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The Gut-Brain Connection: Microbiome and Mental Health in Military Populations



October 22, 2026

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About OneOp

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Strengthening military family service providers through accessible, research-informed learning.

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Free, online professional development through webinars, podcasts, courses, and more.

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This material is based upon work supported by the National Institute of Food and Agriculture, U.S. Department of Agriculture, and the Office of Military Family Readiness Policy, U.S. Department of Defense under Award Number 2023-48770-41333.

Today's Presenters



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Disclosures

This presentation is based on work supported, in part, by the Department of Veterans Affairs (VA) and Department of Defense (DoD) but does not necessarily represent the views of the VA, DoD, or the United States Government.

Learning Objectives

At the conclusion of this webinar, attendees will be able to:

1. Describe the gut–brain axis and biological pathways through which the gut microbiome may influence physical and mental health.

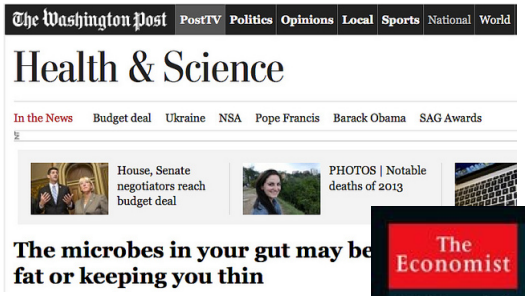
2. Identify factors that can influence the gut microbiome, including diet, medications, environmental and occupational exposures, social determinants of health, and military-related experiences.

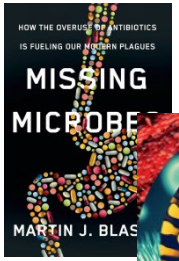
3. Evaluate current evidence linking the gut microbiome and with mental and neurological health outcomes

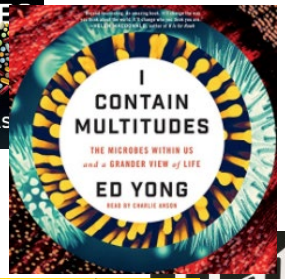
4. Discuss the emerging potential of microbiome-targeted interventions.

Microbiome discussed everywhere

FOUNDATIONS

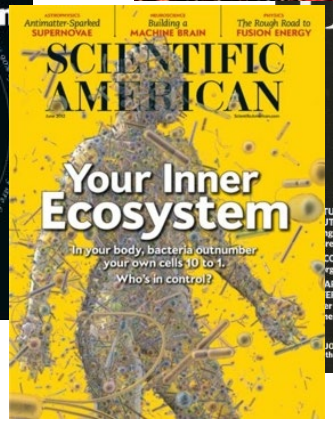


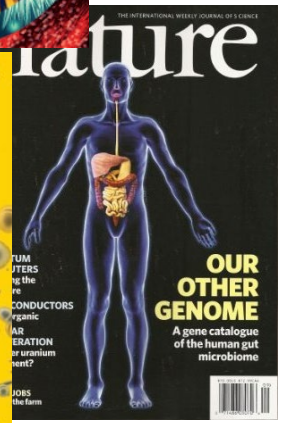


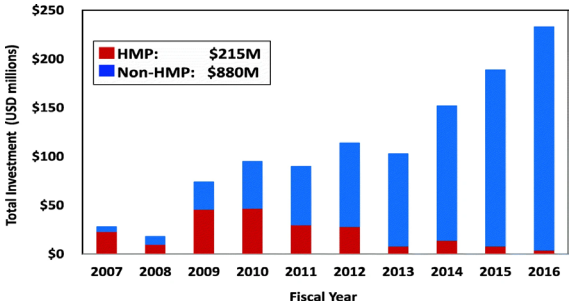




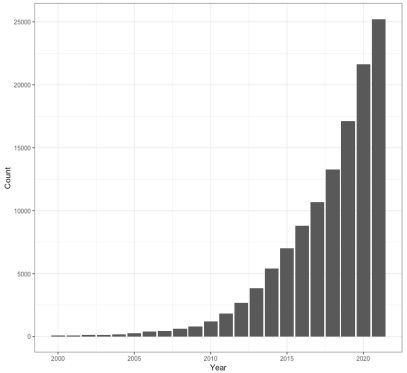








NIH Human Microbiome Portfolio Analysis Team. A review of 10 years of human microbiome research activities at the US National Institutes of Health, Fiscal Years 2007-2016. Microbiome 7, 31 (2019).



Pubmed search of “Microbiome” or “Microbiota”, June 22

Available Near You...

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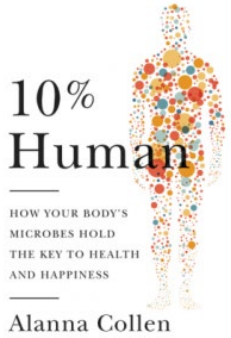




What is a microbe?

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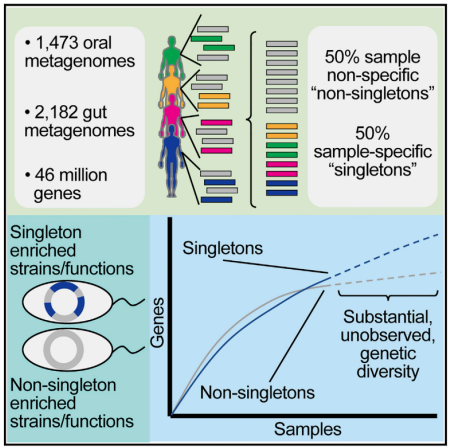
Bacteria*
Archaea
Fungi (mycobiome)
Protists
Viruses (virome)
Phages
Microscopic Animals



Cell Host & Microbe

The Landscape of Genetic Content in the Gut and Oral Human Microbiome

Graphical Abstract



Authors

Braden T. Tierney, Zhen Yang, Jacob M. Luber, ..., Eleanor Mehlenbacher, Chirag J. Patel, Aleksandar D. Kostic

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Chirag_Patel@hms.harvard.edu (C.J.P.), Aleksandar.Kostic@joslin.harvard.edu (A.D.K.)

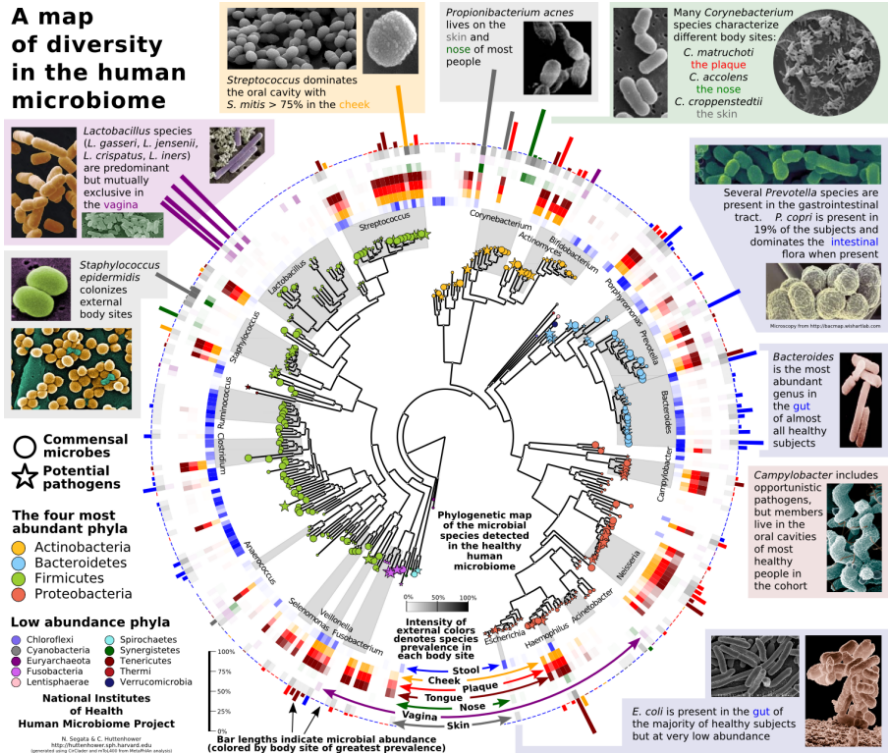
In Brief

Tierney et al. presents a meta-analysis of metagenomes covering 3,655 samples from two body sites. They identify 45,666,334 non-redundant genes in the human oral and gut microbiome, and half of every person's microbial gene content is completely unique. These rare genes, denotes singletons, predominantly arise from extremely rare microbial strains.

The Human Genome Project estimated that humans have between **20,000** and **25,000** genes. Every person has **two** copies of each gene, one inherited from each parent. Most genes are the same in all people, but a small number of genes (less than 1 percent of the total) are slightly different between people.

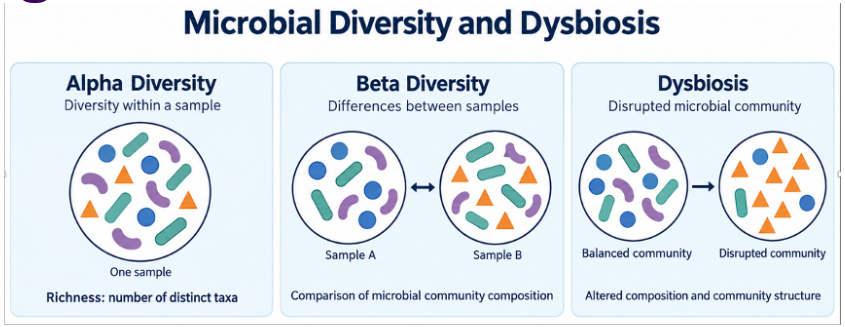
Human Microbiome

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Understanding Microbiome Research

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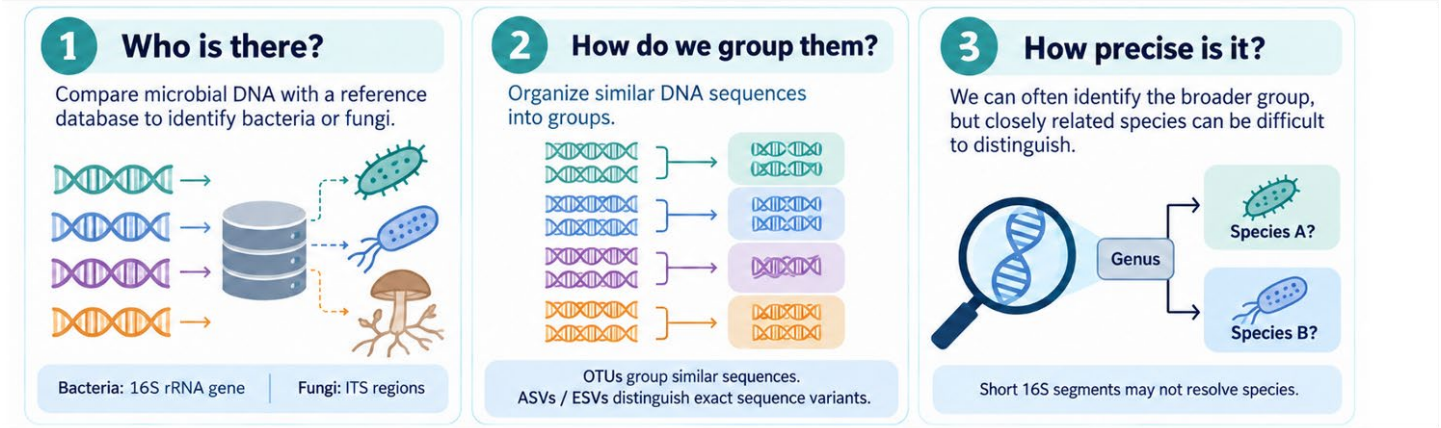
Conceptual Terms	Operational Definitions
Alpha Diversity (α-Diversity)	A measure in microbial ecology of "species" diversity, specifically, the diversity within a sample. For example, one measure of α-diversity, observed species (or observed OTUs [operational taxonomic units]), simply reflects the number of different OTUs present in the sample, a measure of species richness in the sample.
Beta Diversity (β-Diversity)	A measure in microbial ecology of species diversity, specifically, the diversity between samples.
Dysbiosis	Disruption of the gut microbial diversity and community structure, typically due to reductions in beneficial bacteria and overgrowth of harmful bacteria, yeast, and or parasites.

"HEALTH PROMOTING" versus "DISEASE PREDISPOSING"

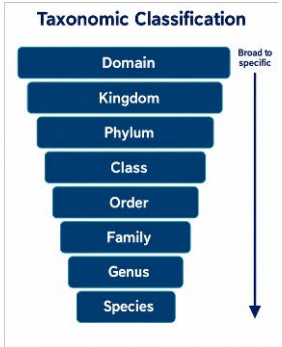


Understanding Microbiome Research Cont.

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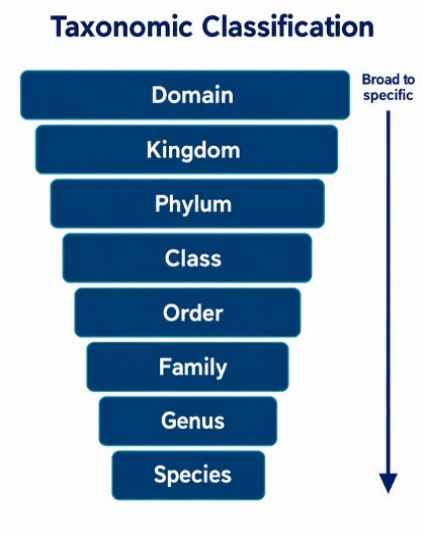


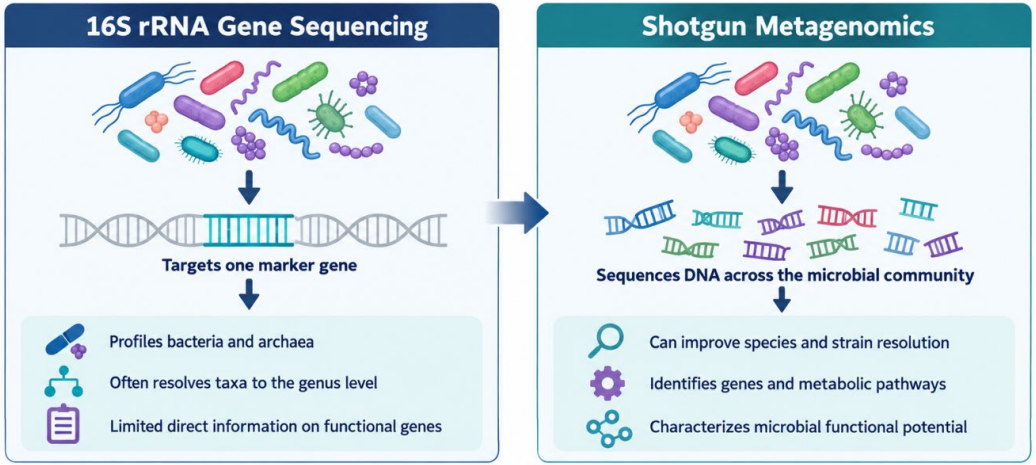
Imagine sorting photographs from a large family reunion. People with similar features are grouped together—**each group is like an OTU**. We then compare the photographs with a labeled family album to help identify who is represented. Sometimes we can recognize the family without identifying the individual.



From Microbial Composition to Functional Potential

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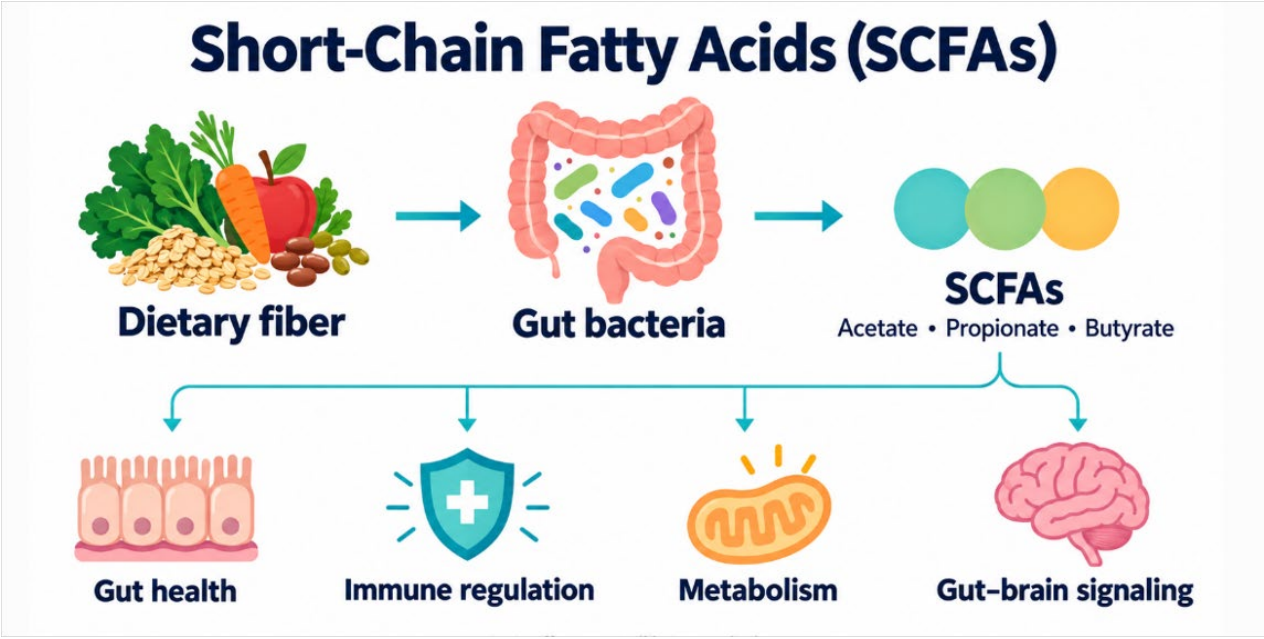




At a family reunion, short-read 16S sequencing is like recognizing family resemblance. Shotgun metagenomics adds detailed biographies, helping identify individual relatives and learn about their potential skills.

Microbial Produced Metabolites

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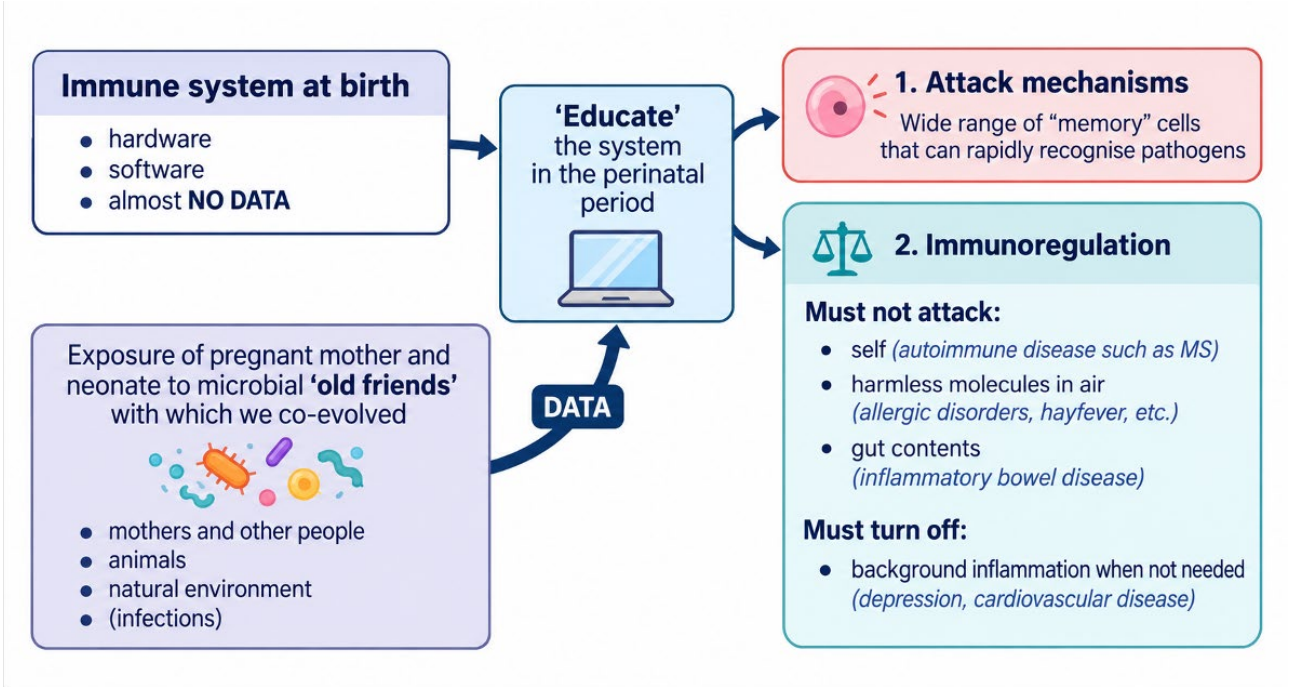


SCFAs are short-chain fatty acids—small molecules made when gut bacteria break down dietary fiber.

