Project Notes:

Project Title:

Modifying the Gut-Microbiota of Drosophila to alleviate symptoms of Seasonal Affective Disorder

Name: Abigail Figueroa

Note Well: There are NO SHORT-cuts to reading journal articles and taking notes from them. Comprehension is paramount. You will most likely need to read it several times, so set aside enough time in your schedule.

Contents:

Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
What are the methods one can induce seasonal depression symptoms besides just modifying light exposure?	Creating an overproduction of melatonin Creating a deficiency in vitamin D (diet?) Reduce serotonin activity by limiting the 5HT2A receptor gene	https://my.clevelandclinic.org/health/diseases/9293-seasonal-depression https://www.mayoclinic.org/diseases-conditions/seasonal-affective-disorder/symptoms-causes/syc-20364651	10/6/23
How would one measure the effects of seasonal depression and then counteract it?	Looking at the links between the gut microbiome and mental health effects. "Bad" bacteria will mean that the organism will also be suffering from a mental imbalance while "good" bacteria will mean it's healthy. "Good" bacteria means that the population is diverse, so steps should be taken to restore it to that level.	How Your Gut B… https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6351938/	10/6/23
What specifically needs to be done directly to the gut-microbiota so that depressive effects are alleviated?	A probiotic should be applied to the sample so that weakened bacteria may reinvigorate, research still needs to be done to figure out which ones should be selected for trial	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3539293/	??

Literature Search Parameters:

These searches were performed between (Start Date of reading) and XX/XX/2019.
List of keywords and databases used during this project.

Database/search engine	**Keywords**	**Summary of search**
Scopus	Neurolinguistics, Bilingualism	Found article: Neurolinguistics in language learning and teaching
Scopus, PubMed	Aphasia, Language Disorders	Found article: Predicting aphasia type from brain damage measured with structural MRI Found article: Cognitive training incorporating temporal information processing improves linguistic and non-linguistic functions in people with aphasia
Scopus, Frontiers, PubMed	Seasonal Depression, Seasonal Affective Disorder, Gut-microbiota, Vagus nerve	Found article: Seasonality and winter-type seasonal depression are associated with the rs731779 polymorphism of the serotonin-2A receptor gene

Tags:

Tag Name	
#Research, #Art-and-Science, #Neurolinguistics, #multiple-demand-system, #fMRI, #brainstudy, #computation	#SAD, #SPLs, #depression, #genetics, #gut-microbiota, #microbiome, #HPA-axis, #SMD
#language disorders, #aphasia, #machine learning, #brain atlas, #multivariate statistical analysis	#bacteria-colonization, #microenvironment

Article #1 Notes: Title [TEMPLATE]

Source Title	
Source citation (APA Format)	
Original URL	
Source type	
Keywords	
Tags	
Summary of key points + notes (include methodology)	
Research Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Article #1 Notes: Bilingualism Comes Naturally to Our Brains

Source Title	Bilingualism Comes Naturally to Our Brains
Source citation (APA Format)	NYU Web Communications. “Bilingualism Comes Naturally to Our Brains.” *Www.nyu.edu*, 3 Nov. 2021, www.nyu.edu/about/news-publications/news/2021/november/bilingualism-comes-naturally-to-our-brains.html.
Original URL	https://www.nyu.edu/about/news-publications/news/2021/november/bilingualism-comes-naturally-to-our-brains.html
Source type	NYU website publication
Keywords	Multilingual, Mixed-language expressions, neural-activity, code-switching
#Tags	#Research, #Art-and-Science, #Neurolinguistics
Summary of key points + notes (include methodology)	Neuroscientists have discovered that the brain uses a shared mechanism for combining words from a single language and for combining words from two different languages. Because of this, when exposed to a combination of languages, the bilingual brain does not detect that the language has switched, allowing for a seamless transition in comprehension. This may possibly indicate that our brains are designed for engaging in multiple languages. ● It is estimated that 60 million people in the United States use two or more languages, however the neurological processes used to produce and understand more than one language are not well understood. ● When speaking, bilinguals often mix two languages together, which raises interesting questions on how the brain handles these changes.

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- A research project arose for Phillips and Liina Pylkkanen, whether bilinguals interpret these mixed-language expressions using the same mechanisms as when comprehending single-language expressions or if understanding mixed-language expressions engages the brain in a unique way.
    - subjects viewed a series of word combinations and pictures on a computer screen - had to indicate whether or not the picture matched the preceding words. The words either formed a two-word sentence or were simply a pair of verbs that did not combine with each other into a meaningful phrase (ex. “ice melt”)
    - project consisted of measuring the neural activity of Korean/English bilinguals by using magnetoencephalography, a technique that maps neural activity by recording magnetic fields generated by the electrical currents produced by the brain.

Their results show that in Korean/English bilinguals, interpreting mixed language expressions uses the same neural mechanisms as with single language expressions. More specifically, the brain’s left anterior lobe was insensitive to whether the words received were from the same or different languages. Overall, the research shows that bilingual brains can, with relative ease, interpret complex expressions containing words from different languages.

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<tr>
<td>Research Question/Problem/ Need</td>
<td>Do bilinguals interpret mixed-language expressions using the same mechanisms as when comprehending single-language expressions or, alternatively, does understanding mixed-language expressions engage the brain in a unique way?</td>
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<td>Important Figures</td>
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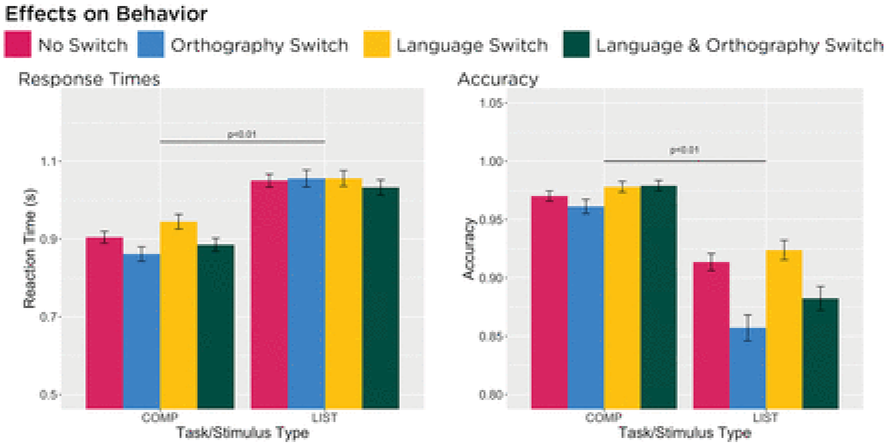

Figures from journal article website publication is based on - Phillips, S. F., & Pylkkänen, L. (2021b). Composition within and between Languages in the Bilingual Mind: MEG Evidence from Korean/English Bilinguals. *ENeuro*, *8*(6). https://doi.org/10.1523/ENEURO.0084-21.2021

