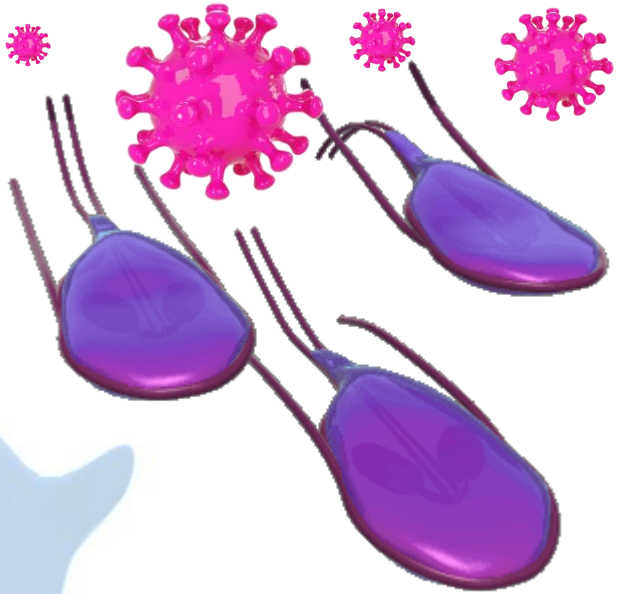

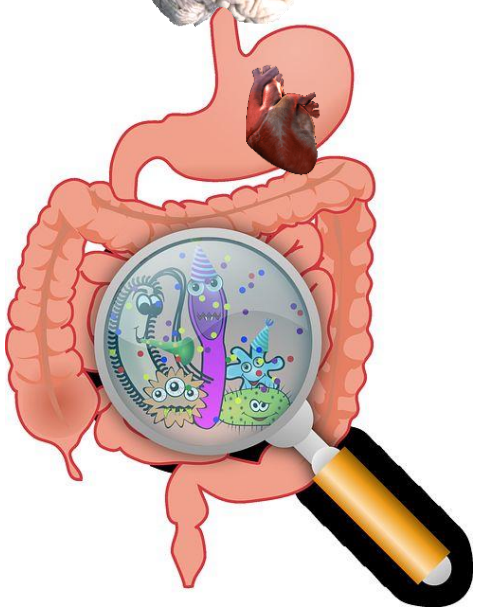

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Review

Cell *167*, November 3, 2016

Neurodevelopment is a complex process governed by both intrinsic and extrinsic signals. While historically studied by researching the brain, inputs from the periphery impact many neurological conditions. Indeed, emerging data suggest communication between the gut and the brain in anxiety, depression, cognition, and autism spectrum disorder (ASD). The development of a healthy, functional brain depends on key pre- and post-natal events that integrate environmental cues, such as molecular signals from the gut. These cues largely originate from the microbiome, the consortium of symbiotic bacteria that reside within all animals. Research over the past few years reveals that the gut microbiome plays a role in basic neurogenerative processes such as the formation of the blood-brain barrier, myelination, neurogenesis, and microglia maturation and also modulates many aspects of animal behavior. Herein, we discuss the biological intersection of neurodevelopment and the microbiome and explore the hypothesis that gut bacteria are integral contributors to development and function of the nervous system and to the balance between mental health and disease.

The Central Nervous System and the Gut Microbiome

Gil Sharon,[1,*] Timothy R. Sampson,[1] Daniel H. Geschwind,[2,3,4,5] and Sarkis K. Mazmanian[1,*]
[1]Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

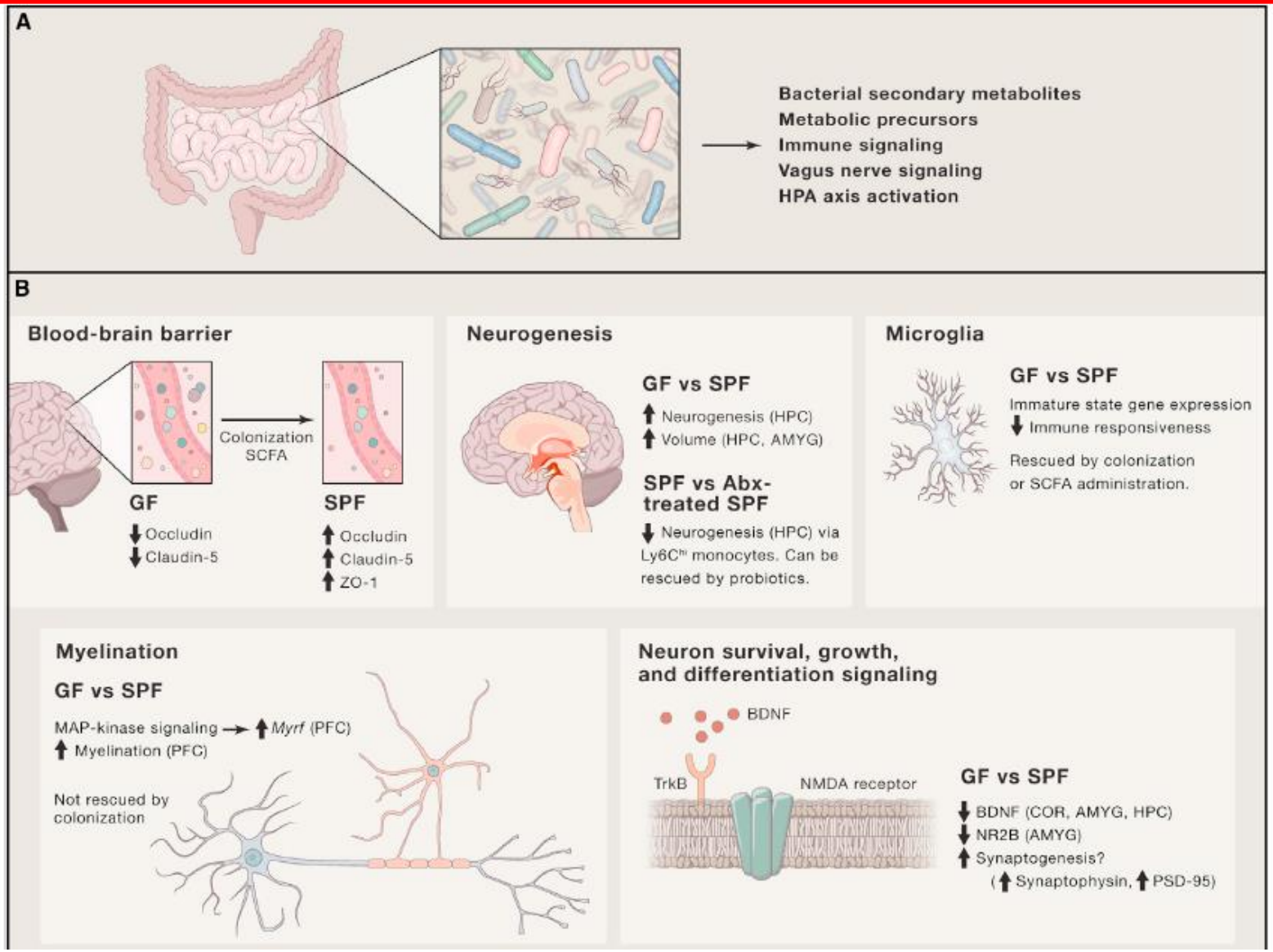
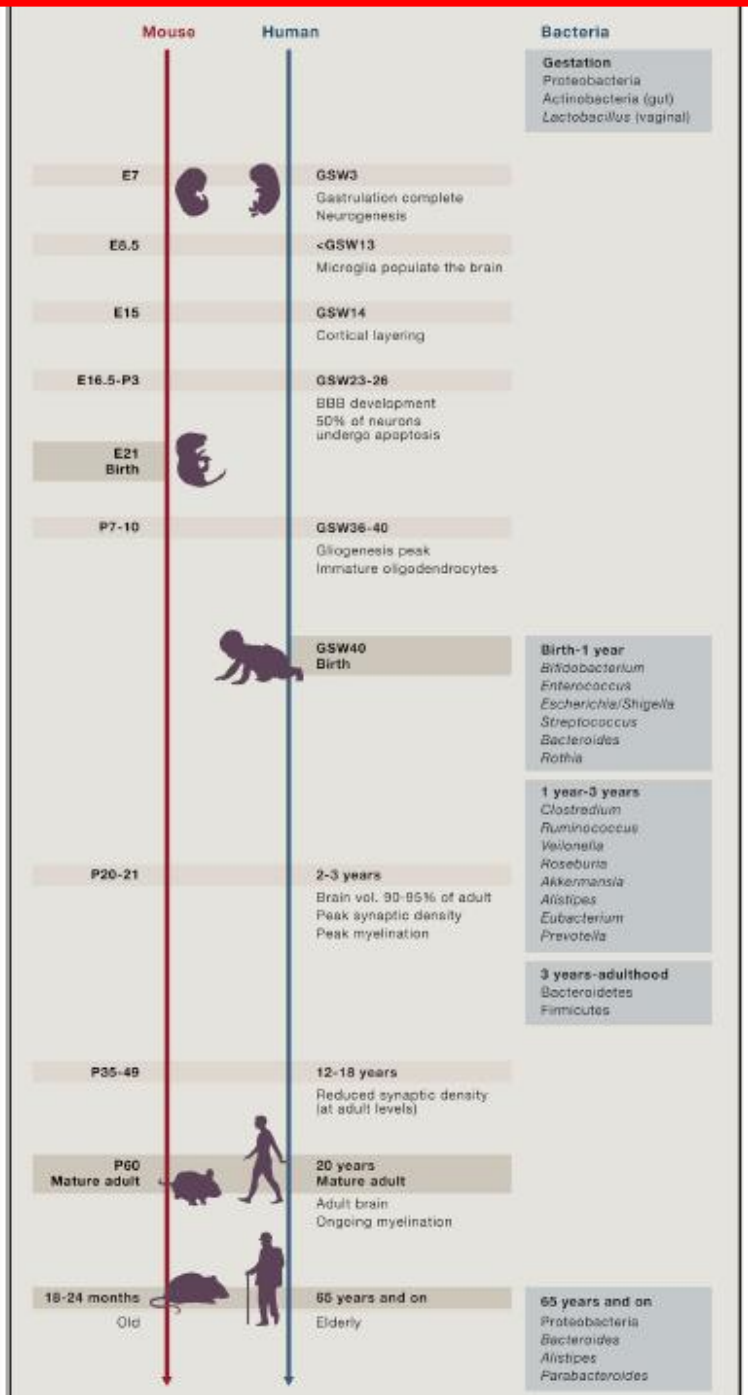


Figure 1. Intersections of Gut Microorganisms and Basic Developmental Processes

Basic developmental processes driven directly or indirectly by gut microbes and their products.

(A) Gut microorganisms relay messages to the brain via various direct and indirect mechanisms.

(B) Basic neurodevelopmental processes are modulated as a result of colonization of GF animals or depletion of gut bacteria by antibiotics. Specifically, the following processes are modulates: blood-brain barrier (BBB) formation and integrity (Braniste et al., 2014), neurogenesis (Möhle et al., 2016; Ogbonnaya et al., 2015), microglia maturation and ramification (Erny et al., 2015; Matcovitch-Natan et al., 2016), myelination (Gacias et al., 2016; Hoban et al., 2016) and expression of neurotrophins (Bercik et al., 2011a, 2011b; Desbonnet et al., 2015), neurotransmitters (Bercik et al., 2011a; O'Mahony et al., 2015), and their respective receptors.



The Central Nervous System and the Gut Microbiome

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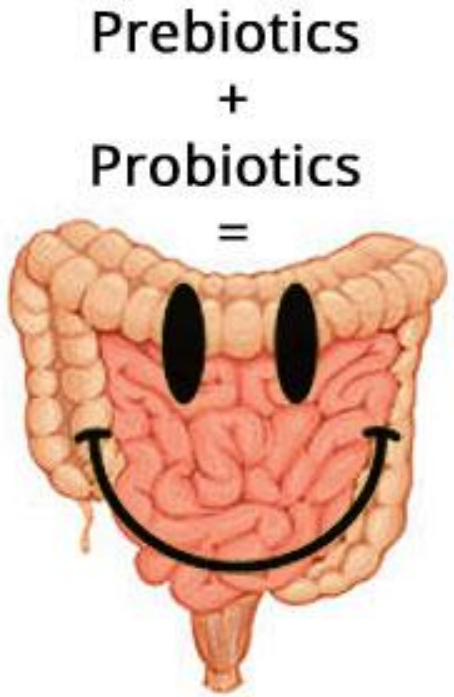
Figure 2. Major Events in Mammalian Brain Development

Developmental trajectories and key neurodevelopmental events in mice and humans (adapted from Knuesel et al., 2014; Pressler and Auvin, 2013; Semple et al., 2013). E, embryonic age; P, postnatal age; GSW, gestational week. Bacterial taxa on the right panel are the dominant ones at each life stage (Bäckhed et al., 2015; Lloyd-Price et al., 2016; Nuriel-Ohayon et al., 2016).



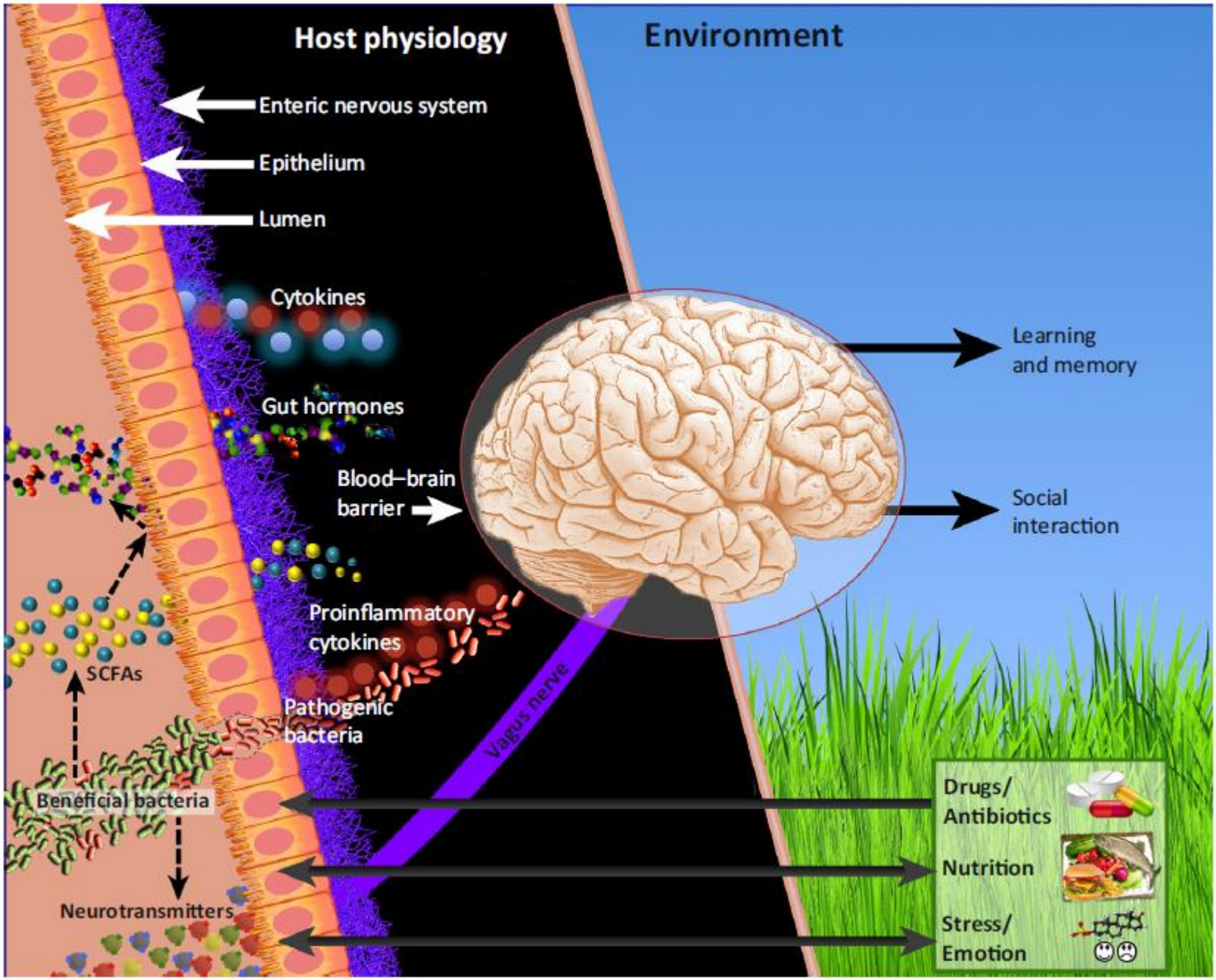
Trends in Cognitive Sciences

The Microbiome in Psychology and Cognitive Neuroscience

Trends in Cognitive Sciences, July 2018, Vol. 22, No. 7

Amar Sarkar,[1,2,3,*] Siobhán Harty,[1,4] Soili M. Lehto,[5,6,7] Andrew H. Moeller,[8] Timothy G. Dinan,[9,10] Robin I.M. Dunbar,[1] John F. Cryan,[10,11] and Philip W.J. Burnet[12]

Psychology and microbiology make unlikely friends, but the past decade has witnessed striking bidirectional associations between intrinsic gut microbes and the brain, relationships with largely untested psychological implications. Although microbe–brain relationships are receiving a great deal of attention in biomedicine and neuroscience, psychologists have yet to join this journey. Here, we illustrate microbial associations with emotion, cognition, and social behavior. However, despite considerable enthusiasm and potential, technical and conceptual limitations including low statistical power and lack of mechanistic descriptions prevent a nuanced understanding of microbiome–brain–behavior relationships. Our goal is to describe microbial effects in domains of cognitive significance and the associated challenges to stimulate interdisciplinary research on the contribution of this hidden kingdom to psychological processes.


Host physiology
Environment
Enteric nervous system
Epithelium
Lumen
Cytokines
Gut hormones
Blood–brain barrier
Proinflammatory cytokines
Pathogenic bacteria
SCFAs
Beneficial bacteria
Neurotransmitters
Vagus nerve
Learning and memory
Social interaction
Drugs/ Antibiotics
Nutrition
Stress/ Emotion

nutrients Review 20 April 2019 MDPI

Review

From Probiotics to Psychobiotics: Live Beneficial Bacteria Which Act on the Brain-Gut Axis

Luis G. Bermúdez-Humarán [1,*], Eva Salinas [2], Genaro G. Ortiz [3], Luis J. Ramirez-Jirano [3], J. Alejandro Morales [4] and Oscar K. Bitzer-Quintero [3,*]

Abstract: There is an important relationship between probiotics, psychobiotics and cognitive and behavioral processes, which include neurological, metabolic, hormonal and immunological signaling pathways; the alteration in these systems may cause alterations in behavior (mood) and cognitive level (learning and memory). Psychobiotics have been considered key elements in affective disorders and the immune system, in addition to their effect encompassing the regulation of neuroimmune regulation and control axes (the hypothalamic-pituitary-adrenal axis or HPA, the sympathetic-adrenal-medullary axis or SAM and the inflammatory reflex) in diseases of the nervous system. The aim of this review is to summarize the recent findings about psychobiotics, the brain-gut axis and the immune system. The review focuses on a very new and interesting field that relates the microbiota of the intestine with diseases of the nervous system and its possible treatment, in neuroimmunomodulation area. Indeed, although probiotic bacteria will be concentrated after ingestion, mainly in the intestinal epithelium (where they provide the host with essential nutrients and modulation of the immune system), they may also produce neuroactive substances which act on the brain-gut axis.

Neuropsychiatric Disease and Treatment

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REVIEW

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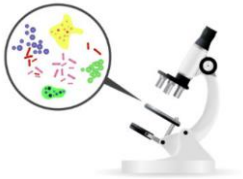
Psychobiotics and the gut–brain axis: in the pursuit of happiness

Prebióticos y Probióticos



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16 March 2015
Number of times this article has been viewed

Linghong Zhou[1]
Jane A Foster[1,2]

[1]Department of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON, Canada; [2]Brain-Body Institute, St Joseph's Healthcare, Hamilton, ON, Canada

Abstract: The human intestine houses an astounding number and species of microorganisms, estimated at more than 10^{14} gut microbiota and composed of over a thousand species. An individual's profile of microbiota is continually influenced by a variety of factors including but not limited to genetics, age, sex, diet, and lifestyle. Although each person's microbial profile is distinct, the relative abundance and distribution of bacterial species is similar among healthy individuals, aiding in the maintenance of one's overall health. Consequently, the ability of gut microbiota to bidirectionally communicate with the brain, known as the gut–brain axis, in the modulation of human health is at the forefront of current research. At a basic level, the gut microbiota interacts with the human host in a mutualistic relationship – the host intestine provides the bacteria with an environment to grow and the bacterium aids in governing homeostasis within the host. Therefore, it is reasonable to think that the lack of healthy gut microbiota may also lead to a deterioration of these relationships and ultimately disease. Indeed, a dysfunction in the gut–brain axis has been elucidated by a multitude of studies linked to neuropsychological, metabolic, and gastrointestinal disorders. For instance, altered microbiota has been linked to neuropsychological disorders including depression and autism spectrum disorder, metabolic disorders such as obesity, and gastrointestinal disorders including inflammatory bowel disease and irritable bowel syndrome. Fortunately, studies have also indicated that gut microbiota may be modulated with the use of probiotics, antibiotics, and fecal microbiota transplants as a prospect for therapy in microbiota-associated diseases. This modulation of gut microbiota is currently a growing area of research as it just might hold the key to treatment.

Keywords: gut microbiota, mental illness, disease, modulation, therapy, probiotics

Prebiotics
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Probiotics
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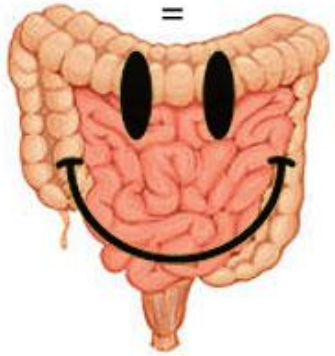

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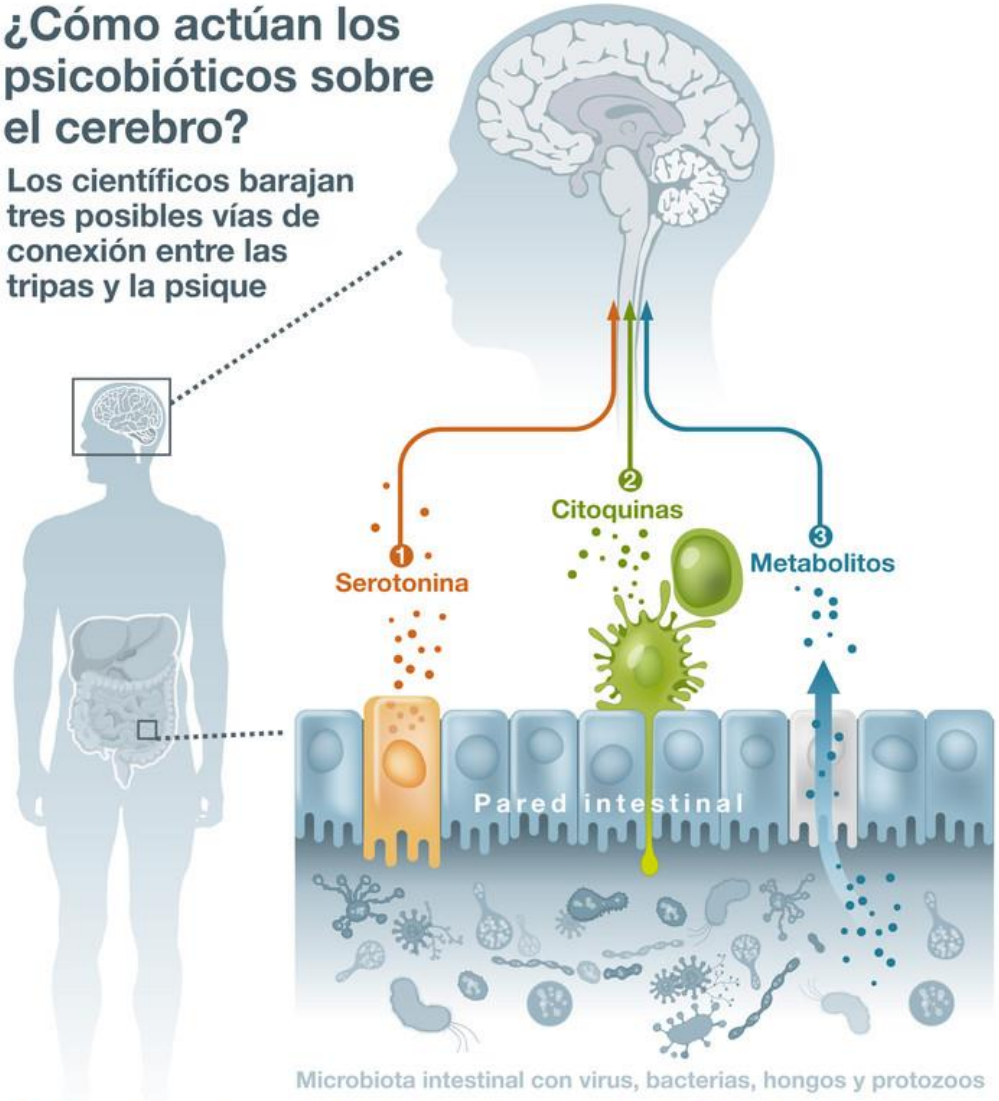
¿Cómo actúan los psicobióticos sobre el cerebro?

Los científicos barajan tres posibles vías de conexión entre las tripas y la psique



Microbiota intestinal con virus, bacterias, hongos y protozoos

1. Neurotransmisores

En el intestino, las células del sistema nervioso entérico producen serotonina, un neurotransmisor, que manda señales al cerebro. Los psicobióticos podrían actuar directamente sobre esas células.

2. Sistema inmunitario intestinal

Los psicobióticos pueden hacer que sus células produzcan citoquinas y estas proteínas influyan sobre el cerebro.

3. Moléculas bacterianas

Los microorganismos también pueden producir metabolitos que alteren la actividad en la barrera hematoencefálica y sean beneficiosos para el cerebro.

Distribución normal de la microbiota en el tracto Gastrointestinal

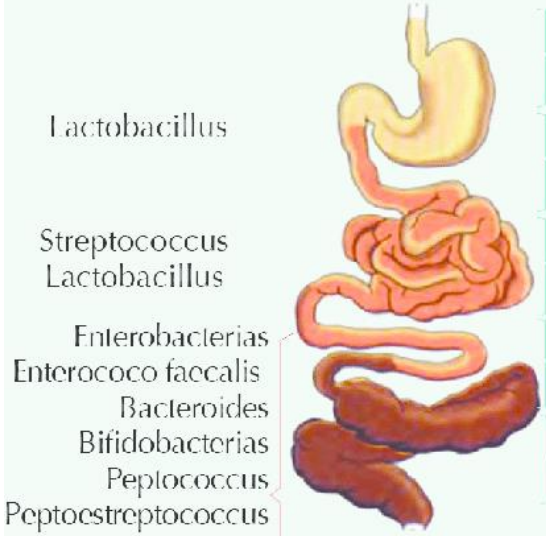
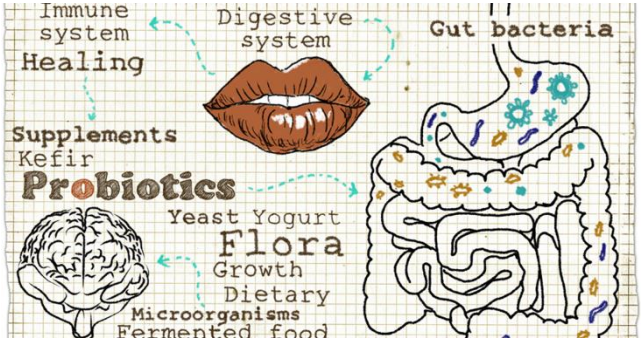
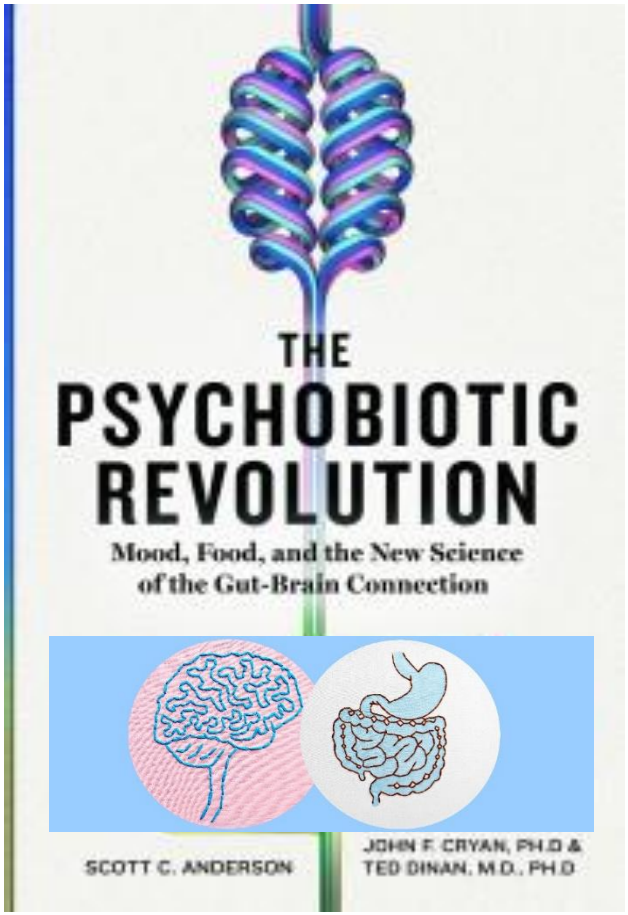


Table 2. Selected Sample of Studies Investigating "Psychobiotics"

Study	Design	Disease	Intervention	Conclusions
Tillisch *et al.*[84]	Clinical; RCT	Healthy Women	Probiotic	Probiotic changed functional connectivity of an emotional recognition network in the brain.
Slykerman *et al.*[85]	Clinical; RCT in pregnancy	Anxiety and Depression	Probiotic	Probiotic significantly lowers postpartum anxiety and depression.
Pinto-Sanchez *et al.*[86]	Clinical; RCT in IBS	Depression	Probiotic	Probiotic reduces depression, increases quality of life; associated with changes in brain activation patterns.
Romijn *et al.*[87]	Clinical; RCT	Depression	Probiotic	No significant effect of probiotic on low mood or inflammatory biomarkers.
Akkasheh *et al.*[88]	Clinical; RCT	Depression	Probiotic	Probiotic reduces depression scores and improves insulin sensitivity.
Takada *et al.*[89]	Clinical; RCT	Stress	Probiotic	Probiotic suppresses cortisol hypersecretion and physical symptoms associated with stress.
Allen *et al.*[90]	Clinical; within-participant placebo controlled trial	Stress	Probiotic	Probiotic reduces stress and improves memory.
Kelly *et al.*[91]	Clinical; RCT	Stress	Probiotic	No significant effect of probiotic on stress.
Ostlund-Lagerstrom *et al.*[92]	Clinical; RCT in older adults	Anxiety and Stress	Probiotic	No significant effect of probiotic on stress.
Schmidt *et al.*[93]	Clinical; RCT	Anxiety	Prebiotic	Prebiotic associated with anxiolytic properties.
Wang *et al.*[94]	Clinical; RCT	Stress	Rifaximin	Rifaximin showed stress-reducing effects.
Burokas *et al.*[95]	Preclinical	Stress	Prebiotic	Prebiotic improves stress-related behaviors.
Desbonnet *et al.*[96]	Preclinical	Depression	Probiotic	Probiotic normalizes markers associated with rat model of depression.
Tarr *et al.*[97]	Preclinical	Anxiety	Prebiotic	Prebiotic improves stressor-induced anxiety behavior.





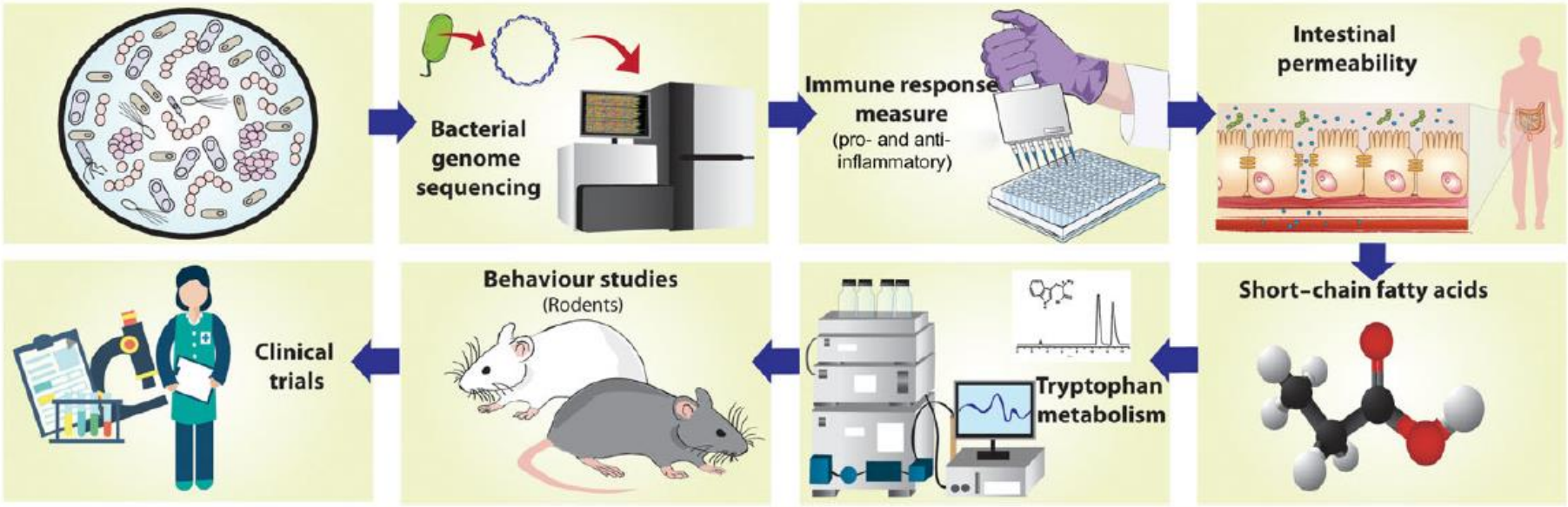
ACCEPTED MANUSCRIPT

British Journal of Pharmacology (2018) **175** 4430–4438

Finding the needle in the haystack: systematic identification of psychobiotics

Aisling Bambury[1,2], Kiran Sandhu[1], John F Cryan[1,3] and Timothy G Dinan[1,2]

The brain–gut–microbiota axis is increasingly viewed as a novel paradigm in neuroscience with the capacity to generate innovative therapies for patients with psychiatric illnesses. Psychobiotics, defined as live bacteria, which when ingested in adequate amounts, confer mental health benefits, are increasingly of interest, as preclinical trials continue to show promising results. Particularly in stress-related, anxiety and depressive disorders, there is potential for psychobiotics to deliver new therapies. The question of which microbes may prove to be the most promising psychobiotic in delivering such therapies at a clinical level is of great importance. Here we look at the characteristics of psychobiotics, in an attempt to present an outline from which the identification of potential new psychobiotics may be possible.