Why microbial exposure matters for immunoregulation

MICROBIOME DRIVERS

- The **immune system** is the body's network of cells, tissues, organs, and signaling molecules that protects against infection and responds to injury.
- **Immunoregulation** is how the body controls those immune responses—when to activate them, how strongly to respond, and when to reduce or stop them. It also helps prevent responses against the body's own tissues or harmless substances.



Revised from Rook GA, Raison CL, Lowry CA. Microbial 'old friends', immunoregulation and socioeconomic status. *Clin Exp Immunol*. 2014;177(1):1-12.

Microbial Connections to Environment

MICROBIOME DRIVERS

ASM | Microbiology and Molecular Biology Reviews®

REVIEW
September 2023 Volume 87 Issue 3 e00212-22
https://doi.org/10.1128/mmbr.00212-22

Microbiome Interconnectedness throughout Environments with Major Consequences for Healthy People and a Healthy Planet

Angela Sessitsch [a], Steve Wakelin [b], Michael Schloter [c], Emmanuelle Maguin [d], Tomislav Cernava [e], Marie-Christine Champomier-Verges [d], Trevor C. Charles [f], Paul D. Cotter [g], Ilario Ferrocino [h], Aicha Kriaa [d], Pedro Lebre [i], Don Cowan [i], Lene Lange [j], Seghal Kiran [k], Lidia Markiewicz [l], Annelein Meisner [m], Marta Olivares [n], Inga Sarand [o], Bettina Schelkle [p], Joseph Selvin [k], Hauke Smidt [q], Leo van Overbeek [m], Gabriele Berg [r], Luca Cocolin [h], Yolanda Sanz [n], Wilson Lemos Fernandes, Jr. [a], S. J. Liu [s], Matthew Ryan [t], Brajesh Singh [u], Tanja Kostic [a]

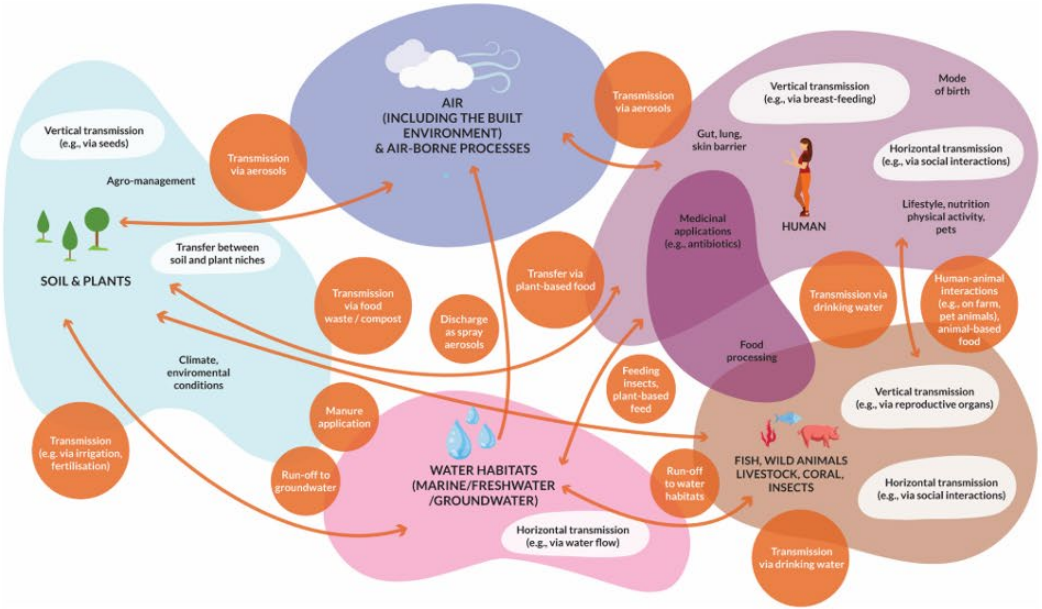
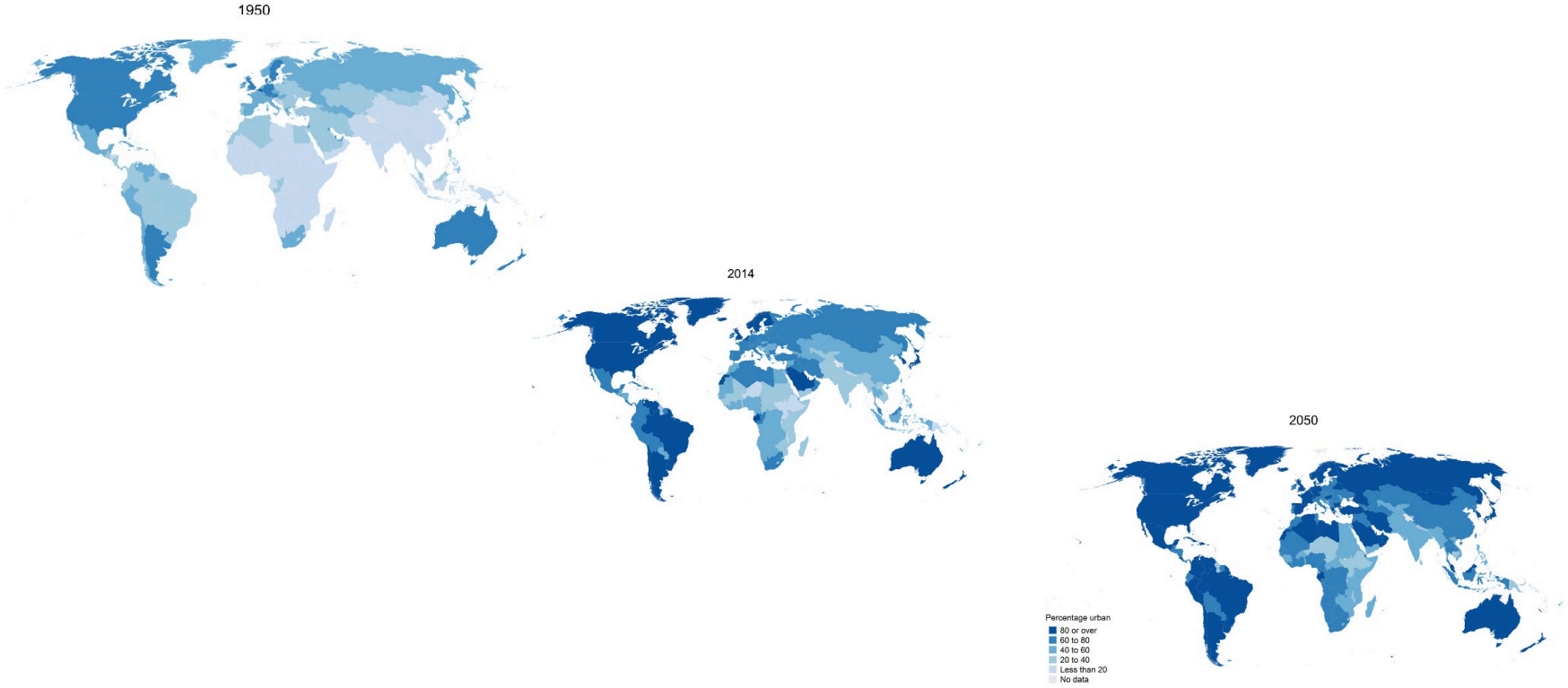


FIG 1 Microbiome transfer between environments and modes of transfer.

Educating our Immune System: Trend Toward Urbanization

MICROBIOME DRIVERS



Microbiome and urbanization

MICROBIOME DRIVERS

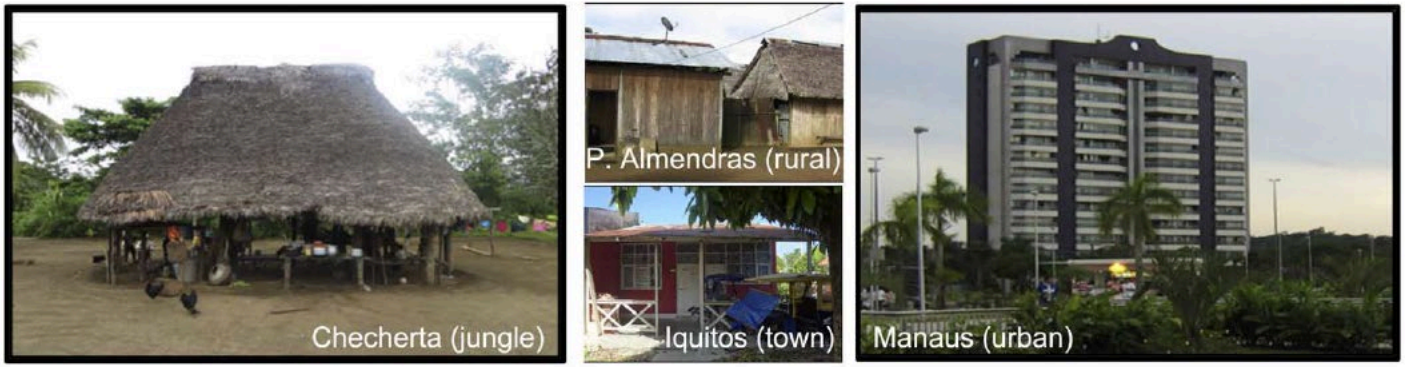
RESEARCH ARTICLE

MICROBIOLOGY

Walls talk: Microbial biogeography of homes spanning urbanization

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10.1126/sciadv.1501061

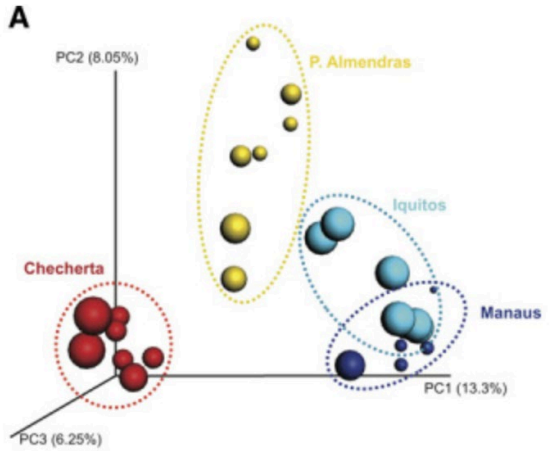
Jean F. Ruiz-Calderon,[1]* Humberto Cavallin,[2]* Se Jin Song,[3]* Atila Novoselac,[4] Luis R. Pericchi,[5] Jean N. Hernandez,[1] Rafael Rios,[6] Oralee H. Branch,[7] Henrique Pereira,[8] Luciana C. Paulino,[9] Martin J. Blaser,[10] Rob Knight,[11] Maria G. Dominguez-Bello[1,10†]



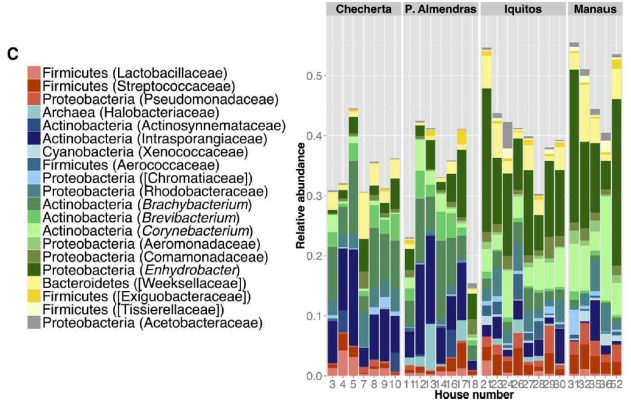
Microbiome and urbanization continued

MICROBIOME DRIVERS





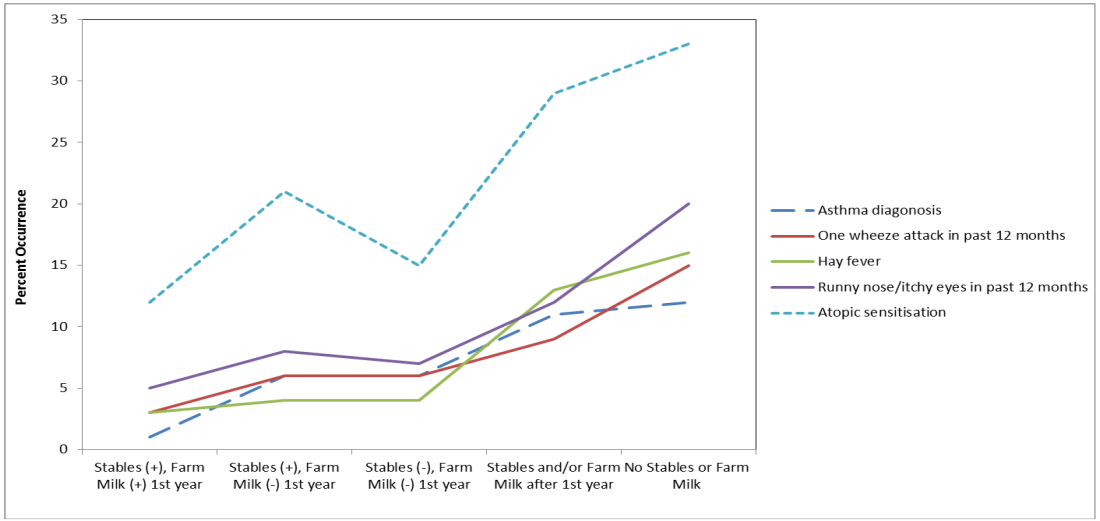
(**A**) Principal coordinates analysis (PCoA) of the seven collapsed samples for each home shows tight clustering of the samples by community ($P < 0.01$, analysis of similarities). Point size shows the α diversity level, measured as phylogenetic diversity (PD) (smallest, <150; largest, >250).



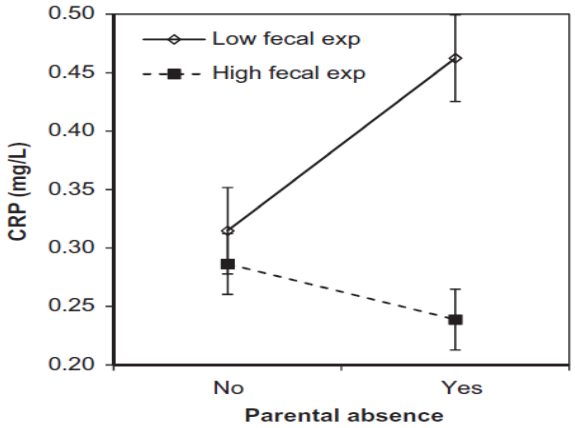
(**C**) Top 20 feature taxa of high relative abundance (>0.1%) that allowed for correct prediction of a sample's source community; these include taxa commonly associated with humans (for example, Streptococcaceae, Lactobacillaceae, and Pseudomonadaceae) (shown in red hues) and taxa commonly associated with the environment (for example, Intrasporangiaceae and Rhodobacteraceae) (shown in blue hues). Taxa shown in the literature to be associated with both the environment and the human body are shown in green hues.

Microbiome from early exposure

MICROBIOME DRIVERS



Riedler et al. (2001) Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey, *Lancet*



McDade et al. (2013) Depressive symptoms are not associated with inflammation in younger and older adults in the Philippines, *Evol Med Public Health*

Biodiversity and Inflammatory Diseases

INFLAMMATION LINKS

Haahtela et al. World Allergy Organization Journal 2013, 6:3
http://www.waojournal.org/content/6/1/3

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES Open Access

The biodiversity hypothesis and allergic disease: world allergy organization position statement

Tari Haahtela[1*], Stephen Holgate[2], Ruby Pawankar[3], Cezmi A Akdis[4], Suwat Benjaponpitak[5], Luis Caraballo[6], Jeffrey Demain[7], Jay Portnoy[8], Leena von Hertzen[1], and WAO Special Committee on Climate Change and Biodiversity

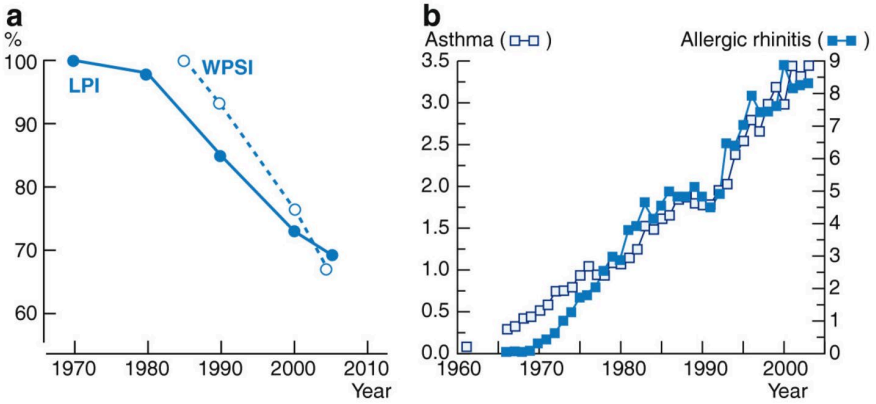


Figure 1
Two global megatrends in biodiversity and public health. (a) Declining biodiversity (percentage change) since 1970 as measured by two indices. WPSI=Waterbird Population Status Index; LPI=Living Planet Index [14]. (b) Increasing trends in the prevalence of inflammatory civilization diseases, asthma and allergic rhinitis among military conscripts in 1966-2003 [165] as an example (modified from ref. [14]).

Farm Microbiome

MICROBIOME DRIVERS





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2016 VOL. 375 NO. 5

Innate Immunity and Asthma Risk in Amish and Hutterite Farm Children

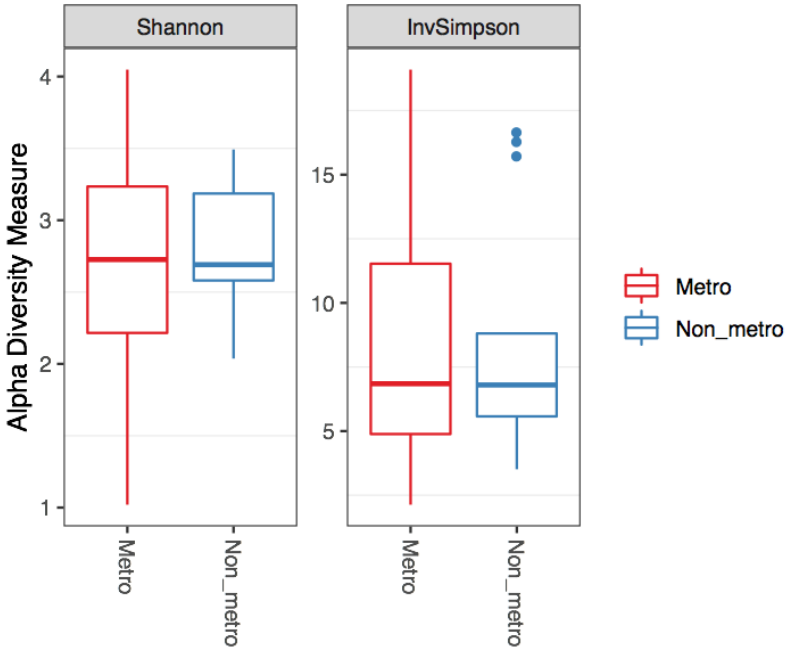
Michelle M. Stein, B.S., Cara L. Hrusch, Ph.D., Justyna Gozdz, B.A., Catherine Igartua, B.S., Vadim Pivniouk, Ph.D., Sean E. Murray, B.S., Julie G. Ledford, Ph.D., Mauricius Marques dos Santos, B.S., Rebecca L. Anderson, M.S., Nervana Metwali, Ph.D., Julia W. Neilson, Ph.D., Raina M. Maier, Ph.D., Jack A. Gilbert, Ph.D., Mark Holbreich, M.D., Peter S. Thorne, Ph.D., Fernando D. Martinez, M.D., Erika von Mutius, M.D., Donata Vercelli, M.D., Carole Ober, Ph.D., and Anne I. Sperling, Ph.D.