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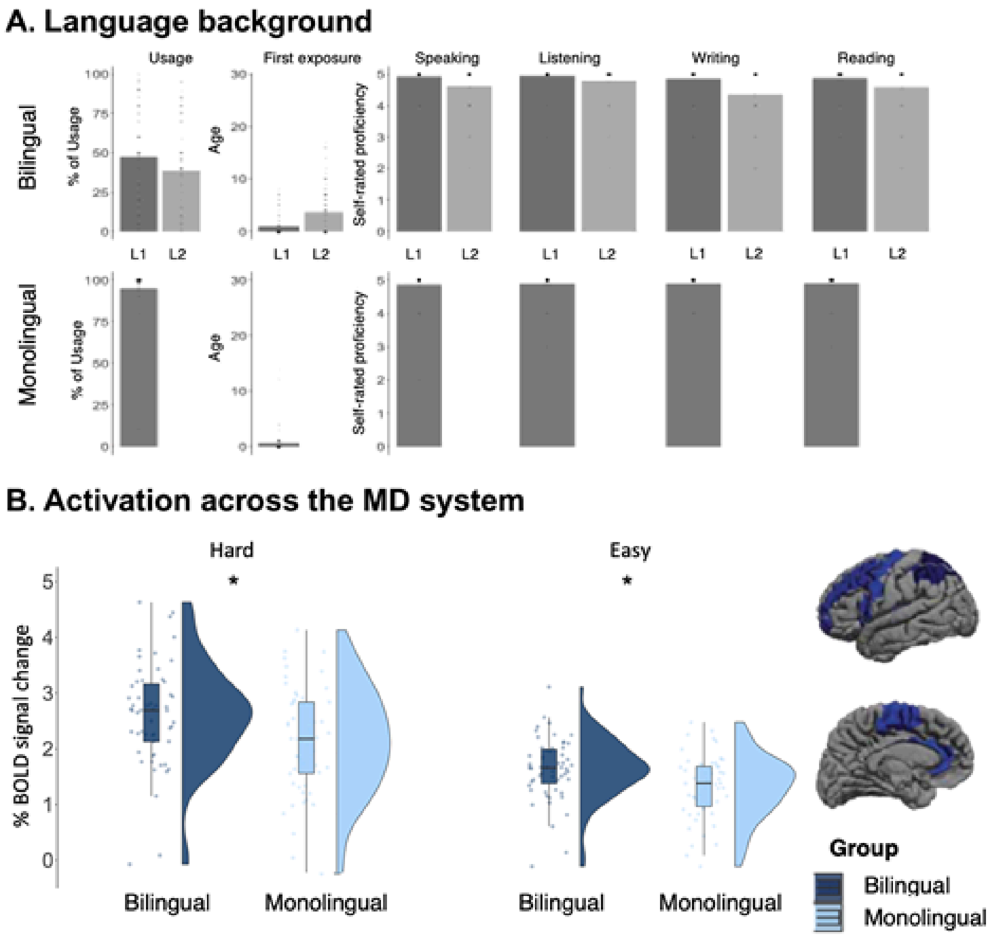
	- Bar graphs represent average response times and average proportion of correct answers, respectively, by each condition - Participants were faster identifying whether pictures matched a two-word sentence than one word of a two-word list - Neither language switching or orthography switching affected response time
VOCAB: (w/definition)	**Magnetoencephalography:** a test that measures the magnetic fields your brain's electrical currents produce, uses sensitive magnetometers **Orthography:** set of conventions for written language **Anterior cingulate cortex:** fundamental cognitive processes, including motivation, decision making, learning, cost-benefit calculation **Dorsolateral prefrontal cortex:** area in prefrontal cortex, responsible for task-switching and reconfiguration
Cited references to follow up on	Phillips, Sarah F., and Liina Pylkkänen. "Composition within and between Languages in the Bilingual Mind: MEG Evidence from Korean/English Bilinguals." *ENeuro*, vol. 8, no. 6, 1 Nov. 2021, www.eneuro.org/content/8/6/ENEURO.0084-21.2021, https://doi.org/10.1523/ENEURO.0084-21.2021.
Follow up Questions	Could this shared mechanism for combining words from different languages have broader implications for language learning or language processing in general? What other techniques can be used to measure the neural activity in bilinguals during research?

Article #2 Notes: The Bilingual Brain

Source Title	The Bilingual Brain
Source citation (APA Format)	Van Deleen, Grace. "The Bilingual Brain." *MIT Technology Review*, 25 Oct. 2022,www.technologyreview.com/2022/10/25/1060386/the-bilingual-brain/.
Original URL	https://www.technologyreview.com/2022/10/25/1060386/the-bilingual-brain/
Source type	MIT Press website article
Keywords	bilingualism, bilingual advantage, executive functioning, multiple demand system
#Tags	#neurolinguistics, #multiple-demand-system, #fMRI
Summary of key points + notes (include methodology)	Bilingualism has been the subject of numerous neurological studies because of the complex language processing the brain undergoes when performing it. Further analyzing this topic is Saima Malik-Moraleda, a fifth-year PhD student in the Harvard/MIT Program in Speech and Hearing Bioscience and Technology. Typically neurobiologists focus on the relative involvement of different brain regions in bilingual activity, however, Malik-Moraleda takes it further by studying neural-networks within the brain. She uses a more localized approach in her investigation by tracking the reaction of specific sets of neurons within brain regions that activate when exposed to linguistic stimuli. Malik, instead of looking just for brain activity, also takes a localized approach and looks specifically at MD (multiple demand) networks and measures their activity. In her 2021 research project "The Domain-General Multiple Demand Network Is More Active in Early Balanced Bilinguals Than Monolinguals During Executive Processing" - - Identified 55 bilingual and 54 monolingual subjects - Participants completed a spatial working memory task as part of a 2-hr fMRI scanning session The MD network responded more strongly in bilinguals than in monolinguals during an executive (spatial working memory) task. Bilinguals performed better than monolinguals behaviorally on the spatial working memory task.
Research Question/Problem/ Need	Is bilingualism linked to superior executive function?

Important Figures	 Figures from journal article website publication is based on - (see cited references) (A) The language background of bilingual and monolingual participants: usage of language in % (B) Activation across the MD system during the Hard and Easy conditions of the spatial working memory task.
VOCAB: (w/definition)	**Multiple Demand system:** a network of fronto-parietal brain regions active during the organization and control of diverse cognitive operations. **Spatial memory:** a cognitive process that enables someone to remember different locations as well as spatial relations between objects.
Cited references to follow up on	Malik-Moraleda, Saima, et al. “The Domain-General Multiple Demand Network Is More Active in Early Balanced Bilinguals than Monolinguals during Executive Processing.” *Neurobiology of*

	Language, 1 Oct. 2021, pp. 1–36, https://doi.org/10.1162/nol_a_00058. Accessed 19 Oct. 2021.
Follow up Questions	Could the enhanced activity in the MD network in bilinguals have broader implications for cognitive abilities beyond language processing? What insights can this research provide into the development of educational strategies that optimize cognitive functions in bilingual and monolingual individuals?

Article #3 Notes: Finding Language in the Brain

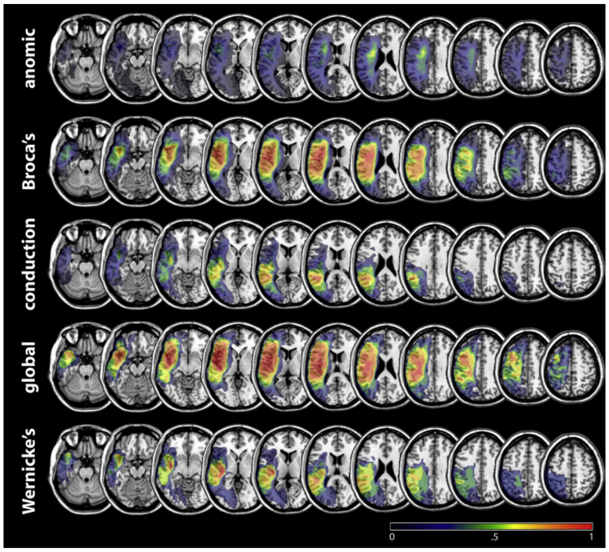
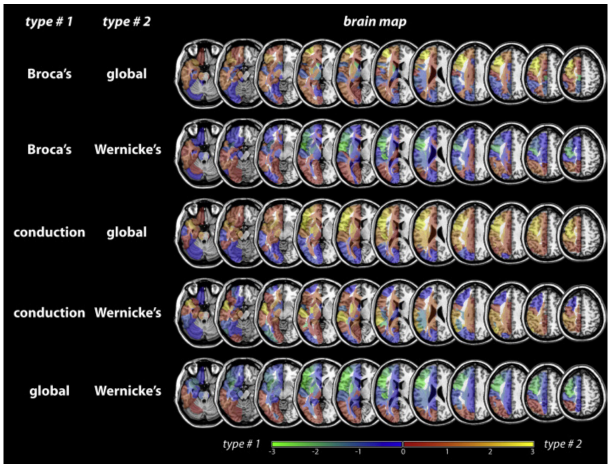
Source Title	*Finding language in the brain*
Source citation (APA Format)	Baggio, G. (2022, December 21). *Finding language in the brain*. The MIT Press Reader. https://thereader.mitpress.mit.edu/finding-language-in-the-brain/
Original URL	https://thereader.mitpress.mit.edu/finding-language-in-the-brain/
Source type	Website article - MIT Press
Keywords	Neurolinguistics
#Tags	#brainstudy #computation #neuroscience
Summary of key points + notes (include methodology)	Despite the fluidity and personality of language, there seems to be a connection between language and computation in regard to the structure of speech. In doing so, the idea of language-as-calculus appears to be the best model for interpreting language in the brain. Still, scientists are in much debate as concrete answers for neurolinguistics remain vague.
Research Question/Problem/ Need	How does language act as a form of mathematical computation in the brain?
Important Figures	“The language-as-calculus idea may well be the best model of language in the brain we currently have — or perhaps the worst, except for all the others.” - Giosue Baggio
VOCAB: (w/definition)	“In silico”- conducted or produced by means of computer modeling or computer simulation.
Cited references to follow up on	https://mitpress.mit.edu/9780262543262/neurolinguistics/?_ga=2.242827591.498704056.1692585944-1094200323.1692304222
Follow up Questions	1. What tools can we use to quantify the information we do have? 2. What forms of investigations can we conduct to dive deeper into the issue? 3. How can we better interpret the language-as-calculus model?