Review

Trends in Neurosciences

Trends in Neurosciences, November 2016, Vol. 39, No. 11

Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals

Amar Sarkar,[1] Soili M. Lehto,[2,3] Siobhán Harty,[1] Timothy G. Dinan,[4] John F. Cryan,[5] and Philip W.J. Burnet[6,*]

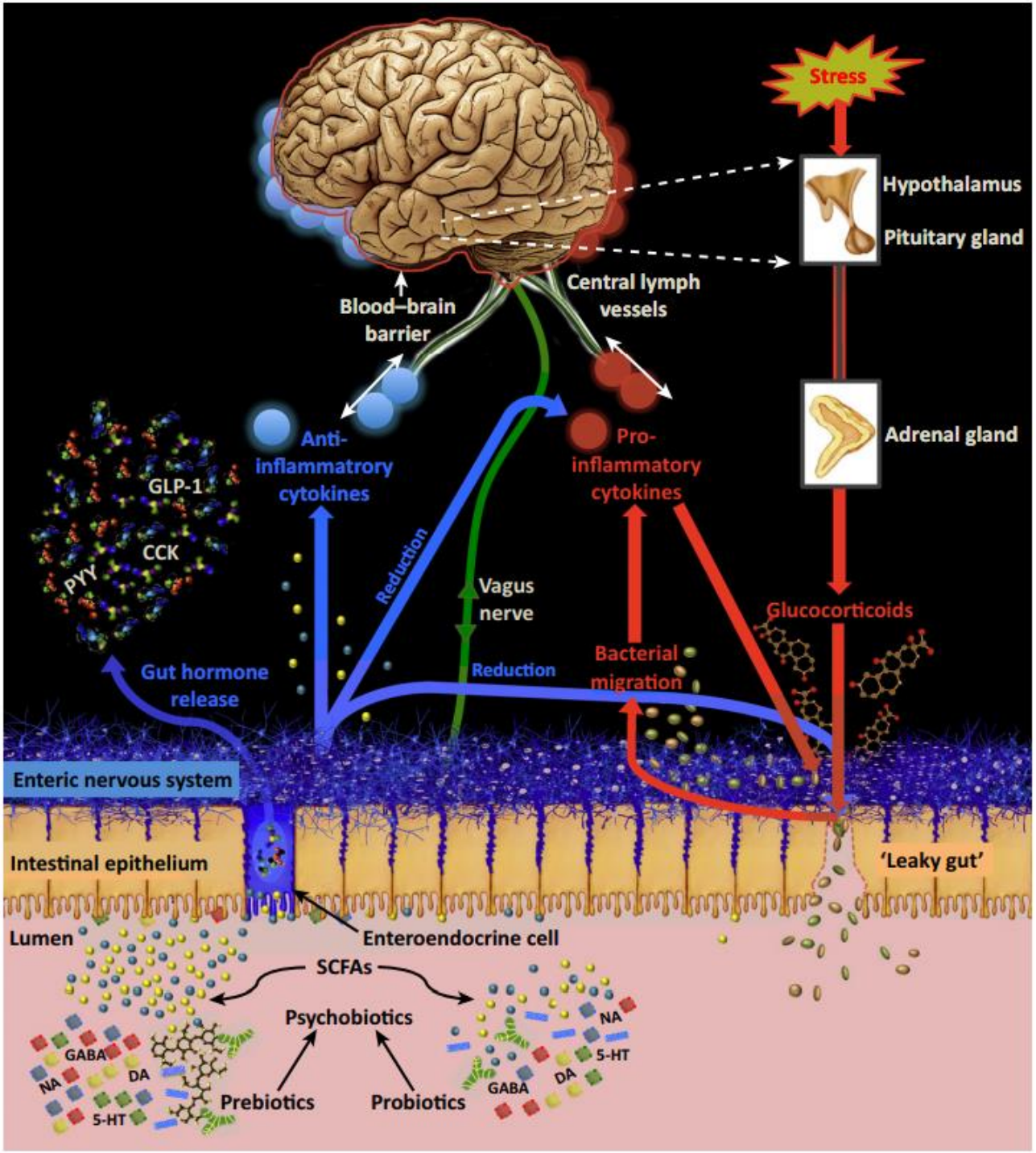
Psychobiotics were previously defined as live bacteria (probiotics) which, when ingested, confer mental health benefits through interactions with commensal gut bacteria. We expand this definition to encompass prebiotics, which enhance the growth of beneficial gut bacteria. We review probiotic and prebiotic effects on emotional, cognitive, systemic, and neural variables relevant to health and disease. We discuss gut–brain signalling mechanisms enabling psychobiotic effects, such as metabolite production. Overall, knowledge of how the microbiome responds to exogenous influence remains limited. We tabulate several important research questions and issues, exploration of which will generate both mechanistic insights and facilitate future psychobiotic development. We suggest the definition of psychobiotics be expanded beyond probiotics and prebiotics to include other means of influencing the microbiome.

Psychobiotics are beneficial bacteria (probiotics) or support for such bacteria (prebiotics) that influence bacteria–brain relationships.

Psychobiotics exert anxiolytic and antidepressant effects characterised by changes in emotional, cognitive, systemic, and neural indices. Bacteria–brain communication channels through which psychobiotics exert effects include the enteric nervous system and the immune system.

Current unknowns include dose-responses and long-term effects.

The definition of psychobiotics should be expanded to any exogenous influence whose effect on the brain is bacterially-mediated.



Outstanding Questions

What are the dose-response functions associated with psychobiotics?

What are the contributions of gut hormones in the mechanisms of action of prebiotics versus probiotics?

How do prebiotics and probiotics differ in terms of their impact on microbiome structure and relative abundance?

Are there undetected psychophysiological costs alongside the observed benefits of psychobiotics?

Does the brain adapt to long-term psychobiotic ingestion?

How do bacteria-derived blood metabolites affect the central nervous system, and how do psychobiotics modulate this relationship?

What is the time-course for emergence of various psychobiotic effects, and how long do they last?

Are there ceiling effects on psychobiotic benefits?

What are the functional implications of altered excitation–inhibition balance (due to alterations in GABA and glutamate concentrations) in specific brain regions?

Why do some strains of probiotic or prebiotic show effects while others do not, and are these linked to dosage?

Do neurotransmitters produced by gut bacteria modulate synaptic transmission in the proximal neurons of the enteric nervous system?

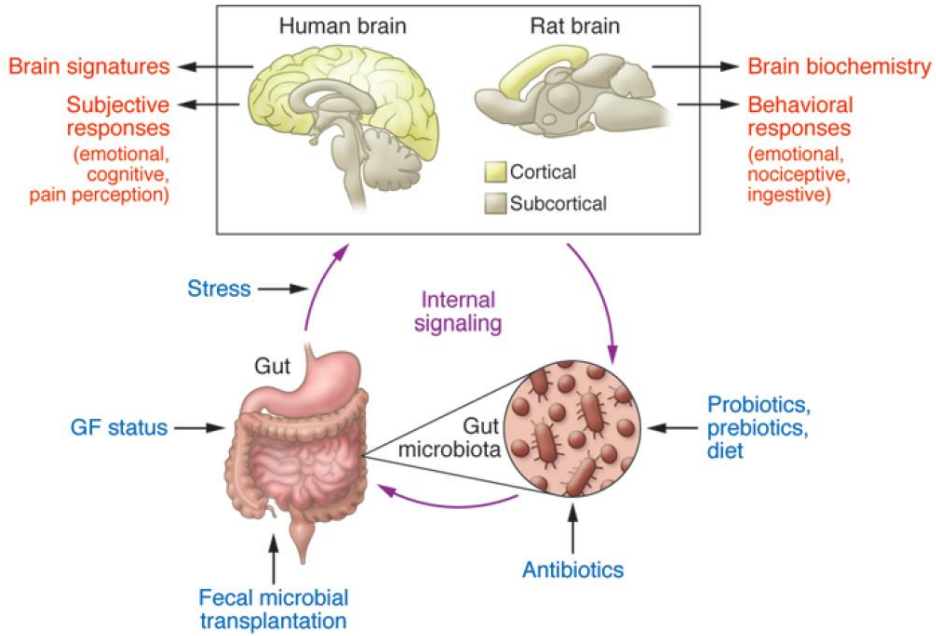
What is the direction of causality between systemic and central changes?

How do factors such as diet, genotype, sex, and age moderate the effects of psychobiotics?

Table 1

Psychobiotics in Rodent Models of Dysfunction

Model	Induction	Psychobiotic	Effects relative to comparison groups
Alzheimer's disease	A β_{1-42}-induced neurotoxicity	Prebiotic, chitosan oligosaccharide	↑ Cognitive function (Morris water maze), ↓ pro-inflammatory cytokines (tumour necrosis factor-α, interleukin-1β)
Amyotrophic lateral sclerosis	High level of mutant human $SOD1^{G93A}$ gene	Prebiotic, galacto-oligosaccharides	↓ Motor neuron death, ↓ muscular atrophy, ↑ serum folate, ↑ vitamin B12, ↑ homocysteine
Autism spectrum disorder	Maternal immune activation	Probiotic, *Bacteroides fragilis*	↑ Intestinal permeability, ↓ pro-inflammatory cytokines (interleukin-6), ↓ anxiety (open field test), ↓ repetitive behaviour (marble burying), ↑ communication (calling), ↑ sensorimotor gating (startle inhibition)
Bacterial infection	*Citrobacter rodentium*–induced colitis	Probiotic *Lactobacillus rhamnosus* R0011 + *Lactobacillus helveticus* R0052	↑ Gut barrier function, ↓ transcription of pro-inflammatory cytokines (tumour necrosis factor-α and interferon-γ, interleukin-17), ↑ transcription of anti-inflammatory cytokines (interleukin-10), normalisation of microbiome
Bacterial infection	*Citrobacter rodentium*–induced colitis	Probiotic *Lactobacillus rhamnosus* R0011 + *Lactobacillus helveticus* R0052	↓ Infection-induced death, ↓ infection-induced weight loss
Bacterial infection	*Citrobacter rodentium*–induced colitis	Probiotic *Lactobacillus reuteri*	↓ Stress-induced gut-to-spleen pathogen migration
Bacterial infection	*Citrobacter rodentium*–induced colitis	Probiotic *Lactobacillus reuteri*	↓ Stress-induced infectious colitis
Diabetes	Streptozotocin injection	Probiotics, *Lactobacillus acidophilus* + *Bifidobacterium lactis* + *Lactobacillus fermentum*	↑ Cognitive function (Morris water maze), ↑ hippocampal long-term potentiation (LTP)
Diabetes	Streptozotocin injection	Probiotics, *Lactobacillus brevis* DPC 6108	↓ Glucose, ↓ hyperglycaemia
Hyperammonemia	Ammonium acetate injection	Probiotic, *Lactobacillus helveticus* NS8	↓ Inflammation (brain-inducible nitric oxide synthase, prostaglandin E2, and interleukin-1β), neurotransmitter processing (↓ abnormal metabolisation of serotonin into 5-hydroxyindole acetic acid), ↓ anxiety (elevated plus maze), ↑ cognitive function (Morris water maze)
Post-inflammatory anxiety	Lipopolysaccharide injection	Prebiotic, Bimuno-galacto-oligosaccharides (B-GOS)	↓ Pro-inflammatory cytokines (interleukin-1β), ↓ cortical 5-HT2A receptors



Asian Journal of Psychiatry 22 (2016) 84–85

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

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

Arpit Parmar
Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, India

Editorial

Gut–brain axis, psychobiotics, and mental health

To conclude, change in the microbial content of the gut as a result of consumption of probiotics cause a variety of changes in human body which includes immune, endocrinal and nervous effects. Person's mood, cognition, behavior, and stress reactivity can potentially be altered using such probiotics (or rather pschobiotics). However, there is a dearth of literature to support its use in clinical practice. More detailed knowledge of gut microbiota along with development of specific probiotics will potentially help in developing more effective drug and diet based therapies for mental illnesses.

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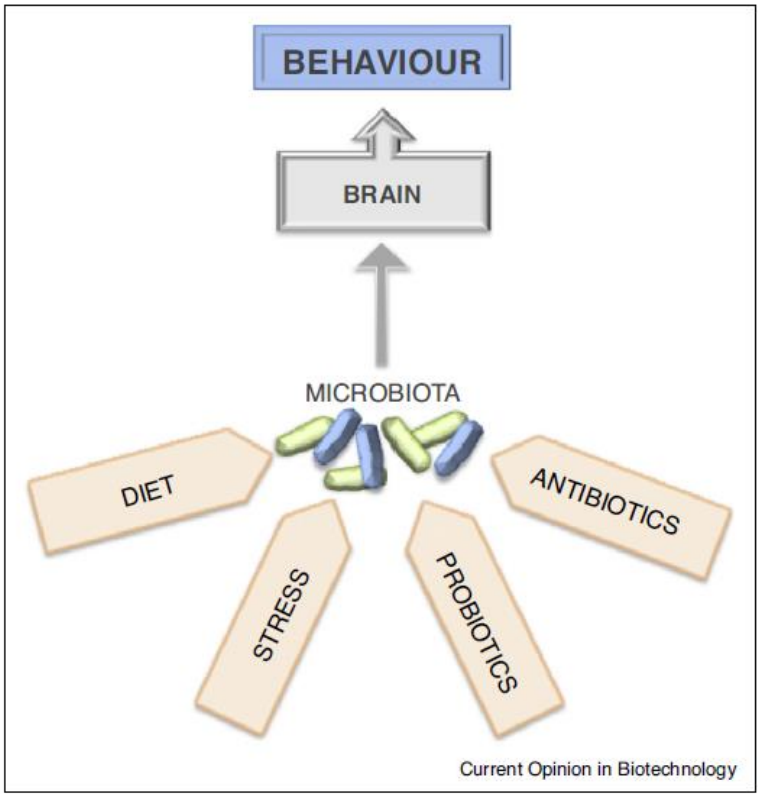
Current Opinion in Biotechnology 2015, 32:35–41

Current Opinion in Biotechnology

Gut brain axis: diet microbiota interactions and implications for modulation of anxiety and depression

Ruth Ann Luna[1,2] and Jane A Foster[3,4]

The human gut microbiome is composed of an enormous number of microorganisms, generally regarded as commensal bacteria. Without this inherent microbial community, we would be unable to digest plant polysaccharides and would have trouble extracting lipids from our diet. Resident gut bacteria are an important contributor to healthy metabolism and there is significant evidence linking gut microbiota and metabolic disorders such as obesity and diabetes. In the past few years, neuroscience research has demonstrated the importance of microbiota in the development of brain systems that are vital to both stress reactivity and stress-related behaviours. Here we review recent literature that examines the impact of diet-induced changes in the microbiota on stress-related behaviours including anxiety and depression.



Factors influencing the gut–brain axis via microbiota. As reviewed in the article, diet, stress, probiotics, and antibiotics can impact gut microbiota community to influence microbiota to brain pathways and thereby impact behaviour.

REVIEW

Psychosomatic Medicine, V 79 • 920-926 October 2017

Brain-Gut-Microbiota Axis and Mental Health

Timothy G. Dinan, MD, PhD, and John F. Cryan, PhD

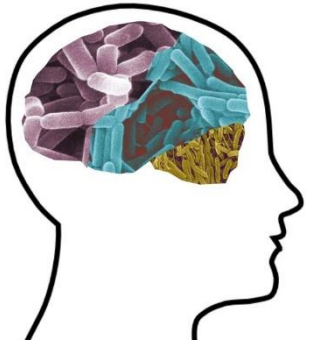
ABSTRACT

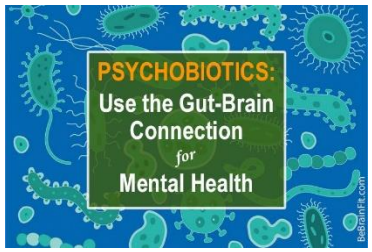
Objective: The brain-gut-microbiota axis has been put forward as a new paradigm in neuroscience, which may be of relevance to mental illness. The mechanisms of signal transmission in the brain-gut-microbiota axis are complex and involve bidirectional communications that enable gut microbes to communicate with the brain and the brain to communicate with the microbes. This review assesses the potential usefulness and limitations of the paradigm.

Methods: A selective literature review was conducted to evaluate the current knowledge in clinical and preclinical brain-gut-microbiota interactions as related to psychiatric disorders.

Results: Most published studies in the field are preclinical, and there is so far a lack of clinical studies. Preliminary studies in psychiatric populations support the view of a dysbiosis in some conditions, but studies are often small scale and marred by potential confounding variables. Preclinical studies support the view that psychobiotics ("bacteria which when ingested in adequate amounts have a positive mental health benefit") might be of use in treating some patients with mental health difficulties. To date, we have no well-conducted studies in clinical populations, although there are some studies in healthy volunteers. A cocktail of probiotics has been shown to alter brain activity as monitored by functional magnetic resonance imaging, and *Bifidobacterium longum* was reported to alter brain electrical activity.

Conclusions: It has yet to be convincingly demonstrated that the exciting findings of psychobiotic efficacy demonstrated in preclinical models of psychiatric illness will translate to patients.

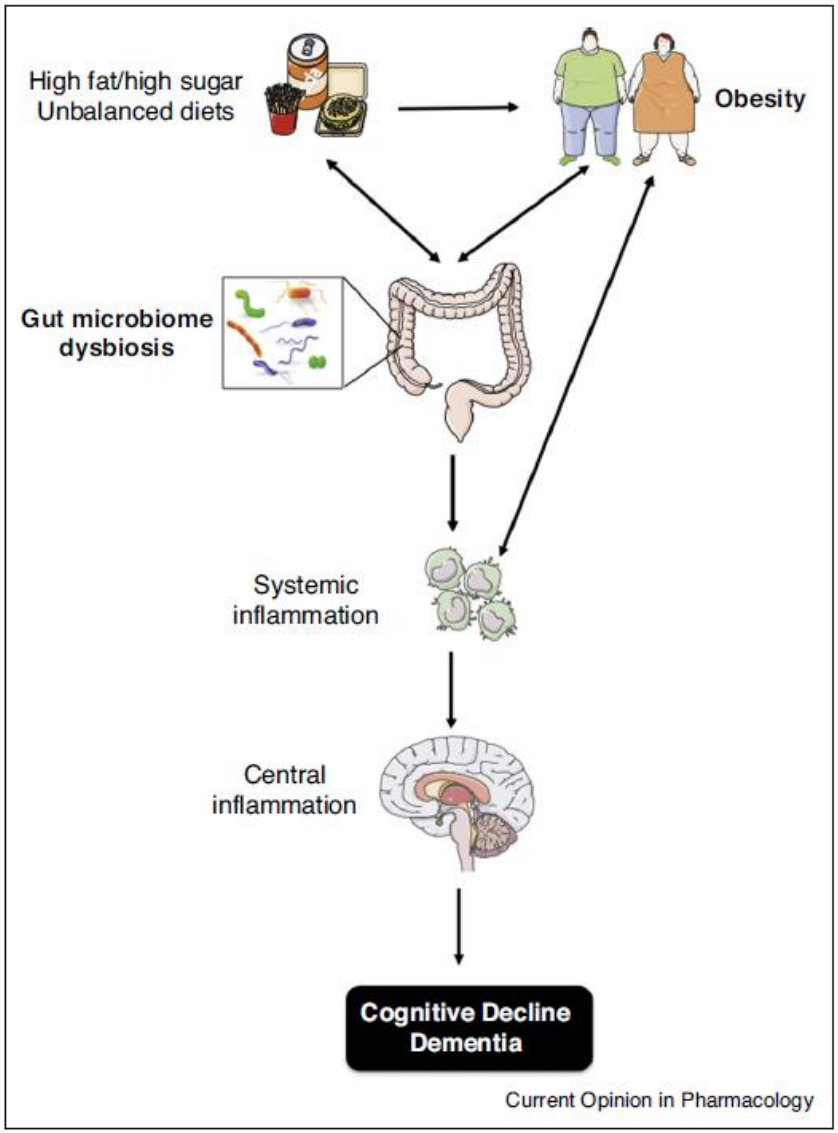


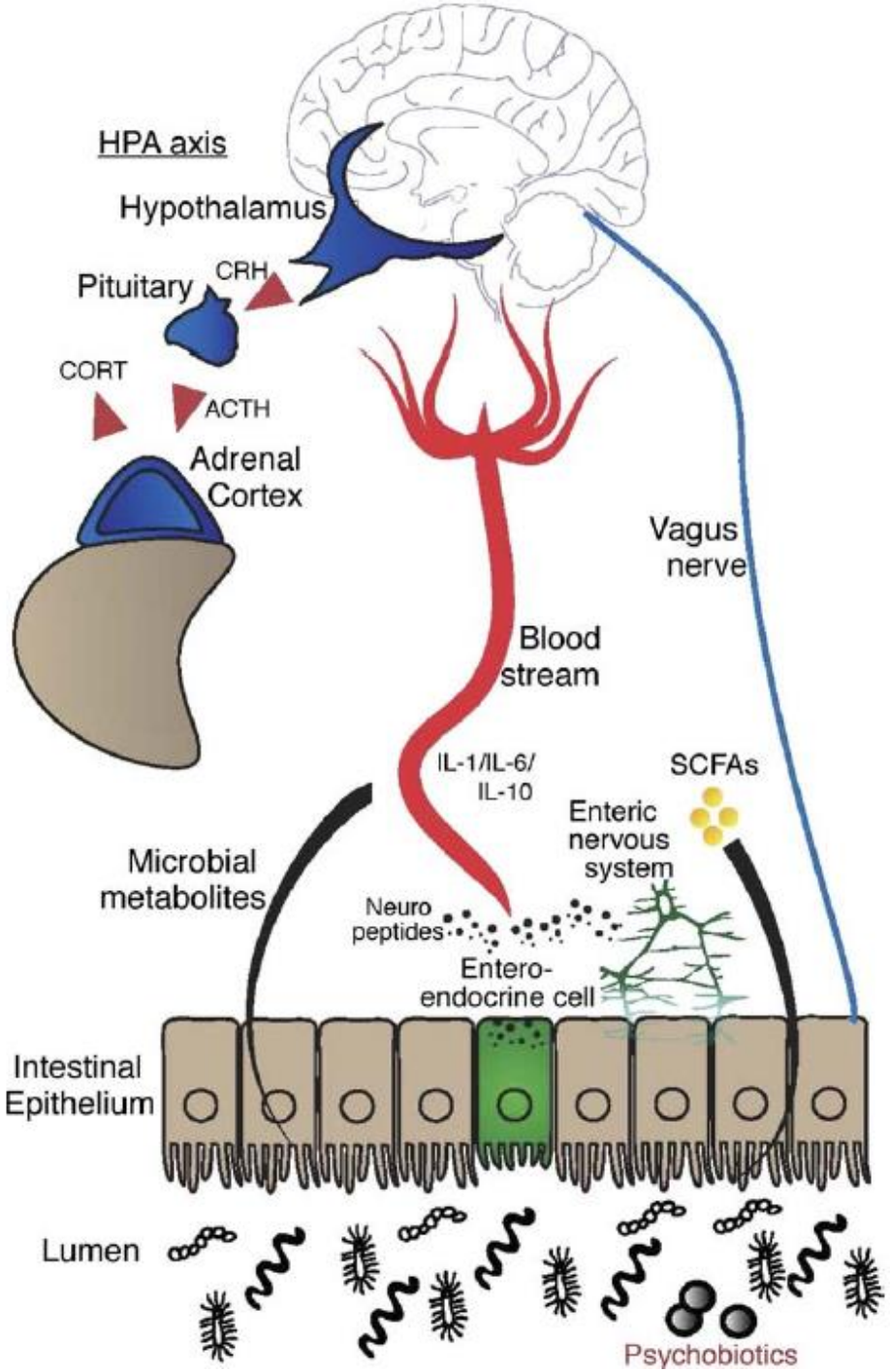


Until February 2017, there were 142 articles focusing on gut microbes and the brain, listed on PubMed. Twenty-three of these articles centered on gut microbes and mental illness, whereas 35 articles focused on psychobiotics. Taking a broader perspective, looking at probiotics and mental health, there were 50 articles. Of the 142 articles on the gut microbiota and the brain, 111 were reviews and 31 were experimental studies, of which only 4 were human studies. This latter fact pinpoints the current weakness of this nascent field.

REVIEW

Psychosomatic Medicine, V 79 • 920-926
October 2017





Article

A microbiome-dependent gut–brain pathway regulates motivation for exercise

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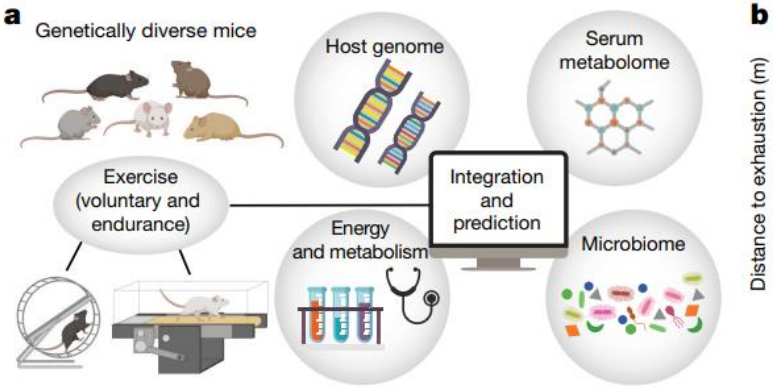
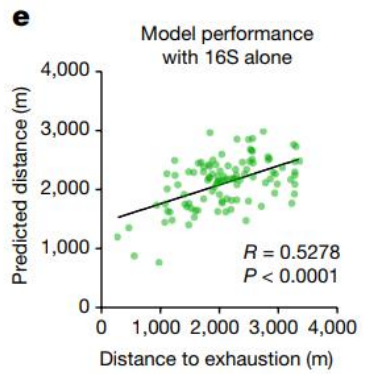
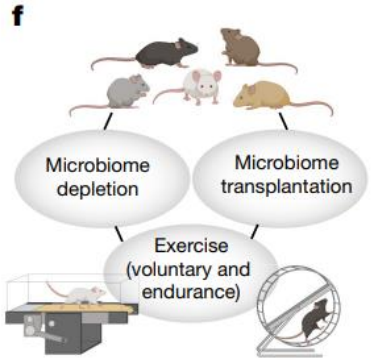
Lenka Dohnalová[1,2,3,4], Patrick Lundgren[1,2,3], Jamie R. E. Carty[5], Nitsan Goldstein[5], Sebastian L. Wenski[4], Pakjira Nanudorn[4], Sirinthra Thiengmag[4], Kuei-Pin Huang[6], Lev Litichevskiy[1,2,3], Hélène C. Descamps[1,2,3], Karthikeyani Chellappa[3,7], Ana Glassman[1,2,3], Susanne Kessler[1,2,3], Jihee Kim[1,2,3], Timothy O. Cox[1,2,3], Oxana Dmitrieva-Posocco[1,2], Andrea C. Wong[1,2], Erik L. Allman[8], Soumita Ghosh[9,10], Nitika Sharma[11], Kasturi Sengupta[7,12], Belinda Cornes[13], Nitai Dean[14], Gary A. Churchill[13], Tejvir S. Khurana[7,12], Mark A. Sellmyer[11], Garret A. FitzGerald[9,10], Andrew D. Patterson[8], Joseph A. Baur[3,7], Amber L. Alhadeff[6,15], Eric J. N. Helfrich[4], Maayan Levy[1,2], J. Nicholas Betley[3,5] & Christoph A. Thaiss[1,2,3] ✉







Exercise exerts a wide range of beneficial effects for healthy physiology[1]. However, the mechanisms regulating an individual's motivation to engage in physical activity remain incompletely understood. An important factor stimulating the engagement in both competitive and recreational exercise is the motivating pleasure derived from prolonged physical activity, which is triggered by exercise-induced neurochemical changes in the brain. Here, we report on the discovery of a gut–brain connection in mice that enhances exercise performance by augmenting dopamine signalling during physical activity. We find that microbiome-dependent production of endocannabinoid metabolites in the gut stimulates the activity of TRPV1-expressing sensory neurons and thereby elevates dopamine levels in the ventral striatum during exercise. Stimulation of this pathway improves running performance, whereas microbiome depletion, peripheral endocannabinoid receptor inhibition, ablation of spinal afferent neurons or dopamine blockade abrogate exercise capacity. These findings indicate that the rewarding properties of exercise are influenced by gut-derived interoceptive circuits and provide a microbiome-dependent explanation for interindividual variability in exercise performance. Our study also suggests that interoceptomimetic molecules that stimulate the transmission of gut-derived signals to the brain may enhance the motivation for exercise.

European Journal of Clinical Nutrition (2007) 61, 355–361
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0954-3007/07 $30.00
www.nature.com/ejcn

https://www.dailymotion.com/video/xi15yg?playlist=x4t2zs

ORIGINAL ARTICLE

Impact of consuming a milk drink containing a probiotic on mood and cognition

D Benton, C Williams and A Brown

Department of Psychology, University of Wales Swansea, Wales, UK

Objective: The impact on mood and memory of consuming a probiotic containing milk drink, or a placebo, was examined as, previously, a poor mood has been found to correlate with the frequency of constipation.
Design: A double-blind placebo-controlled trial with random allocation of subjects.
Setting: Subjects went about their normal life in the community apart from three visits to the laboratory.
Subjects: One hundred and thirty-two healthy members of general population, mean age 61.8 years, volunteered in response to local media coverage. One hundred and twenty-four finished the trial.
Intervention: For a 3-week period, either a probiotic containing milk drink, or a placebo, were consumed daily. Mood and cognition were measured at baseline, and after 10 and 20 days of consumption.
Results: At baseline those who reported themselves to be less frequently constipated were more clearheaded, confident and elated. Although the taking of the probiotic did not generally change the mood, this appeared to be a reflection of the generally good mood in this sample. When those in the bottom third of the depressed/elated dimension at baseline were considered, they selectively responded by reporting themselves as happy rather than depressed after taking the probiotic. The intervention did not, however, influence the reported frequency of defaecation, probably a reflection of the initially low incidence of constipation. An unexpected and possibly chance finding was that the consumption of probiotics resulted in a slightly-poorer performance on two measures of memory.
Conclusions: The consumption of a probiotic-containing yoghurt improved the mood of those whose mood was initially poor. This improvement in mood was not, however, associated with an increased frequency of defaecation.
Sponsorship: Funded by Yakult, Japan.
European Journal of Clinical Nutrition (2007) **61**, 355–361. doi:10.1038/sj.ejcn.1602546; published online 6 December 2006

Keywords: constipation; depression; memory; mood; probiotic

Gastroenterology. 2013 June ; 144(7): . doi:10.1053/j.gastro.2013.02.043.

Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity

KIRSTEN TILLISCH[1], JENNIFER LABUS[1], LISA KILPATRICK[1], ZHIGUO JIANG[1], JEAN STAINS[1], BAHAR EBRAT[1], DENIS GUYONNET[2], SOPHIE LEGRAIN–RASPAUD[2], BEATRICE TROTIN[2], BRUCE NALIBOFF[1], and EMERAN A. MAYER[1]

[1]Oppenheimer Family Center for Neurobiology of Stress, Division of Digestive Diseases, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California

[2]Danone Research, Palaiseau, France

Abstract

BACKGROUND & AIMS—Changes in gut microbiota have been reported to alter signaling mechanisms, emotional behavior, and visceral nociceptive reflexes in rodents. However, alteration of the intestinal microbiota with antibiotics or probiotics has not been shown to produce these changes in humans. We investigated whether consumption of a fermented milk product with probiotic (FMPP) for 4 weeks by healthy women altered brain intrinsic connectivity or responses to emotional attention tasks.

METHODS—Healthy women with no gastrointestinal or psychiatric symptoms were randomly assigned to groups given FMPP (n = 12), a nonfermented milk product (n = 11, controls), or no intervention (n = 13) twice daily for 4 weeks. The FMPP contained *Bifidobacterium animalis* subsp *Lactis*, *Streptococcus thermophiles*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp *Lactis*. Participants underwent functional magnetic resonance imaging before and after the intervention to measure brain response to an emotional faces attention task and resting brain activity. Multivariate and region of interest analyses were performed.

RESULTS—FMPP intake was associated with reduced task-related response of a distributed functional network (49% cross-block covariance; $P = .004$) containing affective, viscerosensory, and somatosensory cortices. Alterations in intrinsic activity of resting brain indicated that ingestion of FMPP was associated with changes in midbrain connectivity, which could explain the observed differences in activity during the task.

CONCLUSIONS—Four-week intake of an FMPP by healthy women affected activity of brain regions that control central processing of emotion and sensation.

Gastroenterology. 2013 June ; 144(7): . doi:10.1053/j.gastro.2013.02.043.

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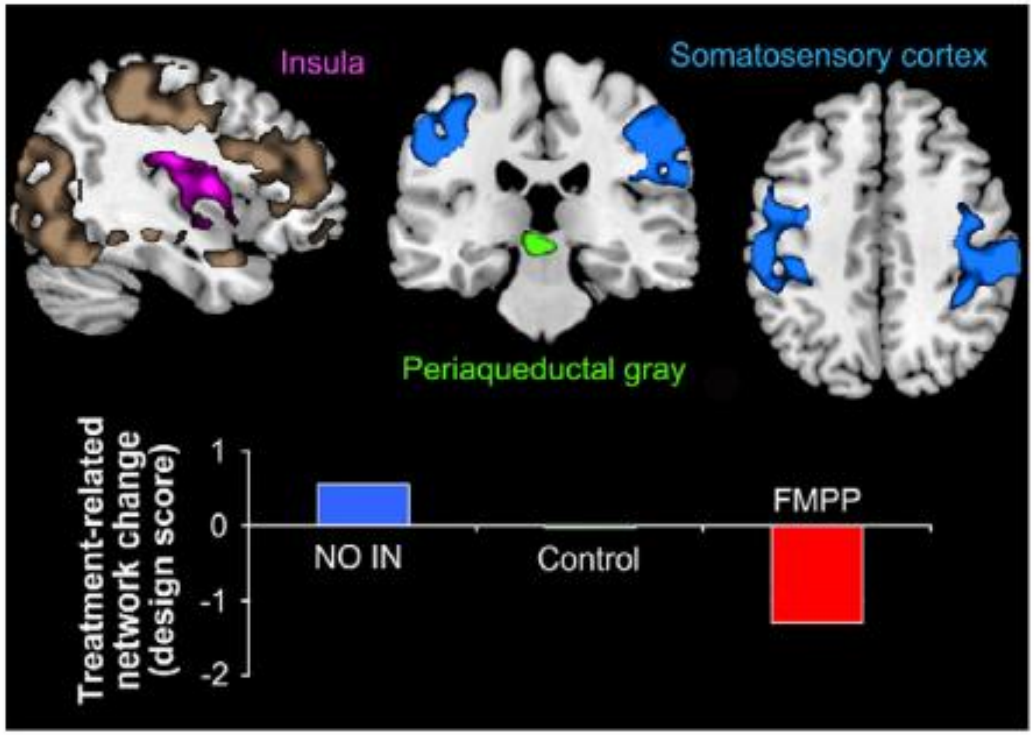


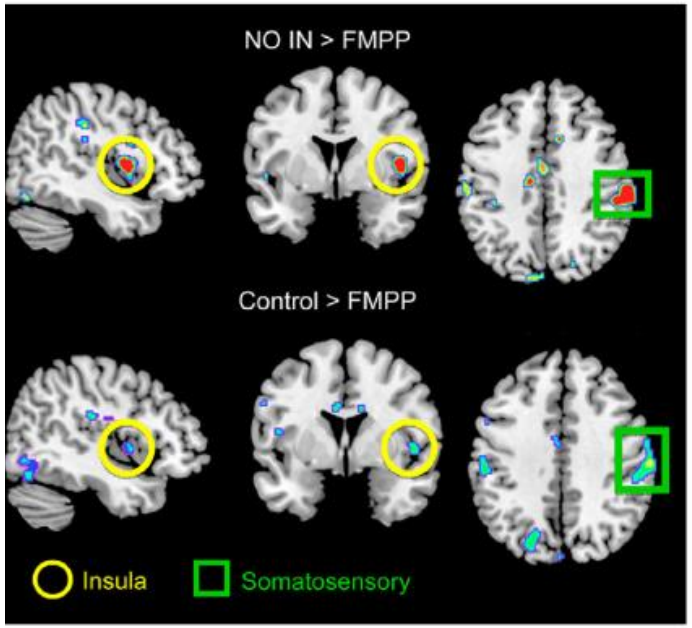


Figure 1.