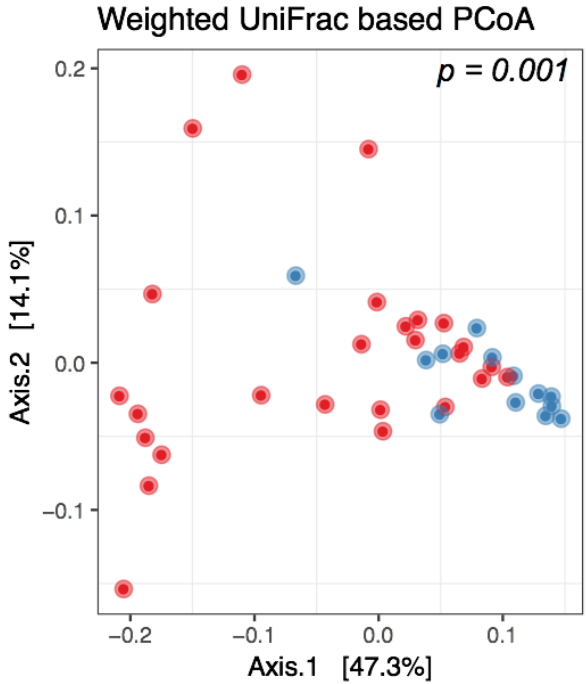
ABSTRACT

- Amish and Hutterite children, the prevalence of asthma and allergic sensitization was 4 and 6 times as low in the Amish
- Median endotoxin levels in Amish house dust was 6.8 times as high.
- Differences in microbial composition were also observed in dust samples from Amish and Hutterite homes.
- Profound differences in the proportions, phenotypes, and functions of innate immune cells were also found between the two groups of children.

The microbiome is shaped across the life course

MICROBIOME DRIVERS





The Increasing Incidence of Immunoregulatory Disorders

INFLAMMATION LINKS

Mechanisms of Disease

The Effect of Infections on Susceptibility to Autoimmune and Allergic Diseases

Jean-François Bach, M.D., D.Sc.

The New England Journal of Medicine

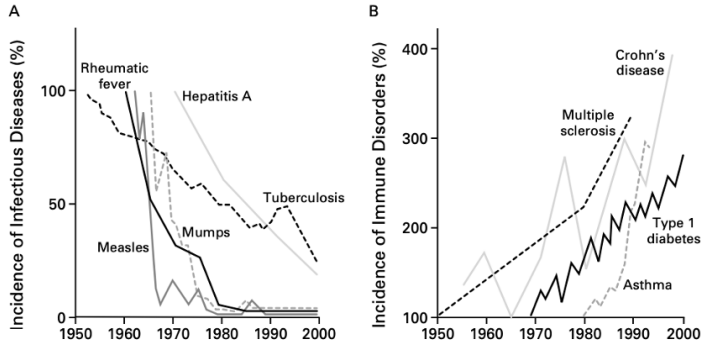
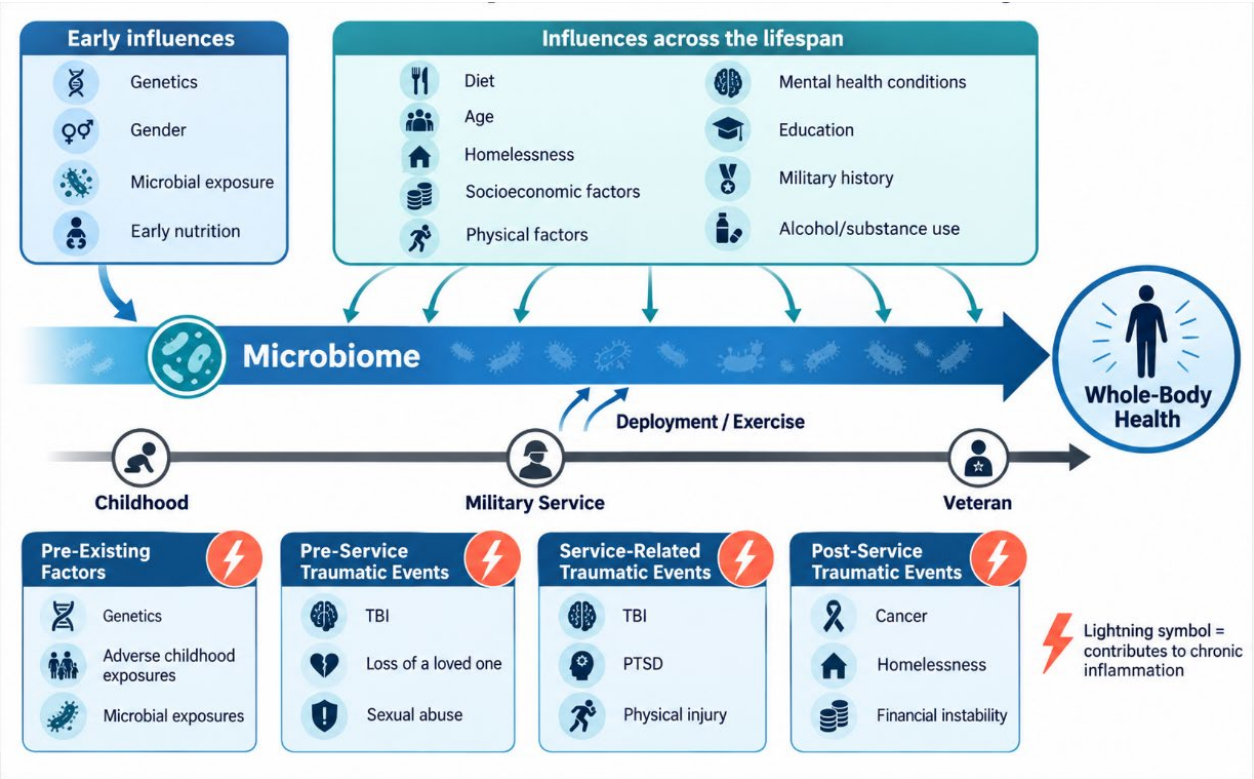


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.[12] In Panel B, data on immune disorders are derived from Swarbrick et al.,[10] Dubois et al.,[13] Tuomilehto et al.,[14] and Pugliatti et al.[15]

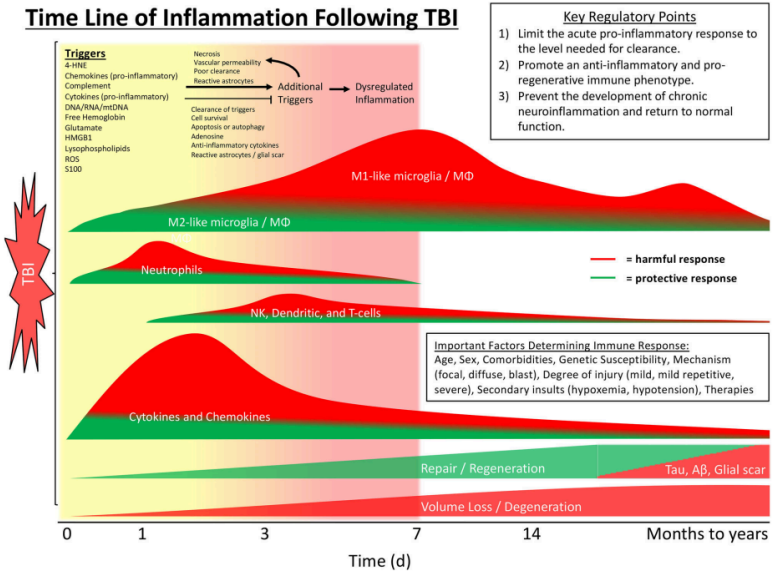
The Microbiome is Shaped Across the Lifecourse

MICROBIOME DRIVERS

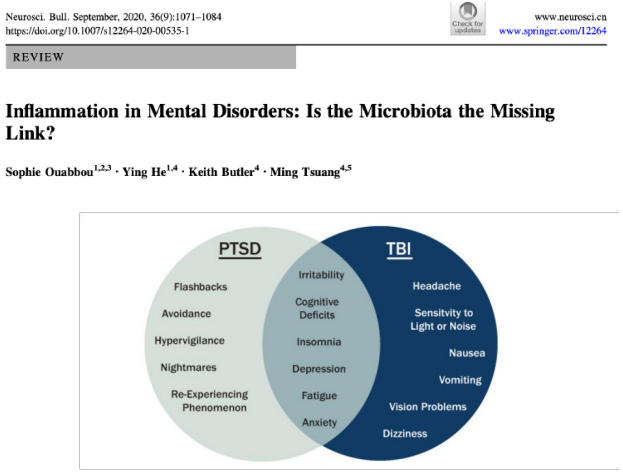


Inflammation Connects Many Signature Military Health Concerns

MENTAL HEALTH EVIDENCE



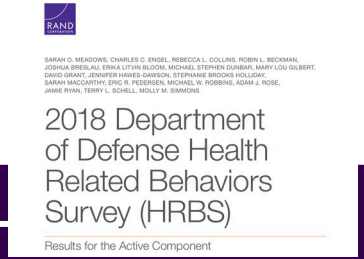
Simon, Dennis W et al. “The far-reaching scope of neuroinflammation after traumatic brain injury.” *Nature reviews. Neurology* vol. 13,3 (2017): 171-191. doi:10.1038/nrneurol.2017.13


Neurosci. Bull. September, 2020, 36(9):1071–1084
https://doi.org/10.1007/s12264-020-00535-1
www.neurosci.cn
www.springer.com/12264
REVIEW

Inflammation in Mental Disorders: Is the Microbiota the Missing Link?

Sophie Ouabbou[1,2,3] · Ying He[1,4] · Keith Butler[4] · Ming Tsuang[4,5]

Approximately one in ten service members (9.8 percent) were current heavy drinkers.



Lifetime History of TBI in Active Duty Soldiers Returning from Deployment (OEF/OIF)

MENTAL HEALTH EVIDENCE

American Psychological Association

In the public domain

Rehabilitation Psychology

2019, Vol. 64, No. 4, 398–406
http://dx.doi.org/10.1037/rep0000286

Characterization of Lifetime TBIs in a Cohort of Recently Deployed Soldiers: The Warrior Strong Study

Lisa M. Betthauser
VA Rocky Mountain Mental Illness Research Education and Clinical Center, Aurora, Colorado, and University of Colorado, Anschutz Medical Campus

Rachel Sayko Adams
Brandeis University and VA Rocky Mountain Mental Illness Research Education and Clinical Center, Aurora, Colorado

Trisha A. Hostetter
VA Rocky Mountain Mental Illness Research Education and Clinical Center, Aurora, Colorado

Ann I. Scher
Uniformed Services University

Karen Schwab
The Defense and Veterans Brain Injury Center, Silver Spring, Maryland, and Uniformed Services University

Lisa A. Brenner
VA Rocky Mountain Mental Illness Research Education and Clinical Center, Aurora, Colorado, and University of Colorado, Anschutz Medical Campus

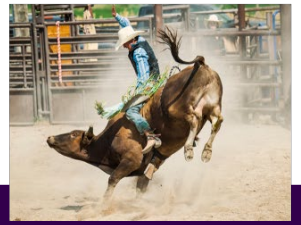
Objective: To describe and characterize the lifetime history of traumatic brain injury (TBI) among active duty soldiers returning from deployment to Afghanistan or Iraq. ***Method:*** Data were extracted from a larger parent study that was conducted at two large United States Army bases between 2009 and 2014 during Post-Deployment Health Assessment. The sample included 1,060 soldiers who sustained at least one TBI during their lifetime. ***Results:*** The Ohio State University TBI-Identification Method interview was administered to characterize individuals' total lifetime history of TBI. Soldiers reported sustaining a median of 2 lifetime TBIs. Slightly more than half of the sample without a most recent deployment-related TBI still reported a history of a lifetime TBI (some of which occurred during previous deployments). Most lifetime injuries reported were of mild severity; however, 6% of individuals reported a history of moderate/severe TBI. Blast was the most frequent mechanism associated with recent deployment-related mild TBIs. ***Conclusion:*** Findings suggest that soldiers who screened positive, as well as those who screened negative, for a history of TBI during their recent deployment still endorsed a lifetime history of TBI. Future research is needed to explore the functional impact of multiple TBIs over one's lifetime to help inform screening, assessment, and treatment among military personnel.

Impact and Implications
Although soldiers in this sample mostly reported mild traumatic brain injuries (TBIs), 6% of individuals reported lifetime moderate to severe TBIs. Moreover, a number of soldiers reported a history of nondeployment TBIs. A history of such injuries may contribute to persistent post-TBI symptoms, as well as postmilitary functional challenges. Additional research to investigate the timing, severity, and history of multiple TBIs on short- and long-term outcomes is indicated.

Keywords: traumatic brain injury, lifetime history, deployment, soldiers, OEF/OIF

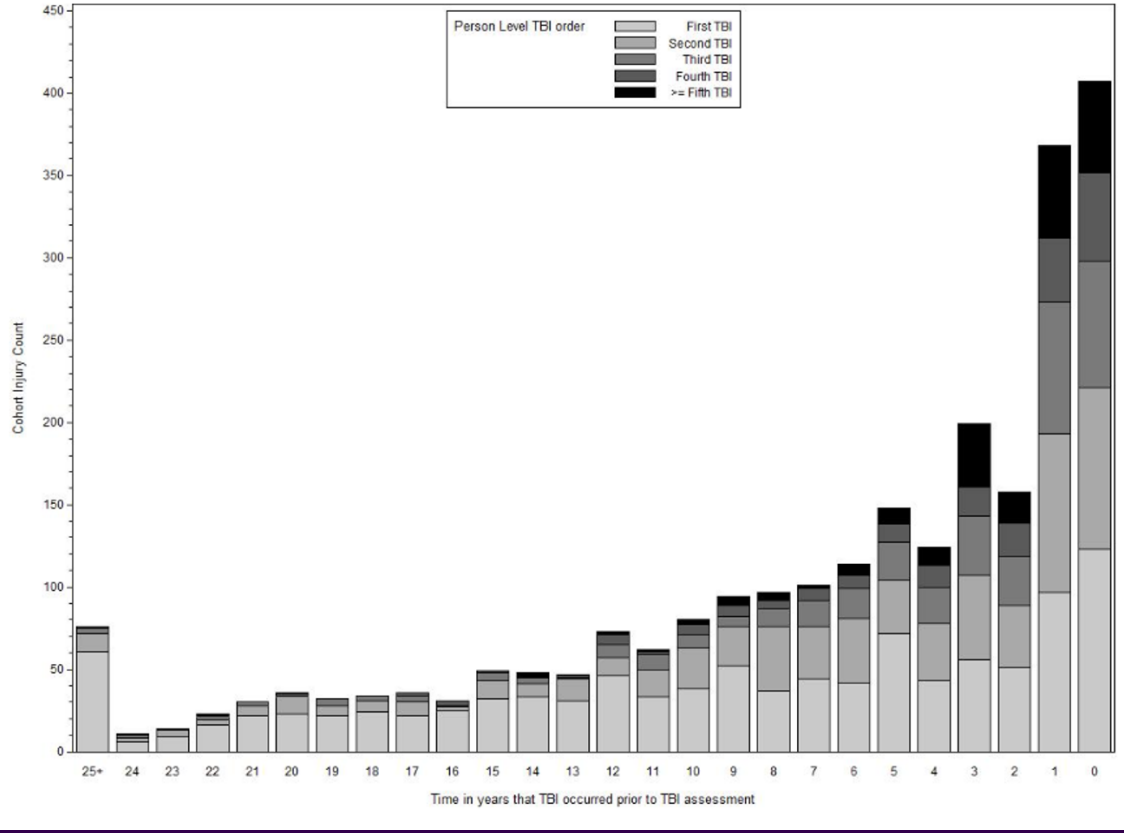






TBI Assessment vs. Injury Date

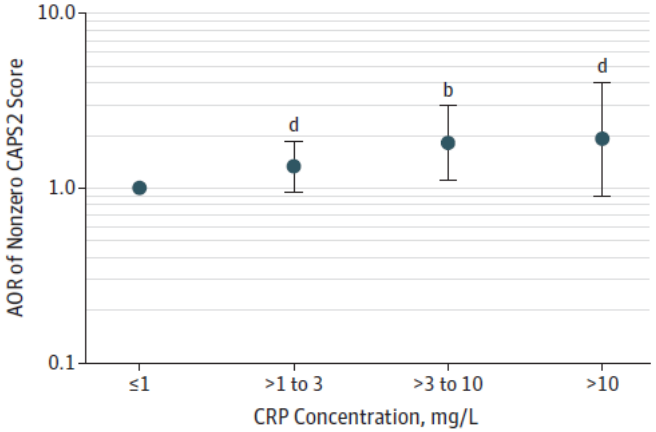
MENTAL HEALTH EVIDENCE



Inflammation Connects Many Signature Military Health Concerns

MENTAL HEALTH EVIDENCE

The Marine Resiliency Study, a prospective study of approximately 2,600 war zone–deployed Marines



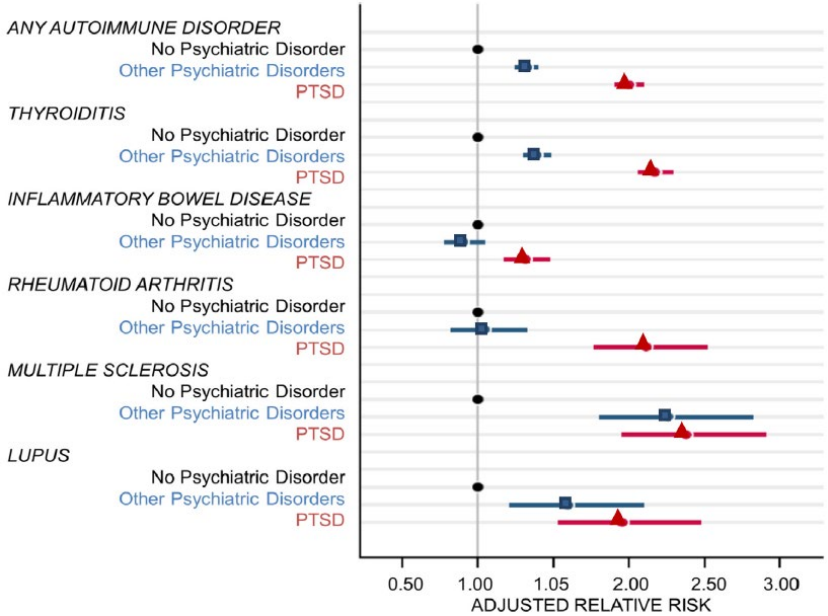
Plasma CRP concentrations before Deployment predict Clinician-Administered PTSD Scale (CAPS) scores ~3 and 6 months following deployment

"Adjusting for the baseline CAPS score, trauma exposure, and other relevant covariates, we found baseline plasma CRP concentration to be a highly significant overall predictor of post-deployment CAPS scores (p = 0.002)."