Article #4 Notes: Neurolinguistics

Source Title	*Neurolinguistics*.
Source citation (APA Format)	Menn, L. (2018). *Neurolinguistics*. Linguistic Society of America. https://www.linguisticsociety.org/resource/neurolinguistics
Original URL	https://www.linguisticsociety.org/resource/neurolinguistics
Source type	Website article
Keywords	Neuroscience
#Tags	#brain, #neuroscience, #language disorders
Summary of key points + notes (include methodology)	Neurolinguistics asks many questions about how our brains process language. Over time, the field of neurolinguistics has made progress with the advancement of modern technology, allowing us to get more accurate data of the brain with the use of MRI and CAT scans. By taking a look at aphasia (the loss of language due to brain damage) and other language disorders, we can better learn how language units interact with the brain.
Research Question/Problem/ Need	How can we further our understanding of neurolinguistics by studying people with aphasia and language disorders?
Important Figures	“Adults who have had brain damage and become aphasic recover more slowly than children who have had the same kind of damage” - Lisa Menn
VOCAB: (w/definition)	Aphasia - loss of ability to understand speech, caused by brain damage
Cited references to follow up on	Caplan, David, Gloria Waters, Gayle DeDe, Jennifer Michaud, & Amanda Reddy 2007. A study of syntactic processing in aphasia I: Behavioral (psycholinguistic) aspects. Brain and Language 101, 103-150. Novick, J.M., Trueswell, J.C., & Thomspon-Schill, S.L. (2010). Broca's Area and Language Processing: Evidence for the Cognitive Control Connection. Language and Linguistics Compass.
Follow up Questions	1. What are some obstacles that might contradict results? 2. To what extent would the degree of brain damage affect the brain? 3. Would there be differences in aphasia of a bilingual person’s brain vs of a monolingual person’s brain?

Article #5 Notes: Predicting aphasia type from brain damage measured with structural MRI

Source Title	Predicting aphasia type from brain damage measured with structural MRI
Source citation (APA Format)	Yourganov, G., Smith, K. G., Fridriksson, J., & Rorden, C. (2015). Predicting aphasia type from brain damage measured with structural MRI. *Cortex*, *73*, 203–215. https://doi.org/10.1016/j.cortex.2015.09.005
Original URL	https://www-sciencedirect-com.ezpv7-web-p-u01.wpi.edu/science/article/pii/S0010945215003299
Source type	Journal article
Keywords	Chronic aphasia; Aphasia typology; Multivariate classification
#Tags	#aphasia, #machine learning, #brain atlas, #multivariate statistical analysis
Summary of key points + notes (include methodology)	Depending on the location of damage in relation to the cortical language regions, aphasic patients can demonstrate very different patterns of language impairment. It's possible that the relationship between symptoms and structural injury reflect specific patterns of injury to a spatially distributed network. The objective was to determine whether automated multivariate classification algorithms could accurately predict aphasia type based on the pattern of brain injury. The study shows that, despite patient heterogeneity, there is a correspondence between the spatial pattern of brain damage and the resulting language deficit.
Research Question/Problem/ Need	How can machine learning algorithms like SVM be utilized in the prediction of aphasia type in patients?

Important Figures	  Overlap of lesions across patients of each aphasia type. A voxel with overlap = 1 indicates that this voxel is lesioned in 100% of the patients.
VOCAB: (w/definition)	- **Multivariate statistical analysis**: comprises a set of advanced techniques for examining relationships among multiple variables at the same time. - **Support Vector Machines (SVM)**: a supervised machine learning algorithm used for both classification and regression - **Lexical** : relating to words or vocabulary - **Locus**: position or place - **Spatial bias**: brain's tendency to process and area of space (right or left) better than the other - **Voxels:** 3D cubic pixels, represent a piece of brain tissue in fMRI
Cited references to follow up on	*Aphasia causes, symptoms, treatment*. Froedtert & the Medical College of Wisconsin. (n.d.). https://www.froedtert.com/aphasia Saini, A. (2023, July 7). *Guide on Support Vector Machine (SVM) algorithm*.

	Analytics Vidhya. https://www.analyticsvidhya.com/blog/2021/10/support-vector-machinessvm-a-complete-guide-for-beginners/
Follow up Questions	What are the steps we can take to produce a more accurate machine learning model that can provide better results on the analysis of fluent vs fluent and non-fluent vs non-fluent aphasia? To what degree are these implements efficient and what are possible margin errors? Can we develop a computer algorithm that along with predicting aphasia type, can predict/model a possible path to recovery? Or can predict/model transformations to other types of aphasia, warning the patient if their condition has the possibility of getting worse?

Article #6 Notes: Seasonality and winter-type seasonal depression are associated with the rs731779 polymorphism of the serotonin-2A receptor gene

Source Title	Seasonality and winter-type seasonal depression are associated with the rs731779 polymorphism of the serotonin-2A receptor gene
Source citation (APA Format)	Molnar, E., Lazary, J., Benko, A., Gonda, X., Pap, D., Mekli, K., Juhasz, G., Kovacs, G., Kurimay, T., Rihmer, Z., & Bagdy, G. (2010). Seasonality and winter-type seasonal depression are associated with the rs731779 polymorphism of the serotonin-2A receptor gene. *European Neuropsychopharmacology*, *20*(9), 655–662. https://doi.org/10.1016/j.euroneuro.2010.04.009
Original URL	https://www-sciencedirect-com.ezpv7-web-p-u01.wpi.edu/science/article/pii/S0924977X1000091X
Source type	Journal Article
Keywords	Seasonal affective disorder, 5-HT2A receptor gene, rs731779, rs985934, rs6311, depression
#Tags	#SAD, #SPLs, #depression, #genetics
Summary of key points + notes (include methodology)	The serotonin-2A (5-HT2A) receptor gene has long been suggested as a reason for the genetic basis of SAD (seasonal affective disorder). It was hypothesized that functional sequence variation in this gene could contribute to seasonality and the development of winter- and/or summer-type seasonal depression. Participants were subjected to two questionnaires, GSS and SHQ, to determine if the participants suffered from SAD and their general sensitivity to seasonality. DNA was collected and analyzed to determine associations between questionnaire scores and 5-HTR2A receptor gene polymorphisms rs731779, rs985934 and rs6311. - Mean score of the GSS was 7.87, with females having significantly higher point scores on GSS scale compared to males. Using the SHQ, the frequency of winter-type SAD was 3.27% in males and 3.49% in females, while the summer-type frequency was 0.81% and 0.97% respectively. Overall, 4.6% of the total population was affected by some form of SAD.

- Significant associations between rs731779 and GSS scores were found using both the recessive genetic model and the codominant genetic model, with GG homozygous individuals scoring significantly higher compared to T allele carriers.
- No significant associations were found between GSS scores and either of the other two SNPs

Research Question/Problem/ Need

Does the functional sequence variation in the serotonin-2A (5-HT2A) receptor gene contribute to seasonality and the development of winter- and/or summer-type seasonal depression?

Important Figures

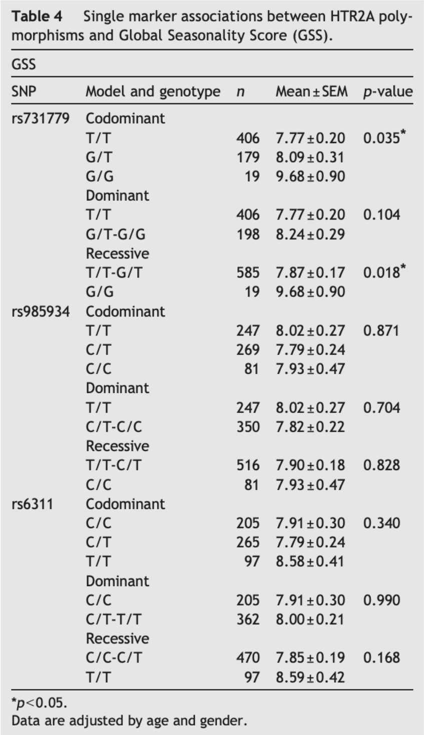


Table 4 Single marker associations between HTR2A polymorphisms and Global Seasonality Score (GSS).