A distributed network of brain regions showing decreases in the FMPP group during the emotional faces attention task is shown in the shaded regions. Three regions of interest selected from the network for study in the resting state are highlighted in *pink* (insula), *green* (periaqueductal gray), and *blue* (somatosensory regions). The change in network strength with intervention is depicted graphically.

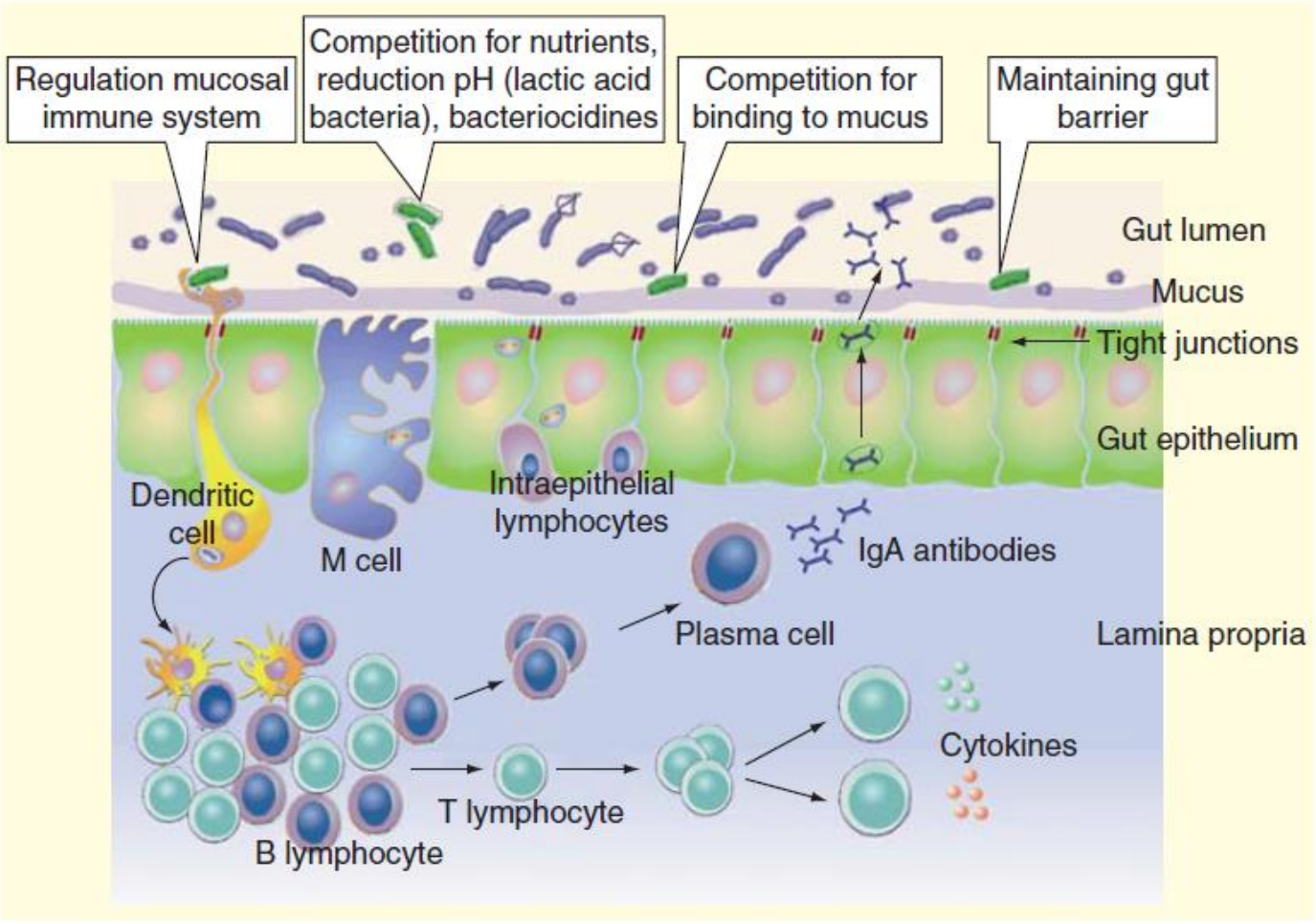
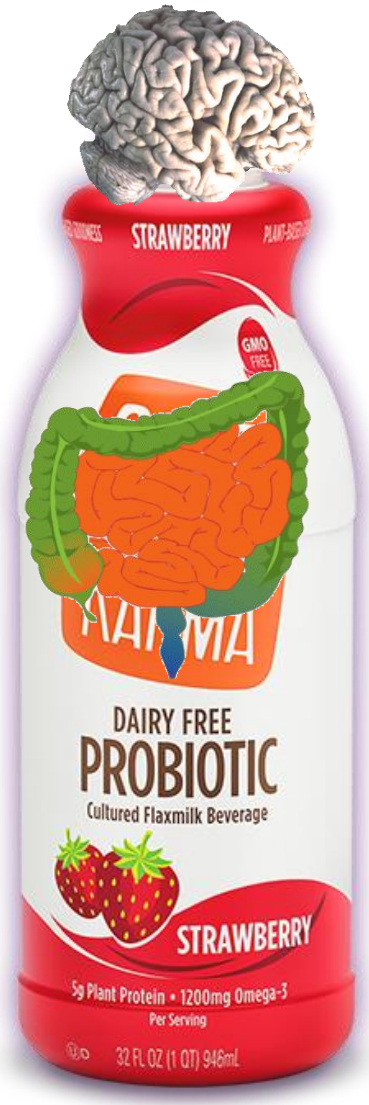


Figure 1. Mechanisms of action of probiotics.



Nutrition, Metabolism & Cardiovascular Diseases (2020) **30**, 11–22

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

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

SYSTEMATIC REVIEWS AND META-ANALYSES

The impact of probiotic yogurt consumption on lipid profiles in subjects with mild to moderate hypercholesterolemia: A systematic review and meta-analysis of randomized controlled trials

Behnaz Pourrajab [a,b], Somaye Fatahi [a,b], Afsaneh Dehnad [c], Hamed Kord Varkaneh [d], Farzad Shidfar [a,*]

Abstract *Background and aims:* Potential beneficial effect of probiotic yogurt on the lipid profile has raised much interest. However, the results are inconsistent in this regard. The aim of the study is to determine the effects of probiotic yogurt on serum lipid profile in individuals with mild to moderate hypercholesterolemia.

Methods and results: Online databases including PubMed, Scopus, ISI Web of Science, Cochrane Central Register of Controlled Trials, Science Direct, Google Scholar and Igaku Chuo Zasshi were searched until March 19th 2019. The effect sizes were expressed as the weighted mean difference (WMD) with 95% confidence interval (CI). Seven eligible trials with 274 participants were included in this systematic review. Pooling of 9 effect sizes from these seven articles revealed a significant reduction in total cholesterol and low density lipoprotein cholesterol levels following probiotic yogurt consumption (mean difference: −8.73 mg/dl, 95% CI: −15.98, −1.48, p-value = 0.018 and mean difference: −10.611 mg/dl, 95% CI: −16.529, −4.693, p-value = 0.000, respectively) without significant heterogeneity among the studies (I^2 = 40.6%, p-value = 0.1 and I^2 = 24.2%, p-value = 0.229, respectively). The results showed no significant changes in high density lipoprotein cholesterol and triglyceride levels. Also, none of the variables showed a significant change for sensitivity analysis.

Conclusion: Available evidence suggests that probiotic yogurt can significantly reduce total cholesterol and LDL-c in subjects with mild to moderate hypercholesterolemia without a significant effect on HDL-c and triglyceride levels.

frontiers in Nutrition

SYSTEMATIC REVIEW
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Higher Yogurt Consumption Is Associated With Lower Risk of Colorectal Cancer: A Systematic Review and Meta-Analysis of Observational Studies

Jiangjie Sun[1†], Jiangyan Song[2†], Jie Yang[3], Le Chen[3], Zuochuan Wang[3], Meiwen Duan[3], Shuhui Yang[3], Chengyang Hu[4] and Qingquan Bi[2,3*]*

Methods: Three databases, namely, PubMed, Web of Science, and Embase, were searched for all relevant studies from July 2021 on the association of yogurt consumption with CRC risk. We pooled the odds ratios (ORs) and their 95% CIs using a random-effects meta-analysis to assess the association.

Results: Finally, 16 studies met the inclusion criteria and were chosen in the meta-analysis. Yogurt consumption was significant with lower risk of CRC risk in the overall comparison (OR = 0.87, 95% CI: 0.81–0.94), in the cohort studies (OR = 0.91, 95% CI: 0.86–0.97), and case-control studies (OR = 0.75, 95% CI: 0.65–0.85). With regard to subgroup analyses by study region, cancer type, publication year, and sex, yogurt consumption significantly decreased overall CRC, colon cancer, and distal colon cancer risks. In stratified analyses, we observed significantly decreased CRC risk in Europe and Africa and published after 2010 and overall population. Sensitivity analysis indicated the result is stable and there is no publication bias in the meta-analysis.

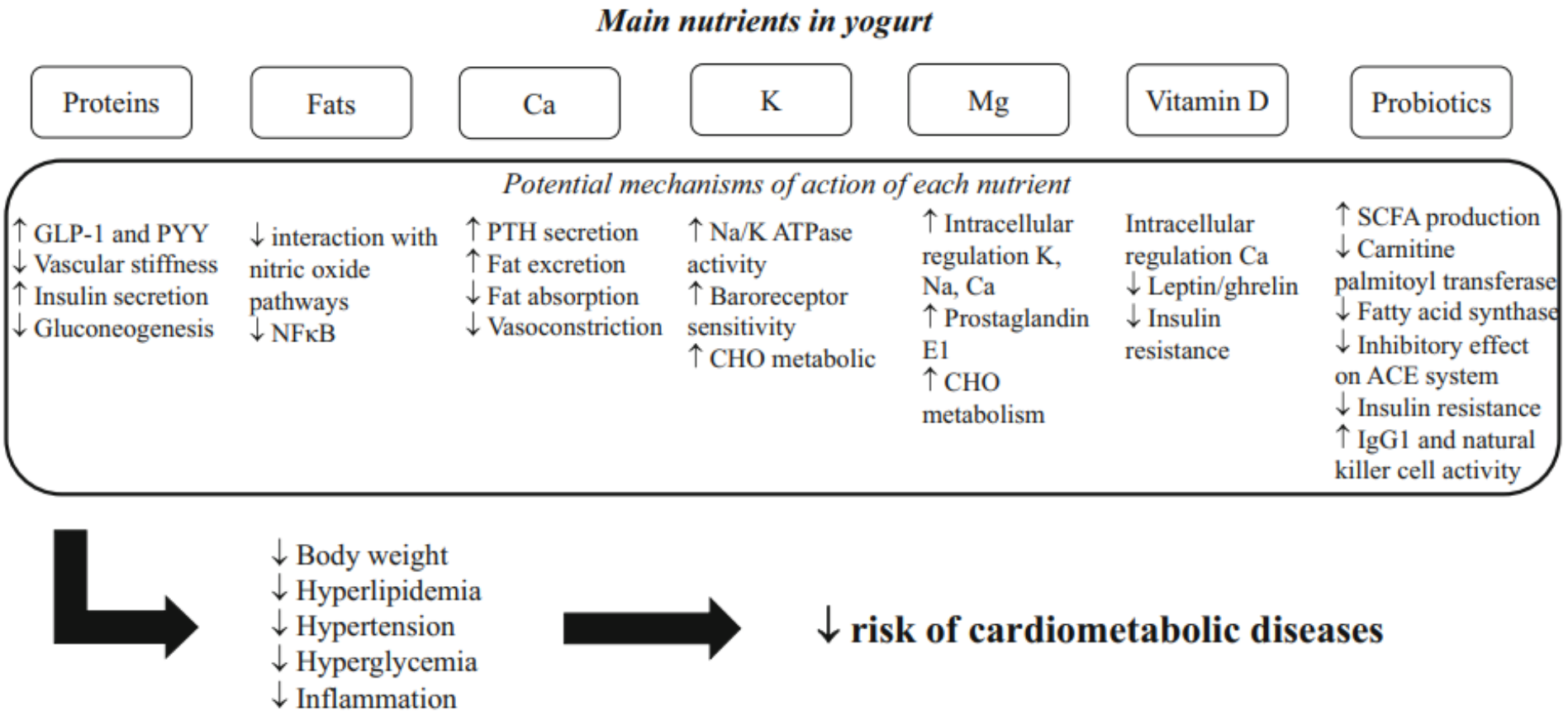
Conclusions: Overall, this study indicated that yogurt intake was related to a decreased risk of CRC.

Current Nutrition Reports (2021) 10:83–92
https://doi.org/10.1007/s13668-020-00344-y

CARDIOVASCULAR DISEASE (JHY WU, SECTION EDITOR)

Effect of Yogurt Consumption on Metabolic Syndrome Risk Factors: a Narrative Review

Leila Khorraminezhad[1] · Iwona Rudkowska[1,2]



Review Article

Bioactive Compounds from Kefir and Their Potential Benefits on Health: A Systematic Review and Meta-Analysis

Carla P. Vieira,[1,2] **Anisio Iuri L. S. Rosario**,[2,3] **Carini A. Lelis**,[1,2] **Bruna Samara S. Rekowsky**,[3] **Anna Paula A. Carvalho**,[1,2] **Denes Kaic A. Rosário**,[1,2] **Thaísa A. Elias**,[2] **Marion P. Costa**,[3] **Debora Foguel**,[4] **and Carlos A. Conte-Junior**[1,2,5]

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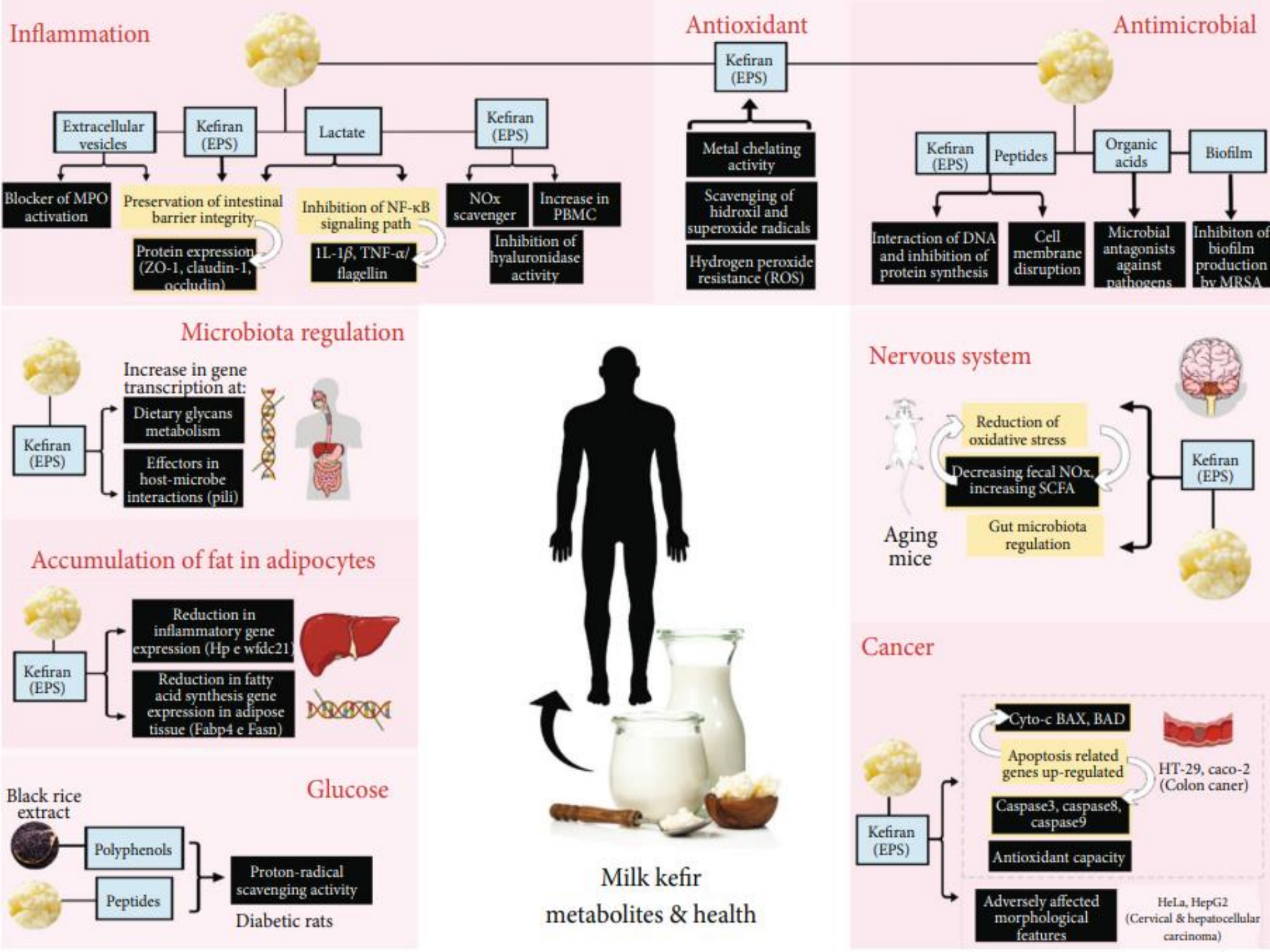

Inflammation
Extracellular vesicles
Kefiran (EPS)
Lactate
Kefiran (EPS)
Blocker of MPO activation
Preservation of intestinal barrier integrity
Protein expression (ZO-1, claudin-1, occludin)
Inhibition of NF-κB signaling path
1L-1β, TNF-α/ flagellin
NOx scavenger
Increase in PBMC
Inhibition of hyaluronidase activity
Antioxidant
Kefiran (EPS)
Metal chelating activity
Scavenging of hidroxil and superoxide radicals
Hydrogen peroxide resistance (ROS)
Antimicrobial
Kefiran (EPS)
Peptides
Organic acids
Biofilm
Interaction of DNA and inhibition of protein synthesis
Cell membrane disruption
Microbial antagonists against pathogens
Inhibiton of biofilm production by MRSA
Microbiota regulation
Kefiran (EPS)
Increase in gene transcription at:
Dietary glycans metabolism
Effectors in host-microbe interactions (pili)
Accumulation of fat in adipocytes
Kefiran (EPS)
Reduction in inflammatory gene expression (Hp e wfdc21)
Reduction in fatty acid synthesis gene expression in adipose tissue (Fabp4 e Fasn)
Glucose
Black rice extract
Polyphenols
Peptides
Proton-radical scavenging activity
Diabetic rats
Milk kefir metabolites & health
Nervous system
Reduction of oxidative stress
Decreasing fecal NOx, increasing SCFA
Gut microbiota regulation
Aging mice
Kefiran (EPS)
Cancer
Cyto-c BAX, BAD
Apoptosis related genes up-regulated
HT-29, caco-2 (Colon caner)
Caspase3, caspase8, caspase9
Antioxidant capacity
Kefiran (EPS)
Adversely affected morphological features
HeLa, HepG2 (Cervical & hepatocellular carcinoma)

Annals of Epidemiology 30 (2019) 66–70

Contents lists available at ScienceDirect

Annals of Epidemiology

Brief communication

Kombucha: a systematic review of the empirical evidence of human health benefit

Julie M. Kapp, MPH, PhD, FACE [a,b,*], Walton Sumner, MD [c]

[a] Department of Health Management and Informatics, School of Medicine, University of Missouri, Columbia
[b] Harry S Truman School of Public Affairs, University of Missouri, Columbia
[c] St. Louis, MO

ABSTRACT

Purpose: Kombucha tea, a fermented beverage, has recently become popular in the United States as part of the functional food movement. This popularity is likely driven by its touted health benefits, coupled with the recent scientific movement investigating the role of the microbiome on human health. The purpose of this systematic review is to describe the literature related to empirical health benefits of kombucha as identified from human subjects research.

Methods: In July 2018, we searched the term "kombucha" for all document types in the following databases across all available years: PubMed, Scopus, and Ovid. To identify federal research grants related to kombucha, we searched the National Institutes of Health Research Portfolio Online Reporting Tools. Finally, to identify ongoing human subjects research, we searched clinicaltrials.gov and clinicaltrialsregister.eu. We reviewed a total of 310 articles.

Results: We found one study reporting the results of empirical research on kombucha in human subjects. We found no results for kombucha in Research Portfolio Online Reporting Tools, clinicaltrials.gov, or clinicaltrialsregister.eu.

Conclusions: The nonhuman subjects literature claims numerous health benefits of kombucha; it is critical that these assertions are tested in human clinical trials. Research opportunities are discussed.

Innovative Food Science and Emerging Technologies 22 (2014) 239–247

Contents lists available at ScienceDirect

Innovative Food Science and Emerging Technologies

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

Gut microbiota modulation and implications for host health: Dietary strategies to influence the gut–brain axis

Tatiana Milena Marques [a,c], John F. Cryan [a], Fergus Shanahan [a], Gerald F. Fitzgerald [a,c], R. Paul Ross [a,b], Timothy G. Dinan [a], Catherine Stanton [a,b,*]

The human intestinal microbiota evolves from an immature and unstable ecosystem during infancy into a more complex and stable ecosystem in adulthood. Diet is one of the main factors contributing to the composition and diversity of the human intestinal microbiota. From birth, breast milk offers the best nutritional regime for maturation of the gut, whereas the introduction of solid food selects the most adapted bacteria, converging towards an adult-like microbiota. The gut microbiota plays an important role in host health, influencing the maturation of the immune system and regulating energy metabolism. Moreover, it has become evident that the microbiota can affect brain function and behaviour. On this bidirectional communication between intestine and the central nervous system (CNS), the so called gut-brain axis, the gut influences brain development and biochemistry, whereas the brain affects gastrointestinal function. In this context, probiotics and prebiotics have been used as dietary strategies aimed at improving host health by modulating the gut ecosystem and, consequently, affecting host stress-responses, behaviour and cognition.

Industrial relevance: Dietary manipulation represents a strategy to preserve a healthy gastrointestinal microbial community and contribute to the well being of the host. Several food products containing probiotics and prebiotics have been developed for specific age groups such as infants and elderly, aiming to enhance the host's immune system and to prevent gastrointestinal diseases. This review presents recent strong evidence suggesting that the use of dietary approaches such as probiotics, prebiotics and diets enriched with fatty acids or proteins not only modulate the microbiota but may also impact on brain function, affecting stress-responses, behaviour and cognition. This new field of research may lead to market opportunities with the development of new dietary strategies targeting the gut–brain axis for enhanced mental health.

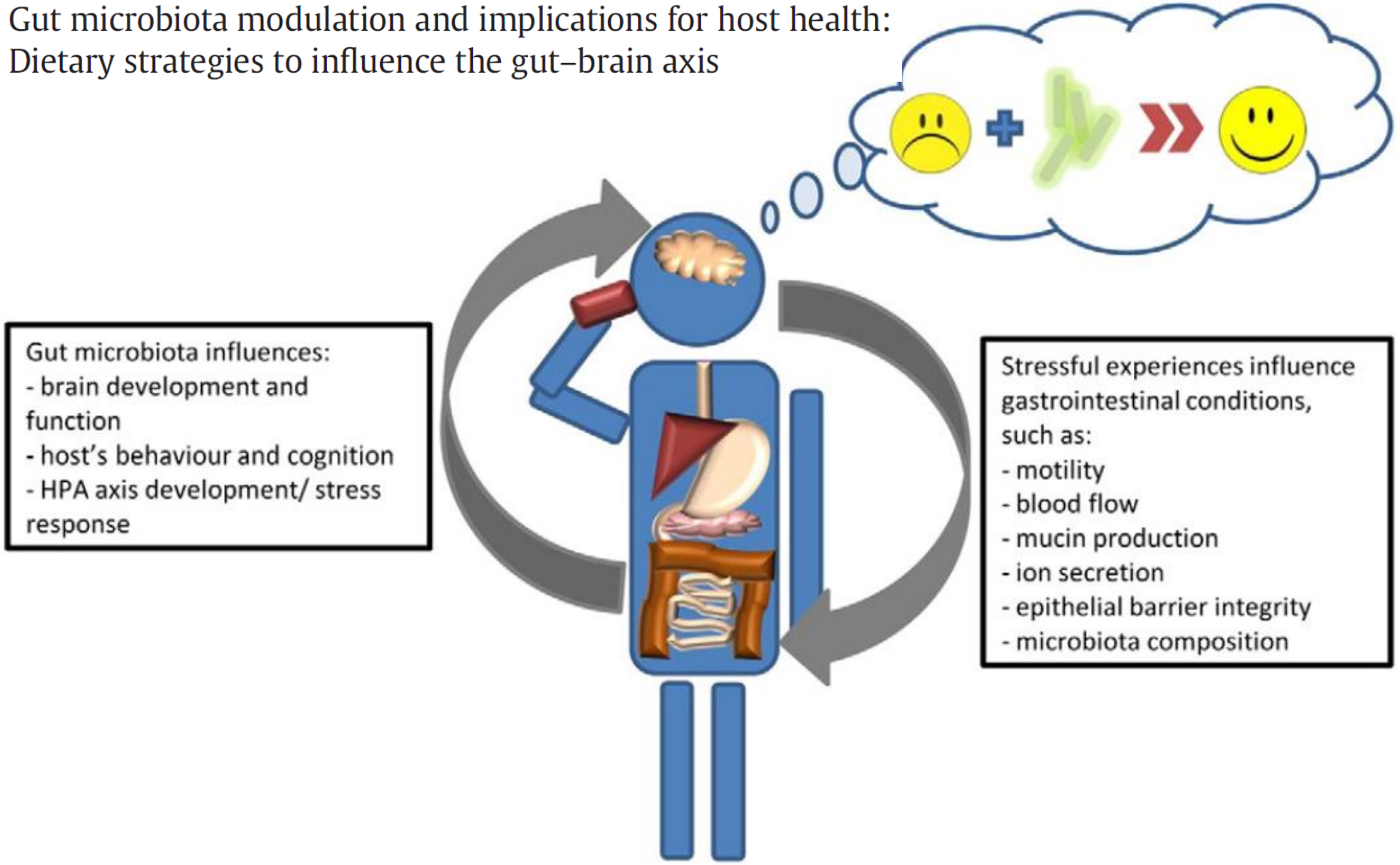


Fig. 1. The microbiota–gut–brain axis. The communication system is bidirectional and integrates neural, hormonal and immunological signalling. Dietary strategies, such as probiotics and prebiotics, aim to modulate the gut microbiota and may affect host's stress-responses, behaviour and cognition.

Effects of probiotics and prebiotics on the immune system, gut microbiota and the peripheral and central nervous system.

Probiotic strain	Model	Trial duration	Effects	Reference
Lactobacillus helveticus R0052 and *L. rhamnosus* R0011	Brown Norway rats	17 days	Prevented stress induced bacterial adherence to enterocytes Prevented bacterial translocation to mesenteric lymph nodes Inhibited chronic stress induced elevated intestinal ion secretion	Zareie et al., 2006
Bifidobacterium infantis 35624	Sprague Dawley rats	2 weeks	Decreased concentration of pro-inflammatory cytokines Increased levels of tryptophan in plasma	Desbonnet et al., 2008
Lactobacillus casei strain Shirota	Humans with chronic fatigue syndrome	8 weeks	Increased *Bifidobacterium* spp. and *Lactobacillus* spp. numbers Decreased anxiety symptoms	Rao et al., 2009
Lactobacillus rhamnosus R0011 and *Lactobacillus helveticus* R0052	C57BL/6 mice infected with *Citrobacter rodentium*	10/30 days	Prevented memory dysfunction after exposition to acute stress	Gareau et al., 2010
Bifidobacterium infantis 35624	SD rats (maternal separation model)	45 days	Normalized the immune response Reversed the behavioural deficits Restored the basal noradrenaline concentrations in the brainstem	Desbonnet et al., 2010
Bifidobacterium longum NCC3001	AKR mice colitis model	14 days	Reduced anxiety-like behaviour in DSS-treated mice	Bercik, Park, et al., 2011
Lactobacillus helveticus R0052 and *Bifidobacterium longum* R0175	Wistar rats and humans	14 days/30 days	Reduced anxiety-like behaviour in rats Alleviated psychological distress in humans	Messaoudi et al., 2011
Lactobacillus rhamnosus JB-1	BALB/c mice	28 days	Reduced stress-induced corticosterone Reduced anxiety- and depression-related behaviour Altered GABA receptors expression in different brain regions	Bravo et al., 2011
Bifidobacterium breve NCIMB 702258	C57BL/6 mice	8 weeks	Increased arachidonic acid and docosahexaenoic acid in the brain	Wall et al., 2012
Prebiotic: trans-galactooligosaccharide mixture	Humans with IBS	12 weeks	Increased *Bifidobacterium* numbers Improved quality of life Decreased anxiety scores in the IBS-D patients group (diarrhoea predominant)	Silk et al., 2009

Gut microbiota modulation and implications for host health: Dietary strategies to influence the gut–brain axis

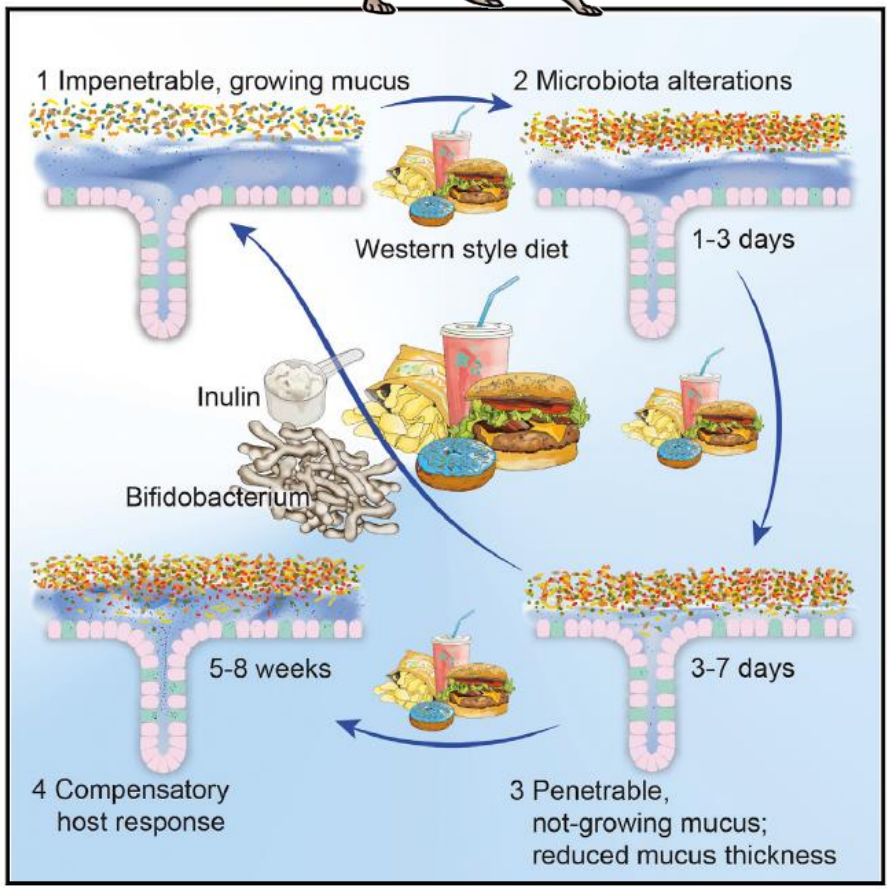
Schroeder et al., 2018, Cell Host & Microbe *23*, 27–40
January 10, 2018 © 2017 Elsevier Inc.
https://doi.org/10.1016/j.chom.2017.11.004

Bifidobacteria or Fiber Protects against Diet-Induced Microbiota-Mediated Colonic Mucus Deterioration

Bjoern O. Schroeder,[1] George M.H. Birchenough,[2] Marcus Ståhlman,[1] Liisa Arike,[2] Malin E.V. Johansson,[2] Gunnar C. Hansson,[2,*] and Fredrik Bäckhed[1,3,4,*]

SUMMARY

Diet strongly affects gut microbiota composition, and gut bacteria can influence the colonic mucus layer, a physical barrier that separates trillions of gut bacteria from the host. However, the interplay between a Western style diet (WSD), gut microbiota composition, and the intestinal mucus layer is less clear. Here we show that mice fed a WSD have an altered colonic microbiota composition that causes increased penetrability and a reduced growth rate of the inner mucus layer. Both barrier defects can be prevented by transplanting microbiota from chow-fed mice. In addition, we found that administration of *Bifidobacterium longum* was sufficient to restore mucus growth, whereas administration of the fiber inulin prevented increased mucus penetrability in WSD-fed mice. We hypothesize that the presence of distinct bacteria is crucial for proper mucus function. If confirmed in humans, these findings may help to better understand diseases with an affected mucus layer, such as ulcerative colitis.



www.nature.com/scientificreports/

Gut microbiota modulation accounts for the neuroprotective properties of anthocyanins

27 July 2018

Cláudia Marques[1,2], Iva Fernandes[3], Manuela Meireles[1,4], Ana Faria[1,2,5], Jeremy P. E. Spencer[6], Nuno Mateus[3] & Conceição Calhau[1,2]

High-fat (HF) diets are thought to disrupt the profile of the gut microbiota in a manner that may contribute to the neuroinflammation and neurobehavioral changes observed in obesity. Accordingly, we hypothesize that by preventing HF-diet induced dysbiosis it is possible to prevent neuroinflammation and the consequent neurological disorders. Anthocyanins are flavonoids found in berries that exhibit anti-neuroinflammatory properties in the context of obesity. Here, we demonstrate that the blackberry anthocyanin-rich extract (BE) can modulate gut microbiota composition and counteract some of the features of HF-diet induced dysbiosis. In addition, we show that the modifications in gut microbial environment are partially linked with the anti-neuroinflammatory properties of BE. Through fecal metabolome analysis, we unravel the mechanism by which BE participates in the bilateral communication between the gut and the brain. BE alters host tryptophan metabolism, increasing the production of the neuroprotective metabolite kynurenic acid. These findings strongly suggest that dietary manipulation of the gut microbiota with anthocyanins can attenuate the neurologic complications of obesity, thus expanding the classification of psychobiotics to anthocyanins.