Eraly et al., 2014, *JAMA Psychiatr*, 71(4): 423-431

PTSD has also been linked with altered immunoregulation

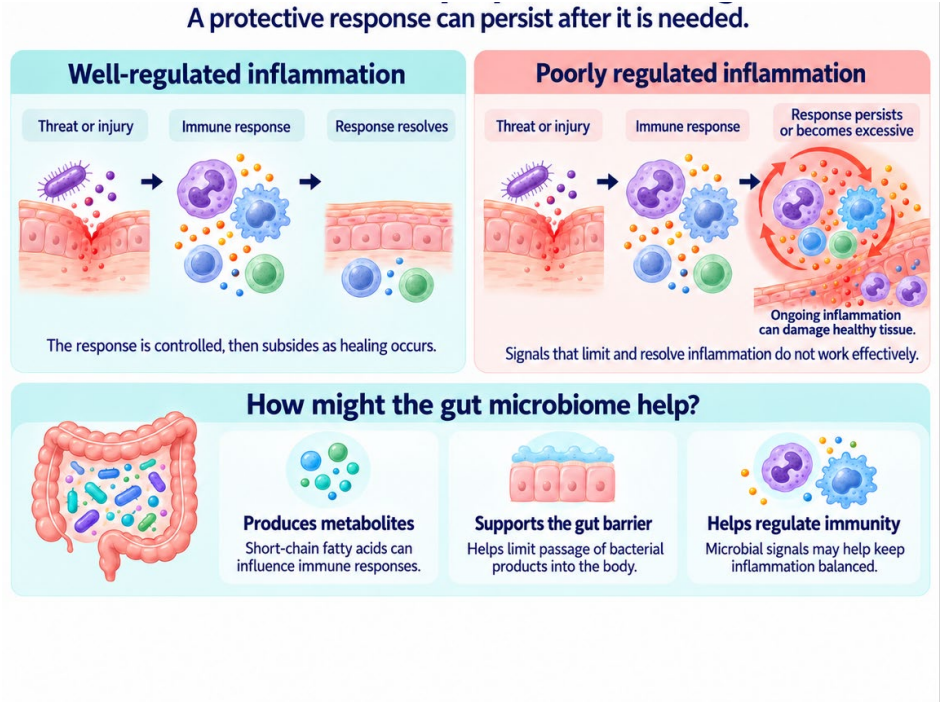
MENTAL HEALTH EVIDENCE



O'Donovan et al., 2015, *Biol Psychiatry* 77: 365-374

Inflammation without Proper Immunoregulation

MENTAL HEALTH EVIDENCE



Trauma history may relate to microbial patterns

MENTAL HEALTH EVIDENCEE

The Microbiome in Posttraumatic Stress Disorder and Trauma-Exposed Controls: An Exploratory Study

Sian M.J. Hemmings, PhD, Stefanie Malan-Müller, PhD, Leigh L. van den Heuvel, MMed (Psych), Brittany A. Demmitt, PhD, Maggie A. Stanislawski, PhD, David G. Smith, BS, Adam D. Bohr, PhD, Christopher E. Stamper, MS, Embriette R. Hyde, PhD, James T. Morton, BS, Clarisse A. Marotz, MS, Philip H. Siebler, BS, Maarten Braspenning, Ir, Wim Van Criekinge, PhD, Ir, Andrew J. Hoisington, PhD, Lisa A. Brenner, PhD, Teodor T. Postolache, MD, Matthew B. McQueen, ScD, Kenneth S. Krauter, PhD, [illegible] A. Lowry, PhD

Psychosomatic Medicine, V 79 • 936-946

October 2017

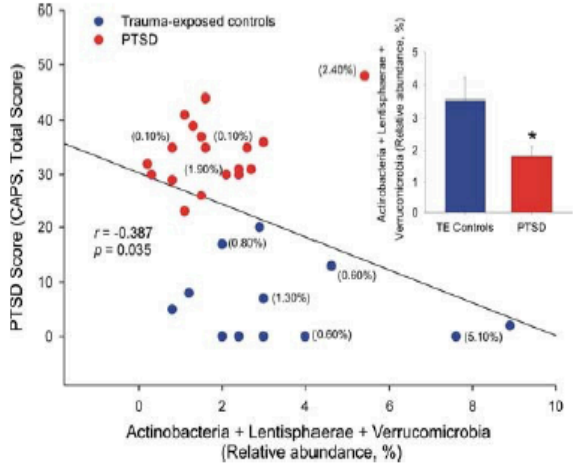
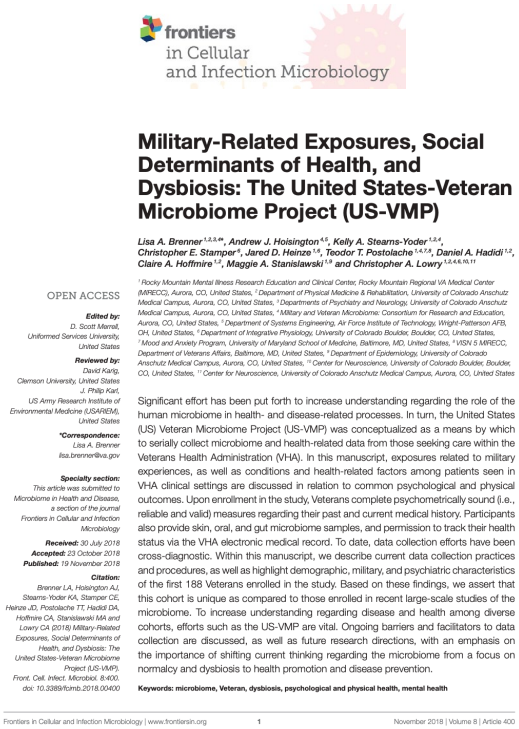


FIGURE 4. Relationship between the random forests interpretation model, relative abundance of [Actinobacteria, Lentisphaerae, Verrucomicrobia] and PTSD scores (CAPS total score). PTSD was negatively correlated with the relative abundance of Actinobacteria, Lentisphaerae, and Verrucomicrobia phyla. In other words, PTSD diagnosis was associated with a decreased abundance of these phyla (Pearson $r = -0.387$; $p = .035$). Percentages in parentheses indicate the percent relative abundance of *Akkermansia*; *Akkermansia* was below the threshold of detection for all other participants. Sample sizes: PTSD participants, $n = 18$; TE controls, $n = 12$. $^*p < .05$, Student's *t*-test. PTSD = posttraumatic stress disorder; CAPS = Clinician-Administered Posttraumatic Stress Disorder Scale for DSM-5; TE = trauma-exposed. Color image is available only in online version (www.psychosomaticmedicine.org).

”The relative abundance of [Actinobacteria, Verrucomicrobia] was also associated with Childhood Trauma Scores (CTQ, total score), with higher CTQ scores associated with lower total relative abundance.”

US-VMP examines microbiota in Veterans over time

VETERAN MICROBIOME



frontiers in Cellular and Infection Microbiology

Military-Related Exposures, Social Determinants of Health, and Dysbiosis: The United States-Veteran Microbiome Project (US-VMP)

Lisa A. Brenner[1,2,3,4], Andrew J. Hoisington[4,5], Kelly A. Stearns-Yoder[1,2,4], Christopher E. Stamper[4], Jared D. Heinze[1,4], Teodor T. Postolache[1,4,7,8], Daniel A. Hadidi[1,2], Claire A. Hoffmire[1,2], Maggie A. Stanislawski[1,9] and Christopher A. Lowry[1,2,4,6,10,11]*

[1] Rocky Mountain Mental Illness Research Education and Clinical Center, Rocky Mountain Regional VA Medical Center (MIRECC), Aurora, CO, United States, [2] Department of Physical Medicine & Rehabilitation, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [3] Departments of Psychiatry and Neurology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [4] Military and Veteran Microbiome: Consortium for Research and Education, Aurora, CO, United States, [5] Department of Systems Engineering, Air Force Institute of Technology, Wright-Patterson AFB, OH, United States, [6] Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO, United States, [7] Mood and Anxiety Program, University of Maryland School of Medicine, Baltimore, MD, United States, [8] VISN 5 MIRECC, Department of Veterans Affairs, Baltimore, MD, United States, [9] Department of Epidemiology, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [10] Center for Neuroscience, University of Colorado Boulder, Boulder, CO, United States, [11] Center for Neuroscience, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

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Brenner LA, Hoisington AJ, Stearns-Yoder KA, Stamper CE, Heinze JD, Postolache TT, Hadidi DA, Hoffmire CA, Stanislawski MA and Lowry CA (2018) Military-Related Exposures, Social Determinants of Health, and Dysbiosis: The United States-Veteran Microbiome Project (US-VMP). Front. Cell. Infect. Microbiol. 8:400. doi: 10.3389/fcimb.2018.00400

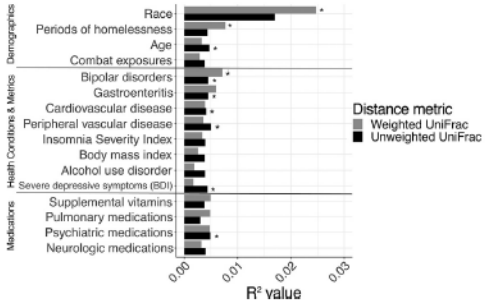
Significant effort has been put forth to increase understanding regarding the role of the human microbiome in health- and disease-related processes. In turn, the United States (US) Veteran Microbiome Project (US-VMP) was conceptualized as a means by which to serially collect microbiome and health-related data from those seeking care within the Veterans Health Administration (VHA). In this manuscript, exposures related to military experiences, as well as conditions and health-related factors among patients seen in VHA clinical settings are discussed in relation to common psychological and physical outcomes. Upon enrollment in the study, Veterans complete psychometrically sound (i.e., reliable and valid) measures regarding their past and current medical history. Participants also provide skin, oral, and gut microbiome samples, and permission to track their health status via the VHA electronic medical record. To date, data collection efforts have been cross-diagnostic. Within this manuscript, we describe current data collection practices and procedures, as well as highlight demographic, military, and psychiatric characteristics of the first 188 Veterans enrolled in the study. Based on these findings, we assert that this cohort is unique as compared to those enrolled in recent large-scale studies of the microbiome. To increase understanding regarding disease and health among diverse cohorts, efforts such as the US-VMP are vital. Ongoing barriers and facilitators to data collection are discussed, as well as future research directions, with an emphasis on the importance of shifting current thinking regarding the microbiome from a focus on normalcy and dysbiosis to health promotion and disease prevention.

Keywords: microbiome, Veteran, dysbiosis, psychological and physical health, mental health

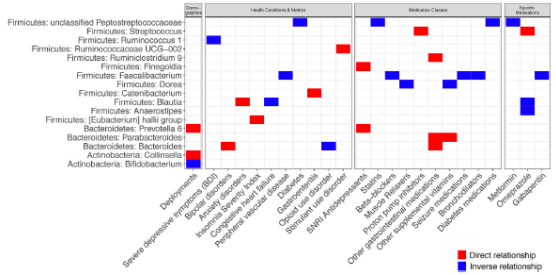
Number of Participant

Military and Veteran health reflects many interacting factors

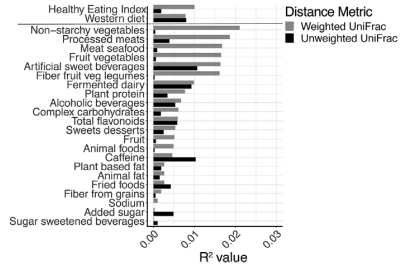
VETERAN MICROBIOME



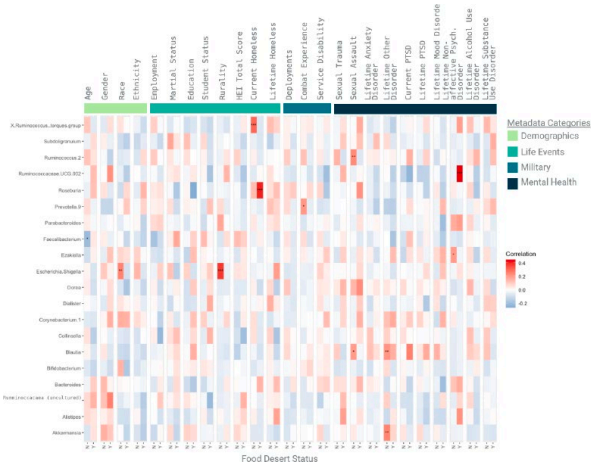
Stanislawksi et al., 2021



Stanislawksi et al., 2021



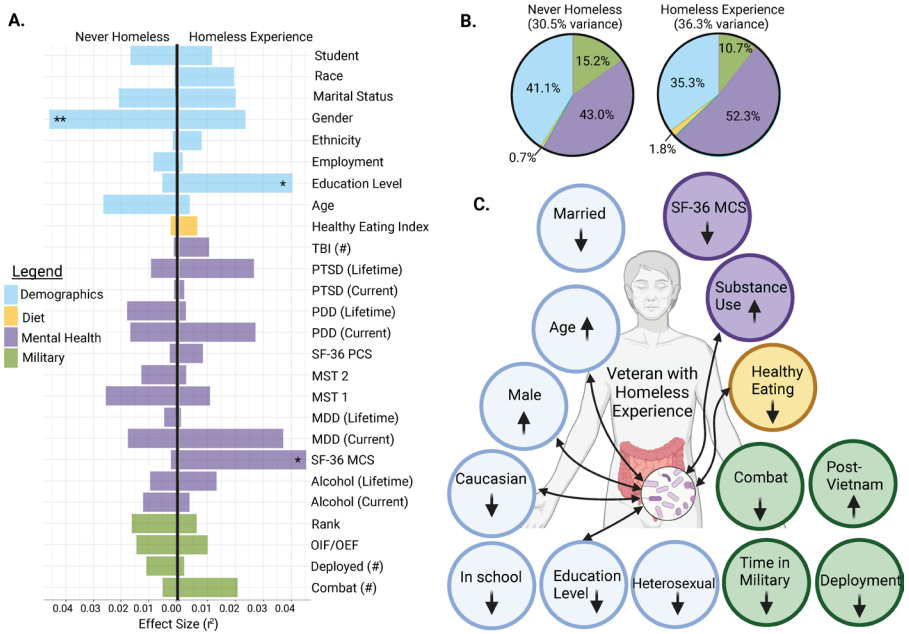
Brostow et al, 2021



Brostow et al, 2023

Social determinants and diet can leave a microbial signal

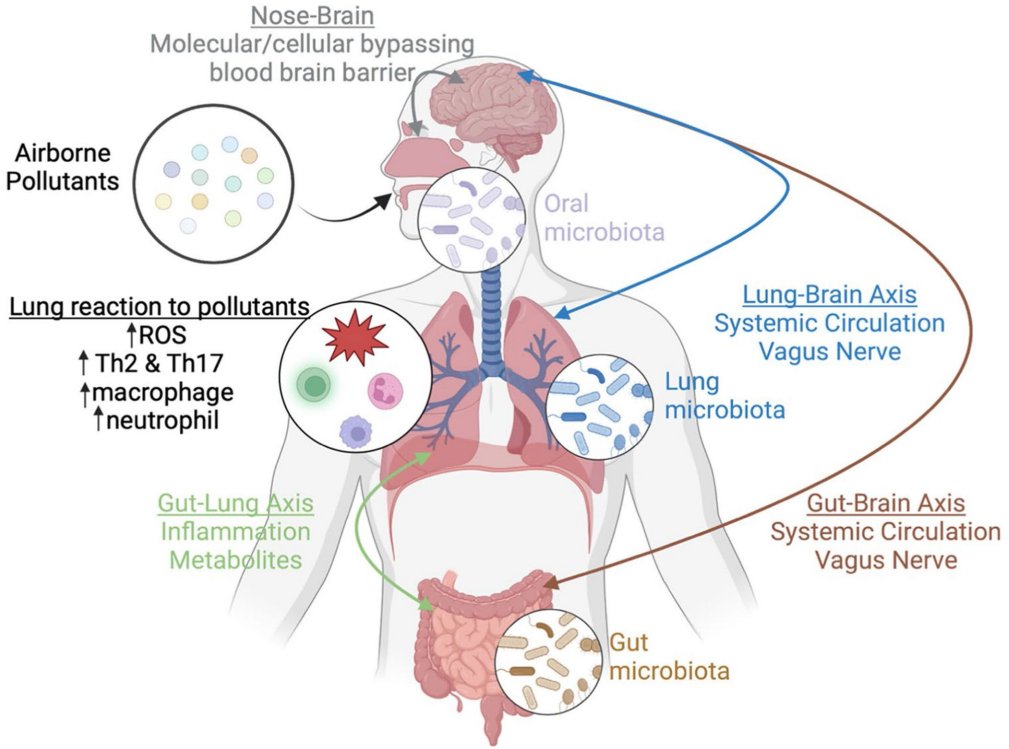
VETERAN MICROBIOME



Hoisington et al, 2023

Military exposures and the microbiome

MICROBIOME EXPOSURES



Review > Curr Environ Health Rep. 2024 Jun;11(2):168-183.
doi: 10.1007/s40572-024-00437-8. Epub 2024 Mar 8.

**Airborne Exposure to Pollutants and Mental Hea
A Review with Implications for United States Veterans**

Andrew J Hoisington [1 2 3 4], Kelly A Stearns-Yoder [5 6 7], Elizabeth J Kovacs [8 9], Teodor T Postolache [5 6 10 11], Lisa A Brenner [5 6 7 12]

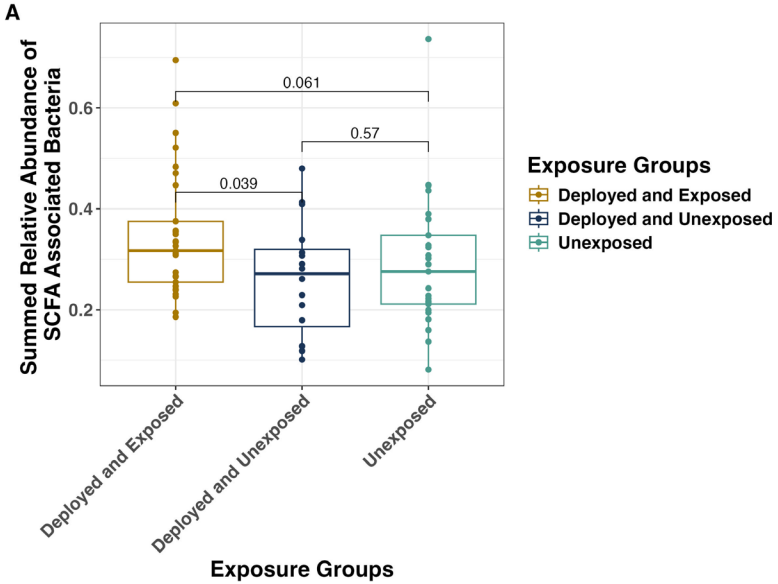
Military exposures associated with changes in microbiome

MICROBIOME EXPOSURES

Limited separation between in beta diversity, but **significant** difference (p=0.001) for **unweighted Unifrac distance**, but not weighted Unifrac (p=0.308)

Military exposures increased beneficial short-chain fatty acid species

MICROBIOME EXPOSURES



- **Beneficial SCFA** producing **microbes** were highest in **Veterans who deployed and were exposed**
- Exposure may have caused a biological response, but it is also possible there is a secondary health outcome we have not considered

Connecting the microbiome to the brain

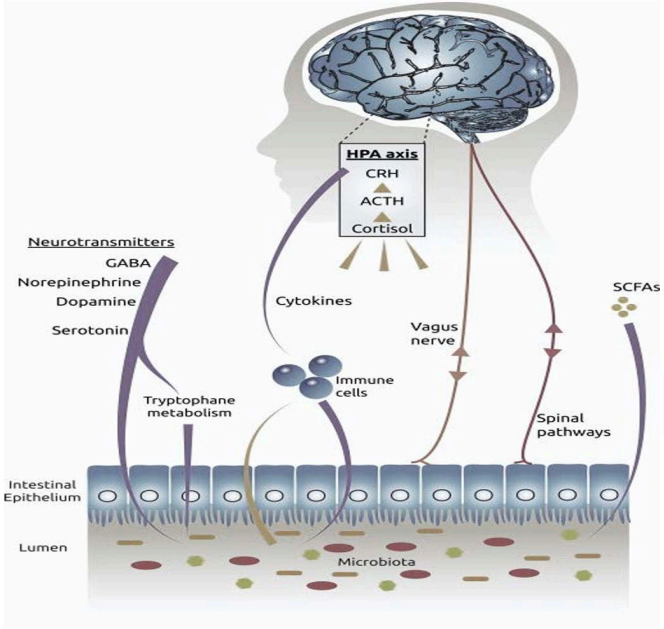
MICROBIOME AND BRAIN HEALTH





Connecting the microbiome to the brain cont.