GSS				
SNP	Model and genotype	*n*	Mean ± SEM	*p*-value
rs731779	Codominant			
	T/T	406	7.77 ± 0.20	0.035*
	G/T	179	8.09 ± 0.31	
	G/G	19	9.68 ± 0.90	
	Dominant			
	T/T	406	7.77 ± 0.20	0.104
	G/T-G/G	198	8.24 ± 0.29	
	Recessive			
	T/T-G/T	585	7.87 ± 0.17	0.018*
	G/G	19	9.68 ± 0.90	
rs985934	Codominant			
	T/T	247	8.02 ± 0.27	0.871
	C/T	269	7.79 ± 0.24	
	C/C	81	7.93 ± 0.47	
	Dominant			
	T/T	247	8.02 ± 0.27	0.704
	C/T-C/C	350	7.82 ± 0.22	
	Recessive			
	T/T-C/T	516	7.90 ± 0.18	0.828
	C/C	81	7.93 ± 0.47	
rs6311	Codominant			
	C/C	205	7.91 ± 0.30	0.340
	C/T	265	7.79 ± 0.24	
	T/T	97	8.58 ± 0.41	
	Dominant			
	C/C	205	7.91 ± 0.30	0.990
	C/T-T/T	362	8.00 ± 0.21	
	Recessive			
	C/C-C/T	470	7.85 ± 0.19	0.168
	T/T	97	8.59 ± 0.42	

*$p < 0.05$.
Data are adjusted by age and gender.

VOCAB: (w/definition)

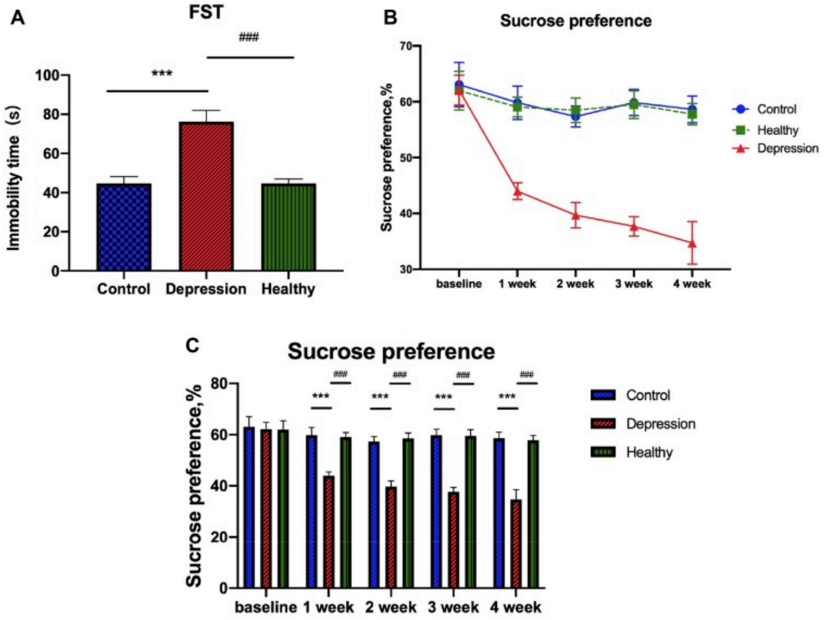
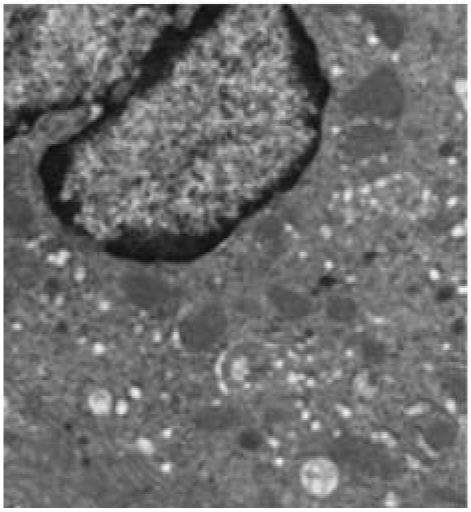
SNPs - the most common types of genetic variation amongst people. Each represents a difference in a single DNA building block (nucleotides). Ex. may replace C with T in a stretch of DNA. - Biological markers

Null Hypothesis - proposes that there is no relationship between the two variables

Cited references to follow up on	"Seasonal Affective Disorder - Mayo Clinic Health System." *Www.youtube.com*, 11 Jan. 2018, www.youtube.com/watch?v=TWtrS8Qvo1Q. Medline Plus. "What Are Single Nucleotide Polymorphisms (SNPs)?" *Medlineplus.gov*, National Library of Medicine, 22 Mar. 2022, medlineplus.gov/genetics/understanding/genomicresearch/snp/.
Follow up Questions	Could some sort of chemical agent be designed to amplify serotonin receptors?

Article #7 Notes: Gut Microbiota Regulates Depression-Like Behavior in Rats Through the Neuroendocrine-Immune-Mitochondrial Pathway

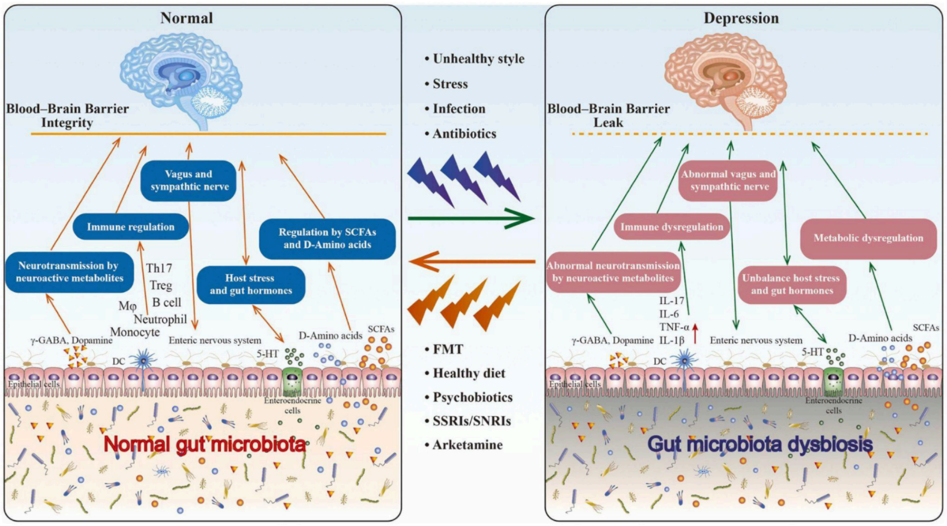
Source Title	Gut Microbiota Regulates Depression-Like Behavior in Rats Through the Neuroendocrine-Immune-Mitochondrial Pathway
Source citation (APA Format)	Liu, S., Guo, R., Liu, F., Yuan, Q., Yu, Y., & Ren, F. (2020). Gut Microbiota Regulates Depression-Like Behavior in Rats Through the Neuroendocrine-Immune-Mitochondrial Pathway. *Neuropsychiatric Disease and Treatment*, *16*, 859–869. https://doi.org/10.2147/NDT.S243551
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7127849/
Source type	Journal article
Keywords	HPA axis; depression; gut microbiota; immune; mitochondrial; neurotransmitter.
#Tags	#gut-microbiota, #microbiome, #depression, #HPA-axis
Summary of key points + notes (include methodology)	In the study, researchers transplanted the gut microbiota from patients with depression, where changes in behavior, hippocampal neurotransmitter levels,Hypothalamic-Pituitary-Adrenocortical (HPA) axis, inflammatory cytokine levels, and mitochondrial structure were analyzed. All of this was done to explore the underlying mechanisms that involve the influence of gut mitochondria on host behavior. - Transplant fecal microbiota from patients with depression and health patients into germ-free rats using fecal transplantation technology - Assessed the affective behavior in the rats using the forced swimming test and a sucrose preference test

	- Used enzyme-linked immunosorbent assay to determine levels of various brain chemicals Rats that received the fecal microbiota from patients with depression developed depressive symptoms. This was presented through decreased levels of hippocampal neurotransmitters, among other chemicals, and increased levels of pro inflammatory cytokines. (swelled up mitochondria)
Research Question/Problem/ Need	What are the underlying mechanisms of the regulation of depressive-like behavior by gut microbiota?
Important Figures	  mitochondria in the depressive microbiota group were oval or round whole; others were swollen, sparse, and even vacuolated.