Brain, Behavior, and Immunity 56 (2016) 140–155

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Brain, Behavior, and Immunity

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Full-length Article

Cognitive impairment by antibiotic-induced gut dysbiosis: Analysis of gut microbiota-brain communication

Esther E. Fröhlich [a,*], Aitak Farzi [a], Raphaela Mayerhofer [a], Florian Reichmann [a], Angela Jačan [a], Bernhard Wagner [b], Erwin Zinser [b], Natalie Bordag [c], Christoph Magnes [d], Eleonore Fröhlich [e], Karl Kashofer [f], Gregor Gorkiewicz [f,g,h], Peter Holzer [a,*]

Emerging evidence indicates that disruption of the gut microbial community (dysbiosis) impairs mental health. Germ-free mice and antibiotic-induced gut dysbiosis are two approaches to establish causality in gut microbiota-brain relationships. However, both models have limitations, as germ-free mice display alterations in blood-brain barrier and brain ultrastructure and antibiotics may act directly on the brain. We hypothesized that the concerns related to antibiotic-induced gut dysbiosis can only adequately be addressed if the effect of intragastric treatment of adult mice with multiple antibiotics on (i) gut microbial community, (ii) metabolite profile in the colon, (iii) circulating metabolites, (iv) expression of neuronal signaling molecules in distinct brain areas and (v) cognitive behavior is systematically investigated. Of the antibiotics used (ampicillin, bacitracin, meropenem, neomycin, vancomycin), ampicillin had some oral bioavailability but did not enter the brain. 16S rDNA sequencing confirmed antibiotic-induced microbial community disruption, and metabolomics revealed that gut dysbiosis was associated with depletion of bacteria-derived metabolites in the colon and alterations of lipid species and converted microbe-derived molecules in the plasma. Importantly, novel object recognition, but not spatial, memory was impaired in antibiotic-treated mice. This cognitive deficit was associated with brain region-specific changes in the expression of cognition-relevant signaling molecules, notably brain-derived neurotrophic factor, N-methyl-D-aspartate receptor subunit 2B, serotonin transporter and neuropeptide Y system. We conclude that circulating metabolites and the cerebral neuropeptide Y system play an important role in the cognitive impairment and dysregulation of cerebral signaling molecules due to antibiotic-induced gut dysbiosis.

General Psychiatry

Effects of regulating intestinal microbiota on anxiety symptoms: A systematic review

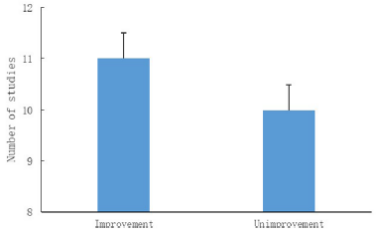
General Psychiatry 2019;

Beibei Yang, Jinbao Wei, Peijun Ju, Jinghong Chen

Background Anxiety symptoms are common in mental diseases and a variety of physical disorders, especially in disorders related to stress. More and more basic studies have indicated that gut microbiota can regulate brain function through the gut-brain axis, and dysbiosis of intestinal microbiota was related to anxiety. However, there is no specific evidence to support treatment of anxiety by regulating intestinal microbiota.

Aims To find evidence supporting improvement of anxiety symptoms by regulation of intestinal microbiota.

Methods This systematic review of randomised controlle trials was searched based on the following databases: PubMed, EMBASE, the Cochrane Library, OVID, Web of Knowledge, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP databases and SinoMed. The retrieval time dated back to 25 July 2018. Then we screened research literatures based on established inclusion and exclusion criteria. Quality evaluation for each included study was done using the Cochrane risk of bias and the Jadad scale.



Results A total of 3334 articles were retrieved and 21 studies were included which contained 1503 subjects. In the 21 studies, 14 chose probiotics as interventions to regulate intestinal microbiota and six chose non-probiotic ways such as adjusting daily diets. Probiotic supplements in seven studies contained only one kind of probiotic, two studies used a product that contained two kinds of probiotics and the supplements used in the other five studies included at least three kinds of probiotics. In the studies that used treatment as usual plus interventions regulating intestinal flora (IRIF) as interventions (five studies), only non-probiotic ways were effective (two studies), which means 40% of studies were effective; in the studies that used IRIF alone (16 studies, 11 studies used probiotic ways and 5 studies used non-probiotic ways), 56% of studies could improve anxiety symptoms, and 80% of studies that conducted the non-probiotic interventions were effective, while 45% of studies that used probiotic supplementations had positive effects on anxiety symptoms. Overall, 11 studies showed a positive effect on anxiety symptoms by regulating intestinal microbiota, which indicated 52% of the 21 studies were effective, and there were five studies that used probiotic supplements as interventions and six used non-probiotic interventions. In addition, it should be noted that six of seven studies showed that regulation of intestinal microbiota could treat anxiety symptoms, the rate of efficacy was 86%.

Conclusions We find that more than half of the studies included showed it was positive to treat anxiety symptoms by regulation of intestinal microbiota. There are two kinds of interventions (probiotic and non-probiotic interventions) to regulate intestinal microbiota, and it should be highlighted that the non-probiotic interventions were more effective than the probiotic interventions. More studies are needed to clarify this conclusion since we still cannot run meta-analysis so far.

Table 1 Basic characteristics of the included literature

ID	Author	Year	Methods	Subjects		Interventions	Scales
				Diagnosis	Sample size (n)		
1	Roman *et al*[28]	2018	Randomised double blind	Fibromyalgia	31	Three probiotic mixtures or above	STAI
2	Farhangi *et al*[21]	2018	Randomised triple blind	T2DM*	62	Resistant dextrin†	GHQ, DASS
3	Schumann *et al*[22]	2018	Randomised single blind	IBS	59	Low FODMAP	HADS
4	Sawada *et al*[17]‡	2017	Randomised double blind	Healthy individuals§	24	*Lactobacillus gasseri*	HADS , STAI
5	Sanchez *et al*[23]	2017	Randomised double blind	Obesity	105	*Lactobacillus rhamnosus*	STAI
6	Romijn *et al*[27]	2017	Randomised double blind	IBS	79	Two probiotic mixtures†	DASS
7	Pinto-Sanchez *et al*[18]	2017	Randomised double blind	IBS	44	*Bifidobacterium longum*	HADS , STAI
8	Kelly *et al* [20]‡	2017	Randomised	Healthy individuals§	29	*L. rhamnosus*	BAI, STAI
9	Eswaran *et al*[26]	2017	Randomised single blind	IBS	84	Low FODMAP†	HADS
10	Colica *et al*[29]	2017	Randomised	Healthy individuals	30	At least three probiotic mixtures	HAM-A
11	Azpiroz *et al*[30]	2017	Randomised double blind	IBS	79	scFOS	HADS
12	Lyra *et al*[31]	2016	Randomised triple blind	IBS	340	*Lactobacillus acidophilus*†	HADS
13	Steenbergen *et al* [32]	2015	Randomised triple blind	Healthy individuals	89	At least three probiotic mixtures	BAI
14	Lorenzo-Zúñiga *et al*[33]	2014	Randomised triple blind	IBS	84	At least three probiotic mixtures	VSI
15	Peters *et al*[34]‡	2014	Randomised double blind	IBS	22	Supplementation of gluten	STPI
16	Alipour *et al*[35]	2014	Randomised double blind	RA*	46	*Lactobacillus casei*†	STAI
17	Yuman and Yingwei[24]	2013	Randomised double blind	Healthy individuals	82	Nutritional interventions	HAM-A
18	Messaoudi *et al*[19]	2011	Randomised double blind	Healthy individuals	55	Two probiotic mixtures	HADS HSCL-90
19	Simrén *et al*[37]	2010	Randomised double blind	IBS	74	At least three probiotic mixtures	HADS
20	Silk *et al* [36]‡	2009	Randomised single blind	IBS	44	*Trans*-galactooligosaccharide mixture	HADS
21	Rao *et al*[39]	2009	Randomised double blind	CFS	39	*L. casei*	BAI

DASS-42 refers to the 42-item self-report questionnaire designed to assess current severity of symptoms relating to depression, anxiety and stress.
*All the subjects were female.
†Studies conducted treatment as usual (TAU) plus interventions regulating intestinal flora (IRIF) interventions.
‡Cross-over study design.
§All the subjects were male.
BAI, Beck Anxiety Inventory; CFS, chronic fatigue syndrome; DASS-42, Depression, Anxiety and Stress Scale; GHQ, General Health Questionnaire; HADS, Hospital Anxiety and Depression Scale; HAM-A, Hamilton Anxiety Rating Scale; HSCL-90, Hopkins Symptom Checklist; IBS, irritable bowel syndrome; RA, rheumatoid arthritis; STAI, State-Trait Anxiety Inventory; STPI, the State Trait Personality Inventory; T2DM, type 2 diabetes mellitus; VSI, Visceral Sensitivity Index; low FODMAP, diet low in fermentable oligosaccharides, disaccharides, and monosaccharides and polyols; scFOS, short-chain fructooligosaccharides.

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Impact of coffee consumption on the gut microbiota: A human volunteer study

Muriel Jaquet, Isabelle Rochat, Julie Moulin, Christophe Cavin, Rodrigo Bibiloni *

A B S T R A C T

The impact of a moderate consumption of an instant coffee on the general composition of the human intestinal bacterial population was assessed in this study. Sixteen (16) healthy adult volunteers consumed a daily dose of 3 cups of coffee during 3 weeks. Faecal samples were collected before and after the consumption of coffee, and the impact of the ingestion of the product on the intestinal bacteria as well as the quantification of specific bacterial groups was assessed using nucleic acid-based methods. Although faecal profiles of the dominant microbiota were not significantly affected after the consumption of the coffee (Dice's similarity index = 92%, $n = 16$), the population of *Bifidobacterium* spp. increased after the 3-week test period ($P = 0.02$). Moreover, in some subjects, there was a specific increase in the metabolic activity of *Bifidobacterium* spp. Our results show that the consumption of the coffee preparation resulting from water co-extraction of green and roasted coffee beans produce an increase in the metabolic activity and/or numbers of the *Bifidobacterium* spp. population, a bacterial group of reputed beneficial effects, without major impact on the dominant microbiota.

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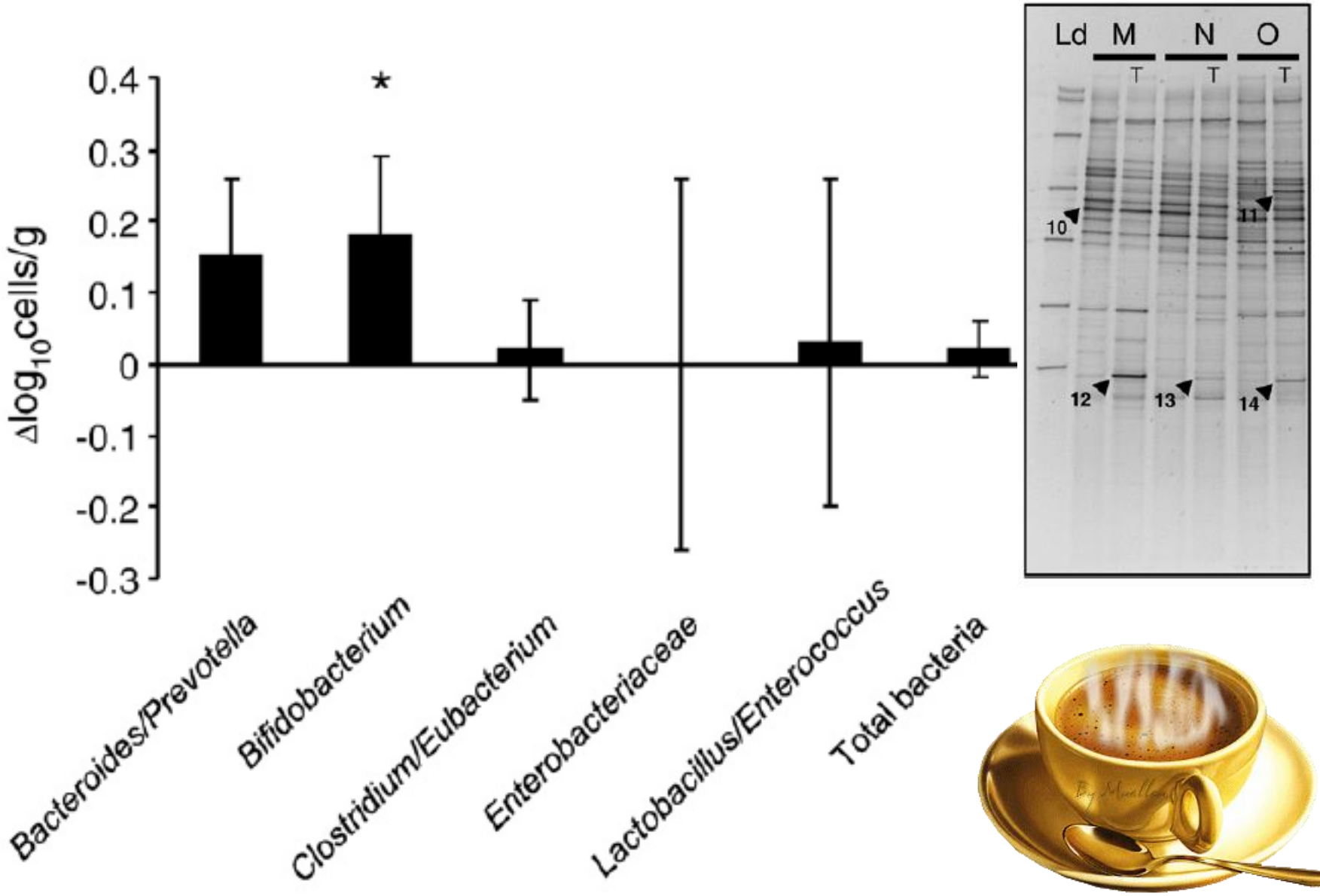

Fig. 2. Increments in bacterial numbers for selected groups after the consumption of coffee. Bacterial counts were determined using FISH technology (P=0.02).

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Original article

Peanuts as a nighttime snack enrich butyrate-producing bacteria compared to an isocaloric lower-fat higher-carbohydrate snack in adults with elevated fasting glucose: A randomized crossover trial

Philip A. Sapp [a], Penny M. Kris-Etherton [a], Elke A. Arnesen [b, c], Jeremy R. Chen See [b, c], Regina Lamendella [b, c], Kristina S. Petersen [a, d, *]

SUMMARY

Background: Tree nuts have glucoregulatory effects and influence gut microbiota composition. The effect of peanuts on the microbiota has not been investigated.

Objectives: The aim was to examine the effect of 28 g/d of peanuts for 6-wks, compared to an isocaloric lower-fat higher-carbohydrate (LFHC) snack, on gut microbiota composition. A secondary aim was to identify functional and active compositional differences in a subset of participants using metatranscriptomics.

Methods: In a randomized, crossover trial, 50 adults (48% female; 42 ± 15 y; BMI 28.3 ± 5.6 kg/m^2; plasma glucose 100 ± 8 mg/dL) consumed 28 g/d of dry roasted, unsalted, peanuts (164 kcal; 11% E carbohydrate, 17% E protein, 73% E fat, and 2.4 g fiber) or a LFHC snack (164 kcal; 53% E carbohydrate, 17% E protein, 33% E fat, and 3 g fiber) for 6-wk (4-wk washout period). Gut bacterial composition was measured using 16S rRNA sequencing in the whole cohort. Exploratory metatranscriptomic analyses were conducted on a random subset (n = 24) of samples from the Peanut condition.

Results: No between-condition differences in α- or β- diversity were observed. Following peanut intake, *Ruminococcaceae* were significantly more abundant [Linear discriminant analysis score (LDA) = 2.8; $P = 0.027$)] compared to LFHC. Metatranscriptomics showed increased expression of the K03518 (aerobic carbon-monoxide dehydrogenase small subunit) gene following peanut intake (LDA = 2.0; $P = 0.004$) and *Roseburia intestinalis L1-82* was identified as a contributor to the increased expression.

Conclusion: An increased abundance of *Ruminococcaceae* was observed following consumption of 28 g/d of peanuts in adults with elevated fasting glucose after 6-wks. Metatranscriptomics revealed increased expression of the K03518 gene. These results suggest peanut intake enriches a known butyrate producer and the increased expression of a gene implicated in butyrate production adds further support for peanut-induced gut microbiome modulation.

Cell Host & Microbe
Review

Control of Brain Development, Function, and Behavior by the Microbiome

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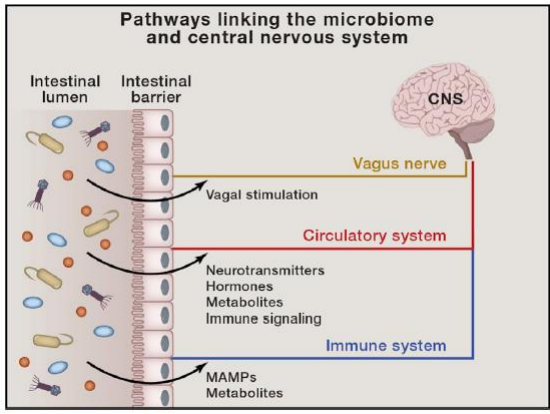
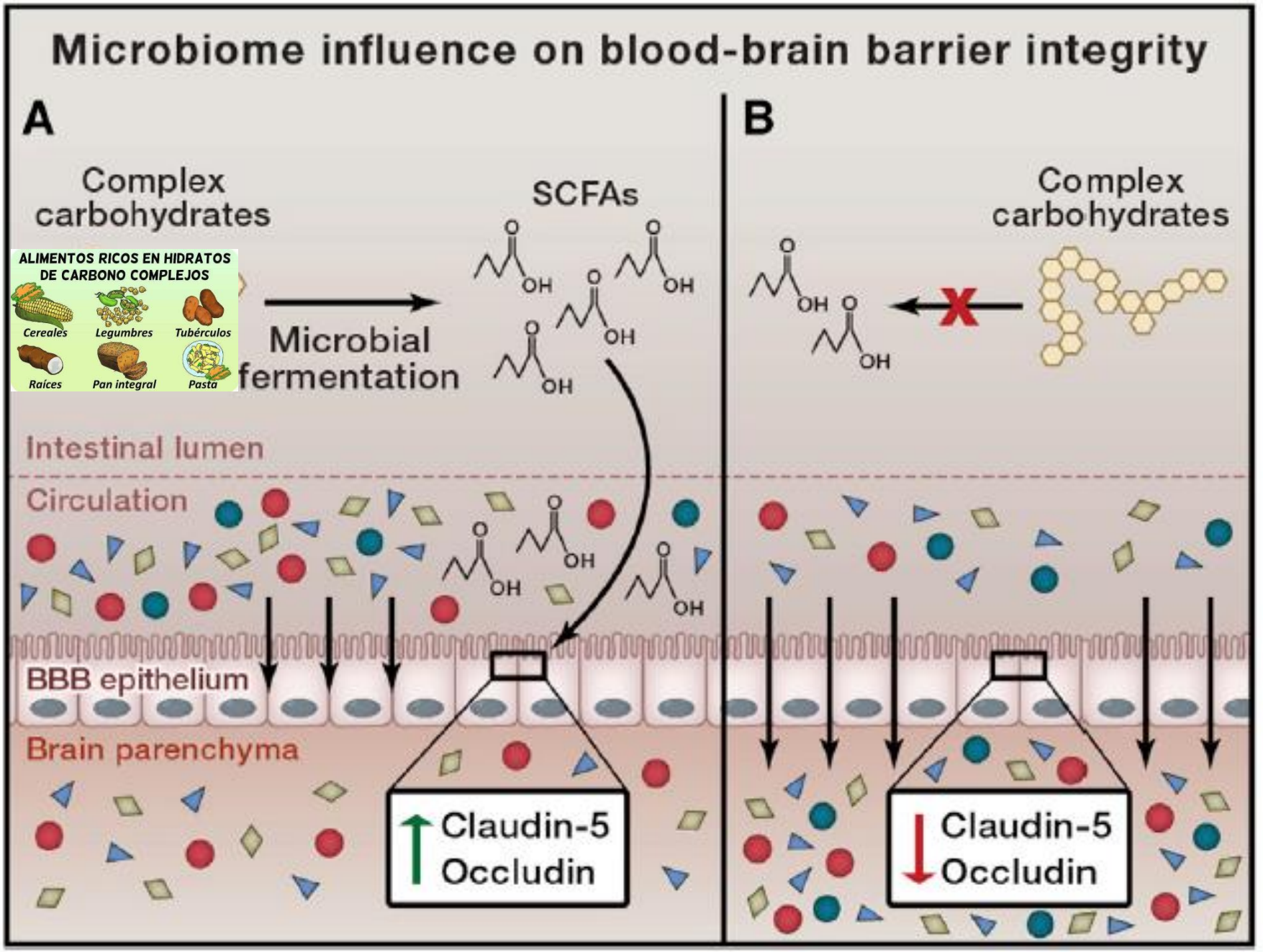
Animals share an intimate and life-long partnership with a myriad of resident microbial species, collectively referred to as the microbiota. Symbiotic microbes have been shown to regulate nutrition and metabolism and are critical for the development and function of the immune system. More recently, studies have suggested that gut bacteria can impact neurological outcomes—altering behavior and potentially affecting the onset and/or severity of nervous system disorders. In this review, we highlight emerging evidence that the microbiome extends its influence to the brain via various pathways connecting the gut to the central nervous system. While understanding and appreciation of a gut microbial impact on neurological function is nascent, unraveling gut-microbiome-brain connections holds the promise of transforming the neurosciences and revealing potentially novel etiologies for psychiatric and neurodegenerative disorders.

Table 1. Selected Phenotypic Attributes Influenced by Gut Microbes

Category	Attribute	Effect	Citation(s)
Behavioral	Anxiety	Reduced self-reported anxiety in humans treated with *L. helveticus* R0052 and *B. longum* R0175	Messaoudi et al., 2011
Behavioral	Anxiety-like behavior	Decreased anxiety-like behavior in GF mice (Swiss Webster, NIH Swiss, and NMRI)	Clarke et al, 2013; Diaz Heijtz et al., 2011; Neufeld et al., 2011; Selkrig et al., 2014
Behavioral	Anxiety-like behavior	Increased anxiety-like behavior in GF mice (BALB/c, C57Bl6)	Bercik et al., 2011; Selkrig et al., 2014
Behavioral	Anxiety-like behavior	Reduced anxiety-like behavior in rodents treated with *Bifidobacterium breve* 1205, *B. longum* 1714, *B. longum* R0175 *Lactobacillus helveticus* R0052, or *L. rhamnosus*JB-1	Bravo et al., 2011; Messaoudi et al., 2011; Savignac et al., 2014
Behavioral	Depression	Reduced self-reported feelings of depression and aggression in humans treated with probiotics	Steenbergen et al., 2015
Behavioral	Depression-like behavior	Decreased depression-like behavior in mice treated with *B. infantis* or *L. rhamnosus* JB-1	Bravo et al., 2011; Desbonnet et al., 2010; Savignac et al., 2014; Savignac et al., 2015
Behavioral	Emotional processing	Reduced activation following emotional stimulus in humans treated with probiotic milk product	Tillisch et al., 2013
Behavioral	Social recognition	Reduced novel and familiar social recognition in GF mice	Desbonnet et al., 2014
Behavioral	Stereotyped behaviors and vocalizations	Restoration of social behaviors in *Bacteroides fragilis*-treated MIA mice	Hsiao et al., 2012
Behavioral	Stress response	Increased response to restraint stress in GF mice	Sudo et al., 2004
Hormonal	Corticosterone	Increased hypothalmic corticosterone in GF mice	Sudo et al., 2004
Hormonal	Cortisol	Reduced urinary cortisol in humans treated with *L. helveticus* R0052 and *B. longum* R0175	Messaoudi et al., 2011
Neurochemical	BBB	Decreased expression of tight junction proteins, and subsequent increase of BBB permeability	Braniste et al., 2014
Neurochemical	BDNF	Decreased hypothalmic BDNF in GF mice	Sudo et al., 2004
Neurochemical	Dopamine and GABA	Decreased serum levels of dopamine and GABA in GF mice	Matsumoto et al., 2012; Velagapudi et al., 2010
Neurochemical	G-CSF	Reduced serum levels of G-CSF in GF mice	Deshmukh et al., 2014
Neurochemical	Peripheral serotonin	Decreased peripheral and intestinal serotonin in GF mice, restored by colonization with spore forming bacteria	Wikoff et al., 2009; Yano et al., 2015
Neurochemical	Serotonin and Serotonin receptor	Decreased serotonin and receptor ($5HT_{1A}$) in the amygdala and hippocampus of GF mice	Bercik et al., 2011; Clarke et al., 2013; Diaz Heijtz et al., 2011; Neufeld et al., 2011; Yano et al., 2015
Neurochemical	Serotonin, noradrenaline, and dopamine	Increased turnover of serotonin, noradrenaline, and dopamine in the striatum of GF mice	Diaz Heijtz et al., 2011




Microbiome influence on blood-brain barrier integrity
A
Complex carbohydrates
ALIMENTOS RICOS EN HIDRATOS DE CARBONO COMPLEJOS
Cereales
Legumbres
Tubérculos
Raíces
Pan integral
Pasta
Microbial fermentation
SCFAs
OH
Intestinal lumen
Circulation
BBB epithelium
Brain parenchyma
Claudin-5
Occludin
B
Complex carbohydrates
X
Claudin-5
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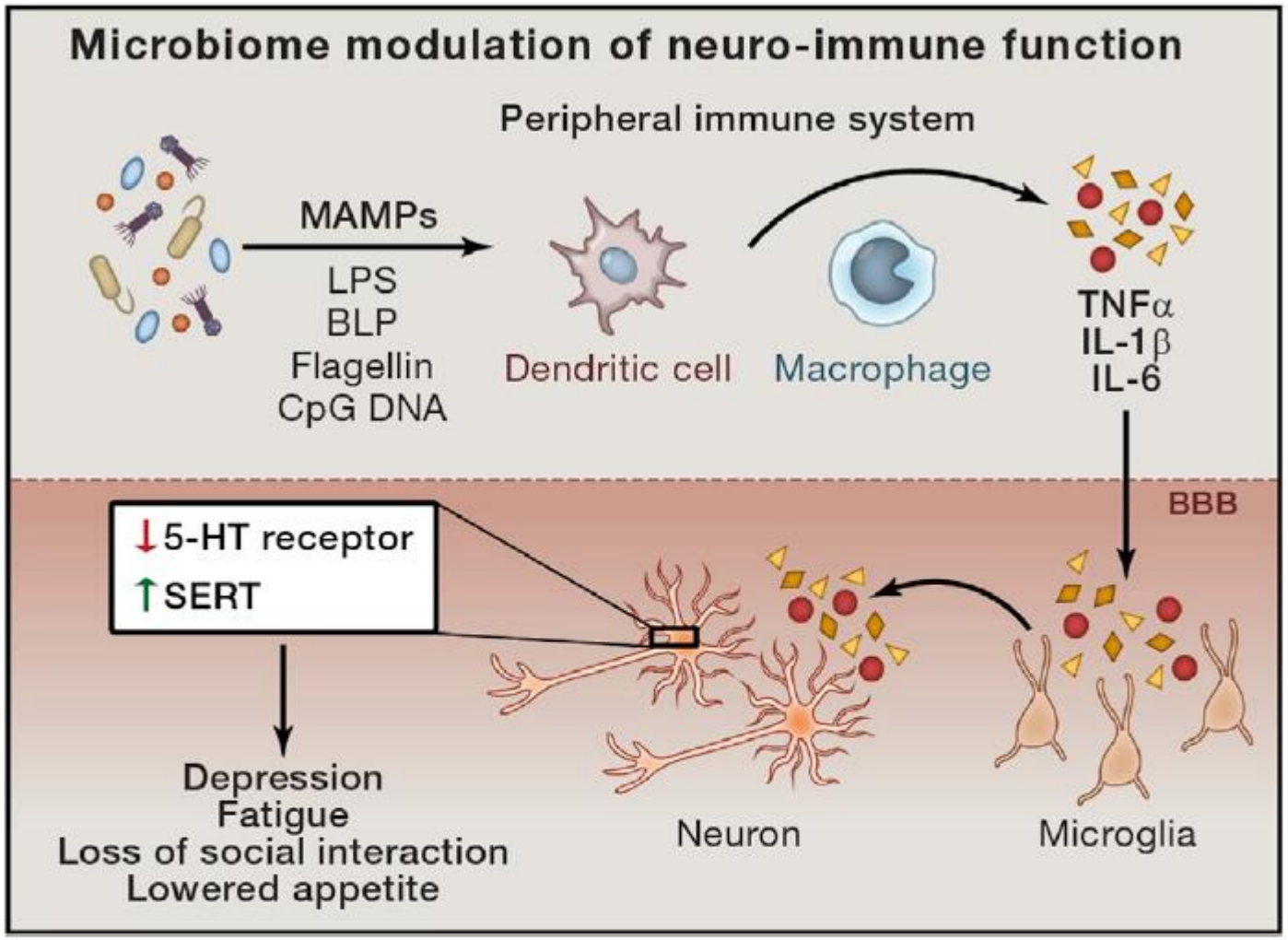

Figure 3. Microbiome Modulation of Neuro-Immune Function
MAMPs derived from the intestinal microbiome can drive various aspects of immune function in the periphery. Cytokine signals, such as TNFα, IL-1β, and IL-6, can cross the BBB and trigger their production by the microglia. Interaction of these cytokines with neurons influences physiology and leads to sickness behavior and depression.

MAMP: Patrón molecular asociado a la microbiota

LPS: lipopolisacáridos

BLP: Lipoproteínas bacterianas

TNF: Factor de necrosis tumoral

IL: Interleucinas

SERT: Transportador de serotinina

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

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

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ABSTRACT

Background: Recent insights into the role of the human microbiota in cognitive and affective functioning have led to the hypothesis that probiotic supplementation may act as an adjuvant strategy to ameliorate or prevent depression. *Objective*: Heightened cognitive reactivity to normal, transient changes in sad mood is an established marker of vulnerability to depression and is considered an important target for interventions. The present study aimed to test if a multispecies probiotic containing *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, and *Lactococcus lactis* (W19 and W58) may reduce cognitive reactivity in non-depressed individuals. *Design*: In a triple-blind, placebo-controlled, randomized, pre- and post-intervention assessment design, 20 healthy participants without current mood disorder received a 4-week probiotic food-supplement intervention with the multispecies probiotics, while 20 control participants received an inert placebo for the same period. In the pre- and post-intervention assessment, cognitive reactivity to sad mood was assessed using the revised Leiden index of depression sensitivity scale. *Results*: Compared to participants who received the placebo intervention, participants who received the 4-week multispecies probiotics intervention showed a significantly reduced overall cognitive reactivity to sad mood, which was largely accounted for by reduced rumination and aggressive thoughts. *Conclusion*: These results provide the first evidence that the intake of probiotics may help reduce negative thoughts associated with sad mood. Probiotics supplementation warrants further research as a potential preventive strategy for depression.

MINIREVIEW

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DOI 10.1007/s12275-018-8079-2

New perspectives of *Lactobacillus plantarum* as a probiotic: The gut-heart-brain axis

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Lactobacillus plantarum **is a non-gas-producing lactic acid bacterium that is generally regarded as safe (GRAS) with Qualified Presumption of Safety (QPS) status. Although traditionally used for dairy, meat and vegetable fermentation, *L. plantarum* is gaining increasing significance as a probiotic. With the newly acclaimed gut-heart-brain axis, strains of *L. plantarum* have proven to be a valuable species for the development of probiotics, with various beneficial effects on gut health, metabolic disorders and brain health. In this review, the classification and taxonomy, and the relation of these with safety aspects are introduced. Characteristics of *L. plantarum* to fulfill the criteria as a probiotic are discussed. Emphasis are also given to the beneficial functions of *L. plantarum* in gut disorders such as inflammatory bowel diseases, metabolic syndromes, dyslipidemia, hypercholesteromia, obesity, and diabetes, and brain health aspects involving psychological disorders.**

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Vol. 48. Fasc. 5 (1997), 297-311

REVISIÓN

Bacterias del ácido láctico en la fermentación de aceitunas de mesa

Por **M. C. Durán Quintana, C. Romero Barranco, P. García García, M. Brenes Balbuena y A. Garrido Fernández***

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RESUMEN

Bacterias del ácido láctico en la fermentación de aceitunas de mesa.

El trabajo hace una revisión de las características del desarrollo de las bacterias ácido lácticas (BAL) en la elaboración de los tres tipos de aceitunas de mesa más importantes en el comercio internacional. El único proceso espontáneo típicamente láctico es el de las verdes estilo español. La presencia de las BAL en la etapa de conservación de las aceitunas tipo negras y en la fermentación de las negras naturales depende de diversos factores tales como variedad, concentración de cloruro sódico, corrección inicial del pH, etc. El conocimiento de las condiciones en las que se produce el crecimiento natural puede permitir un mejor control microbiológico y la utilización eficaz de cultivos iniciadores en dichas fermentaciones.

PALABRAS-CLAVE: Aceituna de mesa – Bacterias del ácido láctico – Fermentación – Revisión (artículo).

frontiers in Microbiology

ORIGINAL RESEARCH
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Biodiversity and Multifunctional Features of Lactic Acid Bacteria Isolated From Table Olive Biofilms

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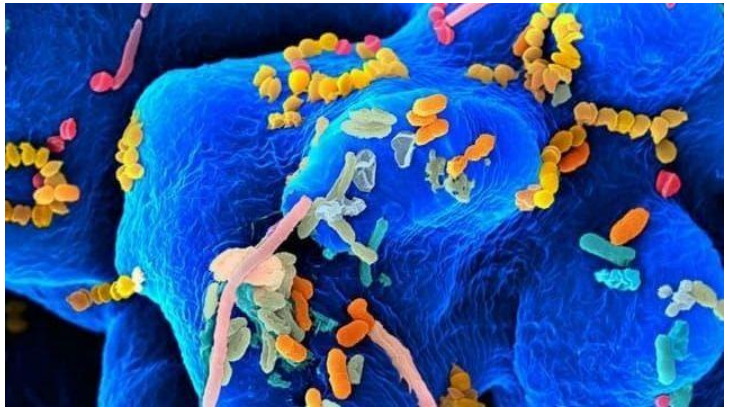
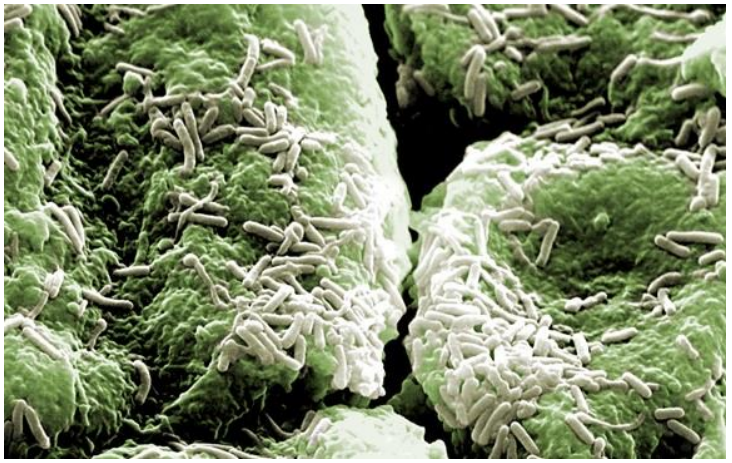


In the present study, a total of 554 lactic acid bacteria (LAB) isolates were obtained from the olive surface of Manzanilla, Gordal, and Aloreña cultivars processed as green Spanish-style or directly brined (natural) olives. The isolates obtained from industrial processes were genotyped by rep-PCR with primer GTG_5, collecting a total of 79 different genotypes. The α-biodiversity indexes showed that the LAB diversity was higher in the biofilms on the fruits which followed the Spanish-style process than in those just brined. Sixteen genotypes had a frequency higher >1% and were identified, by multiplex PCR *recA* gene and 16S gene sequencing, as belonging to *Lactobacillus pentosus* (n = 13) and *Lactobacillus plantarum* (n = 3) species. A multivariate analysis based on a dataset with 89,744 cells, including technological (resistance to salt and pH, production of lactic acid, auto and co-aggregation with yeast species, β-glucosidase and esterase activities), and potential probiotic characteristics (survival to gastric and pancreatic digestions, resistance to antibiotics, inhibition of pathogens, presence of *bsh* genes, cholesterol removal, hemolytic, α-glucosidase, β-galactosidase, and phytase activities) showed that the 16 genotypes could be grouped into 3 great phenotypes. Thus, the genotype biodiversity in table olive biofilms was limited but, at phenotype level, it was even lower since *L. pentosus* predominated clearly (80.15% isolates). *L. pentosus* Lp13 was the genotype with the most promising characteristics for its use as a multifunctional starter, with this strain being and ubiquitous microorganism present in both natural and lye-treated olive fermentations.