MICROBIOME AND BRAIN HEALTH



Dinan, Timothy G., and John F. Cryan. "The microbiome-gut-brain axis in health and disease." *Gastroenterology Clinics* 46.1 (2017): 77-89.

JEM Article

Gut dysbiosis impairs recovery after spinal cord injury

Kristina A. Kigerl,[1] Jodie C.E. Hall,[1] Lingling Wang,[2] Xiaokui Mo,[3] Zhongtang Yu,[2] and Phillip G. Popovich[1]

BRAIN
ORIGINAL ARTICLE

Microbiota from Alzheimer's patients induce deficits in cognition and hippocampal neurogenesis

Stefanie Grabrucker,[1,2,†] Moira Marizzoni,[3,4,†] Edina Silajdžić,[5,†] Nicola Lopizzo,[3,6] Elisa Mombelli,[3] Sarah Nicolas,[1,2] Sebastian Dohm-Hansen,[1,2,7] Catia Scassellati,[3] Davide Vito Moretti,[8] Melissa Rosa,[3] Karina Hoffmann,[5] John F. Cryan,[1,2] Olivia F. O'Leary,[1,2] Jane A. English,[1,7] Aonghus Lavelle,[1,2] Cora O'Neill,[2,9] Sandrine Thuret,[5,†] Annamaria Cattaneo[3,6,†] and Yvonne M. Nolan[1,2,†]

mTBI ED Study: Overview

MICROBIOME AND BRAIN HEALTH

Primary Aim: Evaluate longitudinal change in microbiome for up to one year post mTBI and see if initial brain health is driver of potential microbiome adaptations.

Samples

- Blood – baseline and follow-up only
- Skin, oral, and gut microbiome – monthly throughout study

Surveys

- Structured clinical interviews – 48 hours post injury, 6-month, 12-month follow-up
- Mental Health Surveys – Monthly throughout study



Funding Agency

Assessment of brain health

MICROBIOME AND BRAIN HEALTH

RESEARCH ARTICLE

International Journal of Geriatric Psychiatry

Lifestyle for Brain Health (LIBRA): a new model for dementia prevention

Olga J. G. Schiepers[1], Sebastian Köhler[1], Kay Deckers[1], Kate Irving[2,†], Catherine A. O'Donnell[3], Marjan van den Akker[4], Frans R. J. Verhey[1], Stephanie J. B. Vos[1], Marjolein E. de Vugt[1] and Martin P. J. van Boxtel[1]

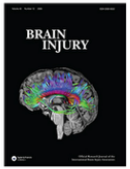
Table 1 Algorithm for calculating individual Lifestyle for Brain Health (LIBRA) score[a]

Modifiable risk factor	Relative risk (RR)	Ln (RR)/beta weight	Score	Available in MAAS
Low/moderate alcohol consumption	0.74	−0.30 (reference)	−1.0	+
Coronary heart disease	1.36	0.31	+1.0	+
Physical inactivity	1.39	0.33	+1.1	+
Renal dysfunction	1.39	0.33	+1.1	+
Diabetes	1.47	0.39	+1.3	+
High cholesterol	1.54	0.43	+1.4	+
Smoking	1.59	0.46	+1.5	+
Obesity	1.60	0.47	+1.6	+
Hypertension	1.61	0.48	+1.6	+
Mediterranean diet	0.60	0.51	−1.7[c]	–
Depression	1.85	0.62	+2.1	+
High cognitive activity	0.38	−0.97	−3.2	+
Low unsaturated fat intake[b]	—	—	–	–

Higher total score means greater risk for worse brain health

mTBI ED Study and Brain Health: LIBRA Model

MICROBIOME AND BRAIN HEALTH



Taylor & Francis

Brain Injury

ISSN: 0269-9052 (Print) 1362-301X (Online) Journal homepage: www.tandfonline.com/journals/ibij20

Feasibility and preliminary validation of the LIBRA model among those with mild TBI

Susan M. Mingils , Christopher E. Stamper , Molly E. Penzenik , Jason B. Gibbons , Matthew J. Igo , Kelly A. Stearns-Yoder , Kevin Beck , Christopher A. Lowry , Andrew J. Hoisington & Lisa A. Brenner

To cite this article: Susan M. Mingils , Christopher E. Stamper , Molly E. Penzenik , Jason B. Gibbons , Matthew J. Igo , Kelly A. Stearns-Yoder , Kevin Beck , Christopher A. Lowry , Andrew J. Hoisington & Lisa A. Brenner (29 Sep 2026): Feasibility and preliminary validation of the LIBRA model among those with mild TBI, Brain Injury, DOI: 10.1080/02699052.2026.2728032

To link to this article: https://doi.org/10.1080/02699052.2026.2728032

Table 1. LIBRA score construction.

LIBRA factor (Lifetime or Current)	Weight	Deckers et al. (10) Population: Midlife and late-life CAIDE study	Brett et al. (2022) Population: Former NFL players	Longitudinal Acute mTBI and Cross-sectional Post-acute mTBI datasets*
Hypertension (Lifetime)	+1.6	SBP ≥140 mmHg or DBP ≥90 mmHg	Self-reported history of hypertension diagnosed by a physician or other healthcare provider	SBP ≥140 mmHg or DBP ≥90 in the EMR, or self-reported lifetime history of hypertension or high blood pressure on NHIS
Obesity (Current)	+1.6	BMI ≥30 kg/m^2	Self-reported history of obesity diagnosed by a physician or other healthcare provider	Current BMI ≥30 kg/m^2 from study data or EMR
High cholesterol (Lifetime)	+1.4	Serum total cholesterol ≥6.5 mmol/L with correction based on different methods of collection	Self-reported history of high cholesterol diagnosed by a physician or other healthcare provider	Self-reported lifetime history of high cholesterol on NHIS
Diabetes (Lifetime)	+1.3	Self-reported history of diabetes diagnosed by a physician OR diagnosis in medical record prior to date of LIBRA score	Self-reported history of diabetes diagnosis	Self-reported lifetime history of diabetes on NHIS
Coronary heart disease (Lifetime)	+1.0	Self-reported history of myocardial infarction or angina diagnosed by a physician OR diagnosis in medical record prior to date of LIBRA score	Self-reported history of coronary heart disease diagnosed by a physician or other healthcare provider	Self-reported lifetime history of heart condition or disease on NHIS
Chronic kidney disease (Lifetime)	+1.1	Diagnosis in medical record prior to date of LIBRA score; self-reports or creatinine measures not available	Self-reported history of chronic kidney disease diagnosed by a physician or other healthcare provider	ICD-9 or ICD-10 code for chronic kidney disease diagnosis present in EMR lifetime history
Physical inactivity (Current)	+1.1	Self-reported participation in leisure-time physical activity that lasts at least 20–30 minutes and causes breathlessness and sweating once a week or less	Self-reported <30 min, 5 days/week of moderate intensity aerobic exercise or resistance training	Self-reported <3 days/week of 20 minutes of vigorous activity or <5 days/week of 30 minutes of moderate activity in the past week on IPAQ-SF
Low/ moderate alcohol use (Current)	−1.0	Self-reported drinking less than once a month on average	Self-reported drinking 2 or less drinks per day on average	Longitudinal Dataset: Self-reported drinking 1–2 drinks on a typical day when drinking or never drinking on AUDIT (acute mTBI); Cross-sectional Dataset: No current alcohol misuse on SCID-5 or no ICD-10 for alcohol misuse ±1 year ago (historical mTBI);
Ever-smoker (Lifetime)	+1.5	'Yes' to question 'Have you ever smoked during your life?'	Self-reported history of ever smoking	'Yes' to question 'Do you currently smoke?' on FND or reported 'current' or 'ever' smoking in EMR (historical mTBI); 'current,' 'ever,' 'former,' or 'quit' is listed under tobacco use history in EMR
Depression (Current)	+2.1	'Somewhat agree' or 'absolutely agree' to two statements measuring hopelessness	Self-reported history of depression diagnosed by a physician or other healthcare provider	PHQ-9 score of ≥10 indicating current moderate- severe depression
High-quality diet (Current)	−1.7	CAIDE Healthy Diet Index Range of >8 points, only available in a limited number of participants in midlife cohort and data not available for late-life cohort	Rapid Eating Assessment for Participants – Shortened Version (REAPS), diet quality score above 22, the median split of the current sample	Upper quartile for self-reported intake of whole grains and fruits/vegetables and lower quartile for self-reported intake of sugar and red/processed meat in the past month on DSQ
High cognitive activity (Current)	−3.2	Not included (data not available)	Score of 1 SD above the normative mean on The Patient Reported Outcomes Measurement Information System (PROMIS) Ability to Participate in Social Roles and Activities scale	Not included (data not available)
Mild Traumatic Brain Injury (Lifetime)	+1.9	Not included	≥6 prior concussions	Not included**

Criteria for LIBRA factors in a study of LIBRA with the general population (10), a study of LIBRA applied to population with history of mTBI (13), and both datasets analyzed in this manuscript. Abbreviations: AUDIT, Alcohol Use Disorders Identification Test (14); BMI, body mass index; BP, blood pressure; CAIDE, Cardiovascular Risk Factors, Aging and Dementia; DBP, diastolic blood pressure, DSQ, Dietary Screener Questionnaire (15); EMR, electronic medical record; FND, Fagerström Test for Nicotine Dependence (16); ICD-9/10, International Classification of Diseases 9 and 10; IPAQ-SF, International Physical Activity Questionnaire – Short Form (17); LIBRA, LIfestyle for BRAin health; mTBI, mild traumatic brain injury; NFL, National Football League; NHIS, National Health Interview Survey of Chronic Conditions (18); PHQ-9, Patient Health Questionnaire-9 (19); PROMIS, Patient Reported Outcomes Measurement Information System (20); SBP, systolic blood pressure; REAPS, Rapid Eating Assessment for Participants – Shortened Version; SCID-5, Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) Axis I Disorders (21); SD, standard deviation. *Measures used to create factor scores were the same for both datasets, with the exception of alcohol use. Additional information regarding score construction is available in Supplemental Materials. **Based on relatively low number of TBIs in our cohort this was not included; however, subsequent analyses were conducted regarding lifetime TBI history.

mTBI ED Study and Brain Health: Demographics

MICROBIOME AND BRAIN HEALTH

Table 2. Participant demographics – longitudinal and cross-sectional datasets.

	Civilians with acute mTBI (*N* = 17; Longitudinal Dataset)	Veterans with historical mTBI (*N* = 92; Cross-sectional Dataset)
Demographics	M ± SD (Min–Max); *n* (%)	M ± SD (Min–Max); *n* (%)
Age (years)	33.12 ± 11.78 (20–57)	49.27 ± 13.52 (24–74)
Sex		
Male	11 (65%)	92 (100%)
Female	6 (35%)	0 (0.0%)
Race		
Black	2 (13%)	13 (14%)
Other*	6 (38%)	13 (14%)
White	8 (50%)	66 (72%)
(Missing)	1	
Ethnicity		
Hispanic	5 (33%)	16 (17%)
Not Hispanic	10 (67%)	76 (83%)
(Missing)	2	
Education		
High school or equivalent	2 (13%)	7 (7.6%)
Some college, no degree	4 (27%)	26 (28%)
Associate's degree	5 (33%)	19 (21%)
Bachelor's degree	3 (20%)	25 (27%)
Master's degree	1 (6.7%)	12 (13%)
Doctoral degree	0 (0.0%)	3 (3.3%)
(Missing)	2	
Number of mTBIs	1.76 ± 1.20 (1-5)**	2.09 ± 1.27 (1-7)

*Other indicates Native American/Alaskan Native, Asian, Pacific Islander, or Multiracial; **Includes index TBI.

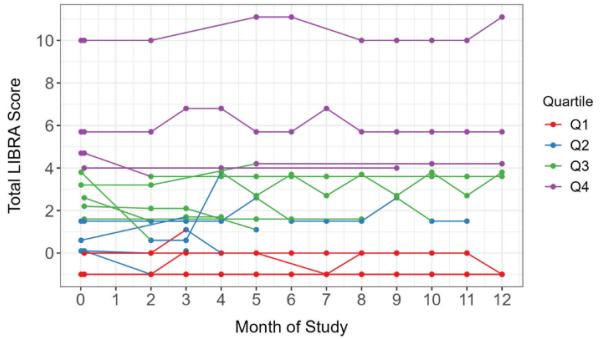


Figure 1. Change in total LIBRA score across time among civilians with acute mTBI. A line plot showing total LIBRA scores for each participant in the longitudinal dataset from the index mild traumatic brain injury (mTBI; timepoint 0) and each month following up to one year after post index mTBI. Line color indicates the quartile across all participants and time points. LIBRA score: Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile.

mTBI ED Study and Brain Health: LIBRA Factor Criteria

MICROBIOME AND BRAIN HEALTH

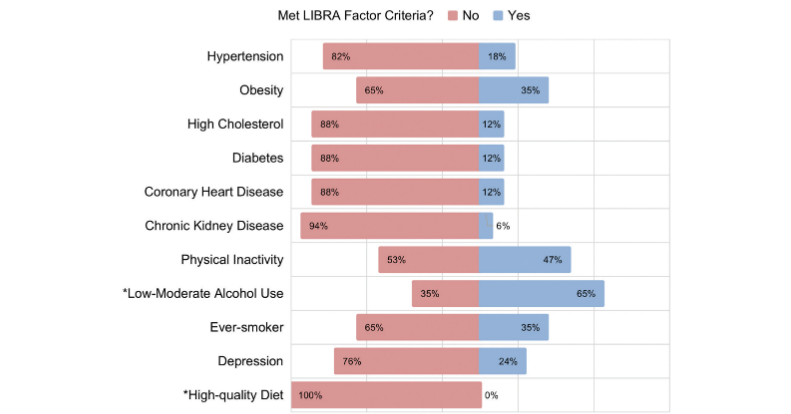


Figure 2. Prevalence of each LIBRA factor among civilians with acute mTBI. Percentages are based on a single timepoint closest to the emergency department visit. The left side shows the percentage of participants that did not meet criteria for a given LIBRA factor. The right side shows the percentage of participants that met criteria for that factor. An asterisk (*) indicates a protective factor, where meeting criteria was considered beneficial for brain health. Meeting criteria for all other factors was indicative of poorer brain health.

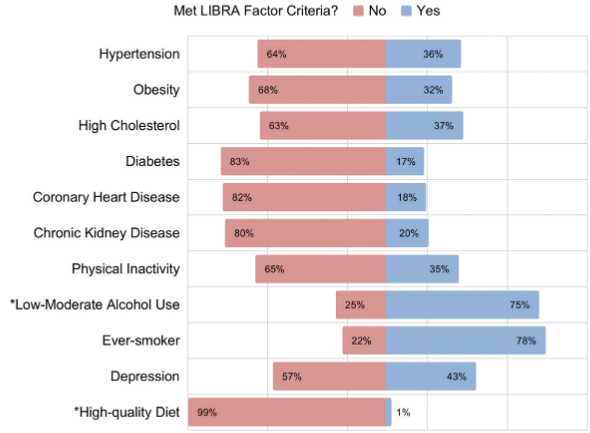


Figure 3. Prevalence of each LIBRA factor among Veterans with historical mTBI. The left side shows the percentage of participants that did not meet criteria for a given LIBRA factor. The right side shows the percentage of participants that met criteria for that factor. An asterisk (*) indicates a protective factor, where meeting criteria was considered beneficial for brain health. Meeting criteria for all other factors was indicative of poorer brain health.

mTBI ED Study and Brain Health

MICROBIOME AND BRAIN HEALTH

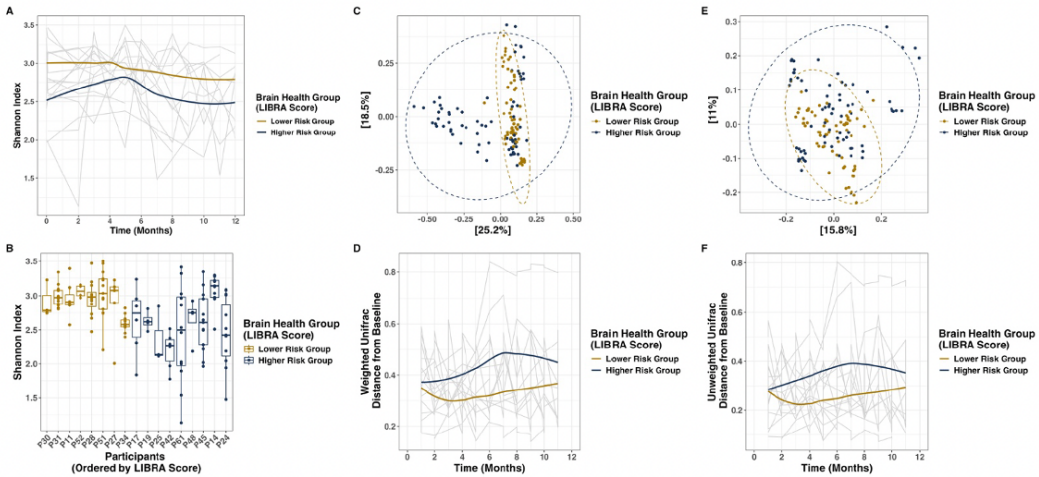


Figure 1. Alpha and beta diversity measurements for all samples, higher brain health risk group (dark blue) and lower brain health risk group (gold) are denoted. Alpha diversity with Shannon Diversity Index as A) continuous value and B) boxplots for each participant, ordered by brain health risk score. C) Principal coordinates analysis (PCoA) plot of beta diversity from Weighted Unifrac measure, D) change from baseline value for Weighted Unifrac Distance, E) PCoA of beta diversity from Unweighted Unifrac measure, F) change from baseline value for Unweighted Unifrac Distance.

mTBI ED Study and Brain Health Cont.