VOCAB: (w/definition)	**Enzyme-linked immunosorbent array:** used to measure antibodies, antigens, proteins, glycoproteins, etc, in biological samples **Microbiota:** consists in the ensemble of microbes, including viruses, bacteria, and eukaryotes, that inhabit several ecological niches of the organism **Vagus nerve:** carries signals between your brain, heart and digestive system. **Neuroendocrine-immune regulatory network** consists of nervous system, endocrine system and immune system; maintains homeostasis
Cited references to follow up on	Morais, Livia H., et al. "The Gut Microbiota–Brain Axis in Behaviour and Brain Disorders." *Nature Reviews Microbiology*, vol. 19, no. 4, 22 Oct. 2020, https://doi.org/10.1038/s41579-020-00460-0. Galland, Leo. "The Gut Microbiome and the Brain." *Journal of Medicinal Food*, vol. 17, no. 12, Dec. 2014, pp. 1261–1272, www.ncbi.nlm.nih.gov/pmc/articles/PMC4259177/, https://doi.org/10.1089/jmf.2014.7000.
Follow up Questions	What changes can be applied to the microbiota directly so that depressive effects are counteracted? What are some non-brain liquidating ways to measure depressive symptoms, (what can I use as an indication of the model organism's state of mind that is minimally invasive?)

Article #8 Notes: The role of gut microbiota in depression: an analysis of the gut-brain axis

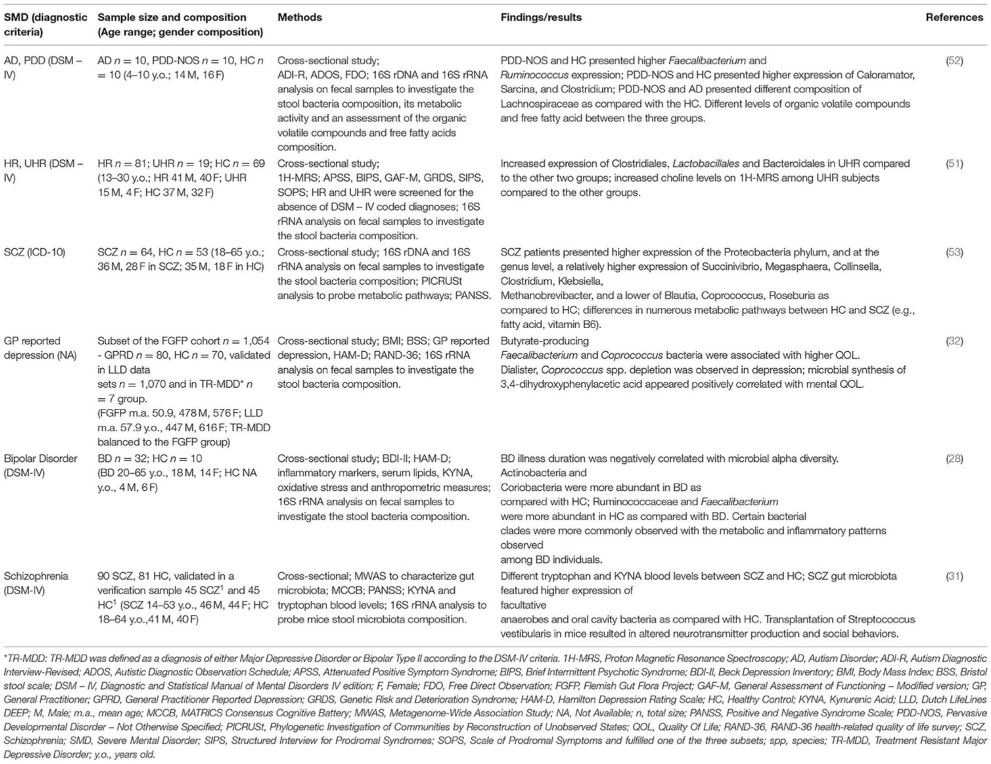
Source Title	The role of gut microbiota in depression: an analysis of the gut-brain axis
Source citation (APA Format)	Irum, N., Afzal, T., Faraz, M. H., Aslam, Z., & Rasheed, F. (2023). The role of gut microbiota in depression: An analysis of the gut-brain axis. *Frontiers in Behavioral Neuroscience*, *17*. https://www.frontiersin.org/articles/10.3389/fnbeh.2023.1185522
Original URL	https://www.frontiersin.org/articles/10.3389/fnbeh.2023.1185522
Source type	Review article
Keywords	gut microbiota, depression, serotonin, gut-brain connection, gut-brain axis, gut normal flora
#Tags	#microbiota, #gut-health, #depression, #SSRI
Summary of key points + notes (include methodology)	The gut-brain axis is a communication pathway that allows for an exchange of information between the microbiota of the gastrointestinal tract and the nervous system. Researchers have found several positive trends by analyzing numerous studies examining the gut microbiota's impact on the effectiveness of SSRIs. There is evidence that selective serotonin reuptake inhibitors (SSRIs) rely on the vagus nerve to exert their therapeutic effects, which has provided further support for the importance for the study of the vagus nerve in the gut-brain axis. The review provides insight on various research linking gut-microbiota to depression ● The gut microbiota of MDD patients differed from that of controls with the same age, gender, and body mass index. There were more Enterobacteriaceae and Alistipes in the guts of MDD patients and fewer Faecalibacterium, Coprococcus, and Dialister according to research conducted by Zheng et al. (2020) ● SSRIs not only modulate serotonin levels in the stomach but also target the role played by the vagus nerve in mood control. ○ McVey Neufeld et al (2019) researched the effectiveness of SSRIs on mice with and without vagotomies. Vagotomized mice

	performed poorly in a tail suspension test, indicating that the SSRI antidepressants they were administered had little effect
Research Question/Problem/ Need	Analyzing the role of the gut microbiota in correlation to depression from various sources
Important Figures	 Infographic shows that an unhealthy lifestyle caused by factors such as stress and infection can lead to dysbiosis in the gut microbiota, which can contribute to depression. However, diverse methods, such as fecal microbiota transplantation, diet, psychobiotics, and antidepressants, can help restore the gut microbiota's equilibrium and alleviate depressive symptoms.
VOCAB: (w/definition)	**Vagotomies:** surgical operations where branches of the vagus nerve are cut **Gut-brain axis (GBA):** communication between the central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions **Probiotics**: live microorganisms intended to be taken as a supplement that improve the bacteria in the body **SSRI**: medications prescribed as antidepressants, works by increasing serotonin levels in the brain
Cited references to follow up on	Zheng, P., Yang, J., Li, Y., Wu, J., Liang, W., Yin, B., et al. (2020). Gut microbial signatures can discriminate unipolar from bipolar depression. Adv. Sci. 7:1902862. doi: 10.1002/advs.201902862 McVey Neufeld, K. A., Bienenstock, J., Bharwani, A., Champagne-Jorgensen, K., Mao, Y., West, C., et al. (2019). Oral selective serotonin reuptake inhibitors activate vagus nerve dependent gut-brain signaling. Sci. Rep. 9:14290. doi:

	10.1038/s41598019- 50807- 8
Follow up Questions	What are the mechanisms by which SSRIs modulate serotonin levels in the stomach and how does this relate to their effectiveness in treating mood disorders? Can findings be applied to personalized treatments for depression based on an individual's gut microbiota composition?