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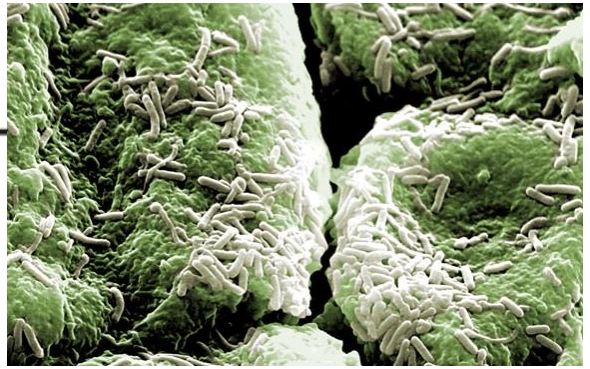

Probiotic Properties of *Lactobacillus* Strains Isolated from Table Olive Biofilms

Antonio Benítez-Cabello[1,2] · Edgar Torres-Maravilla[2] · Luis Bermúdez-Humarán[2] · Philippe Langella[2] · Rebeca Martín[2] · Rufino Jiménez-Díaz[1] · Francisco Noé Arroyo-López[1]

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Abstract

In this work, 16 strains with promising probiotic characteristics belonging to the *Lactobacillus pentosus* (13) and *Lactobacillus plantarum* (3) species and isolated from table olive biofilms were tested for adherence to cell lines and to solvents, immunomodulatory, and anti-proliferative properties on epithelial human cellular lines. Most *Lactobacillus* strains were able to regulate the production of cytokines by stimulating the production of pro-inflammatory (IL-6) and anti-inflammatory (IL-10) interleukins on macrophages, and by suppressing the secretion of IL-8 on HT-29 TNF-α-induced model. *Lactobacillus* strains also showed anti-proliferative activity on the HT-29 cell line. No clear relation was found between adhesion to solvents and adhesion to HT-29 human cell line. *Lactobacillus pentosus LPG1*, which showed the best anti-inflammatory and immunomodulatory properties, was then tested in a dinitro-benzene sulfonic acid (DNBS)-induced chronic colitis murine model. As a measure of the inflammation, gut permeability and weight loss, as well as cytokine profiles, were determined. *Lactobacillus pentosus LPG1* improved mice health as observed by a significant reduction of weight loss, gut permeability, and beneficial cytokine modulation. Macroscopic scores and tissue damage were also lower in mice administered with *LPG1* with respect to the DNBS-treated group. These results showed that *L. pentosus* LPG1 isolated from plant could have potential as probiotic for use as an anti-inflammatory and immunomodulatory agent for patients with inflammatory bowel disease.

foods

Foods 2023, 12, 938.

MDPI

Article

In Silico Evidence of the Multifunctional Features of *Lactiplantibacillus pentosus* LPG1, a Natural Fermenting Agent Isolated from Table Olive Biofilms

Elio López-García [1], Antonio Benítez-Cabello [1,*], Javier Ramiro-García [1], Victor Ladero [2] and Francisco Noé Arroyo-López [1]

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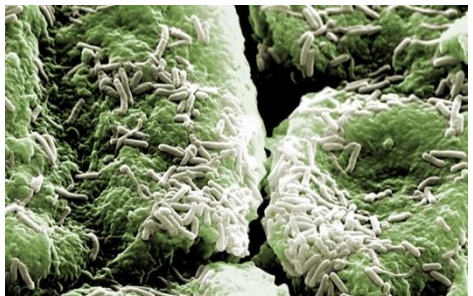
[2] Technology and Biotechnology Department, Instituto de Productos Lácteos de Asturias (IPLA-CSIC),

Abstract: In recent years, there has been a growing interest in obtaining probiotic bacteria from plant origins. This is the case of *Lactiplantibacillus pentosus LPG1*, a lactic acid bacterial strain isolated from table olive biofilms with proven multifunctional features. In this work, we have sequenced and closed the complete genome of *L. pentosus LPG1* using both Illumina and PacBio technologies. Our intention is to carry out a comprehensive bioinformatics analysis and whole-genome annotation for a further complete evaluation of the safety and functionality of this microorganism. The chromosomic genome had a size of 3,619,252 bp, with a GC (Guanine-Citosine) content of 46.34%. *L. pentosus LPG1* also had two plasmids, designated as pl1LPG1 and pl2LPG1, with lengths of 72,578 and 8713 bp (base pair), respectively. Genome annotation revealed that the sequenced genome consisted of 3345 coding genes and 89 non-coding sequences (73 tRNA and 16 rRNA genes). Taxonomy was confirmed by Average Nucleotide Identity analysis, which grouped *L. pentosus LPG1* with other sequenced *L. pentosus* genomes. Moreover, the pan-genome analysis showed that *L. pentosus* LPG1 was closely related to the *L. pentosus* strains *IG8*, *IG9*, *IG11*, and *IG12*, all of which were isolated from table olive biofilms. Resistome analysis reported the absence of antibiotic resistance genes, whilst PathogenFinder tool classified the strain as a non-human pathogen. Finally, in silico analysis of *L. pentosus LPG1* showed that many of its previously reported technological and probiotic phenotypes corresponded with the presence of functional genes. In light of these results, we can conclude that *L. pentosus LPG1* is a safe microorganism and a potential human probiotic with a plant origin and application as a starter culture for vegetable fermentations.



Lactobacillus Pentosus LPG1

BE Well!

— PROBIOTIC —
VEGETABLE DRINK

¿Dónde se aisló Lactobacillus pentosus LPG1?

Lacbobacillus pentosus LPG1 procede de la epidermis de fermentaciones de aceitunas de mesa. Su origen es vegetal.
Además está protegido y patentado por sus características probióticas y tecnológicas.
Seleccionado de un total de 554 cepas aisladas tras 8 años de estudio por el CSIC.

CSIC
Consejo Superior de Investigaciones Científicas

¿Qué lo diferencia de otros probióticos?

Su origen o matriz es vegetal. Los probióticos pueden seleccionarse de distintos ambientes o sustratos tanto de origen animal (suero fetal bovino, secreciones de la leche...) como de origen vegetal como es el caso de Lactobacillus pentosus LGP1.

¿Qué ventajas tiene que su matriz sea vegetal?

Por una parte pueden consumirlo personas con INTOLERANCIA A LA LACTOSA, puesto que no utilizamos la leche ni sus derivados como sustrato y también VEGANOS Y VEGETARIANOS, al no contener nada de origen animal.

¿Está patentado?

Sí, está protegido por sus características probióticas y también tecnológicas.

Diversos artículos científicos y ensayos clínicos respaldan las características probióticas de nuestra cepa L. pentosus LPG1.

¿Es un microorganismo seguro?

Las cepas de Lactobacillus pentosus están incluidas en la QPS (Qualified presumption of Safety) de la EFSA (Junio 2020).

efsa
European Food Safety Authority

¿Qué tipo de estudios se han llevado a cabo con Lactobacillus pentosus LPG1?

Numerosos estudios científicos se han llevado a cabo tanto in vitro, con c. elegans, en murinos... y actualmente se ha concluido un estudio en vivo con humanos en colaboración con el IMIBIC.

¿Qué resultados arrojan estos estudios científicos?

- Reduce los niveles de colesterol (hasta un 25%).
- Retrasa la entrada en senescencia (envejecimiento)
- Presenta una alta actividad antiinflamatoria y antioxidante.
- Presenta actividad inmunomoduladora.
- Reduce la permeabilidad y mejora la integridad de la barrera intestinal.
- La administración de LPG1 aumenta el número de secuencias y personas con Lactobacillus en heces, preserva la biodiversidad y modula favorablemente la microbiota intestinal.

IMIBIC
INSTITUTO MAIMÓNIDES DE INVESTIGACIÓN BIOMÉDICA DE CÓRDOBA

LA CASA D MANOLETE
bistró

la salmoreteca

BE Well!
PROBIOTIC
VEGETABLE DRINK

Fecha de noticia:
Jueves, 2 marzo, 2023

Lactiplantibacillus pentosus **LPG1**

El CSIC desarrolla bebidas probióticas con una bacteria procedente de la aceituna de mesa

El Instituto de la Grasa y las empresas Oleica y La Salmoreteca lanzan al mercado BeWellDrinks, una gama de bebidas vegetales fortificadas con minerales y vitaminas

EL PRIMER SALMOREJO PROBIÓTICO DE LA MANO DE JUANJO RUIZ

portador de más de 1.000 millones de fermentos activos por tarrina de 200 gramos

EL SALMOREJO QUE AYUDA A TU SISTEMA INMUNOLOGICO

Y QUE ADEMÁS ES SOLIDARIO:

COLABORA EN LA INVESTIGACION DE LA ESCLEROSIS MULTIPLE

Fortificado con fermentos naturales activos de origen vegetal (Lactobacillus pentosus LPG1)
el PRIMER SALMOREJO PROBIOTICO DEL MUNDO es el resultado de más de dos años de estudios por parte del chef Juanjo Ruiz y de un equipo multidisciplinar de investigadores pertenecientes al Instituto de la Grasa- CSIC (liderados por el Dr. Francisco Noé Arroyo López), Universidad de Córdoba (Dr. Antonio Valero Díaz), la startup Oleica (Dr. Verónica Romero Gil).

Schroeder et al., 2018, Cell Host & Microbe *23*, 27–40
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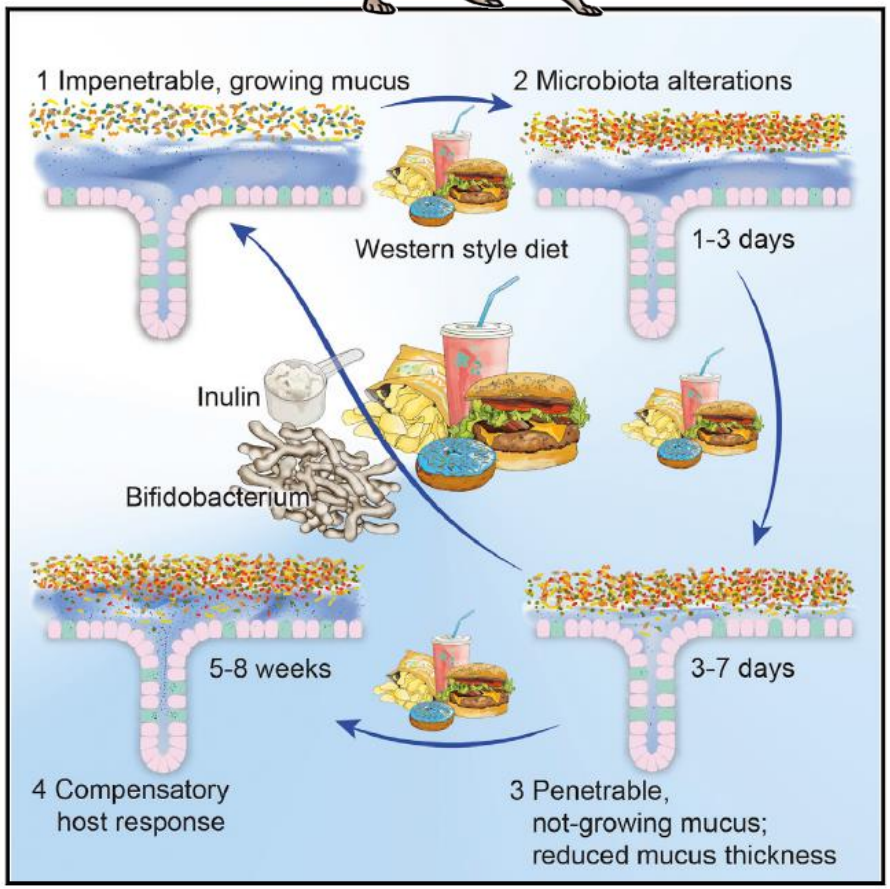
Bifidobacteria or Fiber Protects against Diet-Induced Microbiota-Mediated Colonic Mucus Deterioration

Bjoern O. Schroeder,[1] George M.H. Birchenough,[2] Marcus Ståhlman,[1] Liisa Arike,[2] Malin E.V. Johansson,[2] Gunnar C. Hansson,[2,*] and Fredrik Bäckhed[1,3,4,*]

SUMMARY

Diet strongly affects gut microbiota composition, and gut bacteria can influence the colonic mucus layer, a physical barrier that separates trillions of gut bacteria from the host. However, the interplay between a Western style diet (WSD), gut microbiota composition, and the intestinal mucus layer is less clear. Here we show that mice fed a WSD have an altered colonic microbiota composition that causes increased penetrability and a reduced growth rate of the inner mucus layer. Both barrier defects can be prevented by transplanting microbiota from chow-fed mice. In addition, we found that administration of *Bifidobacterium longum* was sufficient to restore mucus growth, whereas administration of the fiber inulin prevented increased mucus penetrability in WSD-fed mice. We hypothesize that the presence of distinct bacteria is crucial for proper mucus function. If confirmed in humans, these findings may help to better understand diseases with an affected mucus layer, such as ulcerative colitis.



www.nature.com/scientificreports/

Gut microbiota modulation accounts for the neuroprotective properties of anthocyanins

27 July 2018

Cláudia Marques[1,2], Iva Fernandes[3], Manuela Meireles[1,4], Ana Faria[1,2,5], Jeremy P. E. Spencer[6], Nuno Mateus[3] & Conceição Calhau[1,2]

High-fat (HF) diets are thought to disrupt the profile of the gut microbiota in a manner that may contribute to the neuroinflammation and neurobehavioral changes observed in obesity. Accordingly, we hypothesize that by preventing HF-diet induced dysbiosis it is possible to prevent neuroinflammation and the consequent neurological disorders. Anthocyanins are flavonoids found in berries that exhibit anti-neuroinflammatory properties in the context of obesity. Here, we demonstrate that the blackberry anthocyanin-rich extract (BE) can modulate gut microbiota composition and counteract some of the features of HF-diet induced dysbiosis. In addition, we show that the modifications in gut microbial environment are partially linked with the anti-neuroinflammatory properties of BE. Through fecal metabolome analysis, we unravel the mechanism by which BE participates in the bilateral communication between the gut and the brain. BE alters host tryptophan metabolism, increasing the production of the neuroprotective metabolite kynurenic acid. These findings strongly suggest that dietary manipulation of the gut microbiota with anthocyanins can attenuate the neurologic complications of obesity, thus expanding the classification of psychobiotics to anthocyanins.

International Journal of Food Microbiology 130 (2009) 117–121

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

Impact of coffee consumption on the gut microbiota: A human volunteer study

Muriel Jaquet, Isabelle Rochat, Julie Moulin, Christophe Cavin, Rodrigo Bibiloni *

A B S T R A C T

The impact of a moderate consumption of an instant coffee on the general composition of the human intestinal bacterial population was assessed in this study. Sixteen (16) healthy adult volunteers consumed a daily dose of 3 cups of coffee during 3 weeks. Faecal samples were collected before and after the consumption of coffee, and the impact of the ingestion of the product on the intestinal bacteria as well as the quantification of specific bacterial groups was assessed using nucleic acid-based methods. Although faecal profiles of the dominant microbiota were not significantly affected after the consumption of the coffee (Dice's similarity index = 92%, $n = 16$), the population of *Bifidobacterium* spp. increased after the 3-week test period ($P = 0.02$). Moreover, in some subjects, there was a specific increase in the metabolic activity of *Bifidobacterium* spp. Our results show that the consumption of the coffee preparation resulting from water co-extraction of green and roasted coffee beans produce an increase in the metabolic activity and/or numbers of the *Bifidobacterium* spp. population, a bacterial group of reputed beneficial effects, without major impact on the dominant microbiota.

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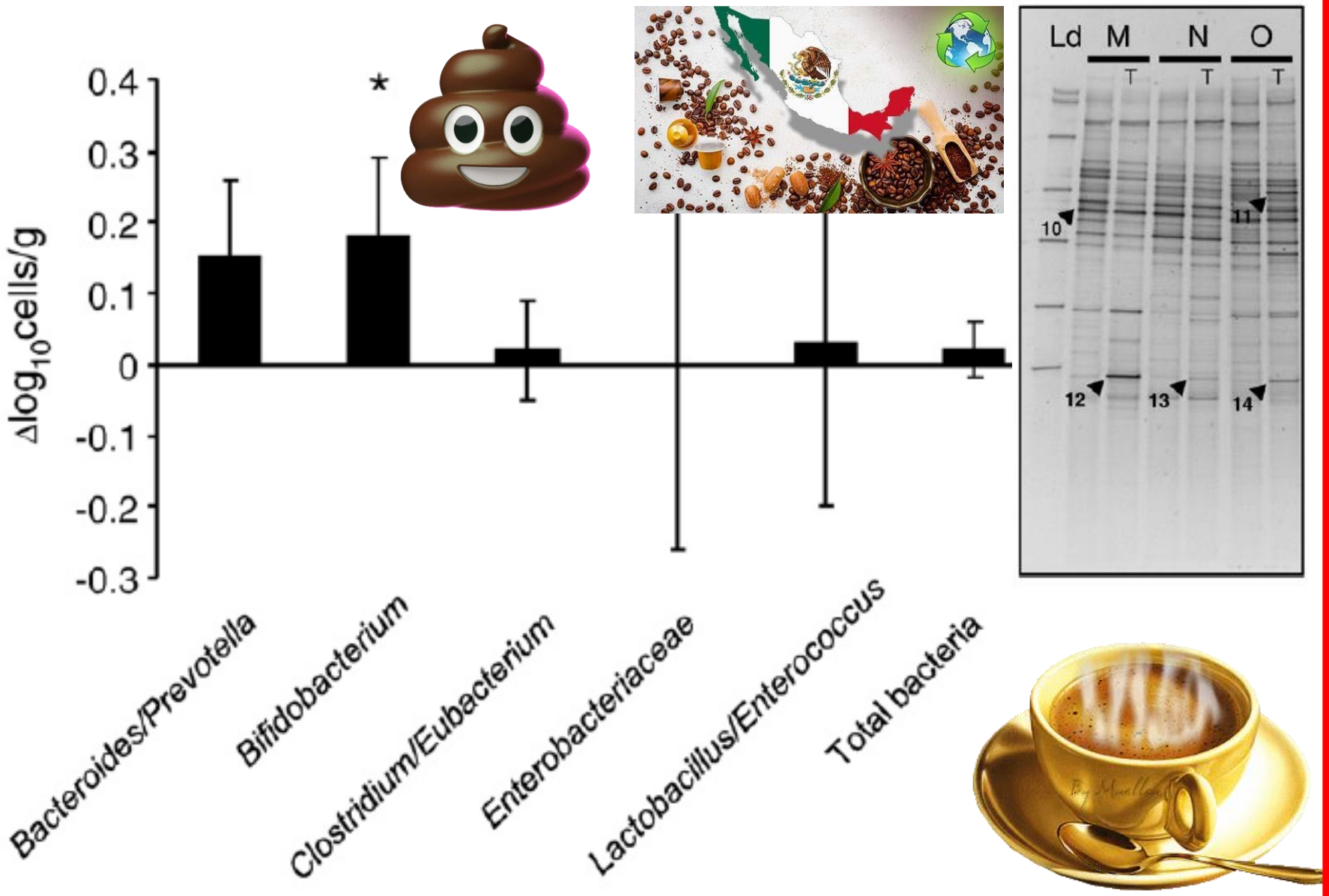


Fig. 2. Increments in bacterial numbers for selected groups after the consumption of coffee. Bacterial counts were determined using FISH technology (P=0.02).

A nuestra microbiota también le gusta el chocolate

El chocolate ocupa un lugar privilegiado entre los alimentos considerados como más tentadores. Este alimento de los dioses, como bien reza su nombre latino Theobroma cacao, atribuido por el ilustre nosólogo sueco Carl Linnaeus en 1753, ha pasado a ostentar

El **chocolate** ocupa un lugar privilegiado entre los alimentos considerados como más tentadores. Este alimento de los dioses, como bien reza su nombre latino *Theobroma cacao*, atribuido por el ilustre nosólogo sueco Carl Linnaeus en 1753, ha pasado a ostentar en muchos países del mundo la categoría de medicamento curativo, delicia culinaria, e incluso moneda de cambio en operaciones comerciales, manteniendo este estatus a lo largo de los siglos. **A ningún otro producto natural se le ha atribuido nunca esa facultad de aliviar males tan diversos como los dolores intestinales o menstruales, o las fiebres y enfermedades cardiovasculares, o incluso potenciar la fuerza de quienes pretendan triunfar militar o sexualmente**. Las crónicas acerca de los beneficios del chocolate para la salud se remontan a las prácticas médicas de los Aztecas y los Mayas, y desde entonces abundan las anécdotas sobre el efecto del chocolate en la salud.

frontiers in PHARMACOLOGY

GENERAL COMMENTARY
published: 07 February 2013
doi: 10.3389/fphar.2013.00011

Chocolate, gut microbiota, and human health

*Nabil Hayek**

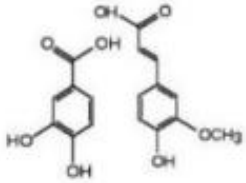
Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON, Canada

Clinical Study

Prebiotic Effect of Lycopene and Dark Chocolate on Gut Microbiome with Systemic Changes in Liver Metabolism, Skeletal Muscles and Skin in Moderately Obese Persons

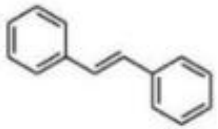
Maria Wiese,[1] Yuriy Bashmakov,[2] Natalia Chalyk,[3] Dennis Sandris Nielsen,[1] Łukasz Krych,[1] Witold Kot,[4] Victor Klochkov,[3] Dmitry Pristensky,[2] Tatyana Bandaletova,[5] Marina Chernyshova,[2] Nigel Kyle,[2] and Ivan Petyaev[2]

POLYPHENOLS



Phenolic acids

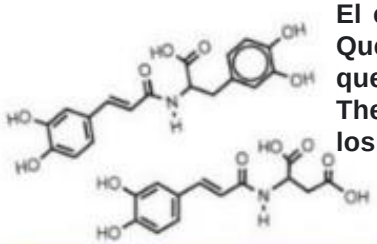
p-hydroxy benzoic, cinnamic, vanillic, caffeic, p-coumaric, Ferulic, chlorogenic acid



Stilbenoids

trans-resveratrol, trans-piceid

Flavonoids

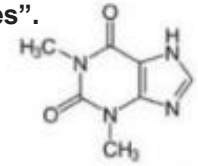


N-phenylpropenoyl-L-amino acids

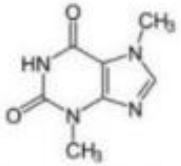
N-caffeoyl-L-tyrosine, N-caffeolyl-Laspartic acid, N-caffeoyl-L-dopa, N-coumaroyl-L-tyrosine

METHYLXANTHINES

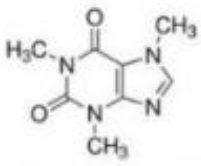
El chocolate tiene su origen en México, donde el dios Quetzalcoatl regaló el árbol de cacao a los hombres, que años después se bautizaría con el nombre científico Theobroma Cacao, que significa en griego "alimento de los dioses".



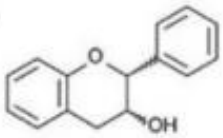
theophylline



theobromine

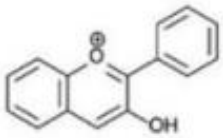


caffeine



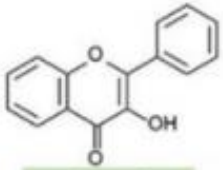
Flavan-3-ols

Epicatechin
Catechin
Gallocatechin
Epicatechin-3-gallate
Epigallocatechin gallate
Epicatechin gallate
Procyanidin B1
Procyanidin B2
Procyanidin B5
Procyanidin C1
Procyanidin D



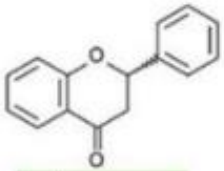
Anthocyanins

cyanidin
ideain
cyanidin 3-arabinoside



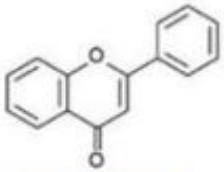
Flavonols

quercitin
rutin
isoquercitrin
hyperin
quercitrin



Flavanones

naringenin
prunin
hesperidin
eriodictyol



Flavones

luteolin
luteolin-7-O-glucoside
orientin
isoorientin
apigenin
vitexin
isovitexin

OTHER COMPONENTS

fat
protein
mono-and polysaccharides
Fiber (insoluble/soluble)

Nomenclature and chemical structures of cocoa phytocomplex.

Available online at www.sciencedirect.com

ScienceDirect

Journal of Nutritional Biochemistry 99 (2022) 108854

Journal of Nutritional Biochemistry

RESEARCH PAPER

Consumption of 85% cocoa dark chocolate improves mood in association with gut microbial changes in healthy adults: a randomized controlled trial

Ji-Hee Shin[a,b,1], Chong-Su Kim[a,1], Lina Cha[a,1], Sojeong Kim[a], Seokoh Lee[a], Suyeon Chae[a], Woo Young Chun[c,*], Dong-Mi Shin[a,d,*]

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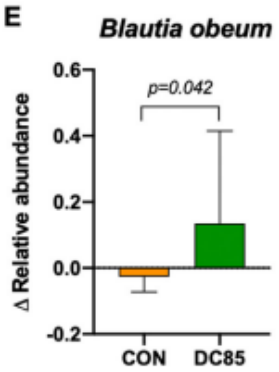

Abstract

Dark chocolate has long been recognized for its mood-altering properties; however, the evidence regarding the emotional effects of daily dark chocolate intake is limited. Therefore, we aimed to investigate the effects of dark chocolate intake on mood in everyday life, with special emphasis on the gut-brain axis. Two different dark chocolates (85% and 70% cocoa content) were tested in this study. In a randomized controlled trial, healthy adults (20–30 y) consumed either 30 g/d of 85% cocoa chocolate (DC85, n=18); 70% cocoa chocolate (DC70, n=16); or no chocolate (control group, CON; n=14); for 3 weeks. Mood states were measured using the Positive and Negative Affect Schedule (PANAS). Daily consumption of dark chocolate significantly reduced negative affect in DC85, but not in DC70. To assess the association between the mood-altering effects of dark chocolate and the gut microbiota, we performed fecal 16S rRNA sequencing analysis for the DC85 and CON groups. Gut microbial diversity was significantly higher in DC85 than CON (P<.05). *Blautia obeum* levels were significantly elevated and *Faecalibacterium prausnitzii* levels were reduced in DC85 compared to CON (P<.05). Furthermore, we found that the observed changes in negative affect scores were negatively correlated with diversity and relative abundance of *Blautia obeum* (P<.05). These findings indicate that dark chocolate exerts prebiotic effects, as evidenced by its ability to restructure the diversity and abundance of intestinal bacteria; thus, it may improve negative emotional states via the gut-brain axis.

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The Role of Nutrition and the Gut-Brain Axis in Psychiatry: A Review of the Literature

Review

Neuropsychobiology
DOI: 10.1159/000492834

Sabrina Mörkl[a] Jolana Wagner-Skacel[a] Theresa Lahousen[a] Sonja Lackner[b] Sandra Johanna Holasek[b] Susanne Astrid Bengesser[a] Annamaria Painold[a] Anna Katharina Holl[a] Eva Reininghaus[a]

[a]Department for Psychiatry and Psychotherapeutic Medicine, Medical University of Graz, Graz, Austria; [b]Unit of Immunology and Pathophysiology, Otto Loewi Research Center (for Vascular Biology, Immunology and Inflammation), Medical University of Graz, Graz, Austria

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Keywords
Nutrition · Psychiatry · Depression · Diet · Nutrients · Gut microbiome · Gut-brain axis · Mediterranean diet

Abstract

Introduction: Individuals suffering from psychiatric disorders experience high levels of illness burden and a significantly reduced quality of life. Despite targeted psychopharmacological strategies and complementary psychotherapeutic procedures only moderate effects are obtained, and the risk of relapse is high in many patients. Worldwide, psychiatric diseases such as depression are continuously increasing, challenging the personal life of the affected as well as their families, but also whole societies by increasing disability, early retirement and hospitalization. According to current scientific knowledge psychiatric disorders are caused by a multifactorial pathogenesis, including genetics, inflammation and neurotransmitter imbalance; furthermore, also lifestyle-associated factors gain rising importance. In line with this, there is growing evidence that the gut microbiota and nutrition have an impact on the onset and course of psychiatric disorders. ***Aim:*** This narrative review highlights the important role of nutrition in psychiatric care and underlines the significance of nutritional advice in the multifactorial, biopsychosocial treatment of patients. It focuses on current dietary interventions such as the Mediterranean diet, dietary supplements and modifications of the gut microbiota with pre-, pro- and postbiotics. ***Results:*** Recent studies support the connection between the quality of diet, gut microbiota and mental health through regulation of metabolic functions, anti-inflammatory and antiapoptotic properties and the support of neurogenesis. Dietary coaching to improve mental health seems to be an additional, cost-effective, practical, nonpharmacological intervention for individuals with psychiatric disorders. ***Conclusion:*** The use of nutritional interventions in psychiatry equips therapists with a promising tool for both the prevention and treatment of psychiatric disorders. Besides pharmacological therapy, psychotherapy and physical activity, nutritional interventions are an important pillar in the multifactorial, biopsychosocial treatment of psychiatric disease and could be used as a potential therapeutic target.

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The Microbiome and Epidemiology

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

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ABSTRACT

Purpose: The accruing data linking the gut microbiome to the development and function of the central nervous system has been proposed as a paradigm shift in neuroscience. The gut microbiota can communicate with the brain via neuroimmune, neuroendocrine, and neural pathways comprising the brain-gut-microbiota axis. Dysfunctional neuroimmune pathways are implicated in stress-related psychiatric disorders.

Methods: Using depression as our primary example, we review both the preclinical and clinical evidence supporting the possible role played by the gut microbiota in stress-related psychiatric disorders. We consider how this can inform future treatment strategies and outline the challenges and necessary studies for moving the field forward.

Results: The role played by the gut microbiota has not been fully elucidated in psychiatric populations. Although tempting to speculate that psychiatric patients may benefit from therapeutic modulation of the brain-gut-microbiota axis, the translational applications of the results obtained in rodent studies have yet to be demonstrated.

Conclusions: Evidence of altered gut microbiota composition and function in psychiatric patients is limited and cannot be regarded as proven. Moreover the efficacy of targeting the gut microbiota has not yet been established, and needs further investigation.

Clinical Nutrition Experimental 6 (2016) 25–38

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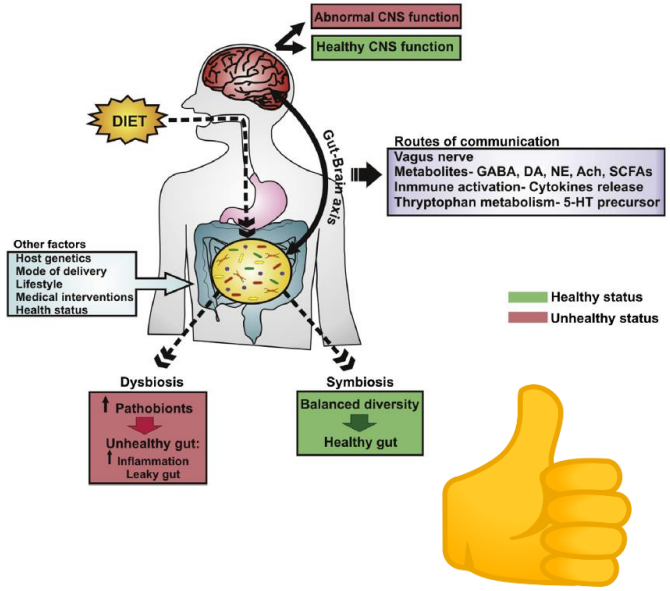
Clinical Nutrition Experimental

journal homepage: http://www.clinicalnutritionexperimental.com

Food for thought: The role of nutrition in the microbiota-gut–brain axis

Clara Seira Oriach [a, d, 1], Ruairi C. Robertson [b, c, d, 1], Catherine Stanton [c, d], John F. Cryan [d, e], Timothy G. Dinan [a, d, *]

Recent research has provided strong evidence for the role of the commensal gut microbiota in brain function and behaviour. Many potential pathways are involved in this bidirectional communication between the gut microbiota and the brain such as immune mechanisms, the vagus nerve and microbial neurometabolite production. Dysbiosis of gut microbial function has been associated with behavioural and neurophysical deficits, therefore research focused on developing novel therapeutic strategies to treat psychiatric disorders by targeting the gut microbiota is rapidly growing. Numerous factors can influence the gut microbiota composition such as health status, mode of birth delivery and genetics, but diet is considered among the most crucial factors impacting on the human gut microbiota from infancy to old age. Thus, dietary interventions may have the potential to modulate psychiatric symptoms associated with gut–brain axis dysfunction. Further clinical and *in vivo* studies are needed to better understand the mechanisms underlying the link between nutrition, gut microbiota and control of behaviour and mental health.



Probiotic interventions and behavioural outcomes.