MICROBIOME AND BRAIN HEALTH

- Fifteen taxa at the species level showed a significant differential expression for abundance based on the interaction between brain health risk and time

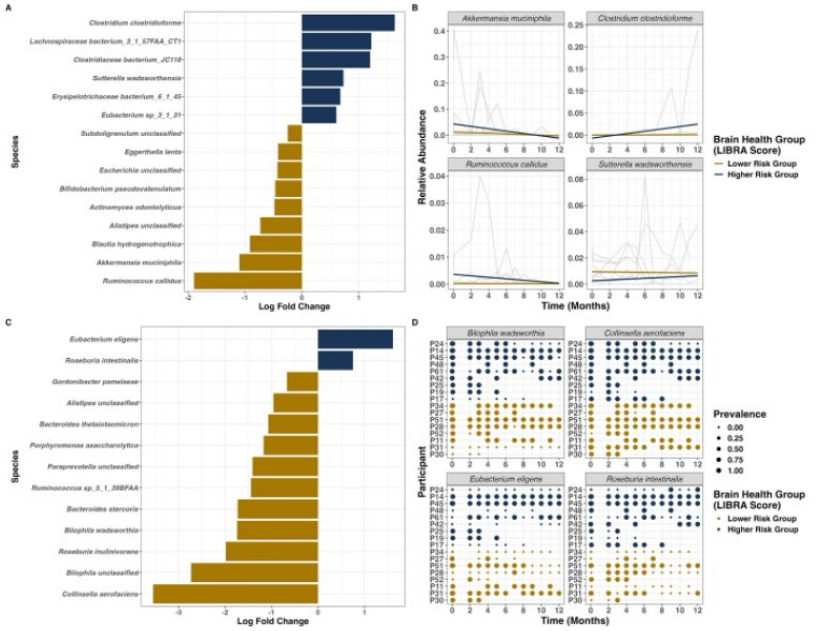
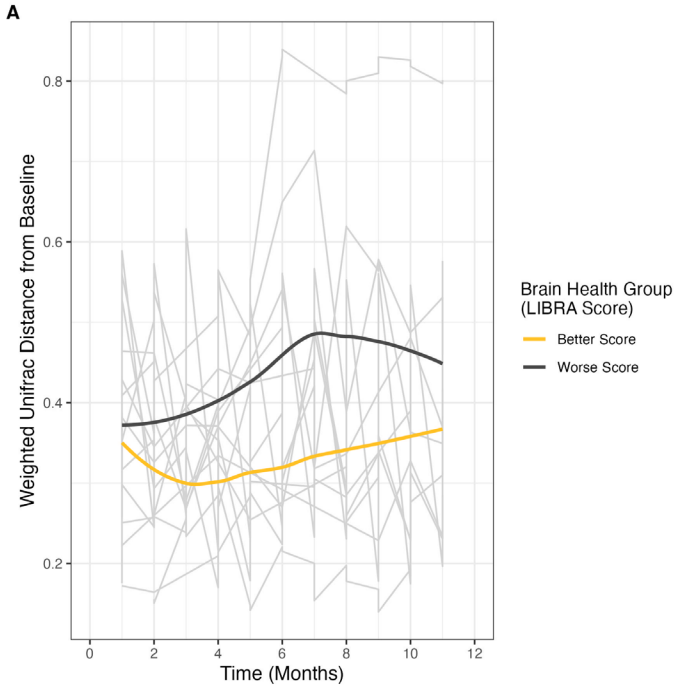
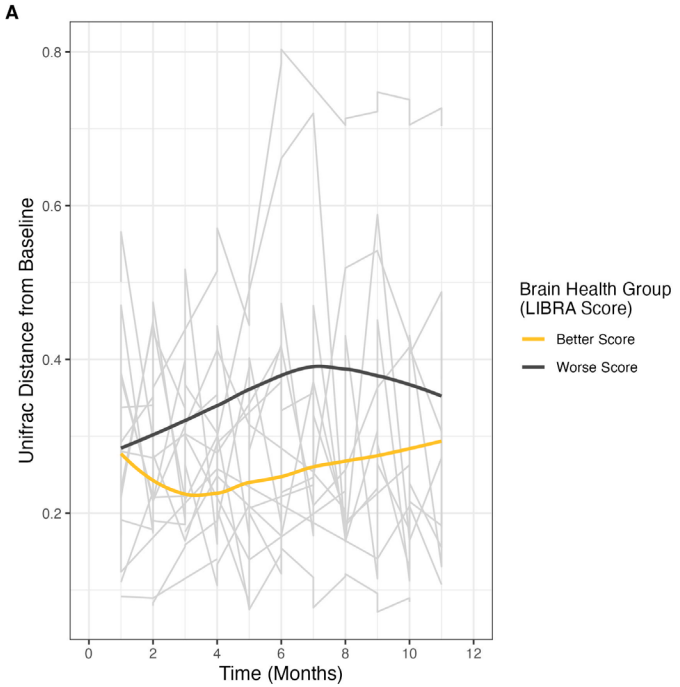


Figure 2. A) Log2 fold changes (LFC) for species that were significantly (FDR <0.3) associated with an increase (dark blue) or decrease (gold) in abundance from change in brain health risk score by time interaction and B) change in abundance of select relevant organism showing trends in higher risk (dark blue) and lower risk (gold) brain health groups. C) Prevalence LFC for species that were significantly (FDR <0.3) associated with an increase (dark blue) or decrease (gold) in abundance from change in brain health risk score by time interaction and D) presence (large dot) or absence (small dot) for select relevant organisms from significant results.

mTBI ED Study: Microbiome more resilient after mTBI for those with better brain health

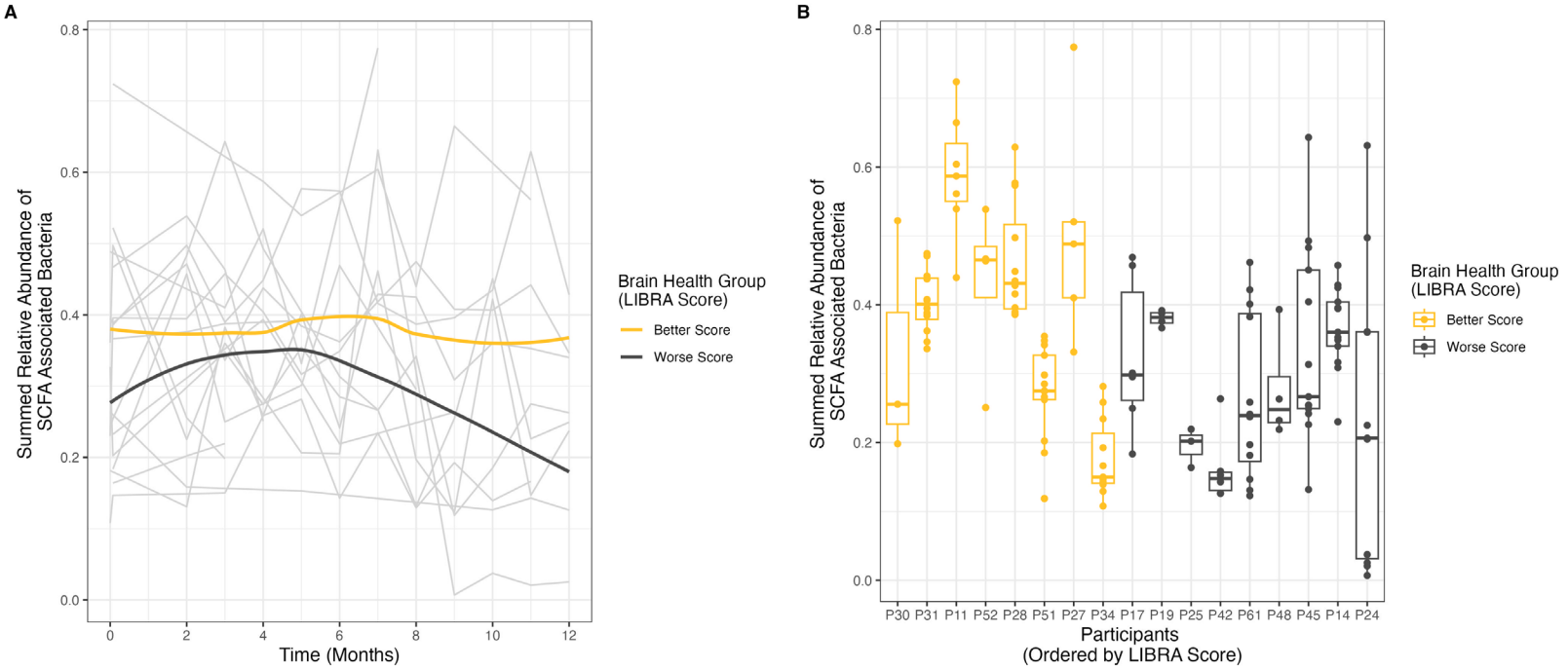
MICROBIOME AND BRAIN HEALTH





mTBI ED Study: Microbiome had more beneficial SCFA for those with better brain health

MICROBIOME AND BRAIN HEALTH



mTBI ED Study: mTBI, future conditions, and the microbiome

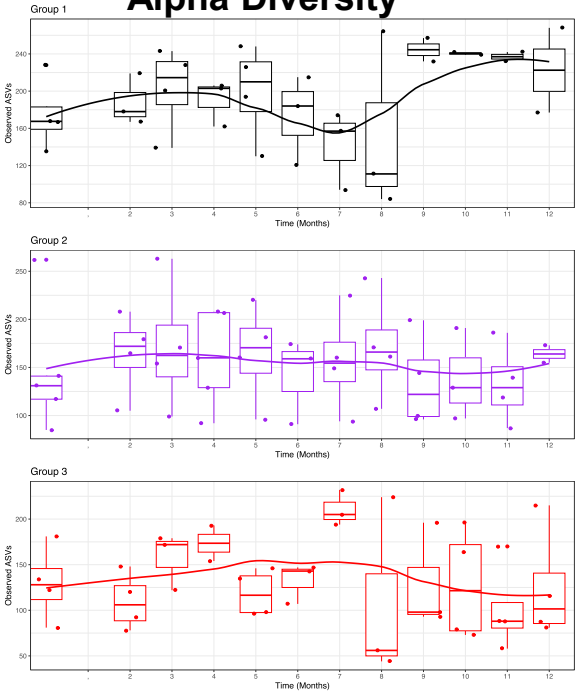
MICROBIOME AND BRAIN HEALTH

Group 1
No psychological disorders

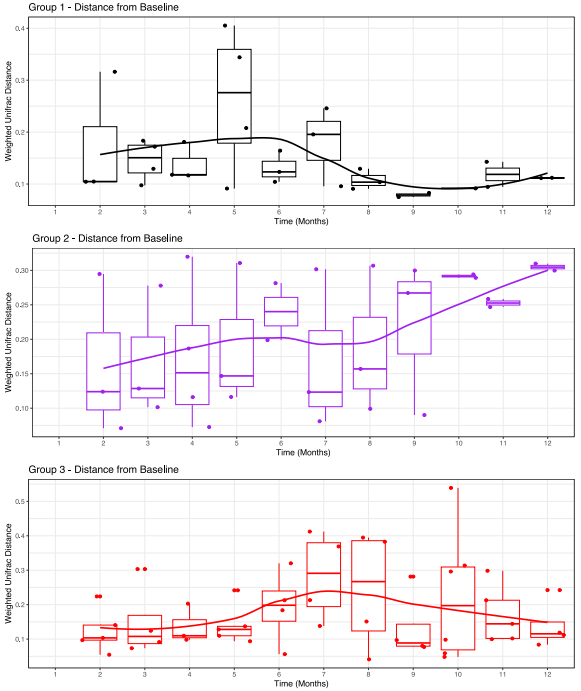
Group 2
Past psychological disorders

Group 3
New/recurrent psychological disorders

Alpha Diversity



Beta Diversity



mTBI ED Study: mTBI, alcohol, and the microbiome

MICROBIOME AND BRAIN HEALTH

mTBI US-VMP Study: Overview

The goal of this study was to assess The LIfestyle for BRAin (LIBRA) scores, a measure of brain health, and their relationship with gut microbiome diversity, taxonomic abundance, and metabolic pathways.

- 92 participants were included in the present study with LIBRA data and preserved microbiome samples from one timepoint, a history of at least one mTBI, and were male to directly correspond to previous studies of NFL players
- Shotgun whole genome sequencing

mTBI US-VMP Study and Brain Health

MICROBIOME AND BRAIN HEALTH

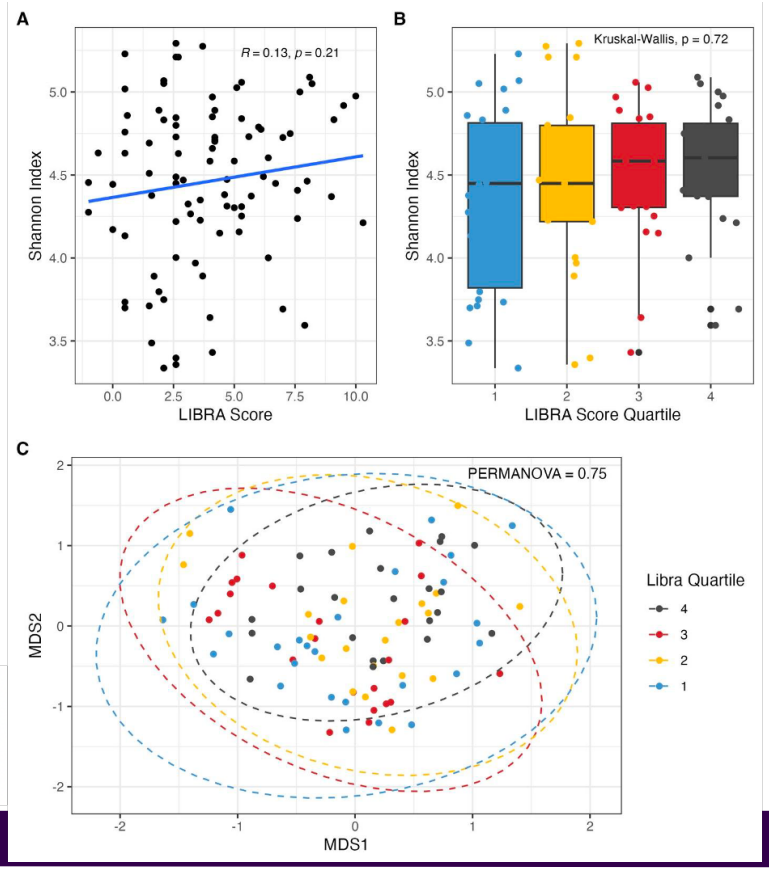
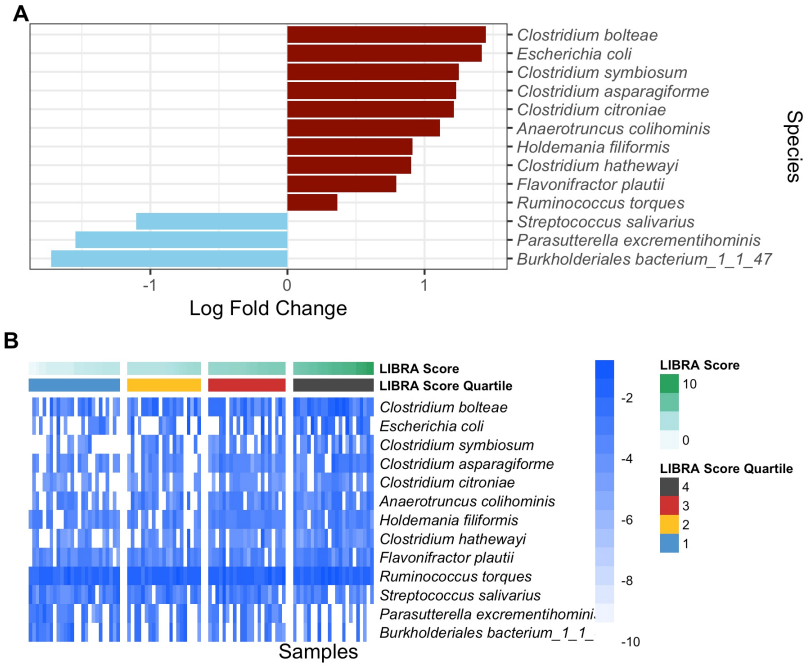


Figure 1. Alpha diversity with Shannon Diversity Index as compared to A) continuous LIBRA and B) quartiles of LIBRA score. C) PCA of beta diversity from Bray-Curtis measure, colored by LIBRA quartiles. Shannon diversity (richness and evenness) was the alpha diversity metric assessed. Lower LIBRA scores are associated with healthier brain health.

mTBI US-VMP brain health and microbiome

MICROBIOME AND BRAIN HEALTH



- Phylum-level shifts in Proteobacteria (*Escherichia coli)* were associated with the LIBRA score. (Figure2B).
- Proteobacteria overrepresentation has been widely linked to systemic inflammation and gut microbiome dysbiosis.

mTBI US-VMP brain health and microbiome cont.

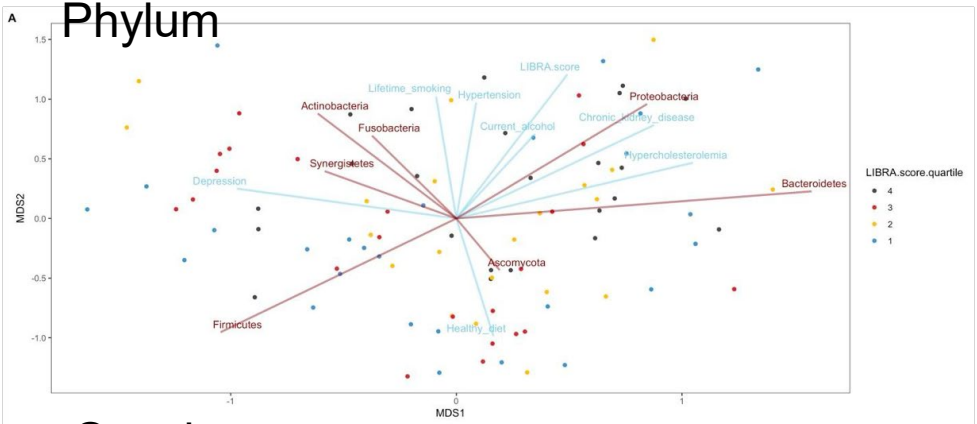
MICROBIOME AND BRAIN HEALTH

A healthy diet was more associated with Ascomycota (**Figure 3A**). One protective behavior (healthy diet) and the absence of two risk behaviors, (physical inactivity, and smoking status) were closely related to the organisms in the genera *Faecalibacterium* and *Coprobacter*, while detrimental factors (chronic kidney disease, diabetes, and high total LIBRA score) were associated with several *Clostridium spp* and organisms from the *Oscillibacter* and *Anaerotruncus* genera. Interestingly, depression was found to be separate from the other detrimental factors and was associated with bacteria from four genera to include *Prevotella* and *Subdoligranulum* (**Figure 3B**).

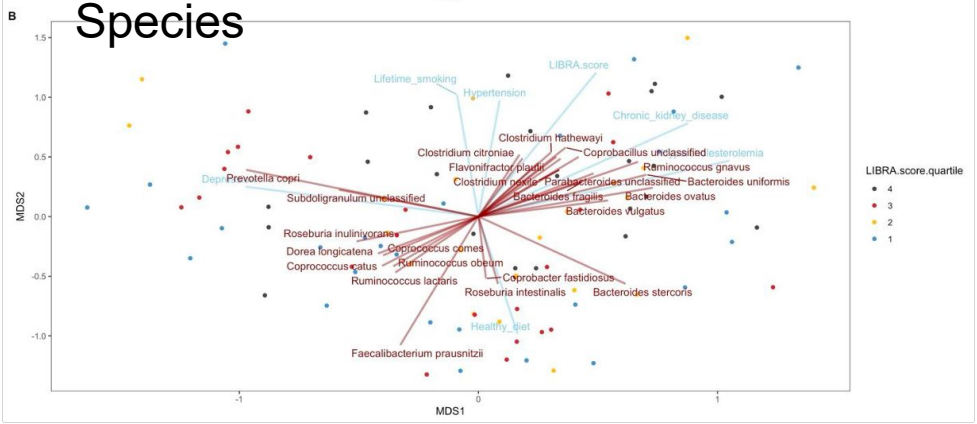
Arrows pointing in similar directions indicate positive associations between cohort characteristics (light blue) and microbial taxa (dark red), whereas arrows pointing in opposite directions indicate inverse associations. For example, the LIBRA score and Proteobacteria arrows point in similar directions, while the LIBRA score arrow points opposite to the arrows for non-smoking and high physical activity.