Article #9 Notes: The Role of Gut Microbiota in the High-Risk Construct of Severe Mental Disorders: A Mini Review

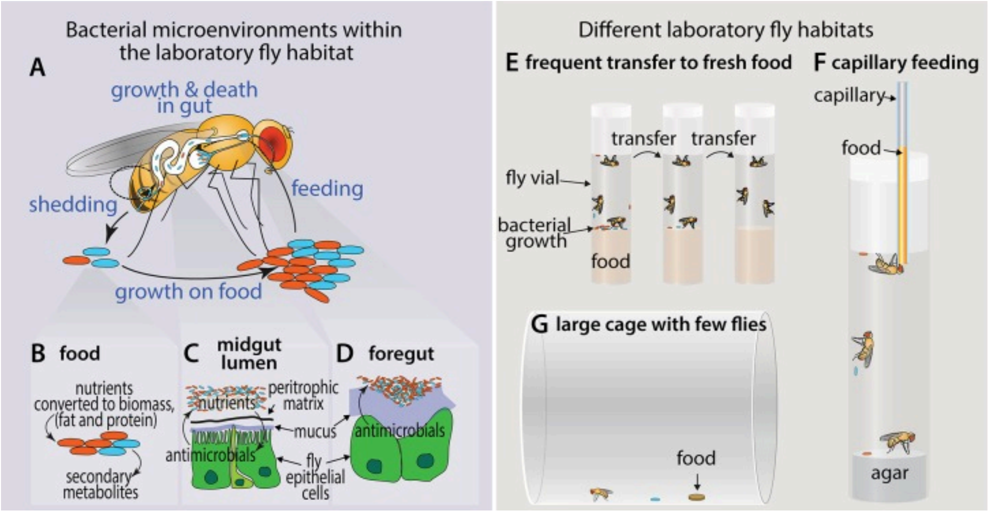
Source Title	The Role of Gut Microbiota in the High-Risk Construct of Severe Mental Disorders: A Mini Review
Source citation (APA Format)	Sani, Gabriele, et al. "The Role of Gut Microbiota in the High-Risk Construct of Severe Mental Disorders: A Mini Review." *Frontiers in Psychiatry*, vol. 11, 12 Jan. 2021, https://doi.org/10.3389/fpsyt.2020.585769. Accessed 7 Feb. 2022.
Original URL	https://www.frontiersin.org/articles/10.3389/fpsyt.2020.585769/full#:~:text=Furthermore%2C%20gut%20microbiota%20can%20modify,bipolar%20disorder%20(72)%2C%20and
Source type	Review article
Keywords	microbiome, schizophrenia, depression, genomics, animal models, autism spectrum disorder, Shannon index, alpha diversity
#Tags	#depression, #gut-microbiome, #SMD
Summary of key points + notes (include methodology)	Recent findings indicate that the development of the microbiome and the central nervous system (CNS) both undergoing critical developmental phases at the same time. This has led to extensive preclinical investigations into how changes in gut microbiota can affect the maturation of the brain and potentially increase the risk of mental disorders in later life. Specifically, studies have shown that alterations in the maternal microbiome can influence the brain development and postnatal development of psychopathological conditions in offspring. - Buffington et al. found that the offspring of mice exposed to a high-fat diet exhibited symptoms resembling autism spectrum disorders and schizophrenia, including reduced social interactions, diminished interest in social novelty, and altered sociability when compared to the offspring of normally fed mice. These behavioral changes were associated with a

<table>
<tr><td></td><td>significant decrease in Lactobacillus reuteri and a reduced number of oxytocin-producing cells in the paraventricular nuclei of the hypothalamus.
Gut microbiota can modify oligodendrocyte products and affect myelination, particularly in the prefrontal cortex, a brain region involved in attention, memory, emotional learning and critically connected to SMD</td></tr>
<tr><td>**Research Question/Problem/ Need**</td><td>Analyzing the impact of the gut microbiota and its effect on various Severe Mental Disorders (SMDs)</td></tr>
<tr><td>**Important Figures**</td><td>

<table>
<tr><th>SMD (diagnostic criteria)</th><th>Sample size and composition (Age range; gender composition)</th><th>Methods</th><th>Findings/results</th><th>References</th></tr>
<tr><td>AD, PDD (DSM – IV)</td><td>AD $n = 10$, PDD-NOS $n = 10$, HC $n = 10$ (4–10 y.o.; 14 M, 16 F)</td><td>Cross-sectional study;
ADI-R, ADOS, FDO; 16S rDNA and 16S rRNA analysis on fecal samples to investigate the stool bacteria composition, its metabolic activity and an assessment of the organic volatile compounds and free fatty acids composition.</td><td>PDD-NOS and HC presented higher *Faecalibacterium* and *Ruminococcus* expression; PDD-NOS and HC presented higher expression of Caloramator, Sarcina, and Clostridium; PDD-NOS and AD presented different composition of Lachnospiraceae as compared with the HC. Different levels of organic volatile compounds and free fatty acid between the three groups.</td><td>(52)</td></tr>
<tr><td>HR, UHR (DSM – IV)</td><td>HR $n = 81$; UHR $n = 19$; HC $n = 69$ (13–30 y.o.; HR 41 M, 40 F; UHR 15 M, 4 F; HC 37 M, 32 F)</td><td>Cross-sectional study;
1H-MRS; APSS, BIPS, GAF-M, GRDS, SIPS, SOPS; HR and UHR were screened for the absence of DSM – IV coded diagnoses; 16S rRNA analysis on fecal samples to investigate the stool bacteria composition.</td><td>Increased expression of Clostridiales, *Lactobacillales* and Bacteroidales in UHR compared to the other two groups; increased choline levels on 1H-MRS among UHR subjects compared to the other groups.</td><td>(51)</td></tr>
<tr><td>SCZ (ICD-10)</td><td>SCZ $n = 64$, HC $n = 53$ (18–65 y.o.; 36 M, 28 F in SCZ; 35 M, 18 F in HC)</td><td>Cross-sectional study; 16S rDNA and 16S rRNA analysis on fecal samples to investigate the stool bacteria composition; PICRUSt analysis to probe metabolic pathways; PANSS.</td><td>SCZ patients presented higher expression of the Proteobacteria phylum, and at the genus level, a relatively higher expression of Succinivibrio, Megasphaera, Collinsella, Clostridium, Klebsiella,
Methanobrevibacter, and a lower of Blautia, Coprococcus, Roseburia as compared to HC; differences in numerous metabolic pathways between HC and SCZ (e.g., fatty acid, vitamin B6).</td><td>(53)</td></tr>
<tr><td>GP reported depression (NA)</td><td>Subset of the FGFP cohort $n = 1{,}054$ - GPRD $n = 80$, HC $n = 70$, validated in LLD data sets $n = 1{,}070$ and in TR-MDD* $n = 7$ group.
(FGFP m.a. 50.9, 478 M, 576 F; LLD m.a. 57.9 y.o., 447 M, 616 F; TR-MDD balanced to the FGFP group)</td><td>Cross-sectional study; BMI; BSS; GP reported depression, HAM-D; RAND-36; 16S rRNA analysis on fecal samples to investigate the stool bacteria composition.</td><td>Butyrate-producing
Faecalibacterium and *Coprococcus* bacteria were associated with higher QOL.
Dialister, *Coprococcus* spp. depletion was observed in depression; microbial synthesis of 3,4-dihydroxyphenylacetic acid appeared positively correlated with mental QOL.</td><td>(32)</td></tr>
<tr><td>Bipolar Disorder (DSM-IV)</td><td>BD $n = 32$; HC $n = 10$
(BD 20–65 y.o., 18 M, 14 F; HC NA y.o., 4 M, 6 F)</td><td>Cross-sectional study; BDI-II; HAM-D; inflammatory markers, serum lipids, KYNA, oxidative stress and anthropometric measures; 16S rRNA analysis on fecal samples to investigate the stool bacteria composition.</td><td>BD illness duration was negatively correlated with microbial alpha diversity.
Actinobacteria and
Coriobacteria were more abundant in BD as
compared with HC; Ruminococcaceae and *Faecalibacterium*
were more abundant in HC as compared with BD. Certain bacterial
clades were more commonly observed with the metabolic and inflammatory patterns
observed
among BD individuals.</td><td>(28)</td></tr>
<tr><td>Schizophrenia (DSM-IV)</td><td>90 SCZ, 81 HC, validated in a verification sample 45 SCZ[1] and 45 HC[1] (SCZ 14–53 y.o., 46 M, 44 F; HC 18–64 y.o.,41 M, 40 F)</td><td>Cross-sectional; MWAS to characterize gut microbiota; MCCB; PANSS; KYNA and tryptophan blood levels; 16S rRNA analysis to probe mice stool microbiota composition.</td><td>Different tryptophan and KYNA blood levels between SCZ and HC; SCZ gut microbiota featured higher expression of
facultative
anaerobes and oral cavity bacteria as compared with HC. Transplantation of Streptococcus vestibularis in mice resulted in altered neurotransmitter production and social behaviors.</td><td>(31)</td></tr>
</table>
**TR-MDD: TR-MDD was defined as a diagnosis of either Major Depressive Disorder or Bipolar Type II according to the DSM-IV criteria. 1H-MRS, Proton Magnetic Resonance Spectroscopy; AD, Autism Disorder; ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autistic Diagnostic Observation Schedule; APSS, Attenuated Positive Symptom Syndrome; BIPS, Brief Intermittent Psychotic Syndrome; BDI-II, Beck Depression Inventory; BMI, Body Mass Index; BSS, Bristol stool scale; DSM – IV, Diagnostic and Statistical Manual of Mental Disorders IV edition; F, Female; FDO, Free Direct Observation; FGFP, Flemish Gut Flora Project; GAF-M, General Assessment of Functioning – Modified version; GP, General Practitioner; GPRD, General Practitioner Reported Depression; GRDS, Genetic Risk and Deterioration Syndrome; HAM-D, Hamilton Depression Rating Scale; HC, Healthy Control; KYNA, Kynurenic Acid; LLD, Dutch LifeLines DEEP; M, Male; m.a., mean age; MCCB, MATRICS Consensus Cognitive Battery; MWAS, Metagenome-Wide Association Study; NA, Not Available; n, total size; PANSS, Positive and Negative Syndrome Scale; PDD-NOS, Pervasive Developmental Disorder – Not Otherwise Specified; PICRUSt, Phylogenetic Investigation of Communities by Reconstruction of Unobserved States; QOL, Quality Of Life; RAND-36, RAND-36 health-related quality of life survey; SCZ, Schizophrenia; SMD, Severe Mental Disorder; SIPS, Structured Interview for Prodromal Syndromes; SOPS, Scale of Prodromal Symptoms and fulfilled one of the three subsets; spp, species; TR-MDD, Treatment Resistant Major Depressive Disorder; y.o., years old.*
Summary of findings of clinicals studies done on various SMD types and the role of the gut microbiota</td></tr>
<tr><td>**VOCAB: (w/definition)**</td><td>**Choline**: necessary nutrient, part of the methyl group needed for metabolism
Histone deacetylases: enzymes that remove acetyl groups, may result in inhibition of gene transcription
Brain-derived neurotrophic factor: serves as a neurotransmitter modulator, participates in neuronal plasticity, which is essential for learning and memory. It is expressed in the CNS, gut and other tissues.
Lactobacillus reuteri: lactic acid bacterium that can break down food, absorb nutrients, and fight off organisms that might cause diseases.</td></tr>
</table>