Intervention	Species	Health status	Microbiota changes	Behavioural/neurochemical outcomes	References
Lactobacillus casei	Humans	Healthy	—	↑ mood (self reported) ↓ memory	[66]
Bifidobacteria longum	Mice	Healthy anxious strain (BALB/c)	—	↑ memory and cognitive performance (novel object recognition, barnes maze, fear conditioning)	[67]
VSL#3	Rats	Aged	↑ *Bacteroidetes*	↓ deficit in age-related LTP ↓ microglial activation ↑ BDNF and synapsin	[68]
Lactobacillus helveticus	Mice	Healthy or fed western-diet	Normalized the increase in *Proteobacteria* following "western diet" feeding	↑ memory (Barnes maze) ↓ anxiety-like behaviour (Barnes maze)	[59]
Bacteroides fragilis	Mice	MIA treated	Restored relative abundance of *lachnospiraceae* following MIA treatment	↓ anxiety-like behaviour (Open field) ↑ communication (ultrasonic vocalization) ↓ stereotyped behaviour (marble burying)	[69]
Lactobacillus casei	Humans	Chronic fatigue syndrome	↑ *Bifidobacteria* ↑ *Lactobacillus*	↓ anxiety	[70]
Lactobacillus helveticus and *Bifidobacterium longum*	Rats Humans	Healthy Healthy	— —	↓ anxiety (conditioned defensive burying) ↓ anxiety	[71]
Bifidobacteria infantis	Rats	Healthy	—	↓ proinflammatory immune response ↑ tryptophan	[72]
Lactobacillus rhamnosus and *Bifidobacterium animalis*	Humans	Schizophrenic	Microbiota data not reported however probiotic group significantly less likely to experience severe bowel difficulty	No observed differences	[73]
Bifidobacterium infantis	Rats	Healthy normosensitive (Sprague–Dawley) and healthy hypersensitive (Wistar–Kyoto)	—	↓ visceral pain (colorectal distension)	[74]
Lactobacillus rhamnosus	Mice	Healthy anxious strain (BALB/C)	—	↓ corticosterone, anxiety behaviour, depressive behaviour. Altered GABA receptor expression	[44]

Abbreviations: MIA, maternal immune activation; LTP, long-term potentiation; GABA, gamma-aminobutyric acid.

frontiers in Neuroscience

Interplay Between the Gut-Brain Axis, Obesity and Cognitive Function

REVIEW
published: 16 March 2018
doi: 10.3389/fnins.2018.00155

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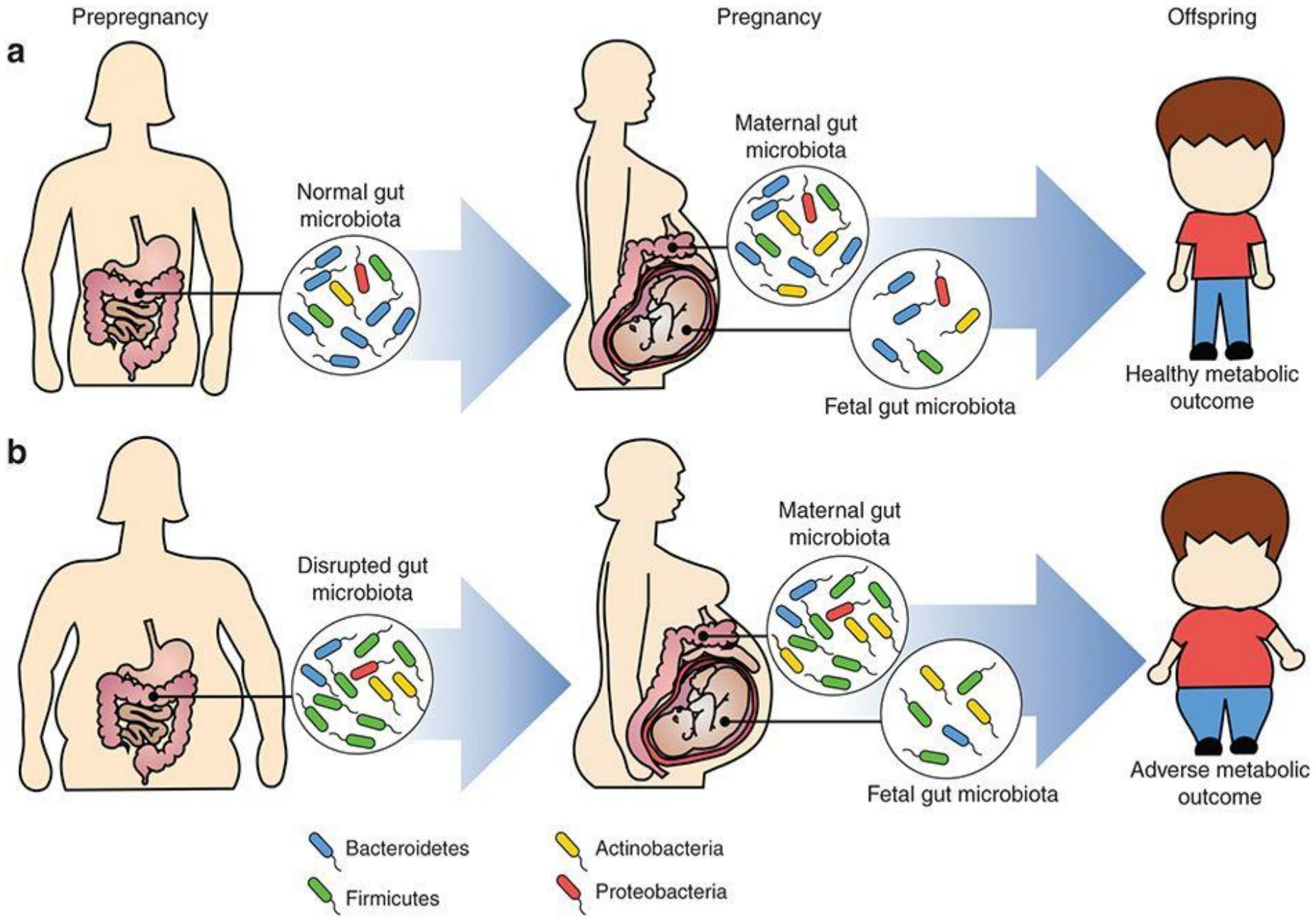
Obesity continues to be one of the major public health problems due to its high prevalence and co-morbidities. Common co-morbidities not only include cardiometabolic disorders but also mood and cognitive disorders. Obese subjects often show deficits in memory, learning and executive functions compared to normal weight subjects. Epidemiological studies also indicate that obesity is associated with a higher risk of developing depression and anxiety, and *vice versa*. These associations between pathologies that presumably have different etiologies suggest shared pathological mechanisms. Gut microbiota is a mediating factor between the environmental pressures (e.g., diet, lifestyle) and host physiology, and its alteration could partly explain the cross-link between those pathologies. Westernized dietary patterns are known to be a major cause of the obesity epidemic, which also promotes a dysbiotic drift in the gut microbiota; this, in turn, seems to contribute to obesity-related complications. Experimental studies in animal models and, to a lesser extent, in humans suggest that the obesity-associated microbiota may contribute to the endocrine, neurochemical and inflammatory alterations underlying obesity and its comorbidities. These include dysregulation of the HPA-axis with overproduction of glucocorticoids, alterations in levels of neuroactive metabolites (e.g., neurotransmitters, short-chain fatty acids) and activation of a pro-inflammatory milieu that can cause neuro-inflammation. This review updates current knowledge about the role and mode of action of the gut microbiota in the cross-link between energy metabolism, mood and cognitive function.

https://www.dailymotion.com/video/xiooc2?playlist=x4t2zs


Prepregnancy
Pregnancy
Offspring
a
Normal gut microbiota
Maternal gut microbiota
Fetal gut microbiota
Healthy metabolic outcome
b
Disrupted gut microbiota
Maternal gut microbiota
Fetal gut microbiota
Adverse metabolic outcome
Bacteroidetes
Firmicutes
Actinobacteria
Proteobacteria

REVIEW
published: 16 March 2018
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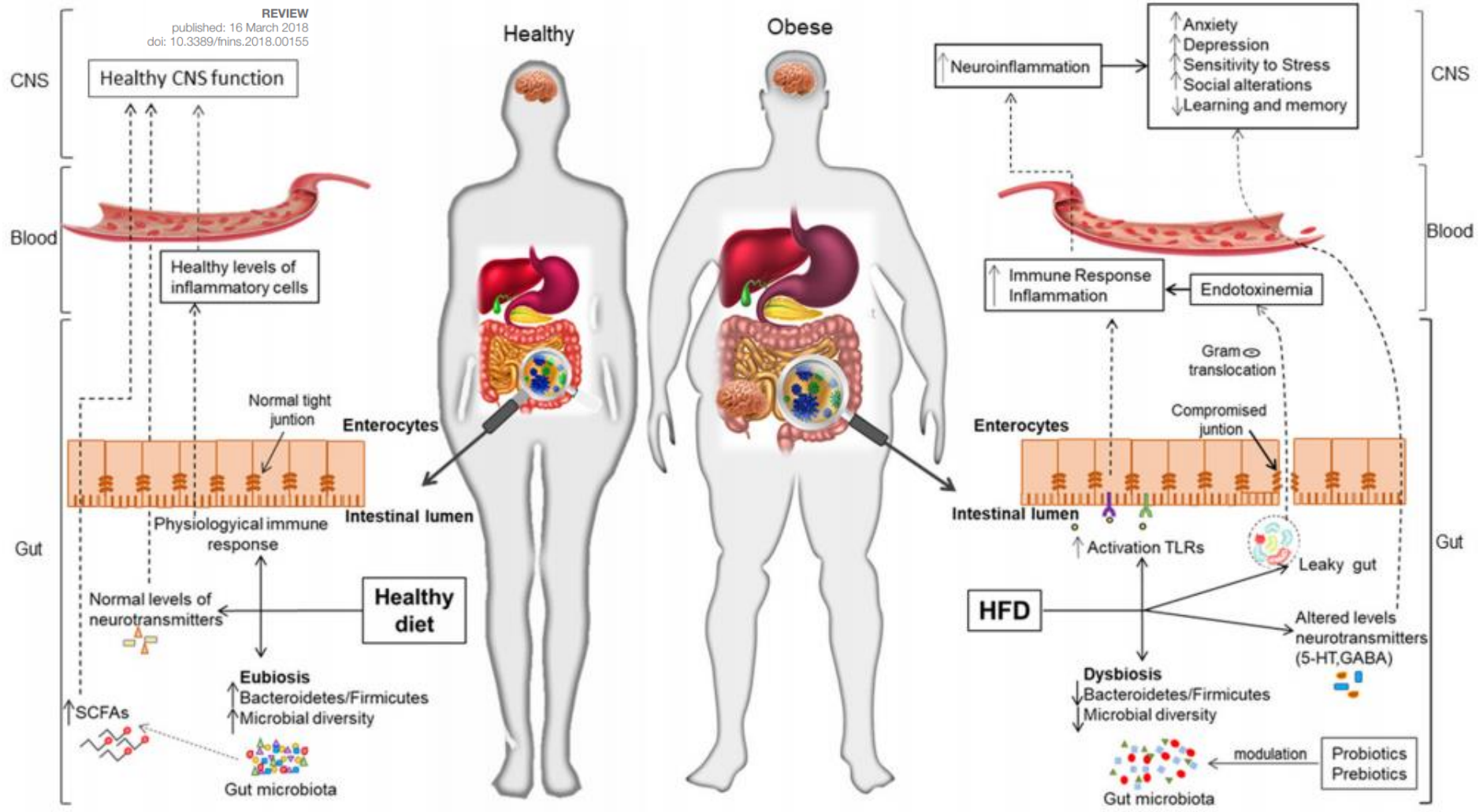

FIGURE 1 | Interplay between the microbiota and the gut-brain axis in obesity and associated mental disorders. Gut microbiota contributes to regulating the gut-brain axis and maintaining health, while its alteration (dysbiosis) due to lifestyle factors (unhealthy diets, stress) is related to obesity and its adverse consequences on mood and cognition. A healthy dietary pattern (e.g., rich in fibers, vegetables, etc.) is thought to increase gut microbiota diversity and, thereby, contribute to epithelial gut integrity, immune homeostasis and normal CNS function through the gut-brain axis. On the contrary, Western-dietary patterns (rich in simple sugars and saturated fat) seem to reduce microbial diversity, promote inflammation and contribute to the *leaky gut* syndrome; this facilitates the translocation of components of Gram-negative bacteria, which increases the peripheral inflammatory tone and produces neuroinflammation and alterations in the CNS. The use of dietary strategies (e.g., probiotics, healthier diets rich in fiber, prebiotics, etc.) could beneficially impact on obesity and mental complications, via restoration of a healthy microbiota and its regulatory role in the gut-brain axis.

REVIEW
published: 16 March 2018
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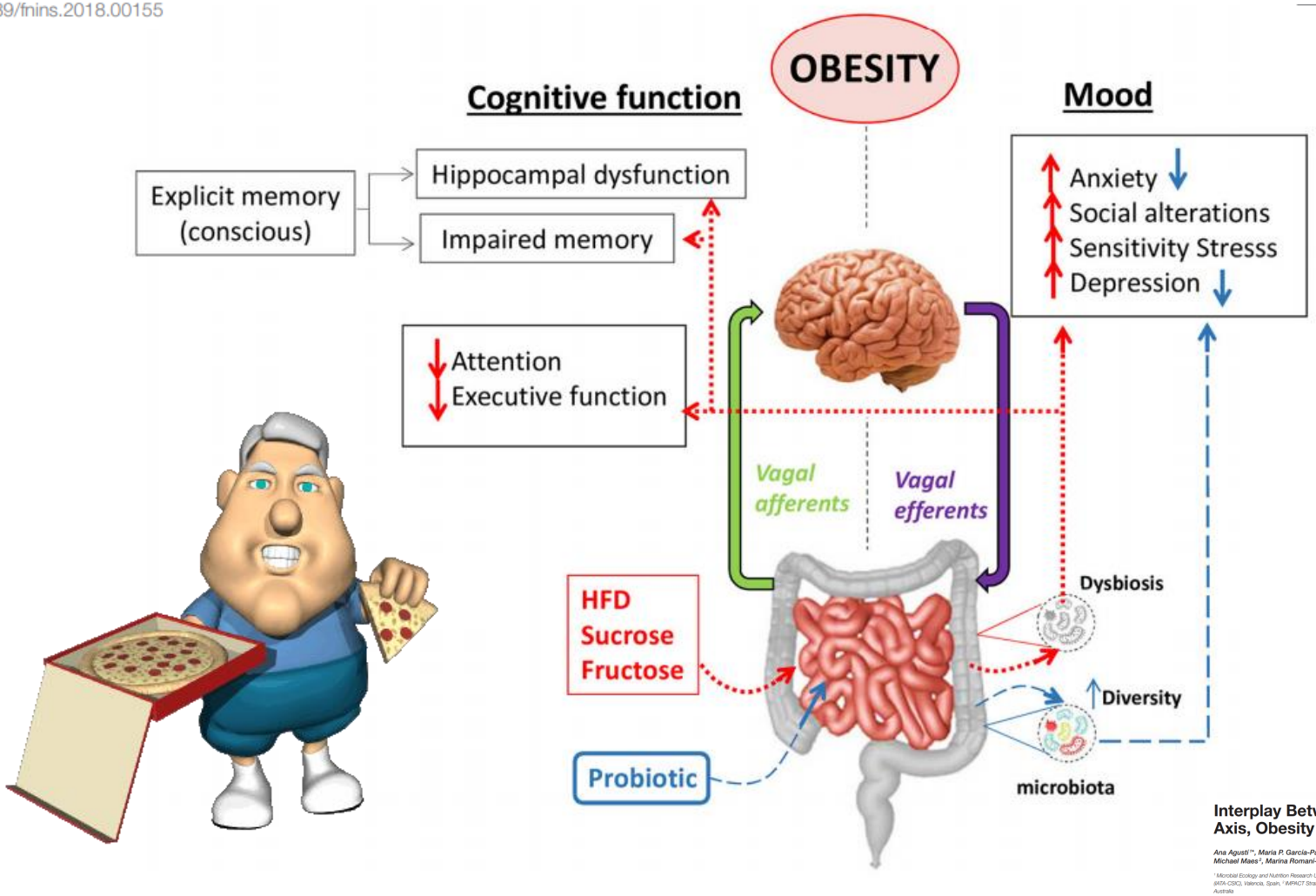


FIGURE 2 | Mood and cognitive alterations in obesity: the role of the gut-brain axis. The diversity and stability of the gut microbiota can be affected by high-fat diets (HFD) or high carb diets leading to dysbiosis, which is a typical alteration observed in obesity. A dysbiotic microbiota is thought to alter the communication between the gut and the brain axis contributing to mood alterations like anxiety, depression, sensitivity to stress, social behavioral alterations and cognitive alterations like hippocampal dysfunction, impaired memory and reduction of attention or the executive function. The use of some probiotics has demonstrated to ameliorate some of the mood alterations like anxiety or depression through different mechanisms in animal models.

Nutrition, the gut microbiome and the metabolic syndrome.
Petia Kovatcheva-Datchary, Tulika Arora · Published in Best practice & research. Clinical... 2013 · DOI: 10.1016/j.bpg.2013.03.017

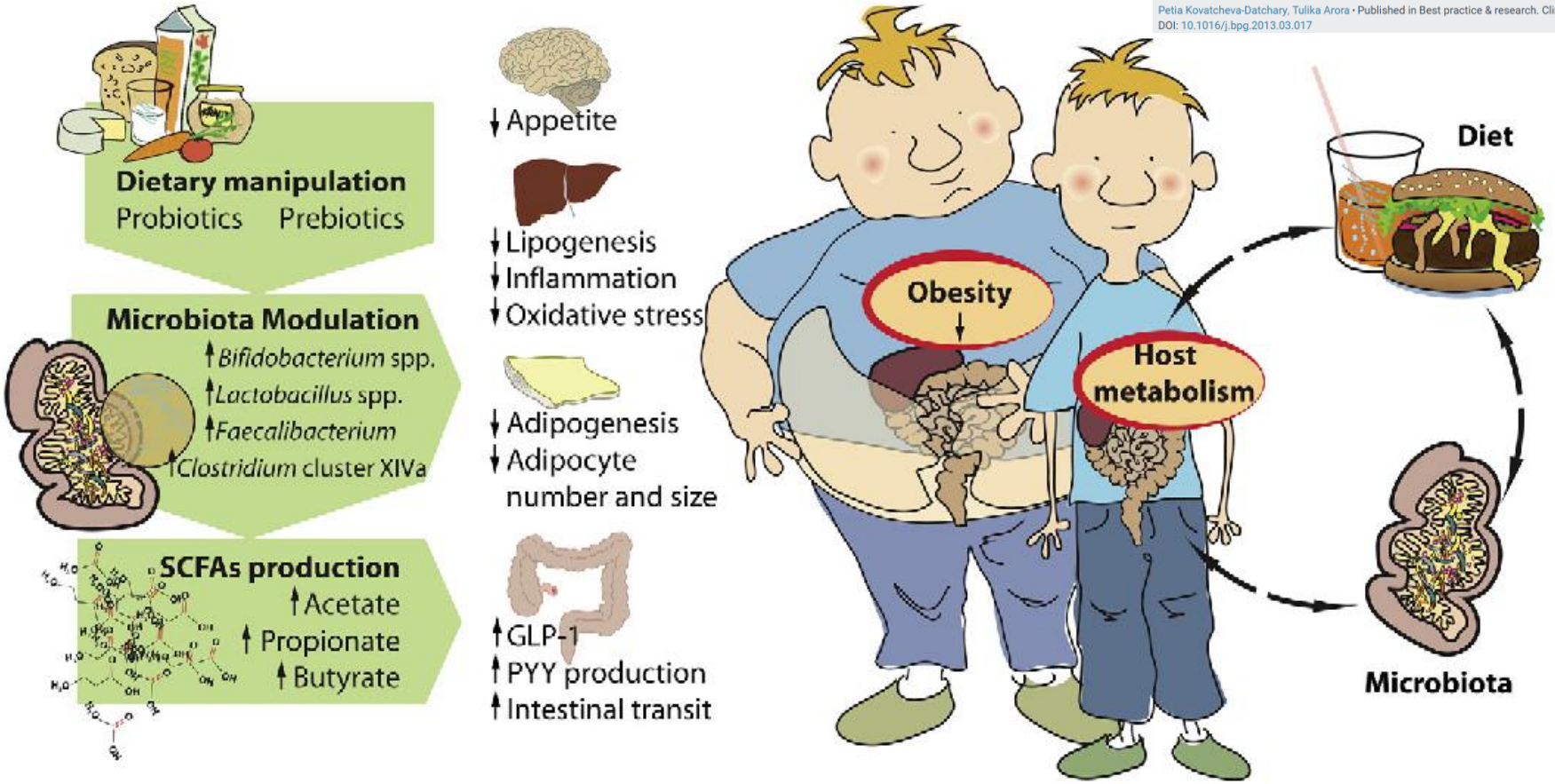
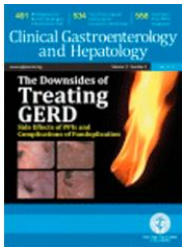


Fig. 1. Interaction between diet and gut microbiota affects host metabolism. Dietary manipulation with probiotics and prebiotics alters the composition and metabolic capacity of gut microbiota. Dietary manipulation in obesity with prebiotics and probiotics changes gut microbiota by favouring bacteria beneficial to the host and enhances the production of short chain fatty acids (SCFAs) – acetate, propionate and butyrate. These result in decreased lipogenesis, reduced inflammation and oxidative stress in liver; decreased adipogenesis, and reduced adipocyte size and number in adipose tissue; increased production of gut hormones and intestinal transit in the large intestine; reduced appetite in the brain. GLP-1: Glucagon like peptide-1, PYY: Peptide YY.

Title: The Gut-Brain Axis and the Microbiome: Mechanisms and Clinical Implications

To appear in: *Clinical Gastroenterology and Hepatology*
Accepted Date: 1 October 2018



Vadim Osadchiy[1], Clair R. Martin[1], Emeran A. Mayer[1]

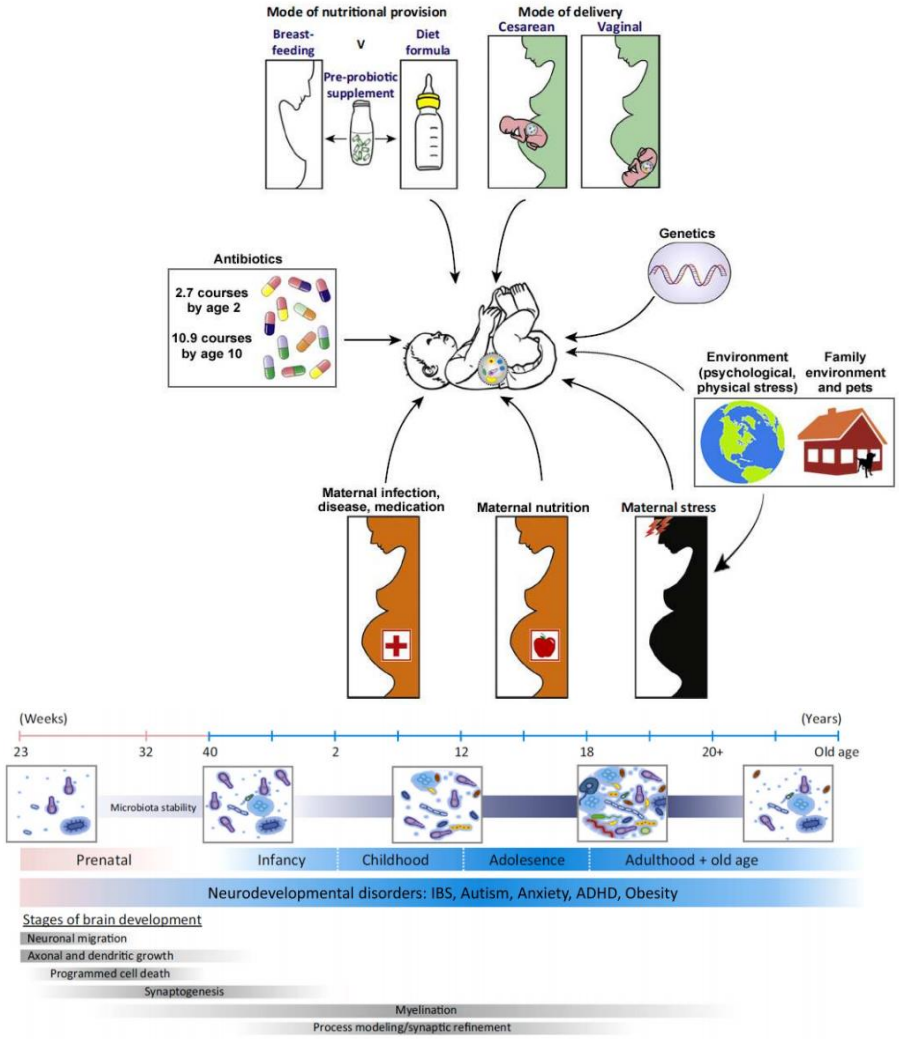
1 G. Oppenheimer Center for Neurobiology of Stress and Resilience, Vatche and Tamar Manoukian Division of Digestive Diseases, UCLA, Los Angeles, CA

Background and Aims: Based largely on results from preclinical studies, the concept of a brain gut microbiome axis has been established, mediating bidirectional communication between the gut, its microbiome and the nervous system. Limited data obtained in humans suggests that alterations in these interactions may play a role in several brain gut disorders.

Methods: We reviewed the preclinical and clinical literature related to the topic of brain gut microbiome interactions.

Results: Well characterized bidirectional communication channels, involving neural, endocrine and inflammatory mechanisms exist between the gut and the brain. Communication through these channels may be modulated by variations in the permeability of the intestinal wall and the blood brain barrier. Brain gut microbiome interactions are programmed during the first 3 years of life, including the prenatal period, but can be modulated by diet, medications and stress throughout life. Based on correlational studies, alterations in these interactions have been implicated in the regulation of food intake, obesity and in irritable bowel syndrome, even though causality remains to be established.

Conclusions: Targets within the brain gut microbiome axis have the potential to become targets for novel drug development for brain gut disorders.



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microorganisms

MDPI

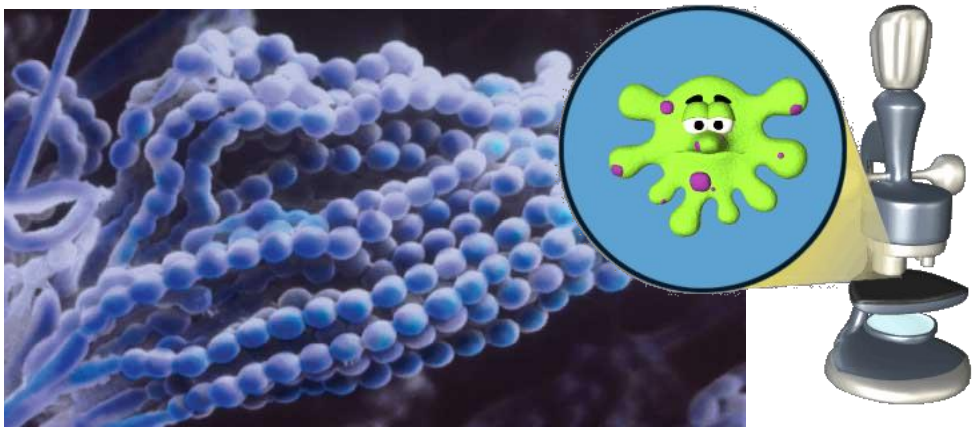
Microorganisms **2018**, *6*, 22; doi:10.3390/microorganisms6010022

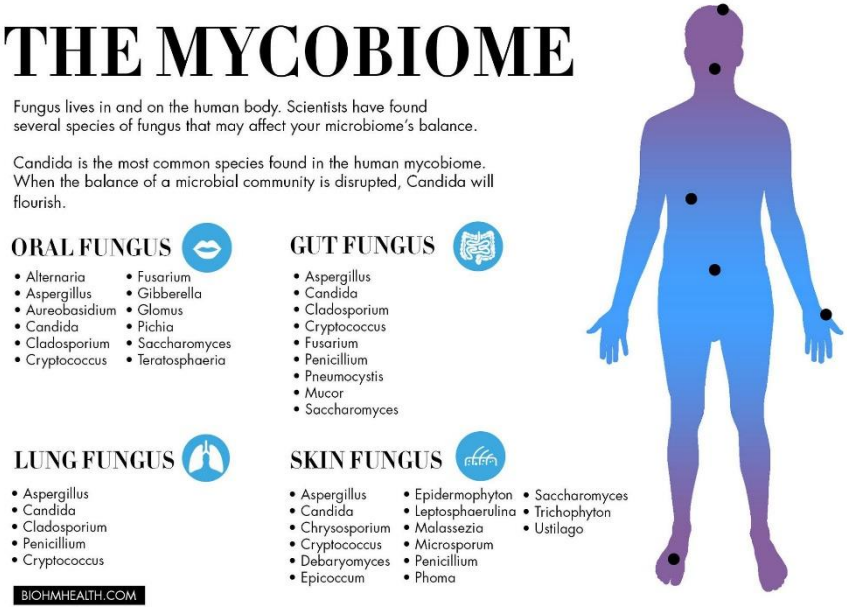
Review

The Mycobiome: A Neglected Component in the Microbiota-Gut-Brain Axis

Raphaël Enaud [1,2,3,*], Louise-Eva Vandenborght [1,3,4], Noémie Coron [1,2,3], Thomas Bazin [1,2], Renaud Prevel [1], Thierry Schaeverbeke [1,2], Patrick Berger [1,2,3], Michael Fayon [1,2,3], Thierry Lamireau [1,2] and Laurence Delhaes [1,2,3]

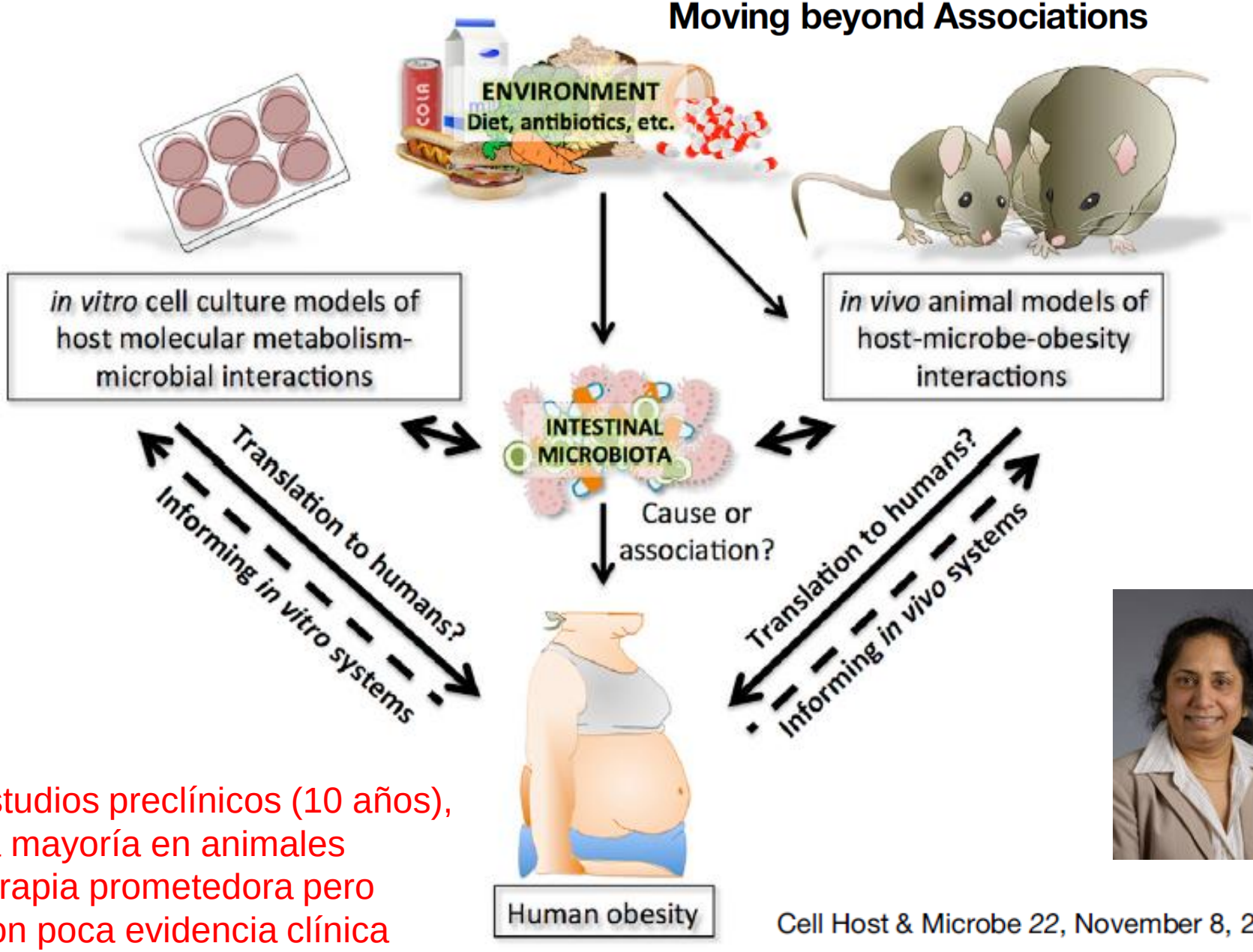
[1] Centre de Recherche Cardio-Thoracique de Bordeaux, U1045, FHU ACRONIM, University Bordeaux, 33000 Bordeaux, France; louise-eva.vandenborght@genoscreen.fr (L.-E.V.);





Abstract: In recent years, the gut microbiota has been considered as a full-fledged actor of the gut–brain axis, making it possible to take a new step in understanding the pathophysiology of both neurological and psychiatric diseases. However, most of the studies have been devoted to gut bacterial microbiota, forgetting the non-negligible fungal flora. In this review, we expose how the role of the fungal component in the microbiota-gut-brain axis is legitimate, through its interactions with both the host, especially with the immune system, and the gut bacteria. We also discuss published data that already attest to a role of the mycobiome in the microbiota-gut-brain axis, and the impact of fungi on clinical and therapeutic research.

The Human Microbiome and Obesity: Moving beyond Associations



Estudios preclínicos (10 años),
La mayoría en animales
Terapia prometedora pero
Con poca evidencia clínica

Cell Host & Microbe 22, November 8, 2017

Padma Maruvada,[1] Vanessa Leone,[2] Lee M. Kaplan,[3] and Eugene B. Chang[2,*]

1521-0081/73/4/198–232$35.00
PHARMACOLOGICAL REVIEWS
https://doi.org/10.1124/pharmrev.120.000063
Pharmacol Rev 73:198–232, October 2021
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Pharmacological Modulation of Immune Responses by Nutritional Components

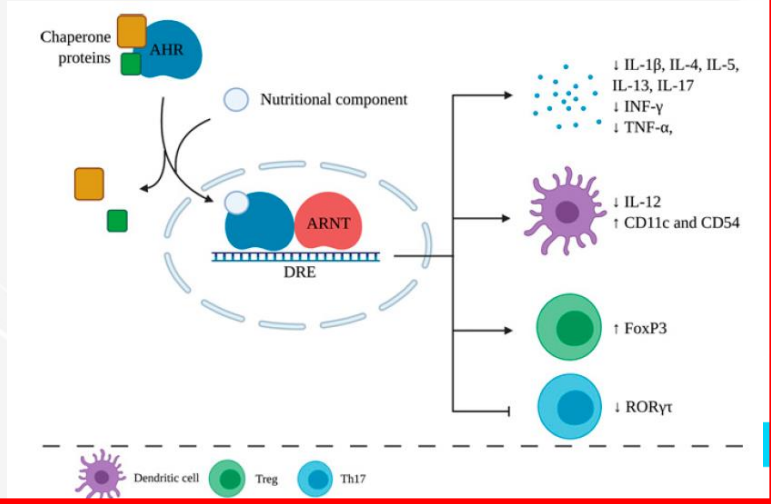
Marthe T. van Daal, Gert Folkerts, Johan Garssen, and Saskia Braber

Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, 3584 CG, Utrecht, The Netherlands (M.T.v.D., G.F., J.G., S.B.); and Danone Nutricia Research, 3584 CT, Utrecht, The Netherlands (J.G.)