Lower LIBRA scores (blue quartile) are associated with healthier lifestyles and better brain health. Higher LIBRA scores (black quartile) are associated with poorer lifestyles and brain health.

Phylum



Species



Ways to alter the gut microbiome

INTERVENTIONS

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Article | Published: 11 January 2021

Microbiome connections with host metabolism and habitual diet from 1,098 deeply phenotyped individuals

Francesco Asnicar, Sarah E. Berry, Ana M. Valdes, Long H. Nguyen, Gianmarco Piccinno, David A. Drew, Emily Leeming, Rachel Gibson, Caroline Le Roy, Haya Al Khatib, Lucy Francis, Mohsen Mazidi, Olatz Mompeo, Mireia Valles-Colomer, Adrian Tett, Francesco Beghini, Léonard Dubois, Davide Bazzani, Andrew Maltez Thomas, Chloe Mirzayi, Asya Khleborodova, Sehyun Oh, Rachel Hine, Christopher Bonnett, ... Nicola Segata + Show authors

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Article | Open Access | Published: 27 October 2020

The trans-kingdom battle between donor and recipient gut microbiome influences fecal microbiota transplantation outcome

Negin Kazemian, Milad Ramezankhani, Aarushi Sehgal, Faizan Muhammad Khalid, Amir Hossein Zeinali Kalkhoran, Apurva Narayan, Gane Ka-Shu Wong, Dina Kao & Sepideh Pakpour

Scientific Reports **10**, Article number: 18349 (2020) | Cite this article

3680 Accesses | **14** Citations | **71** Altmetric | Metrics

Brain, Behavior, & Immunity - Health 18 (2021) 100346

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journal homepage: www.editorialmanager.com/bbih/default.aspx

Full Length Article

Characterization of the gut microbiota among Veterans with unique military-related exposures and high prevalence of chronic health conditions: A United States-Veteran Microbiome Project (US-VMP) study

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[c] Military and Veteran Microbiome: Consortium for Research and Education, Aurora, CO, USA
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[k] Center for Neuroscience, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
[l] Department of Neurology, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

Table 3
The subsets of variables demonstrating the strongest correlation with the gut microbial community composition.

Distance metric	Exposure	Variable	*P*
Unweighted UniFrac	Demographics	Age	0.014
	Health conditions/ metrics	PVD	0.018
		Bipolar disorders	0.038
		Stimulant use disorder	0.046
		Gastroenteritis	0.050
		Severe depressive symptoms (BDI)	0.050
	Medication class	Beta blockers	0.008
		SNRI antidepressants	0.014
		Diabetes medications	0.028
Weighted UniFrac	Demographics	Sex	0.002
		Race	0.012
	Health conditions/ metrics	Stimulant use disorder	0.022
		Bipolar disorders	0.028
		Opioid use disorder	0.046
	Medication class	Other GI medications	0.010
		PPIs	0.050
	Specific medications	Omeprazole	0.032

Footnote. Microbial composition as measured by unweighted and weighted UniFrac distance metrics. The exposures were grouped into four categories: 1) demographics; 2) health conditions and metrics; 3) medication classes; and 4) specific medications. *P*-values were generated by a stepwise contrained ordination model. Abbreviations: BDI, Beck Depression Inventory; GI, gastrointestinal; PPI, proton pump inhibitor; PVD; peripheral vascular disease; SNRI, serotonin and norepinephrine reuptake inhibitor.

Probiotics and Inflammation

INTERVENTIONS

frontiers in Immunology

RE
published: 26 February
doi: 10.3389/fimmu.2021.57

Anti-Inflammatory and Immunomodulatory Effects of Probiotics in Gut Inflammation: A Door to the Body

*Fernanda Cristofori [1], Vanessa Nadia Dargenio [1], Costantino Dargenio [1], Vito Leonardo Miniello [1], Michele Barone [2] and Ruggiero Francavilla [1]**

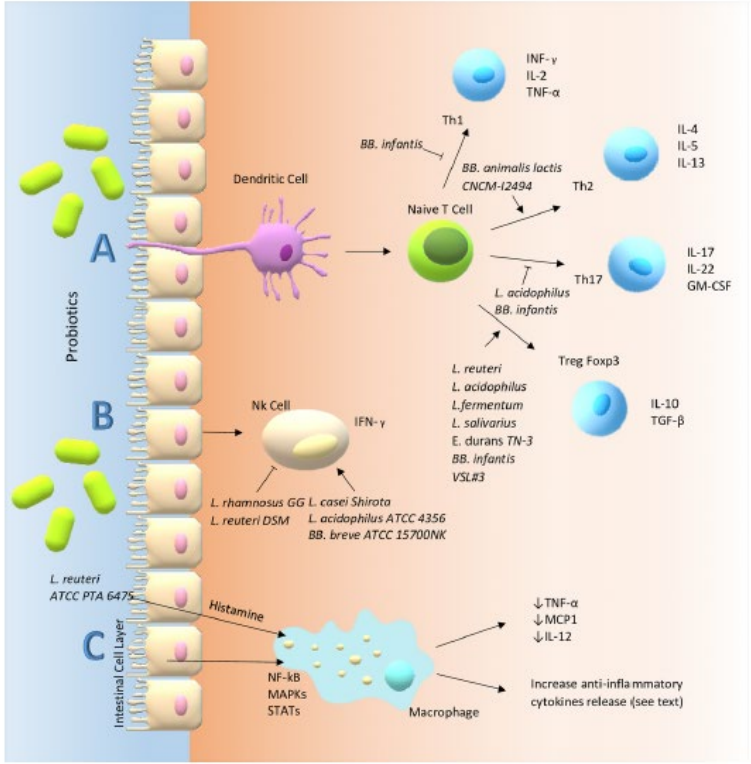


FIGURE 1 | Main probiotic immune-modulatory pathways in the gut. **(A)** T cells are considered the masters of inflammation in that they can differentiate into different

Probiotics Mechanisms

INTERVENTIONS

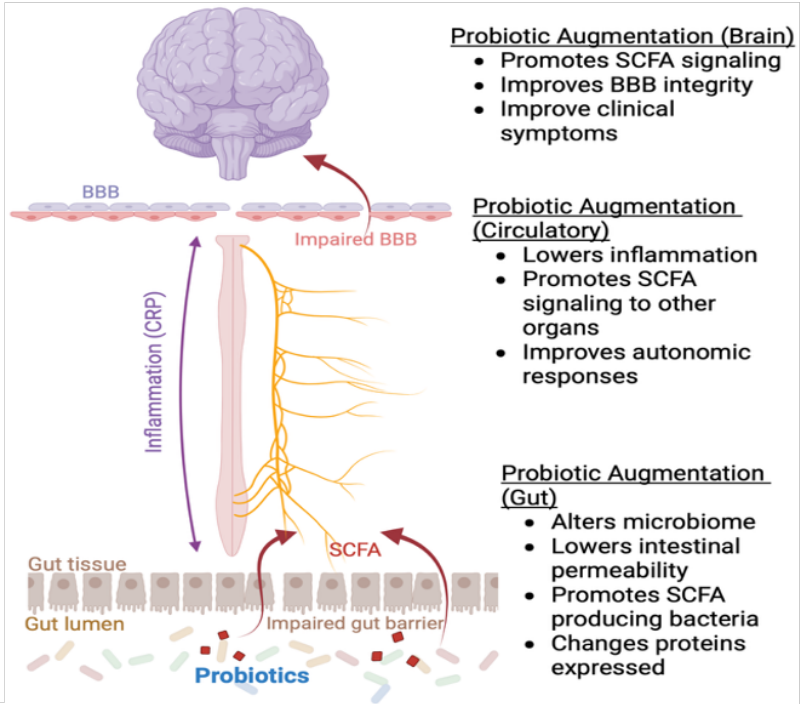


Figure 1. Mechanistic Model. Abbreviations: BBB, Blood Brain Barrier; CRP, C-Reactive Protein; IP, Intestinal Permeability; SCFA, Short-Chain Fatty Acids.

Past Findings - Lactobacillus reuteri DSM 17938

INTERVENTIONS

TABLE 3 | Mean change in plasma concentrations of C-reactive protein (CRP), plasma concentrations of cytokines and plasma concentrations of biomarkers of intestinal permeability from Visit 2 to Visit 3.

	Placebo		Probiotic		*p*-value
	N	**Mean (SD) and Median (range)[a]**	***N***	**Mean (SD) and Median (range)[a]**	
Biomarkers of Inflammation					
CRP (mg/L)	14	0.113 (1.2) 0.09 (−2.3, 2.4)	10	−0.625 (1.1) −0.565 (−2.3, 1.5)	0.056
IFNγ (pg/ml)	14	0.36 (1.2) 0.04 (−1.4, 3.9)	9	−0.33 (1.2) −0.04 (−3.1, 1.1)	0.22
IL1α (pg/ml)	14	0.98 (4.0) 0.28 (−4.4, 12.7)	9	−1.6 (11.2) 1.64 (−30.4, 9.6)	0.45
IL1β (pg/ml)	14	0.70 (2.7) 0.04 (−3.5, 9.1)	9	−0.25 (2.5) −0.03 (−6.1, 3.3)	0.37
IL2 (pg/ml)	14	0.02 (0.34) −0.02 (−0.60, 0.81)	9	−0.12 (1.3) 0 (−3.4, 1.3)	0.51
IL6 (pg/ml)	14	0.22 (2.4) −0.10 (−5.1, 4.0)	9	−0.07 (7.7) −0.24 (−13.5, 16.3)	0.64
IL8 (pg/ml)	14	−4.8 (11.2) −0.49 (−39.2, 3.6)	9	1.4 (5.9) 1.1 (−8.8, 11.4)	0.12
IL10 (pg/ml)	14	0.15 (0.85) 0.09 (−1.4, 2.2)	9	−0.23 (2.0) −0.23 (−3.0, 2.4)	0.72
IL12p70 (pg/ml)	14	−1.6 (9.3) −0.41 (−28.5, 11.2)	9	−10.1 (46.2) −0.61 (−129, 34.3)	0.89
IL-6:IL-10 ratio	14	−0.08 (1.0) −0.004 (−3.2, 1.6)	9	−0.003 (0.97) −0.12 (−0.7, 1.6)	0.52
TNFα (pg/ml)	14	−0.62 (1.4) −0.27 (−3.7, 1.3)	9	−2.1 (8.2) 0 (−23.7, 3.2)	0.26
Intestinal Permeability					
DAO (ng/ml)	10	−0.11 (0.24) −0.08 (−0.55, 0.29)	8	0.03 (0.12) 0.08 (−0.12, 0.16)	0.17
IFABP (pg/ml)	12	−0.09 (0.45) −0.17 (−1.0, 0.72)	10	−0.04 (0.16) −0.03 (−0.35, 0.21)	0.54

[a]*Negative numbers indicate a decrease from Visit 2 to Visit 3. Wilcoxon rank-sum test was used to compare the change from Visit 2 to Visit 3 between the Placebo and Probiotic groups. CRP, C-reactive protein; DAO, D-amino acid oxidase; IFABP, intestinal fatty acid binding protein; IFNγ, interferon gamma; IL, interleukin; mg/L, milligrams/liter; ng/ml, nanograms/ milliliter; pg/ml, picograms/ milliliter; TNFα, tumor necrosis factor alpha.*

C-Reactive Protein (CRP)

frontiers in Neurology

CLINICAL TRIAL
published: 20 October 2020
doi: 10.3389/fneur.2020.01015

Evaluation of an Immunomodulatory Probiotic Intervention for Veterans With Co-occurring Mild Traumatic Brain Injury and Posttraumatic Stress Disorder: A Pilot Study

Lisa A. Brenner[1,2,3,4], Jeri E. Forster[1,2,4], Kelly A. Stearns-Yoder[1,2,4], Christopher E. Stamper[1,2,4], Andrew J. Hoisington[1,2,4,5], Diana P. Brostow[1,2,4], Meredith Mealer[1,2], Hal S. Wortzel[1,3], Teodor T. Postolache[1,4,6,7] and Christopher A. Lowry[1,2,4,8,9,10]*

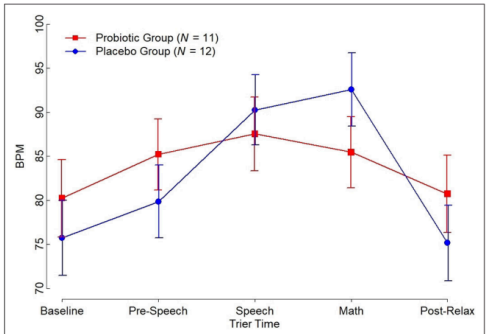
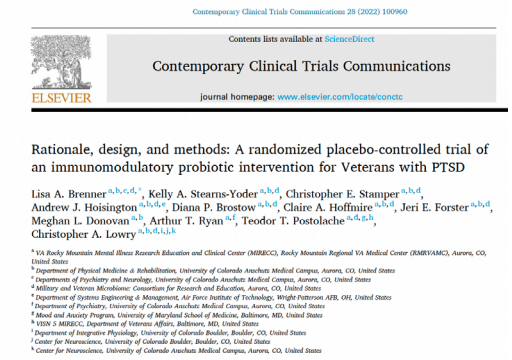


FIGURE 2 | Beats per Minute (BPM) with Standard Error Bars by Trier Social Stress Test.

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Trial Rationale and Design - Lactobacillus rhamnosus GG ATCC 53103

INTERVENTIONS



Contemporary Clinical Trials Communications 28 (2022) 100960

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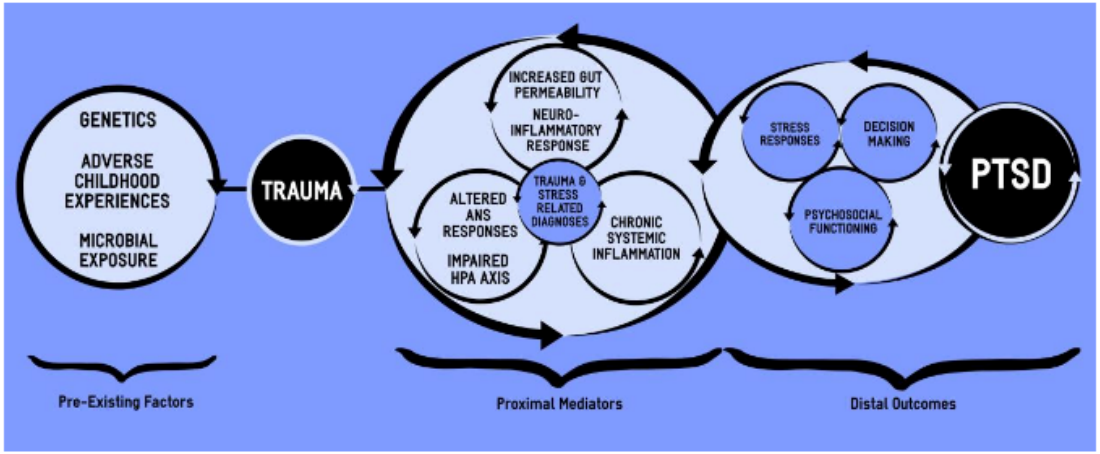
Contemporary Clinical Trials Communications

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

Rationale, design, and methods: A randomized placebo-controlled trial of an immunomodulatory probiotic intervention for Veterans with PTSD

Lisa A. Brenner [a,b,c,d,*], Kelly A. Stearns-Yoder [a,b,d], Christopher E. Stamper [a,b,d], Andrew J. Hoisington [a,b,d,e], Diana P. Brostow [a,b,d], Claire A. Hoffmire [a,b,d], Jeri E. Forster [a,b,d], Meghan L. Donovan [a,b], Arthur T. Ryan [a,f], Teodor T. Postolache [a,d,g,h], Christopher A. Lowry [a,b,d,i,j,k]

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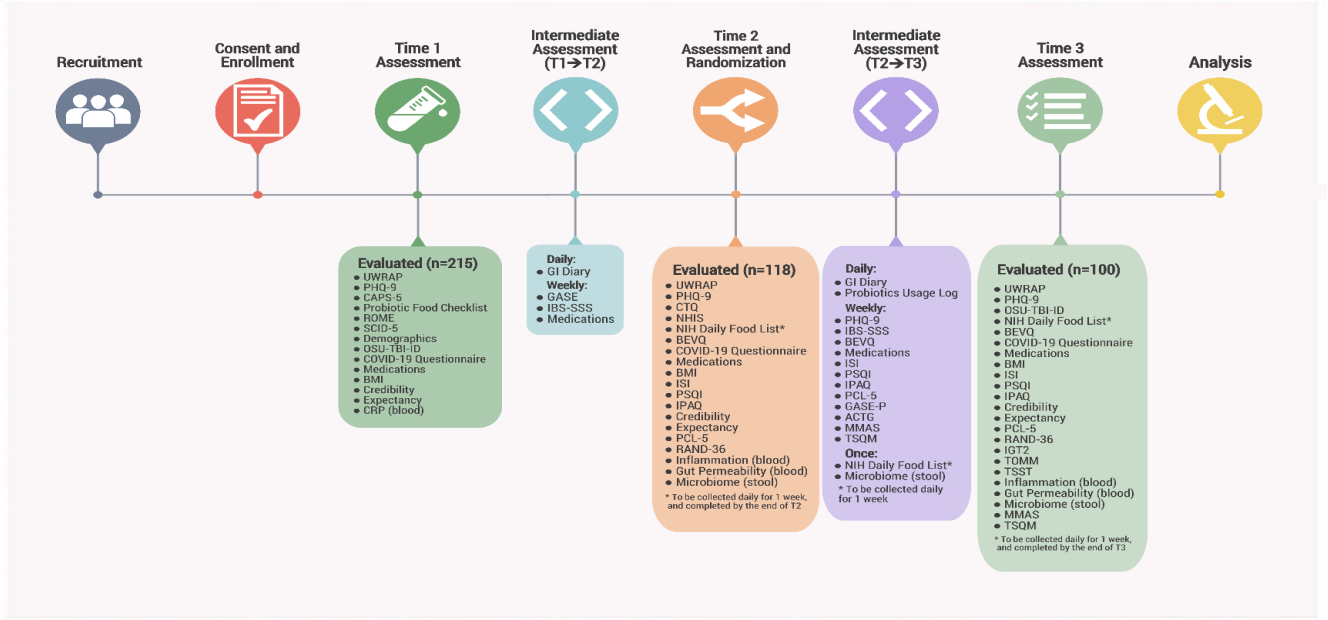
National Center for Complementary and Integrative Health