Cited references to follow up on	Rehm J, Shield KD. Global burden of disease and the impact of mental and addictive disorders. *Curr Psychiatr Rep.* (2019) 21:10. doi: 10.1007/s11920-019-0997-0 Zwicker A, MacKenzie LE, Drobinin V, Howes Vallis E, Patterson VC, Stephens M, et al. Basic symptoms in offspring of parents with mood and psychotic disorders. *BJPsych Open.* (2019) 5:e54. doi: 10.1192/bjo.2019.40
Follow up Questions	What are the potential mechanisms that link alterations in the gut microbiota during critical developmental windows to brain maturation and the risk of mental disorders later in life? Are there ongoing studies investigating the specific roles of different microbial species in influencing brain development and behavior, beyond Lactobacillus reuteri?

Article #10 Notes: *Drosophila* as a model for the gut microbiome

Source Title	*Drosophila* as a model for the gut microbiome
Source citation (APA Format)	Ludington, W. B., & Ja, W. W. (2020). Drosophila as a model for the gut microbiome. *PLoS Pathogens*, *16*(4), e1008398. https://doi.org/10.1371/journal.ppat.1008398
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7179820/
Source type	Journal Article/Review
Keywords	gut microbiome, bacteria, growth cycles,
#Tags	#gut-microbiota, #bacteria-colonization, #microenvironment
Summary of key points + notes (include methodology)	Invertebrate systems offer valuable opportunities for studying intricate interactions between hosts and microbes. Notably, Drosophila melanogaster, stands out as a suitable model for animal genetics. Its uncomplicated microbiome consists of 5 to 20 microbial species, which can be deliberately reconstructed in a laboratory setting through a short egg treatment with bleach, followed by the introduction of specific bacterial species. Recent work has identified gut symbionts that stably colonize specific niches in the gut. Identifying these symbionts is a critical step in establishing a fly model for the gut microbiome. ● Obadia and colleagues attempted the colonization of individual flies after ingesting a single dose of a bacterial strain. They found that colonization is probabilistic, with the odds increasing with higher doses. Out of the 17 strains screened, 11 were categorized as stable colonizers, including the genera *Lactobacillus*, *Leuconostoc*, *Enterococcus*, and *Acetobac* ● Flies live on top of their food which serve to amplify microbial growth. Methods such as capillary feeding are used in an attempt to differentiate and minimize the interaction of fly food bacteria and fly gut bacteria
Research Question/Problem/ Need	By developing an understanding of the symbiosis of drosophila and the gut-microbiota, one can solidify the standing of Drosophila as an exemplary model of microbiome analysis.

Important Figures	
VOCAB: (w/definition)	**Symbionts**: an organism associated and in a symbiotic relationship with a much larger organism, in this case the bacteria in the gut microbiota and the fruit fly **Colonization**: presence of a microorganism in a host, with growth and multiplication of the organism but without interaction between host and organism **Acidic copper cell region:** region of the Drosophila midgut characterized by an acidic pH **Gnotobiotic**: state of an organism in which all forms of life in or on it, including its microbiota, have been identified.
Cited references to follow up on	Gilbert JA, Blaser MJ, Caporaso JG, Jansson JK, Lynch SV, Knight R. Current understanding of the human microbiome. *Nature Medicine*. 2018;24(4):392–400. 10.1038/nm.4517 [PMC free article] [PubMed] [CrossRef] [Google Scholar] Steinfeld HM. Length of life of Drosophila melanogaster under aseptic conditions. Dissertation thesis. University of California, Berkeley. 1927:1–23.
Follow up Questions	How do the findings regarding colonization probabilities and doses of bacterial strains in Drosophila aid our understanding of host-microbe interactions in other organisms, including humans? What insights do these findings provide for the development of Drosophila as a robust model for studying the gut microbiome, and what further research is needed?

Article #11 Notes: Serotonin modulates a depression-like state in Drosophila responsive to Lithium treatment

Source Title	Serotonin modulates a depression-like state in Drosophila responsive to Lithium treatment
Source citation (APA Format)	Ries, AS., Hermanns, T., Poeck, B. *et al.* Serotonin modulates a depression-like state in *Drosophila* responsive to lithium treatment. *Nat Commun* 8, 15738 (2017). https://doi.org/10.1038/ncomms15738
Original URL	https://www.nature.com/articles/ncomms15738#Sec7
Source type	Research Article
Keywords	Depression, Motivation, Stress and Resilience, Neural circuits
#Tags	#5-HT signaling, #MDD, #LithiumChloride
Summary of key points + notes (include methodology)	In this study, the researchers introduce a new protocol to induce a depression-like state in Drosophila melanogaster flies through repeated exposure to uncontrollable 300 Hz vibrations over several days. They demonstrate that the flies' climbing decisions at a challenging gap provide a reliable measure of their motivational state. Flies in the depression-like state exhibit fewer climbing attempts compared to unstressed, sated control flies, while unstressed but hungry flies display increased climbing attempts. This depression-like state not only reduces activity in various voluntary behaviors but also leaves reactive behaviors, such as escape running, unchanged. The induced depression-like state is distinguished from sexual deprivation effects and can be reversed by administering different antidepressants or sugars, even without caloric value. The study further reveals that serotonergic signaling to α- and γ-lobes of the mushroom bodies through various 5-HT receptors regulates behavioral activity, as evidenced by neurogenetic and pharmacological interventions. ● To measure the motivational state of a fly, they have the fly make climbing decisions at a calculated insurmountable gap, 4.5mm ● To measure walking activity, wings of flies were clipped and flies were individually placed in a Buridian's arena ● To test for anhedonia, or the stop-for-sweet paradigm, flies' wings were clipped and were individually placed in a rectangular chamber with a strip of glycerol. Flies were shaken down and had to walk to eat the glycerol.
Research Question/Problem/	To establish a novel method of inducing a depressive-state in Drosophila