Hipócrates, "deja que la comida sea tu medicina, y que la medicina sea tu comida", a pesar de datar del año 400 aC, los **investigadores hicieron una lista de quince tipos de receptores celulares y de los nutrientes capaces de unirse a ellos**, lo que permitió crear una amplia descripción de decenas de nutrientes capaces de unirse a estos receptores y modular respuestas inmunes, para bien o para mal. Así, se sabe que algunos nutrientes producirían efectos **proinflamatorios, mientras que otros tendrían efectos antiinflamatorios de forma natural**.

El 'paracetamol' que se come: estos son los alimentos que funcionan como medicamentos

Una enorme cantidad de nutrientes tendrían los mismos efectos que algunos compuestos farmacológicos actuales según un nuevo estudio.



LA DIETA MEDITERRANEA


Mi desayuno pre y
probiótico desde 2010
NATURAL
KEFIR
consum
Zumo DE
Granada
SIN AZÚCAR AÑADIDO
Kombucha
ORGANIC KOMBUCHA
Berryvida
FRUTOS ROJOS

ALCOHOL RESEARCH: *Current Reviews*

Alcohol and Gut-Derived Inflammation

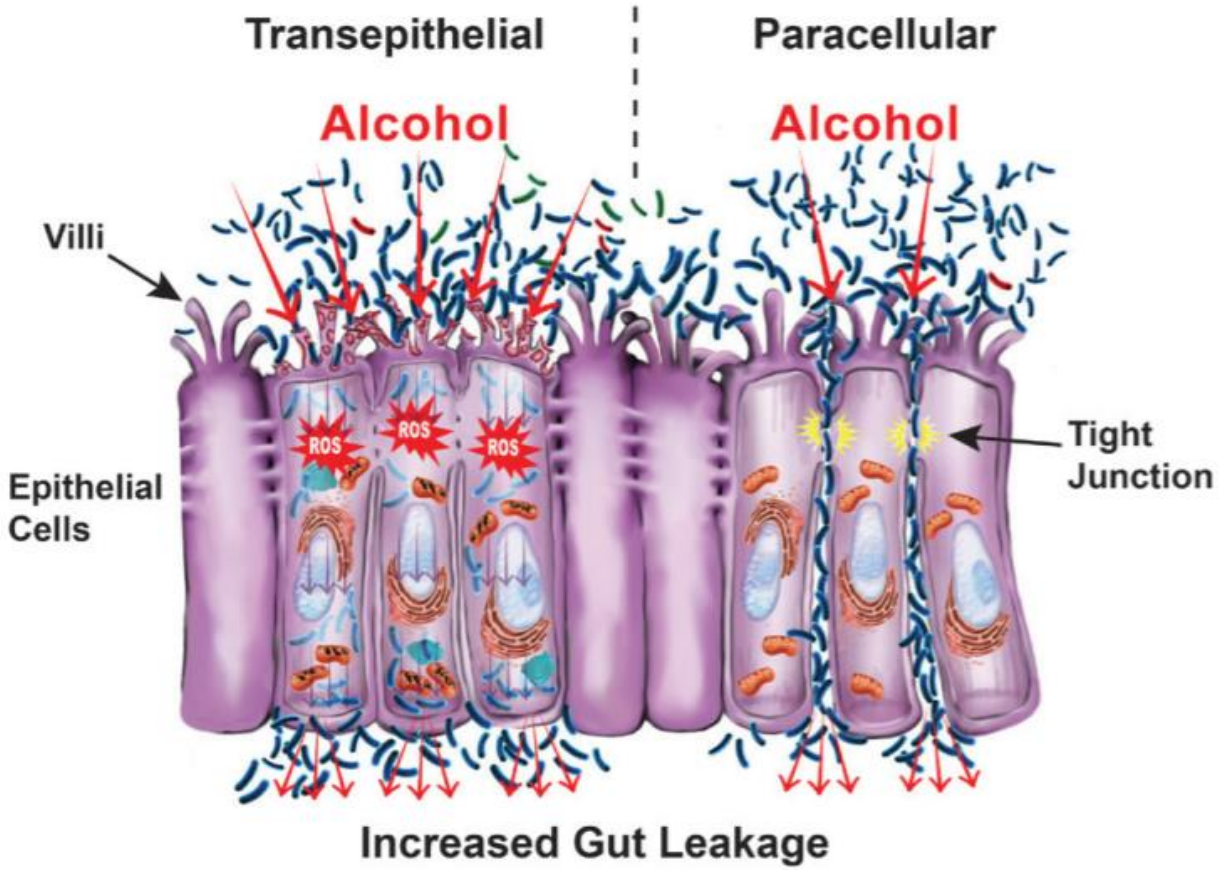
Faraz Bishehsari, M.D., Ph.D.; Emmeline Magno, M.D.; Garth Swanson, M.D.; Vishal Desai, M.D.; Robin M. Voigt, Ph.D.; Christopher B. Forsyth, Ph.D.; and Ali Keshavarzian, M.D.

Faraz Bishehsari, M.D., Ph.D., is an Assistant Professor; Garth Swanson, M.D., is an Assistant Professor; Vishal Desai, M.D., is a Physician; Robin M. Voigt, Ph.D., is an Assistant Professor; Christopher B. Forsyth, Ph.D., is an Associate Professor; and Ali Keshavarzian, M.D., is a Professor, all in the Department of Internal Medicine, Division of Gastroenterology, Rush University Medical Center, Chicago, Illinois.

Emmeline Magno, M.D., is an Internist in the Department of Internal Medicine, Rush University

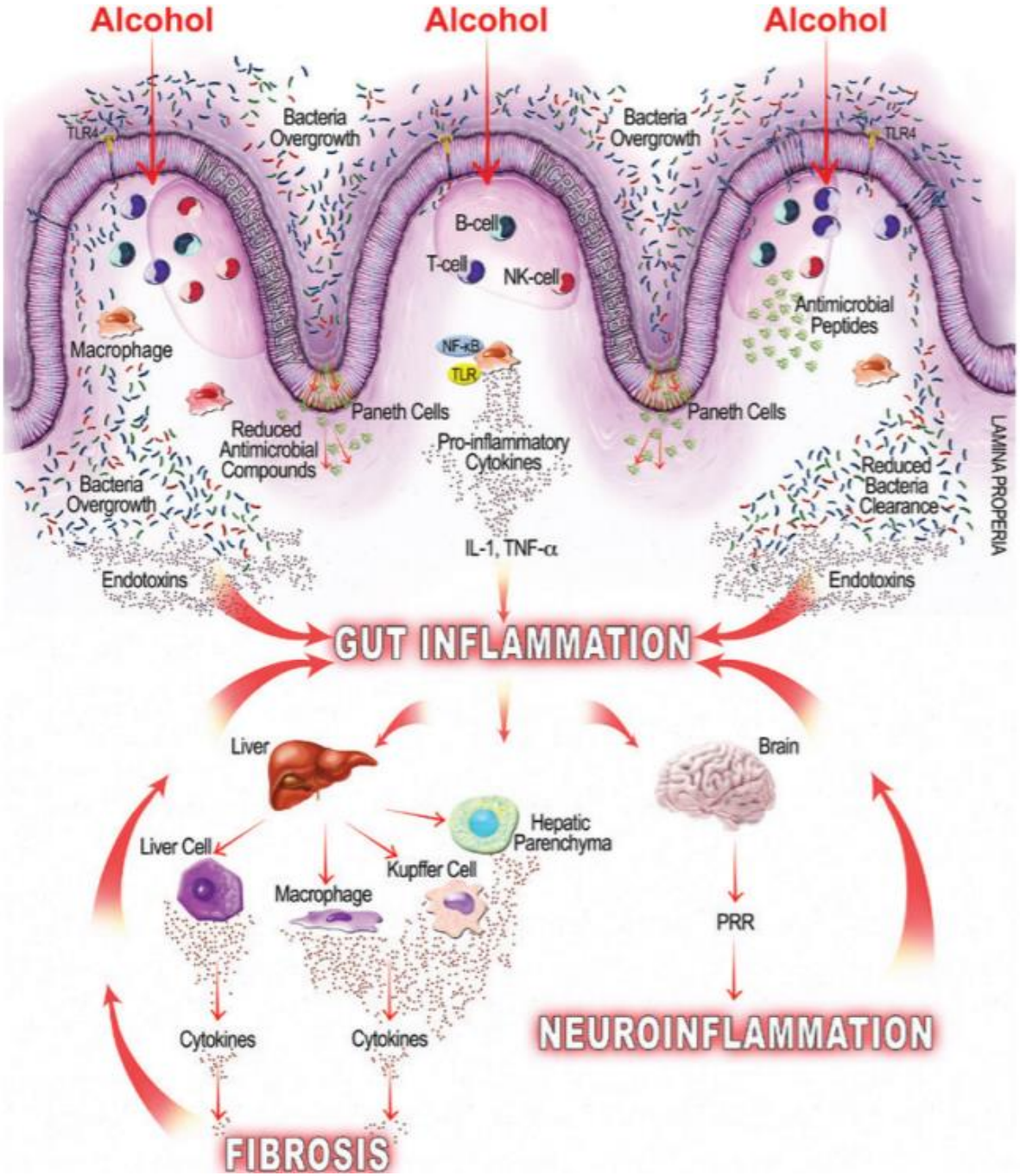
In large amounts, alcohol and its metabolites can overwhelm the gastrointestinal tract (GI) and liver and lead to damage both within the GI and in other organs. Specifically, alcohol and its metabolites promote intestinal inflammation through multiple pathways. That inflammatory response, in turn, exacerbates alcohol-induced organ damage, creating a vicious cycle and leading to additional deleterious effects of alcohol both locally and systemically. This review summarizes the mechanisms by which chronic alcohol intake leads to intestinal inflammation, including altering intestinal microbiota composition and function, increasing the permeability of the intestinal lining, and affecting the intestinal immune homeostasis. Understanding the mechanisms of alcohol-induced intestinal inflammation can aid in the discovery of therapeutic approaches to mitigate alcohol-induced organ dysfunctions.

Key words: Alcohol consumption; alcohol use, abuse, and dependence; chronic alcohol use; organ damage; gastrointestinal (GI) tract; liver; metabolites; gut-derived inflammation; intestinal inflammation; intestinal microbiota



La barrera intestinal regula el paso de materiales entre el interior del intestino y las células y los vasos sanguíneos en el otro lado de la capa de células epiteliales que recubre el interior del intestino. El alcohol interrumpe la barrera intestinal, aumentando su permeabilidad, de dos maneras: a través de mecanismos **transepiteliales** (células a la izquierda), que permiten que el material pasen directamente a través de las células epiteliales y los mecanismos **paracelulares** que permiten que el material pase a través de las uniones entre las células epiteliales.

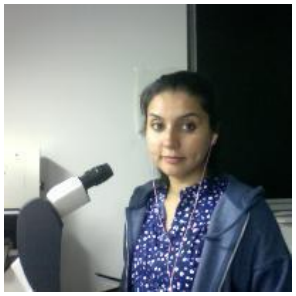
El alcohol y sus metabolitos desencadenan mecanismos transepiteliales al dañar las células directamente y debilitar las membranas celulares a través de varios mecanismos, incluido el estrés oxidativo causado por especies reactivas de oxígeno (ROS). Los metabolitos del alcohol desencadenan mecanismos paracelulares al alterar las proteínas que crean las uniones estrechas que unen las células y las proteínas que estabilizan los citoesqueletos de las células. El aumento de la permeabilidad de la barrera intestinal permite que las bacterias y las toxinas abandonen el intestino y se infiltren en otros órganos a través del torrente sanguíneo.



El alcohol puede inducir inflamación intestinal través de una cascada de mecanismos que posteriormente conducen a la inflamación, en particular en el hígado y el cerebro, permitiendo que las bacterias se filtren y liberen endotoxinas. El alcohol también produce una inmunosupresión de la mucosa colónica, suprimiendo uno de las principales líneas de defensa del intestino contra bacterias (células de Paneth) que secretan compuestos antibacterianos. Las células de Paneth suprimidas secretan menos compuestos antibacterianos, que puede permitir el crecimiento excesivo de bacterias intestinales adicionales y permitir la entrada de endotoxinas a través de la barrera intestinal, causando una liberación de citocinas proinflamatorias. Las endotoxinas y las citocinas pueden ingresar al hígado, interactuando directamente con hepatocitos y con las células inmunes del hígado, lo que provoca la liberación local de citocinas que conduce a la fibrosis y causa adicional inflamación. La inflamación intestinal también puede propagar endotoxinas.

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

KIRAN V. SANDHU, EOIN SHERWIN, HARRIËT SCHELLEKENS, CATHERINE STANTON, TIMOTHY G. DINAN, and JOHN F. CRYAN



Translational Research
January 2017

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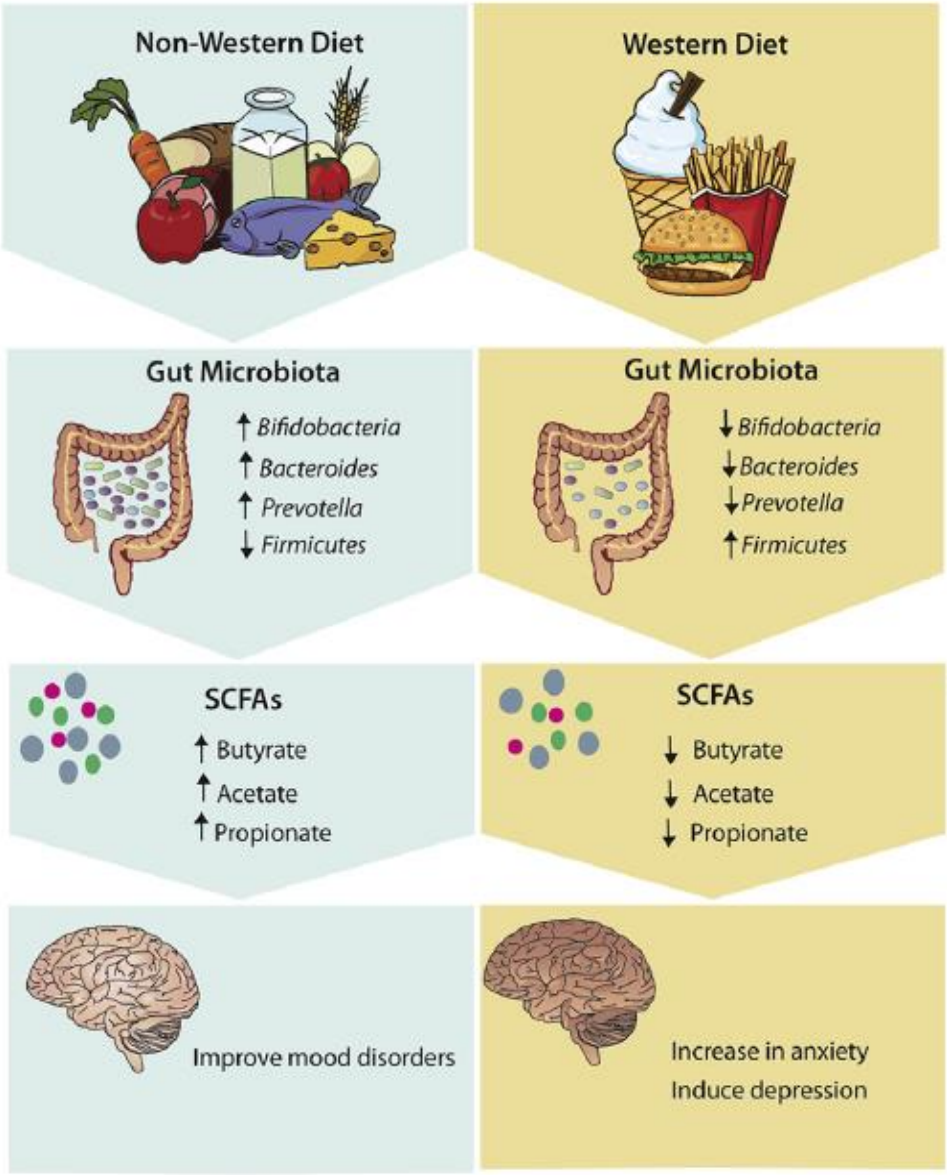
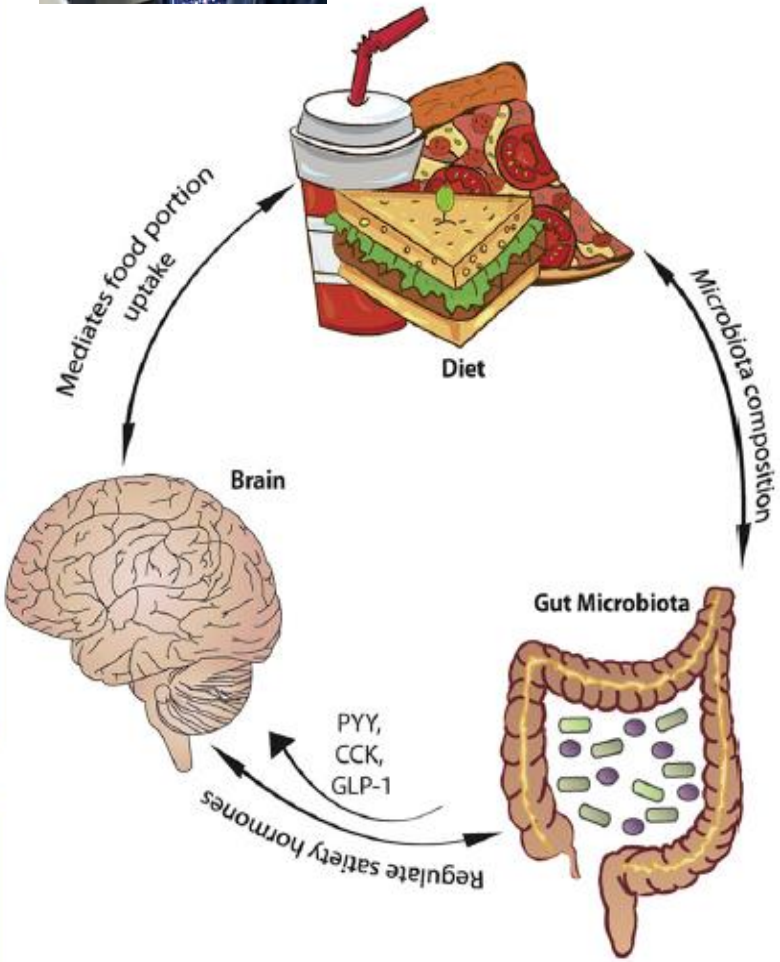




Review

Clinical Nutrition

Feeding melancholic microbes: MyNewGut recommendations on diet and mood

Timothy G. Dinan [a, b, *], Catherine Stanton [a, c], Caitriona Long-Smith [a], Paul Kennedy [a], John F. Cryan [a, f], Caitlin S.M. Cowan [a], María Carmen Cenit [d], Jan-Willem van der Kamp [e], Yolanda Sanz [d]

Accepted 12 November 2018

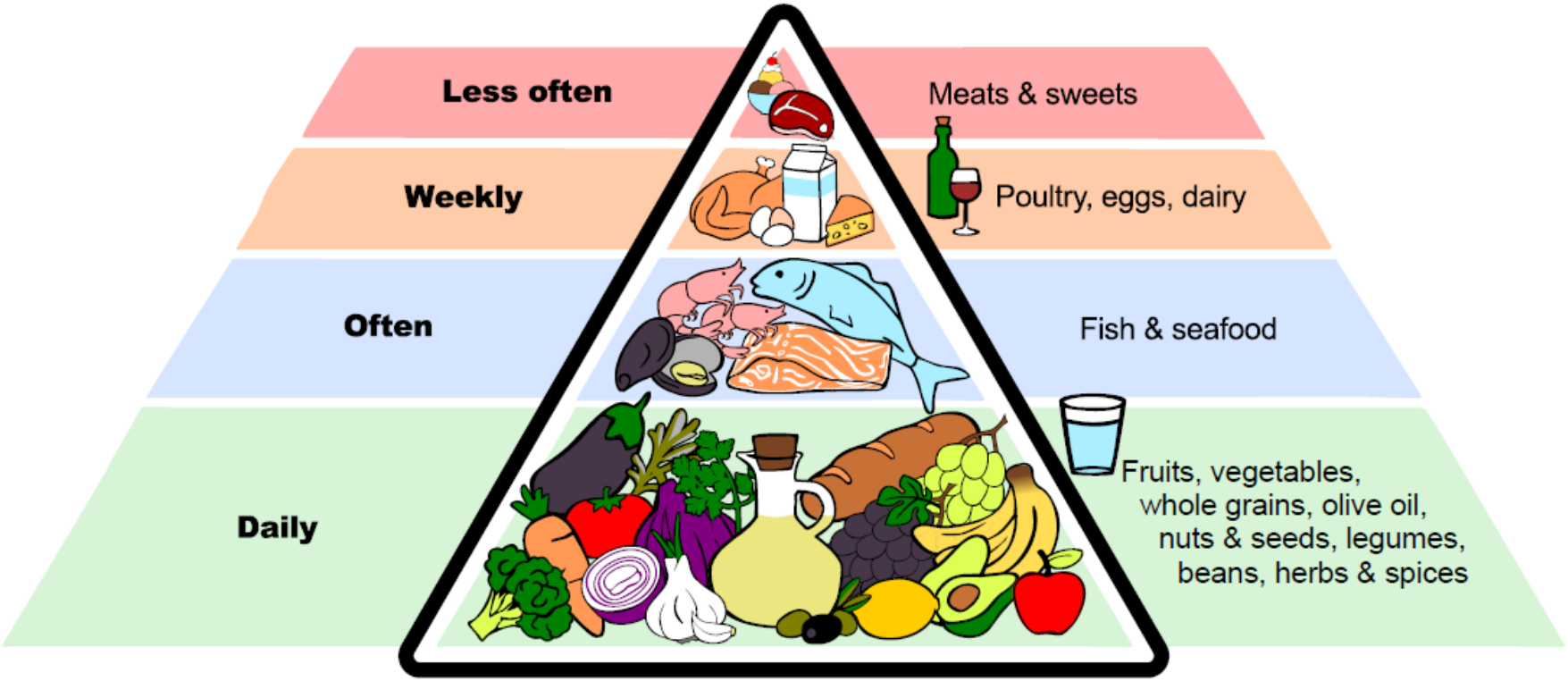


Fig. 2. Illustrates a food pyramid optimal for mental health.

THE MICROBIOME DIET

FOODS TO EAT

Fresh vegetables
beets, carrots, cruciferous veggies, leafy greens, onions, peas, salad greens, sea vegetables, squash

Whole pieces of fruit
apples, blackberries, blueberries, cherries, nectarines, oranges, pears, pink grapefruit, plums, pomegranates, red grapefruit, strawberries

Herbs, spices and teas
turmeric, ginger, basil, oregano, thyme, green tea, organic coffee

Probiotic foods
yogurt, kefir, kombucha, kvass, cultured veggies

Wild-caught fish, cage-free eggs and grass-fed/pasture-raised meat

Healthy fats
grass-fed butter, coconut oil, extra virgin olive oil, nuts/seeds

Ancient grains and legumes/beans
Ansazi beans, adzuki beans, black beans, black-eyed peas, chickpeas, lentils, black rise, amaraneth, buckwheat, quinoa

Red wine and dark chocolate/cocoa
(in moderation)

FOODS TO AVOID

Refined vegetable oils
canola, corn, soybean

Refined carbohydrates and processed grain products

Pasteurized dairy products

Conventional meat, poultry and eggs

Added sugars
packaged snacks, breads, condiments, canned items, cereals

Trans fats/ hydrogenated fats
packaged/processed products, fried foods

ALIMENTOS FERMENTADOS

Yogur

Kéfir

Tempeh

Natto

Miso

Tamari y shoyu

Kimchi

Chucrut

Pickles

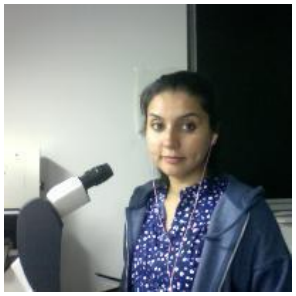
Umeboshi

Amasake

Kombucha

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

KIRAN V. SANDHU, EOIN SHERWIN, HARRIËT SCHELLEKENS, CATHERINE STANTON, TIMOTHY G. DINAN, and JOHN F. CRYAN



Translational Research
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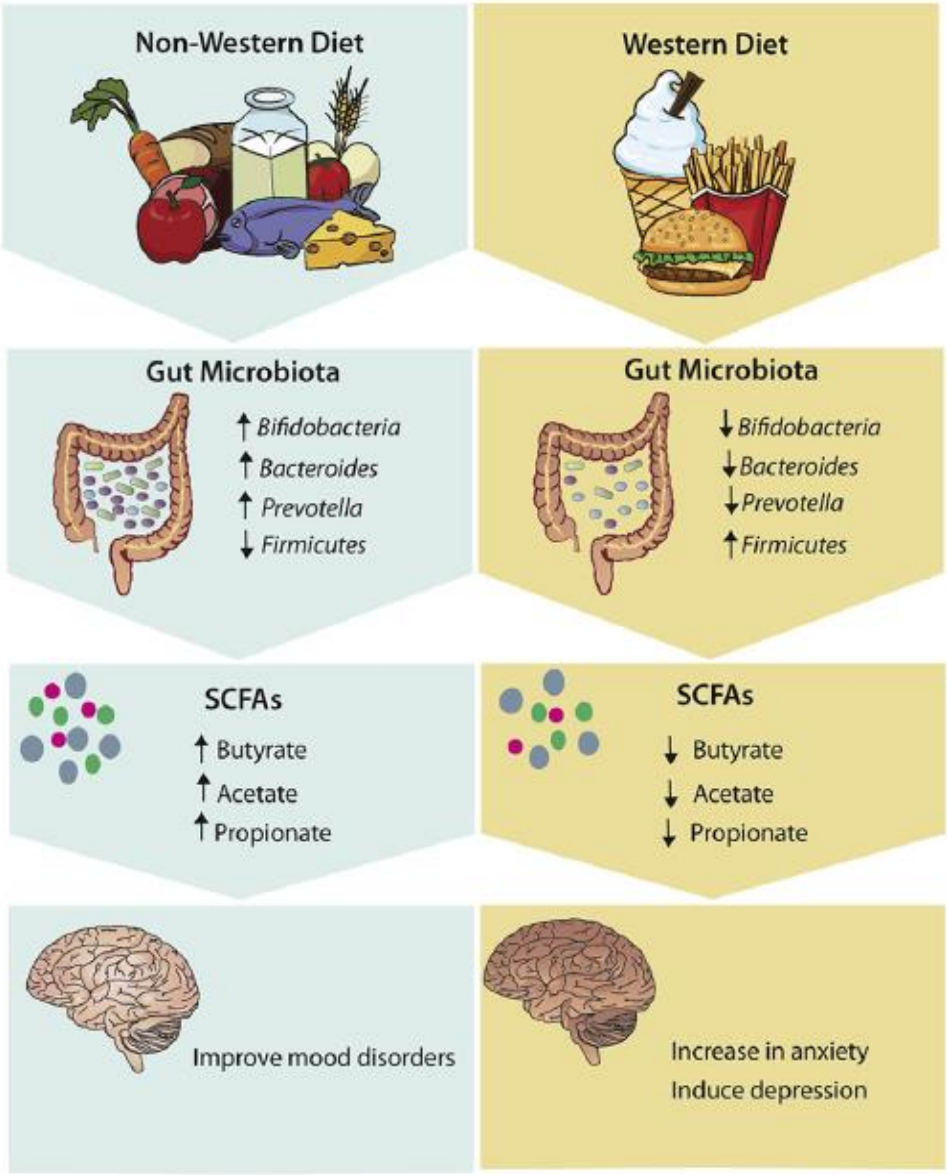
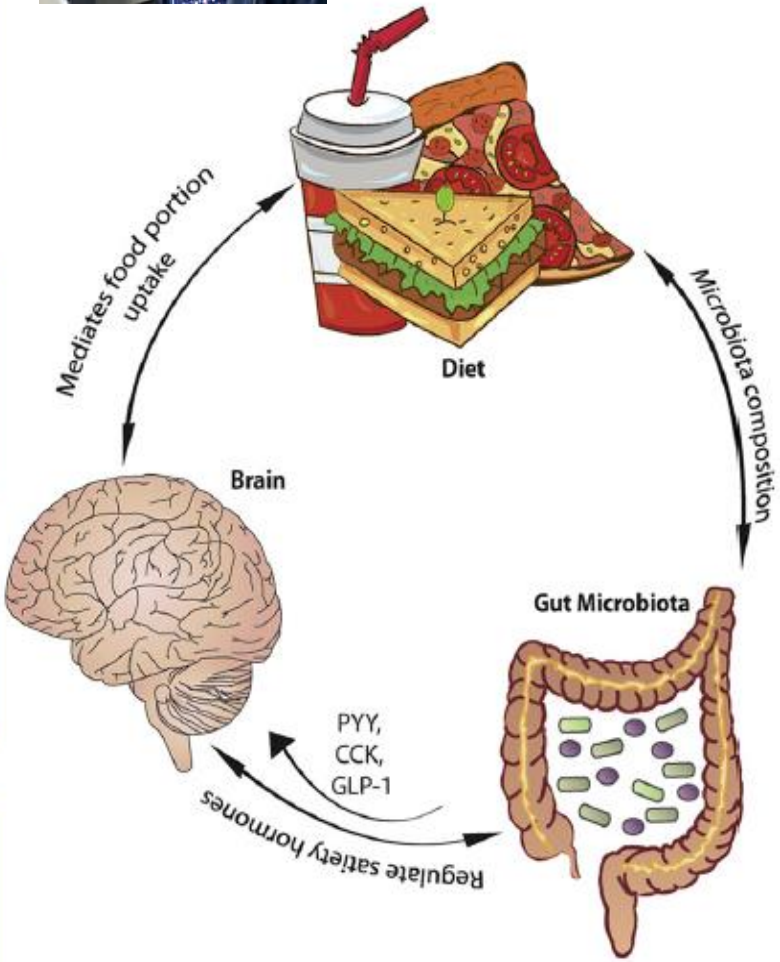
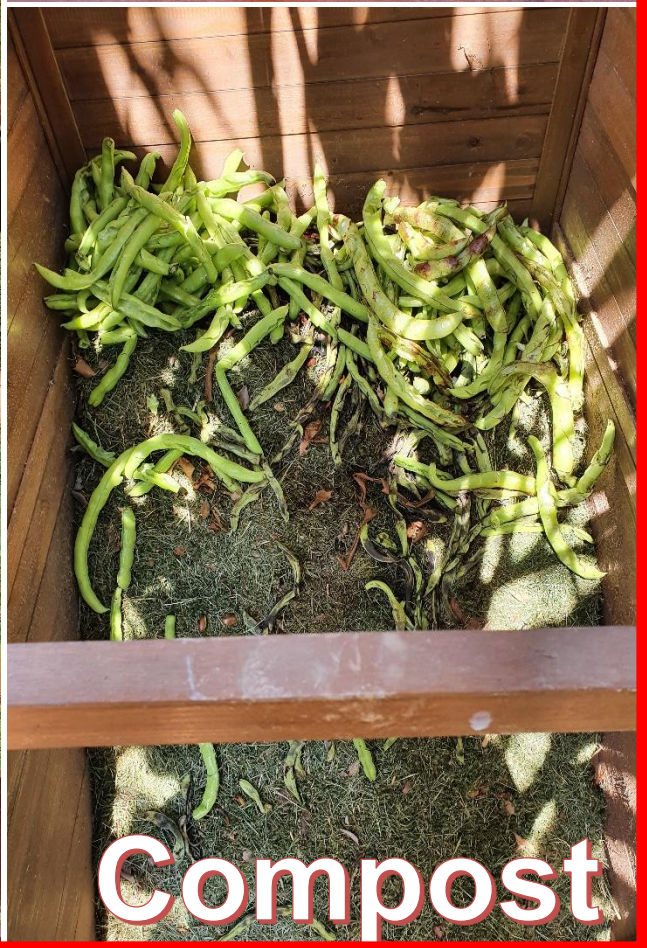




HUERTOS URBANOS
Y MACETOHUERTOS

HUERTOS URBANOS
Y MACETOHUERTOS


Agricultura ecológica


Compost


Overtime
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Dread
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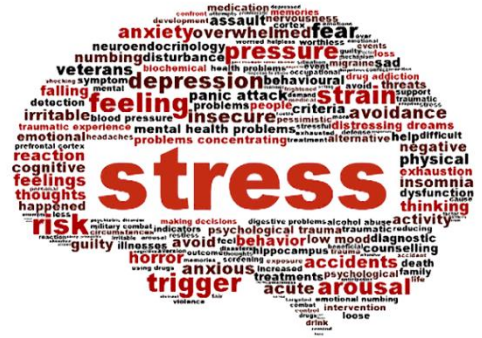
No Time
Tired
Headache
Stress
Bills
Payments
No Sleep
Stress
Debt
Fear
Work
Worry
Job
Anxiety
Retirement
Savings
Anxiety
Overdue
Expectations
Insuran
Time Management
Fear
Late Nights


stress
anxiety
overwhelmed
fear
pressure
depression
feeling
strain
insecure
avoidance
risk
trigger
arousal
horror
accidents
behavior
negative
physical
exhaustion
insomnia
thinking

Brain, Behavior, and Immunity xxx (xxxx) xxx–xxx

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

2019

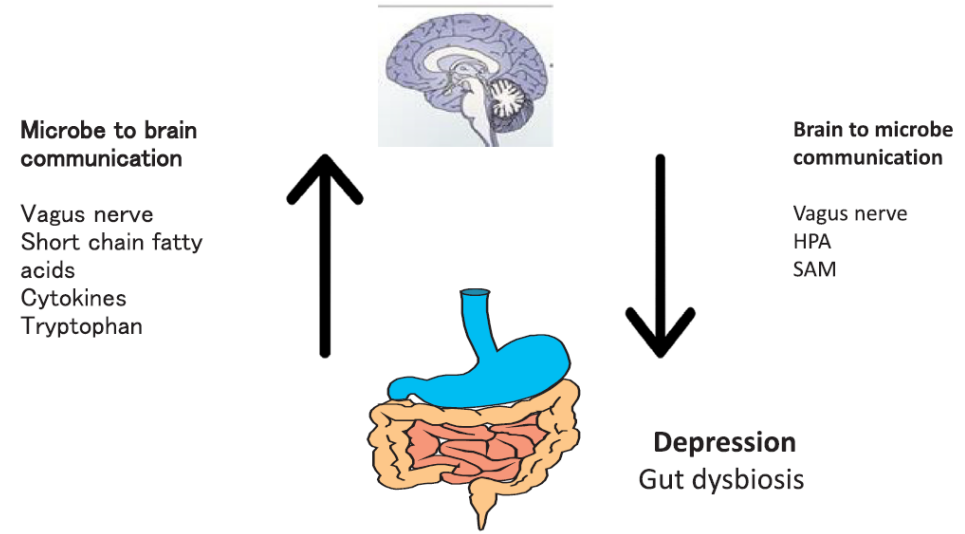
Viewpoint

Gut microbes and depression: Still waiting for Godot

Timothy G. Dinan[a,b,*], John F. Cryan[a,c]

[a] APC Microbiome Ireland, University College Cork, Cork, Ireland
[b] Department of Psychiatry and Neurobehavioral Science, University College Cork, Cork, Ireland
[c] Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

While enormous progress has been made in this field over the past decade, we patiently await definitive developments that will impact patient care. Hopefully, the field will not meet the characters in Waiting for Godot!



medical sciences

Med. Sci. 2019, 7, 21

MDPI

Review

Therapeutic Potential of the Microbiome in the Treatment of Neuropsychiatric Disorders

Alper Evrensel [1,2,*], Barış Önen Ünsalver [3] and Mehmet Emin Ceylan [4]

Abstract: The search for rational treatment of neuropsychiatric disorders began with the discovery of chlorpromazine in 1951 and continues to evolve. Day by day, new details of the intestinal microbiota–brain axis are coming to light. As the role of microbiota in the etiopathogenesis of neuropsychiatric disorders is more clearly understood, microbiota-based (or as we propose, "fecomodulation") treatment options are increasingly discussed in the context of treatment. Although their history dates back to ancient times, the importance of psychobiotics and fecal microbiota transplantation (FMT) has only recently been recognized. Despite there being few preclinical and clinical studies, the evidence gathered to this point suggests that consideration of the microbiome in the treatment of neuropsychiatric disorders represents an area of significant therapeutic potential. It is increasingly hoped that such treatment options will be more reliable in terms of their side effects, cost, and ease of implementation. However, there remains much to be researched. Questions will be answered through germ-free animal experiments and randomized controlled trials. In this article, the therapeutic potential of microbiota-based options in the treatment of neuropsychiatric disorders is discussed in light of recent research.