R01AT010005

ClinicalTrials.gov Identifier: NCT04150380

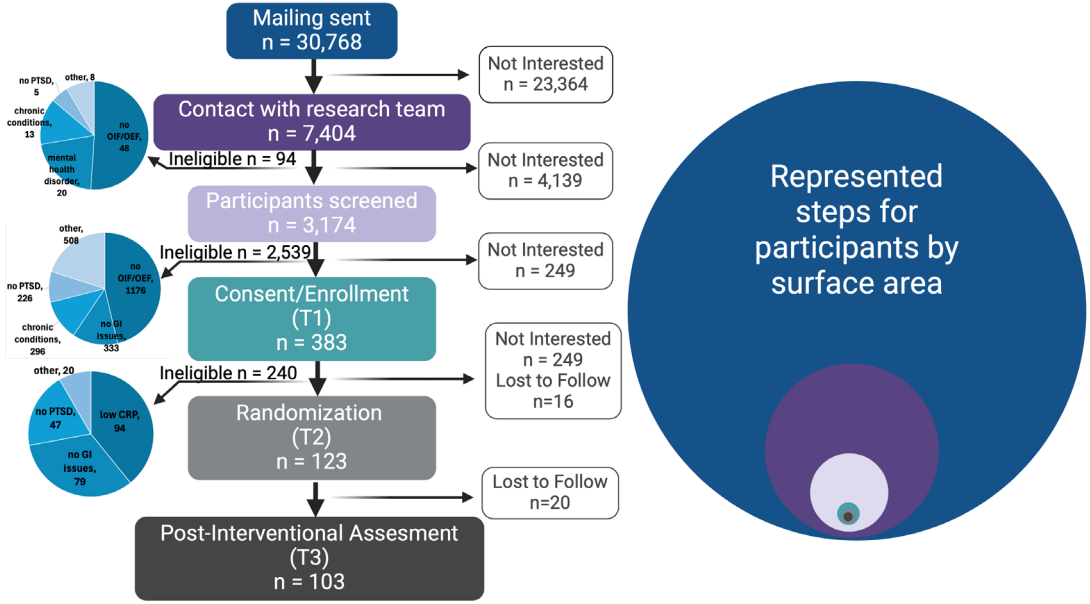
LGG Trial Rationale and Design - Participant Flow

INTERVENTIONS



LGG Challenges in Finding Right Participants

INTERVENTIONS

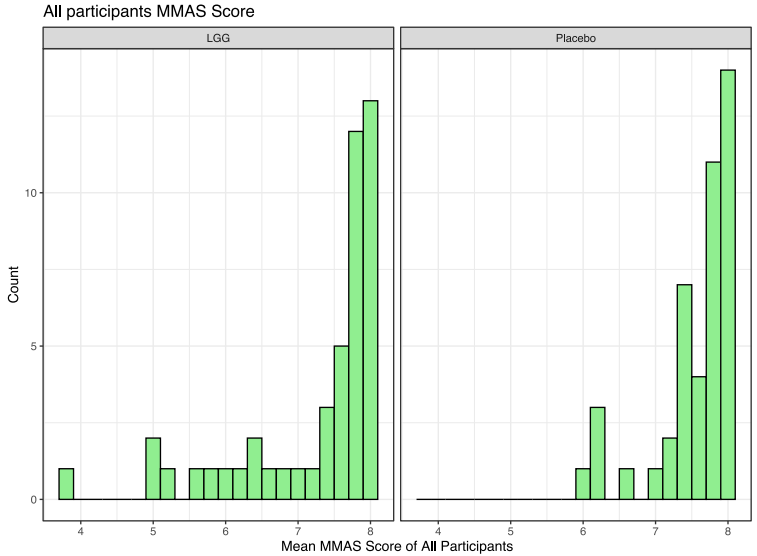


LGG Adherence and Side Effects

INTERVENTIONS

Adherence: Morisky Medication Adherence Scale (MMAS)

- Mean LGG = 7.3, Placebo = 7.6
- Total 6 participants under 6
  - Low adherence cutpoint, All LGG



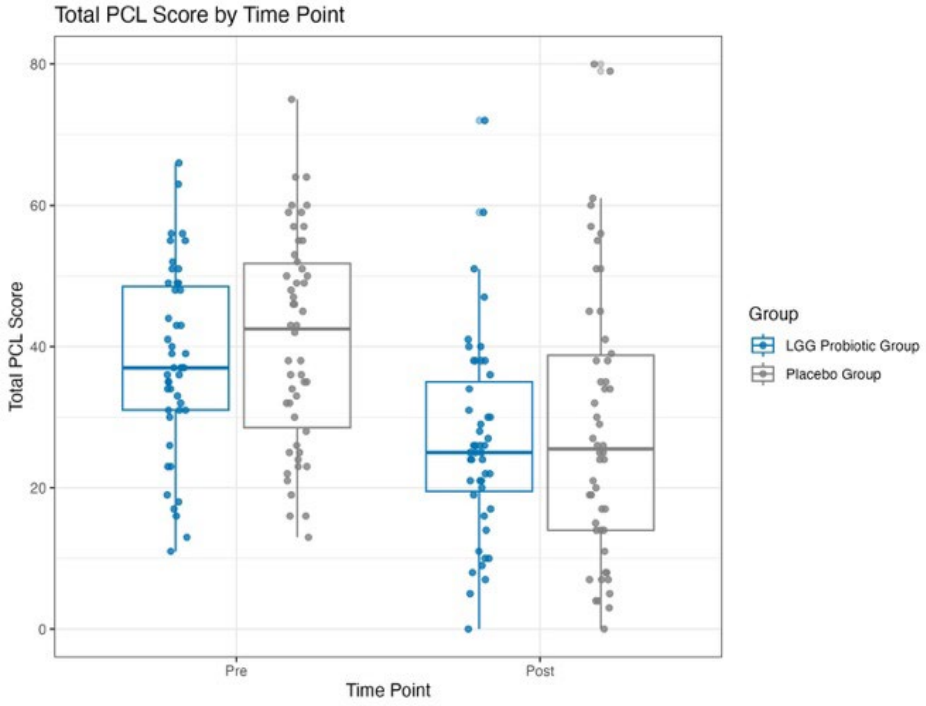
Side Effects: GASE-P

Adverse events defined as at least one GASE-P symptom was rated severe (3) and attributed to the supplement

- At least one adverse event: LGG = 7 participants, Placebo = 7 participants
- Those with adverse event that did not complete study: LGG = 1 participants, Placebo = 1 participants

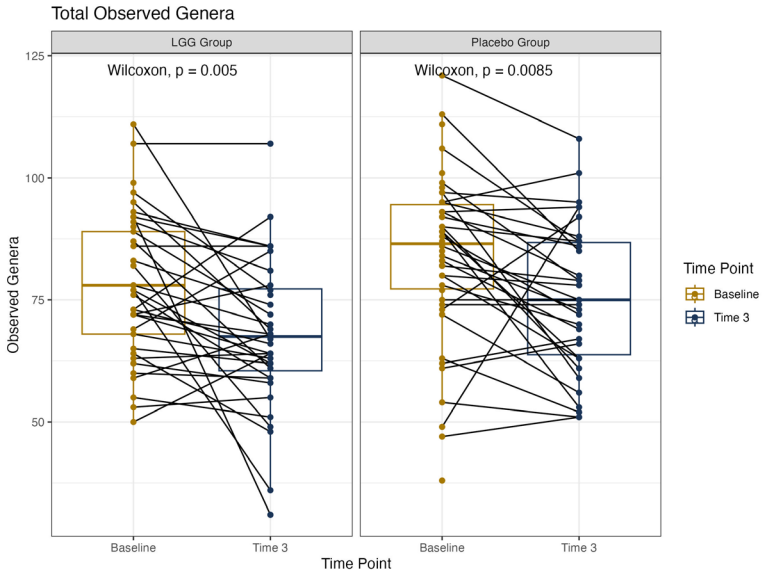
LGG Study Placebo Effect

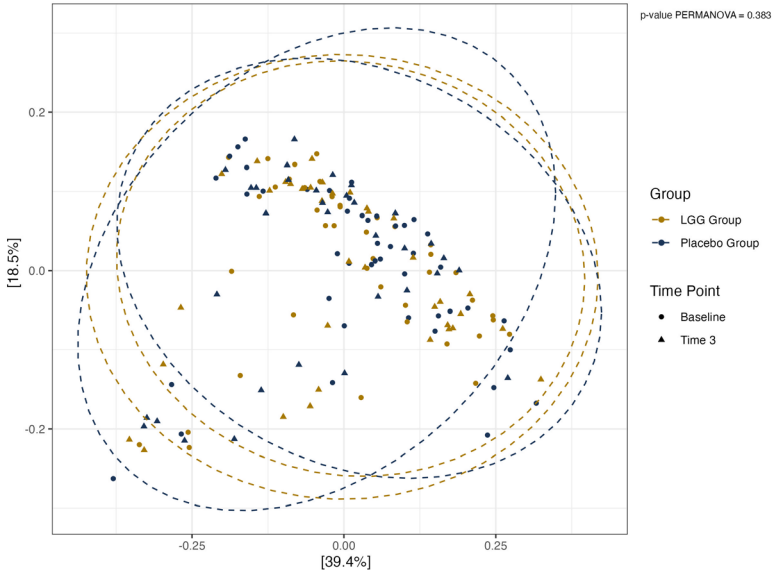
INTERVENTIONS



LGG Alpha/Beta Diversity Levels by Group

INTERVENTIONS





Mixed effects model showed no effect for Group x Time interaction for Shannon and slight decrease in Observed OTUs (p=0.03)

No significance for Weighted (p = 0.383) or Unweighted (0.589) UniFRAC through PERMANOVA

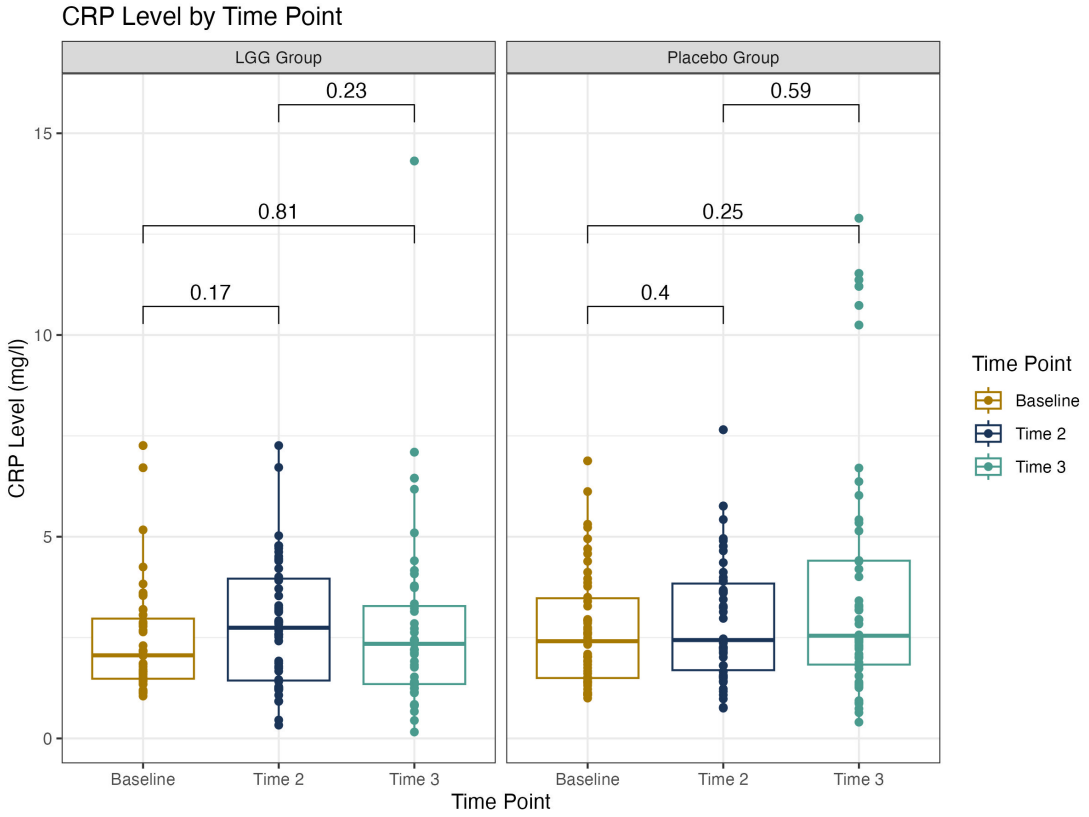
LGG Inflammatory Levels by Group

INTERVENTIONS

Adjusted difference in CRP change

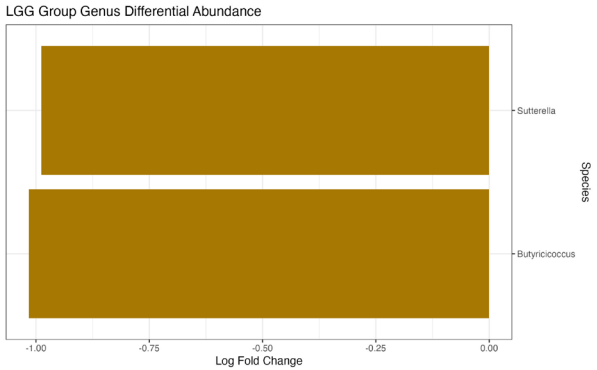
-0.542 mg/L

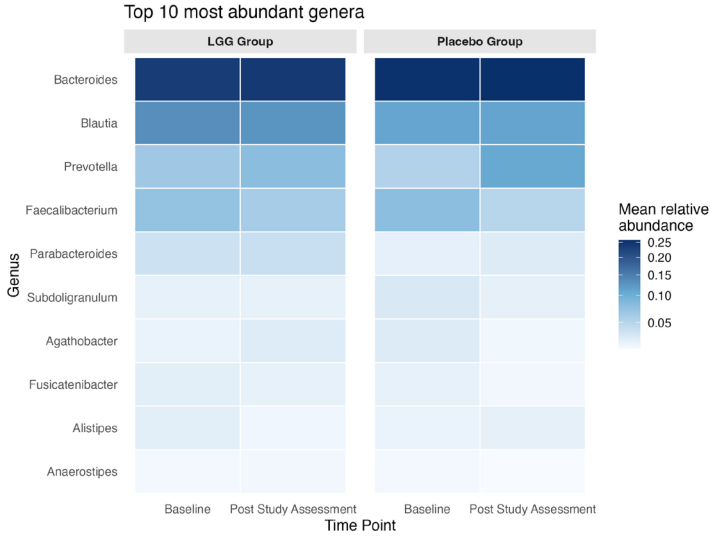
95% CI: -1.84, 0.75; p = 0.41



LGG Microbes by Group

INTERVENTIONS

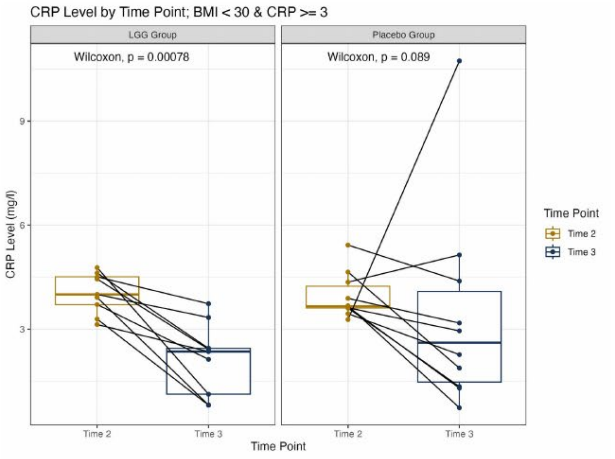


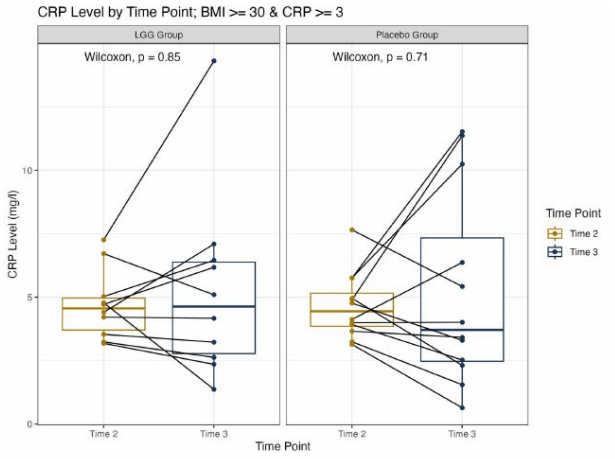


LGG group showed slightly greater stability in 10 most abundant genera

Future Directions – Targeted Interventions?

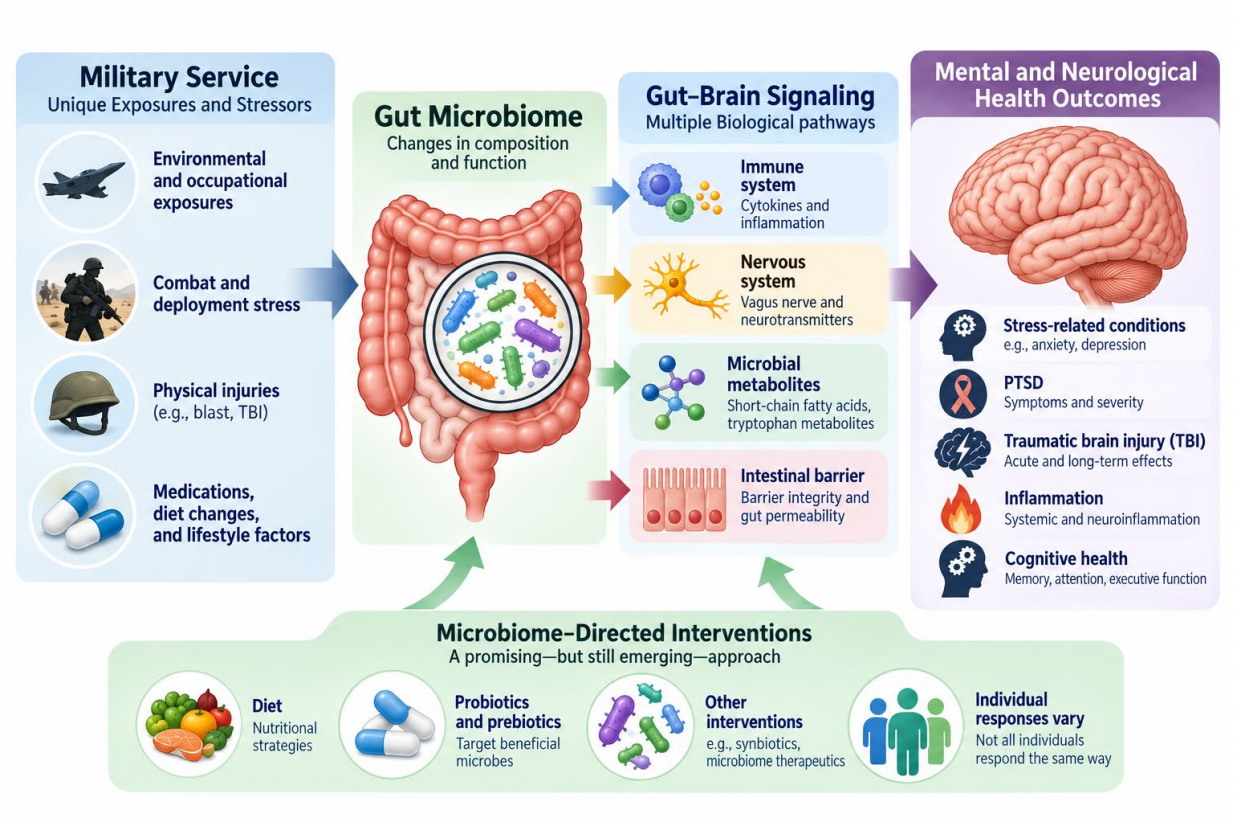
INTERVENTIONS





LGG showed greater effect for those with BMI < 30 and initial CRP > 3; offering a potential precision medicine group

Conclusions



Conclusions Cont.

- The gut and brain are connected through multiple biological pathways, including the immune system, nervous system, microbial metabolites, and intestinal barrier.
- The gut microbiome is highly dynamic and influenced by our environment and experiences, including diet, medications, stress, environmental/occupational exposures, and other lifestyle factors.
- Military service can introduce unique exposures and stressors that may alter the gut microbiome and gut–brain signaling, with potential implications for long-term health.
- Growing evidence links the gut microbiome with mental and neurological health, including stress-related conditions, PTSD, traumatic brain injury, inflammation, and cognitive health.
- The microbiome represents a promising—but still emerging—target for improving health and resilience, including through diet, probiotics, and other microbiome-directed interventions; individual responses can vary substantially.

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