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Applied nutritional investigation

Probiotic food consumption is associated with lower severity and prevalence of depression: A nationwide cross-sectional study

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Depression
KNHANES

ABSTRACT

Objective: It has been suggested that probiotics have beneficial effects on a variety of health problems including immunologic diseases and metabolic disorders, however, the effects on brain function are yet to be fully studied. The aim of this study was to evaluate the association between probiotic food consumption and depression status through a cross-sectional analysis of a nationwide, large population-based data.

Methods: The study population included 26 118 individuals 19 to 64 y of age who participated in the Korean National Health and Nutrition Examination Survey (KNHANES, 2012–2016). A food frequency questionnaire was used to assess probiotic food consumption. Depression status was determined by two different methods including a Patient Health Questionnaire (PHQ-9) and self-reported clinical diagnosis.

Results: Compared with the lowest tertile of probiotic food consumption, the highest tertile had significantly lower odds in PHQ-9 depression severity (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.28–0.81; $P = 0.0065$) and self-reported clinical depression (OR, 0.59; 95% CI, 0.35–0.96; $P = 0.0129$). Although there was no significant association between probiotic food consumption and clinical depression in women (OR, 0.85; 95% CI, 0.47–1.54; $P = 0.3081$), men showed a significantly lower prevalence of clinical depression (OR, 0.24; 95% CI, 0.06–0.92; $P = 0.0256$) in the highest tertile.

Conclusions: These results suggest that probiotic food consumption might have beneficial effects on depression, particularly in men. Further studies are required to identify the mechanistic relations between probiotics and depression.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
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Psychobiotics: A new approach for treating mental illness?

Snigdha Misra [a] and Debapriya Mohanty[b]

ABSTRACT

Gut microbiomes may have a significant impact on mood and cognition, which is leading experts towards a new frontier in neuroscience. Studies have shown that increase in the amount of good bacteria in the gut can curb inflammation and cortisol level, reduces symptoms of depression and anxiety, lowers stress reactivity, improves memory and even lessens neuroticism and social anxiety. This shows that, probably the beneficial gut bacteria or probiotics function mechanistically as delivery vehicles for neuroactive compounds. Thus, a psychobiotic is a live organism, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. Study of these novel class of probiotics may open up the possibility of rearrangement of intestinal microbiota for effective management of various psychiatric disorders.

Table 1. Gut microbes having psychotropic properties.

Lactobacillus spp	*Bifidobacterium* spp
L. acidophilus	*B. infantis,*
L. casei	*B. longum,*
L. rhamnosus	*B. bifidum*
L. helveticus	*B. lactis*
L. plantarum	*B. breve*
L pentosus	
L casei Shirota	
L. hilgardii,	

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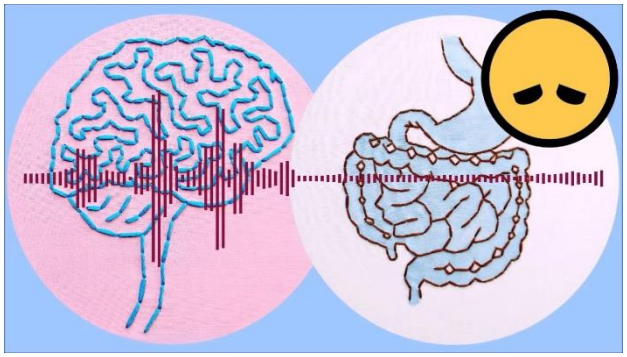
Psychobiotics: A new approach for treating mental illness?

Snigdha Misra [a] and Debapriya Mohanty[b]



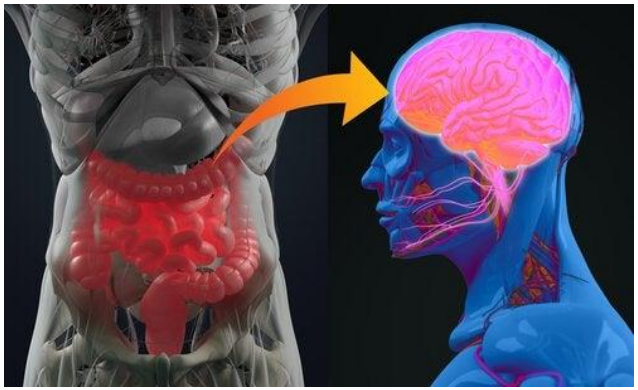


Table 2. Pyscobiotics used in different neurological conditions.

Neurological Condition	Gut microbes	Psychobiotic Strains
Anxiety	*Lactobacillus* spp	*L. fermentum* NS9,
		Lactobacillus casei Shirota,
		L. rhamnosus JB-1
		L. helveticus ROO52
	Bifidobacterium spp	*B. breve* 1205
		B. infantis
		B. longum 1714
		B. longum NCC3001
		B. longum R0175
Depression	*Lactobacillus* spp	*L. acidophilus*
		L. acidophilus W37
		L. brevis W63
		L. casei
		L. casei Shirota
		L. casei W56
		L. gasseri OLL2809
		L. helveticus NS8
	Lactococcus	*L. lactis* W19
		L.lactis W58
	Bifidobacterium spp	*B. infantis*
		B. bifidum
		B. bifidum W23
		B. lactis W52
		B. longum R0175
Stress	*Lactobacillus* spp	*L. casei Shirota*
		L. helveticus
		L. helveticus R0052
		L. plantarum PS128
		L. rhamnosus
	Bifidobacterium spp	*B. infantis*
		B. longum R0175

nutrients

MDPI

Review

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

Ruixue Huang, Ke Wang and Jianan Hu *

Department of Occupational and Environmental health, Xiangya school of Public Health, Central South University, Changsha 410078, Hunan, China; huangruixue@csu.edu.cn (R.H.); wangke2138@126.com (K.W.)

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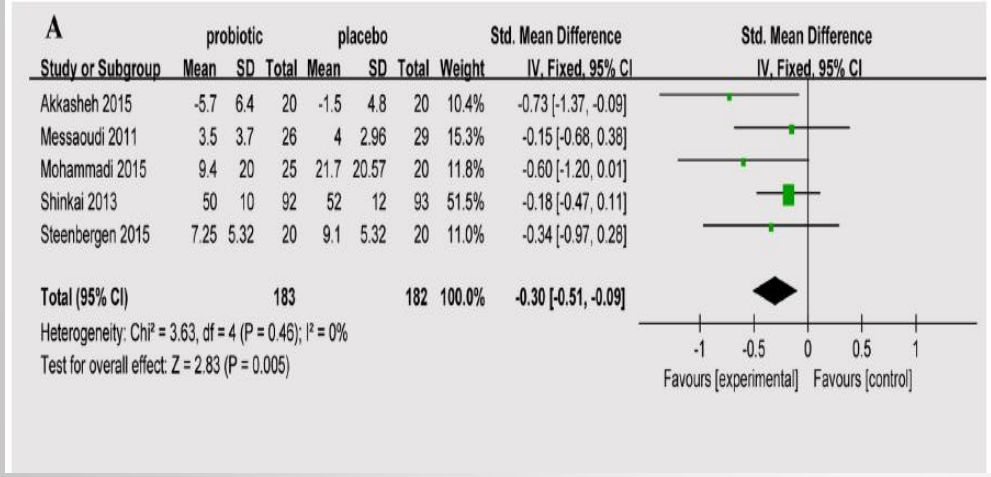
Received: 1 June 2016; Accepted: 3 August 2016; Published: 6 August 2016

Abstract: It has been reported that gut probiotics play a major role in the bidirectional communication between the gut and the brain. Probiotics may be essential to people with depression, which remains a global health challenge, as depression is a metabolic brain disorder. However, the efficacy of probiotics for depression is controversial. This study aimed to systematically review the existing evidence on the effect of probiotics-based interventions on depression. Randomized, controlled trials, identified through screening multiple databases and grey literature, were included in the meta-analysis. The meta-analysis was performed using Review Manager 5.3 software using a fixed-effects model. The meta-analysis showed that probiotics significantly decreased the depression scale score (MD (depressive disorder) = −0.30, 95% CI (−0.51–−0.09), $p = 0.005$) in the subjects. Probiotics had an effect on both the healthy population (MD = −0.25, 95% CI (−0.47–−0.03), $p = 0.03$) and patients with major depressive disorder (MDD) (MD = −0.73, 95% CI (−1.37–−0.09), $p = 0.03$). Probiotics had an effect on the population aged under 60 (MD = −0.43, 95% CI (−0.72–−0.13), $p = 0.005$), while it had no effect on people aged over 65 (MD = −0.18, 95% CI (−0.47–0.11), $p = 0.22$). This is the first systematic review and meta-analysis with the goal of determining the effect of probiotics on depression. We found that probiotics were associated with a significant reduction in depression, underscoring the need for additional research on this potential preventive strategy for depression.

Aunque el tamaño del efecto fue pequeño (¨X¨< 0.05) se evidenciaron resultados favorables que inducen a interpretar que algún efecto positivo tiene el consumo de probióticos asociado a la disminución de la depresión, evidenciando que los probióticos probablemente puede tener una influencia potencial en la reducción de la misma



Psychiatry Research 282 (2019) 112568

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Psychiatry Research

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Effect of probiotics on depressive symptoms: A meta-analysis of human studies

Kah Kheng Goh[a], Yen-Wenn Liu[b,c], Po-Hsiu Kuo[d,e], Yu-Chu Ella Chung[d], Mong-Liang Lu[a,f], Chun-Hsin Chen[a,f,*]

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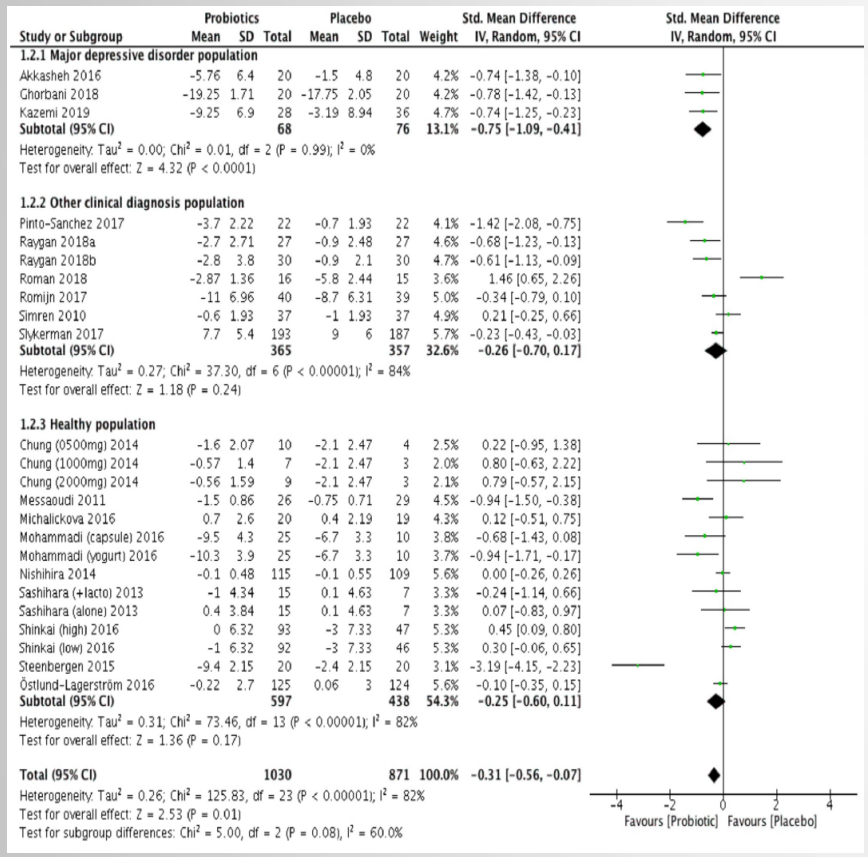
ARTICLE INFO

Keywords:
Depressive symptoms
Major depressive disorder
Meta-analysis
Microbes
Probiotics

ABSTRACT

Accumulating data show that probiotics may be beneficial in reducing depressive symptoms. We conducted an updated meta-analysis and evaluated the effects of probiotics on depressive symptoms. A systematic search of six databases was performed, and the results were reported according to Preferred Reporting Items for Systematic Reviews and Meta-analyses, with the priori-defined protocol registered at PROSPERO (CRD42018107426). In total, 19 double-blind, randomized, placebo-controlled trials with a total of 1901 participants were included in the qualitative synthesis. Participants treated with probiotics showed significantly greater improvement in depressive symptoms than those receiving placebo. The clinical population was stratified by clinical diagnosis into those with major depressive disorder (MDD) and those with other clinical conditions. The beneficial effect of probiotics on depressive symptoms was significant in patients with MDD, but not in those with other clinical conditions and in the general population. In addition, multiple strains of probiotics were more effective in reducing depressive symptoms. In conclusion, altering the gut–brain axis with probiotics may be an approach to improve depression severity. It is essential to verify the efficacy of specific combinations or strains of probiotics for depressive symptoms by conducting studies with a larger sample size in the future.



Resultados obtenidos estadísticamente significativos (p=0.01). Los pacientes con trastorno de depresión mayor, que consumieron probióticos evidenciaron una mejora mucho más significativa respecto al grupo control, resultado que no fue tan significativo en aquellos incluidos en el grupo de otros trastornos.

Se evidenció también un efecto estadísticamente significativo de los probióticos en la reducción de síntomas depresivos (DME=-0.31; IC=95%, -0.56-0.07; P=0.01)

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Neurosci Biobehav Rev. Author manuscript; available in PMC 2020 July 01.

Published in final edited form as:

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Prebiotics and probiotics for depression and anxiety: A systematic review and meta-analysis of controlled clinical trials

Richard T. Liu, **Rachel F. L. Walsh**, and **Ana E. Sheehan**

Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University

Abstract

With growing interest in the gut microbiome, prebiotics and probiotics have received considerable attention as potential treatments for depression and anxiety. We conducted a random-effects meta-analysis of 34 controlled clinical trials evaluating the effects of prebiotics and probiotics on depression and anxiety. Prebiotics did not differ from placebo for depression ($d = -.08$, $p = .51$) or anxiety ($d = .12$, $p = .11$). Probiotics yielded small but significant effects for depression ($d = -.24$, $p < .01$) and anxiety ($d = -.10$, $p = .03$). Sample type was a moderator for probiotics and depression, with a larger effect observed for clinical/medical samples ($d = -.45$, $p < .001$) than community ones. This effect increased to medium-to-large in a preliminary analysis restricted to psychiatric samples ($d = -.73$, $p < .001$). There is general support for antidepressant and anxiolytic effects of probiotics, but the pooled effects were reduced by the paucity of trials with clinical samples. Additional randomized clinical trials with psychiatric samples are necessary fully to evaluate their therapeutic potential.

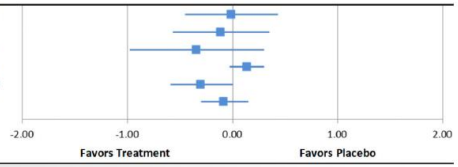
Keywords

anxiety; depression; microbiome; prebiotic; probiotic

efecto de los prebióticos en la depresión

Statistics for Each Study

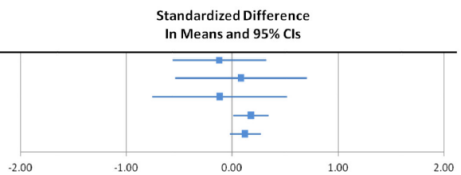
First Author, Year	Standardized Difference in Means	Lower Limit	Upper Limit	p
Azpiroz et al. (2017)	-0.01	-0.45	0.43	0.96
Kazemi et al. (in press)	-0.11	-0.57	0.35	0.64
Silk et al. (2009)	-0.34	-0.98	0.30	0.30
Smith et al. (2005)	0.14	-0.03	0.30	0.10
Smith et al. (2015)	-0.30	-0.59	<0.01	<0.05
Total	**-0.08**	**-0.30**	**0.15**	**0.51**



efecto de los prebióticos en la ansiedad

Statistics for Each Study

First Author, Year	Standardized Difference in Means	Lower Limit	Upper Limit	p
Azpiroz et al. (2017)	-0.12	-0.56	0.32	0.59
Schmidt et al. (2015)	0.08	-0.54	0.70	0.80
Silk et al. (2009)	-0.12	-0.76	0.52	0.71
Smith et al. (2005)	0.17	0.01	0.34	0.04
Total	**0.12**	**-0.03**	**0.27**	**0.11**



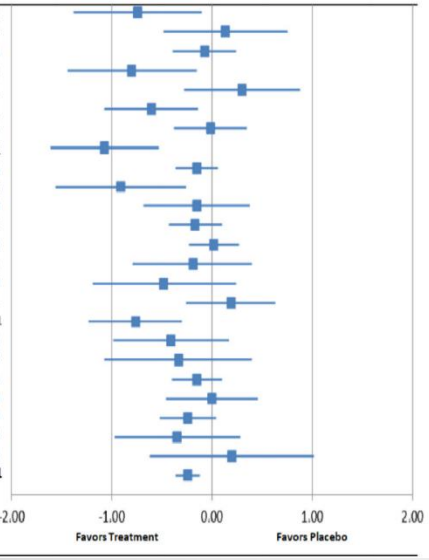
No se observan evidencias significativas entre el consumo de prebióticos en la depresión (p=0.51) o en la ansiedad (p=0-11)

- ✓ aquellos a los que se les administró probióticos, la depresión fue menor
- ✓ La administración de probióticos se asoció con menor ansiedad

Efecto de los probióticos para la depresión

Statistics for Each Study

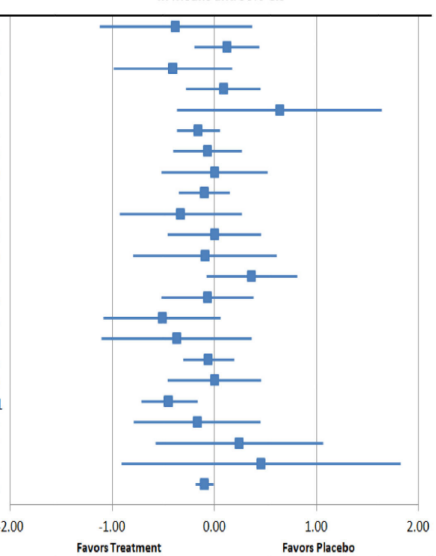
First Author, Year	Standardized Difference in Means	Lower Limit	Upper Limit	p
Akkasheh et al. (2016)	-0.74	-1.38	-0.10	0.02
Chung et al. (2014)	0.13	-0.48	0.75	0.67
Cremon et al. (2018)	0.07	0.39	0.24	0.65
Ghorbani et al. (2018)	-0.80	-1.44	-0.15	0.02
Kato-Kataoka et al. (2016)	0.30	-0.28	0.88	0.31
Kazemi et al. (in press)	-0.60	-1.07	-0.14	0.01
Kelly et al. (2017)	-0.01	-0.38	0.35	0.95
Kouchaki et al. (2017)	-1.07	-1.61	-0.53	<0.01
Lyra et al. (2016)	-0.15	-0.36	0.06	0.16
Majeed et al. (2018)	-0.91	-1.56	-0.26	<0.01
Messaoudi et al. (2011)	-0.15	-0.68	0.38	0.58
Nishihira et al. (2014)	-0.17	-0.43	0.10	0.22
Östlund-Lagerström et al. (2016)	0.02	-0.23	0.27	0.88
Pinto-Sanchez et al. (2017)	-0.19	-0.79	0.40	0.52
Roman et al. (2018)	-0.48	-1.19	0.24	0.19
Romjin et al. (2017)	0.19	-0.26	0.63	0.41
Sanchez et al. (2017) Female subsample	-0.76	-1.23	-0.30	< 0.01
Sanchez et al. (2017) Male subsample	-0.41	-0.98	0.17	0.16
Sashihara et al. (2013)	-0.33	-1.07	0.40	0.38
Shinkai et al. (2012)	-0.15	-0.40	0.10	0.25
Simrén et al. (2010)	0.00	-0.46	0.46	1.00
Slykerman et al. (2018)	-0.24	-0.52	0.04	0.09
Steenbergen et al. (2015)	-0.35	-0.97	0.28	0.28
Tillisch et al. (2013)	0.20	-0.62	1.02	0.63
Total	**-0.24**	**-0.36**	**-0.12**	**< 0.01**



Efecto de los probióticos para la ansiedad.

Statistics for Each Study

First Author, Year	Standardized Difference in Means	Lower Limit	Upper Limit	p
Colica et al. (2017)	-0.38	-1.13	0.37	0.32
Cremon et al. (2018)	0.12	-0.20	0.44	0.48
Kato-Kataoka et al. (2016)	-0.41	-0.99	0.17	0.16
Kelly et al. (2017)	0.09	-0.28	0.45	0.64
Kitaoka et al. (2009)	0.64	-0.37	1.64	0.21
Lyra et al. (2016)	-0.16	-0.37	0.05	0.14
Marcos et al. (2004)	-0.07	-0.41	0.27	0.68
Messaoudi et al. (2011)	<0.01	-0.52	0.52	1.00
Östlund-Lagerström et al. (2016)	-0.10	-0.35	0.15	0.44
Pinto-Sanchez et al. (2017)	-0.33	-0.93	0.27	0.28
Reale et al. (2012)	< 0.01	-0.46	0.46	1.00
Roman et al. (2018)	-0.09	-0.80	0.61	0.80
Romjin et al. (2017)	0.36	-0.08	0.81	0.11
Sanchez et al. (2017) Female subsample	-0.07	-0.52	0.38	0.76
Sanchez et al. (2017) Male subsample	-0.51	-1.09	0.06	0.08
Sashihara et al. (2013)	-0.37	-1.11	0.36	0.32
Shinkai et al. (2012)	-0.06	-0.31	0.19	0.66
Simrén et al. (2010)	0.00	-0.46	0.46	1.00
Slykerman et al. (2018)	-0.45	-0.72	-0.17	< 0.01
Steenbergen et al. (2015)	-0.17	-0.79	0.45	0.59
Tillisch et al. (2013)	0.24	-0.58	1.06	0.57
Vaghef-Mehrabany et al. (2014)	0.46	-0.91	1.82	0.51
Total	**-0.10**	**-0.19**	**-0.01**	**0.03**



Entonces…

consumo de prebióticos
- Ansiedad
- Depresión

consumo de probióticos
- Ansiedad
- Depresión

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Meta-analyses

Can psychobiotics "mood" ify gut? An update systematic review of randomized controlled trials in healthy and clinical subjects, on anti-depressant effects of probiotics, prebiotics, and synbiotics

Elnaz Vaghef-Mehrabany [a], Vahid Maleki [a], Maryam Behrooz [a], Fatemeh Ranjbar [b], Mehrangiz Ebrahimi-Mameghani [c, *]

SUMMARY

Background & aims: Depression is a major debilitating health problem with high global prevalence. Gut microbiota dysbiosis might be implicated in pathophysiology of depression. Hence, probiotics, prebiotics and synbiotics (psychobiotics) have been administered in clinical trials in attempt to relieve depressive symptoms. This update systematic review aimed to evaluate the current body of research concerning the effects of psychobiotics on depression.

Methods: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed in this review. Search was performed in MEDLINE, ProQuest, EMBASE, PsycNET, and Scopus databases for randomized clinical trials which assessed the effects of psychobiotics on depressive symptoms among adults, and were published in English language, since inception until September 2018.

Results: Out of 3374 records screened, 32 articles met the study criteria; only seven studies reported significant anti-depressant effects of psychobiotics. Some probiotic strains showed beneficial effects on depressive symptoms; the results were inconsistent, though. Few studies investigated the effects of prebiotics or synbiotics on depression, and did not come up with much promising results The overall risk of bias was judged to be unclear across the included studies, and major confounding factors were not considered in their design.

Conclusion: Since probiotics may affect depression in strain-specific manner, the current evidence is not sufficient to either support or decline anti-depressant effects of probiotics; results of studies on prebiotics and synbiotics are not conclusive, either. More well-designed studies with emphasis on specific probiotic strains, inter-individual gut microbiota variations, and depression subtypes are warranted.

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The effects of probiotic supplementation on mental health, biomarkers of inflammation and oxidative stress in patients with psychiatric disorders: A systematic review and meta-analysis of randomized controlled trials

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ARTICLE INFO

Keywords:
Probiotic supplementation
Inflammation
Oxidative stress
Psychiatric disorders
Meta-analysis

ABSTRACT

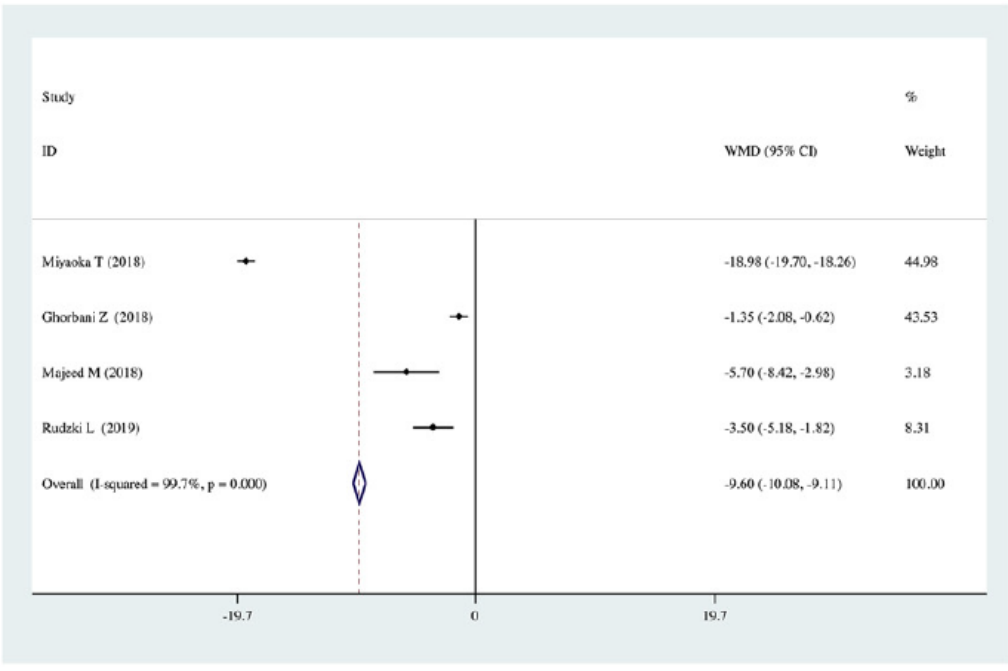
Background and objective: In the current meta-analysis of randomized controlled trials (RCTs), the effects of probiotic supplementation on mental health, biomarkers of inflammation and oxidative stress in patients with psychiatric disorders were assessed.

Methods: The following databases were search up to February 2019: PubMed, Scopus, Web of Science, Google scholar and Cochrane Central Register of Controlled Trials.

Results: Twelve studies were included in the current meta-analysis. The findings demonstrated that probiotic supplementation resulted in a significant reduction in Hamilton Depression Rating Scale (HAMD) [Weighted Mean Difference (WMD): -9.60; 95 % CI: -10.08, -9.11]. In addition, a significant reduction in C-reactive protein (CRP) (WMD: -1.59; 95 % CI: -2.22, -0.97), interleukin 10 (IL-10) (WMD: -0.29; 95 % CI: -0.48, -0.11) and malondialdehyde (MDA) levels (WMD: -0.38; 95 % CI: -0.63, -0.13) was found after probiotics supplementation. No significant change was seen in Beck Depression Inventory (BDI) score (WMD: -11.17; 95 % CI: -24.99, 2.65), tumor necrosis factor-α (TNF-α) (WMD: -0.12; 95 % CI: -0.20, -0.05), IL-1B (WMD: -0.34; 95 % CI: -1.43, 0.74), IL-6 (WMD: 0.03; 95 % CI: -0.32, 0.38), nitric oxide (NO) (WMD: -0.54; 95 % CI: -2.16, 1.08), glutathione (GSH) (WMD: 46.79; 95 % CI: -17.25, 110.83) and total antioxidant capacity (TAC) levels (WMD: 15.21; 95 % CI: -59.96, 90.37) after probiotics supplementation.

Conclusion: Overall, the current meta-analysis demonstrated that taking probiotic by patients with psychiatric disorders had beneficial effects on HAMD, CRP, IL-10 and MDA levels, but it did not affect BDI score, other markers of inflammation and oxidative stress.

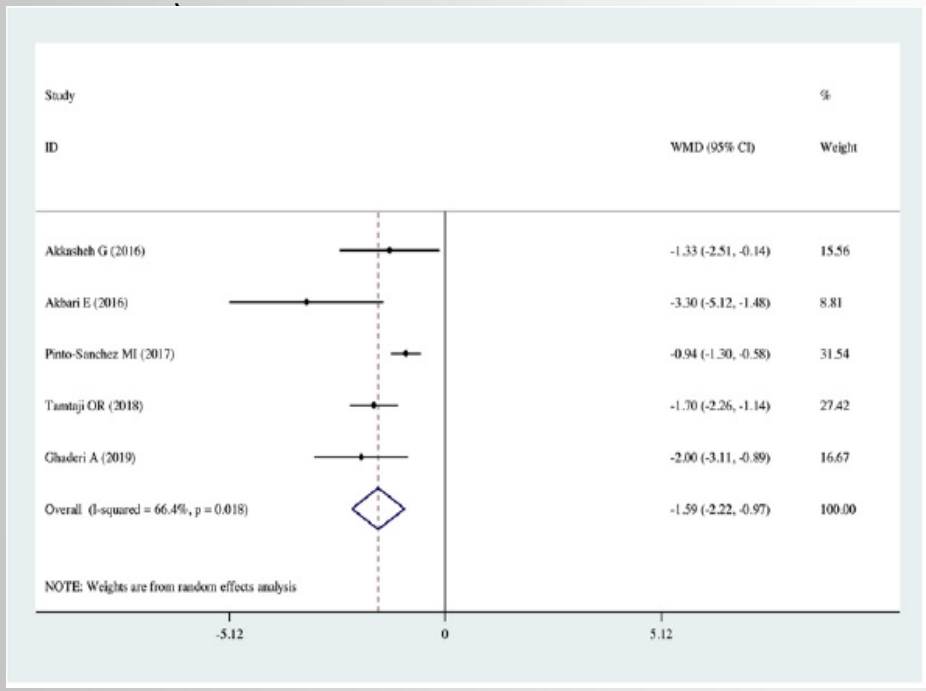
Análisis de los suplementos probióticos en la escala HAMD



Reducción significativa en los marcadores de la Escala de Depresión de Hamilton (HAMD), dando indicios relevantes de que el consumo de suplementos probióticos es capaz de reducir, en pacientes con síntomas psiquiátricos, los estándares de depresión

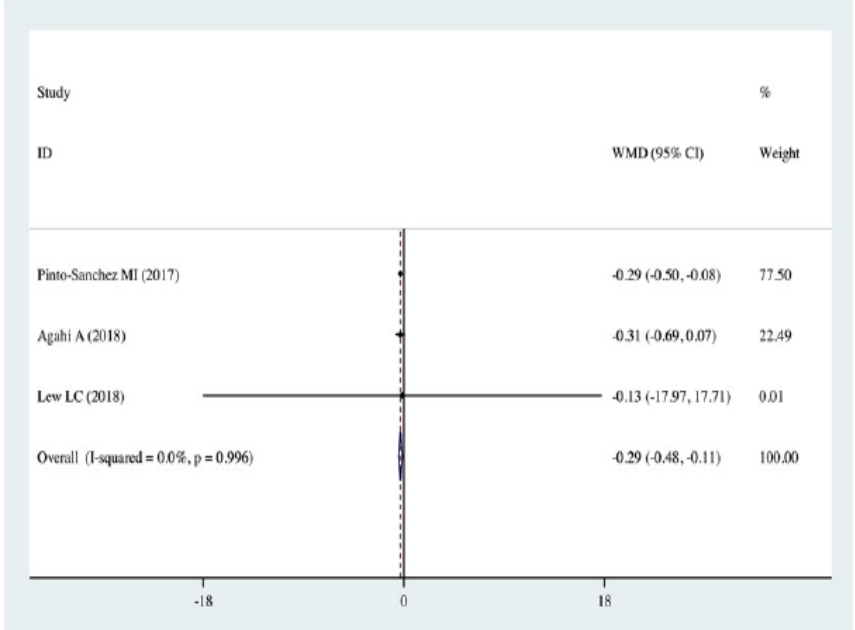
suplementos probióticos en los marcadores inflamatorios

Probióticos y proteína C-reactiva (CRP) (aumenta al haber inflamación en el



Se evidenció una reducción significativa de dichos marcadores inflamatorios producto de la ingesta de probióticos

Marcadores IL-10



Sí se observó un efecto significativo (aunque sea mínimo) en la reducción de los niveles IL-10 (WMD: -0.29; 95 % CI: -0.48, -0.11) (fig.22) interviniente en la respuesta inflamatoria.

LA DIETA PRE Y PROBIÓTICA TIENE UN PAPEL CRUCIAL EN NUESTRA SALUD (HUMOR, INMUNOLOGÍA, PSICOPATOLOGÍAS, REGULACIÓN DE 5-HT y PATOLOGÍAS DE LA TERCERA EDAD)

Ensayos preclínicos
Estudios preliminares
Falta investigación con Humanos
¿Dosis? ¿Qué probióticos?

CONCLUSIONES