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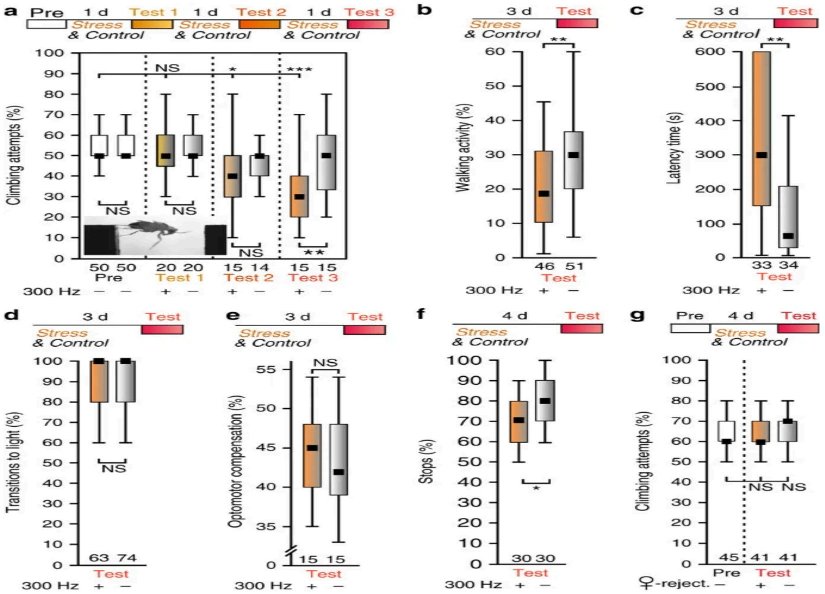
<tr><td>**Need**</td><td></td></tr>
<tr><td>**Important Figures**</td><td>


a) Males were tested for their motivation to climb (Pre-test) an insurmountable 4.5 mm-wide gap in a catwalk. Decreasing fractions of climbing attempts were observed after 2 days (Test 2), or 3 days (Test 3) of vibration treatment (orange bars) but not in sham-treated males (gray bars).
</td></tr>
<tr><td>**VOCAB: (w/definition)**</td><td>
Learned Helplessness: A state for an organism exposed to constant stressors; unavoidable punishment

MB: prominent structures structures in the the drosophila brain essential for olfactory (smell) learning and memory;process sensory and internal state information

MPT: Mitochondrial trifunctional proteins; enzyme; play a critical role in the oxidation of long chain fatty-acids

Kruskal-Wallis test: used to determine if there are statistically significant differences between two or more groups of an independent variable on a continuous or ordinal dependent variable.

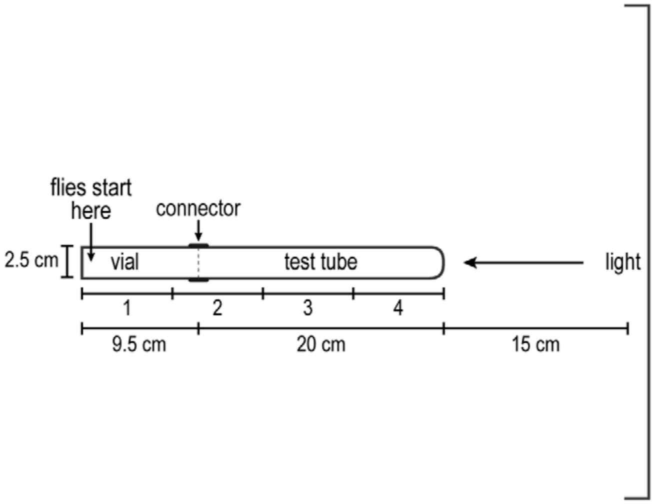
Optomotor response: shifts an animal in motion has to make as a result of unplanned course perturbations
</td></tr>
<tr><td>**Cited references to follow up on**</td><td>
Abelaira, H. M., Reus, G. Z., & Quevedo, J. (2013). Animal models as tools to study the pathophysiology of depression. *Revista Brasileira de Psiquiatria*, *35*(suppl 2), S112–S120.
</td></tr>
</table>

	https://doi.org/10.1590/1516-4446-2013-1098 Yang, Z., Bertolucci, F., Wolf, R., & Heisenberg, M. (2013). Flies Cope with Uncontrollable Stress by Learned Helplessness. *Current Biology*, *23*(9), 799–803. https://doi.org/10.1016/j.cub.2013.03.054
Follow up Questions	What was the process for performing the Epsiolid Body imaging and with what equipment?

Article #12 Notes: Simple Ways to Measure Behavioral Responses of Drosophila to Stimuli and Use of These Methods to Characterize a Novel Mutant

Source Title	Simple Ways to Measure Behavioral Responses of Drosophila to Stimuli and Use of These Methods to Characterize a Novel Mutant
Source citation (APA Format)	Vang LL, Medvedev AV, Adler J (2012) Simple Ways to Measure Behavioral Responses of Drosophila to Stimuli and Use of These Methods to Characterize a Novel Mutant. PLoS ONE 7(5): e37495. doi:10.1371/journal.pone.0037495
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3359294/
Source type	Journal article
Keywords	Drosophila Melanogaster, mutant-strain, Behavioral assays
#Tags	#behavioral study, #lab-oriented, #stimulus,

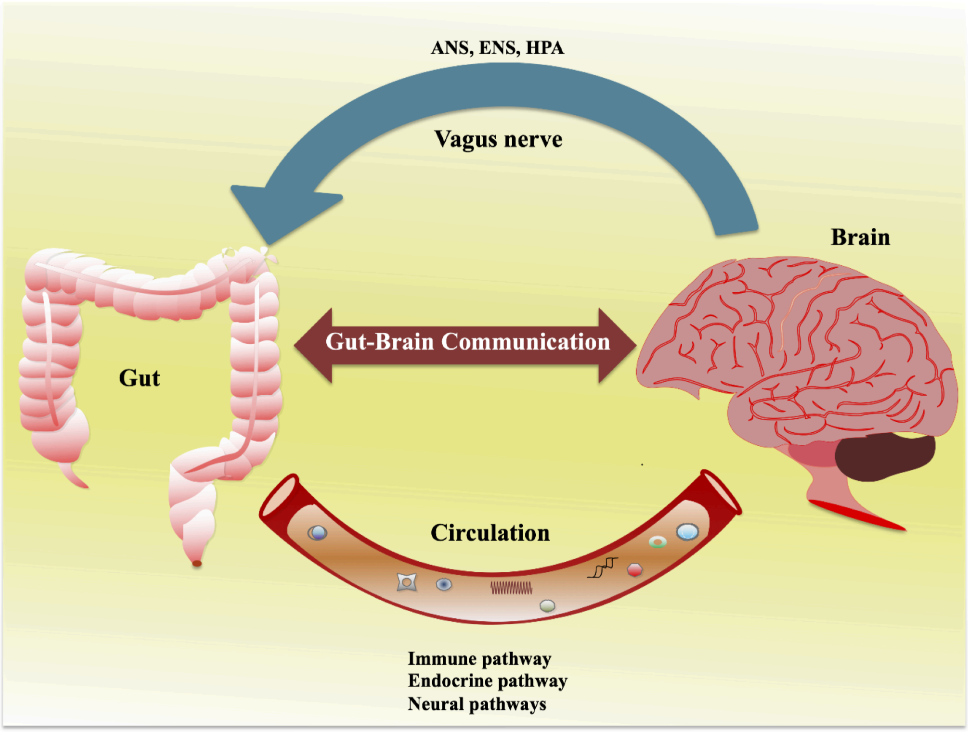
Summary of key points + notes (include methodology)	Previously, studies have extensively measured the behavioral responses of adult Drosophila fruit flies to different sensory stimuli, including light, chemicals, temperature, humidity, gravity, and sound. Some of these assays are quite intricate. The goal in this study was to develop affordable and straightforward methods for assessing the behavior of adult Drosophila fruit flies. These new assays have been applied to characterize a newly identified mutant, which, despite its ability to move, does not exhibit attraction or repulsion to various sensory stimuli.
	- Methods introduced:
	  - **Phototaxis:** - In a dark room, a vial containing approximately 20 flies, sealed with cotton, and a test tube were left separately for 30 minutes to allow the flies to adapt to darkness. The flies were then positioned away from the cotton, the cotton was removed, and the vial was connected to the test tube. This apparatus, placed horizontally and perpendicular to a light source 15 cm away, was used to conduct an experiment. The light was turned on, and a timer was started to count the flies every minute in each quarter of the apparatus. In a control group, a similar setup was used but placed 15 cm away from and parallel to the light source.
	  - **Smell Chemotaxis**: experiment involved testing the volatile repellent, benzaldehyde, on approximately 20 flies in two different methods. In Method 1, flies were placed in a vial, adapted to darkness for 30 minutes, and then exposed to benzaldehyde. The

	experiment was conducted in a dark room 15 cm away from a visible-light source. Flies' reactions were observed and counted every minute for 20 minutes. Method 2 involved placing flies in a test tube, adapting them to darkness, and introducing benzaldehyde in a similar setup. The flies' responses were counted every minute for 10 minutes. Control experiments without benzaldehyde were also conducted in both methods. The purpose was to assess the flies' reactions to benzaldehyde in controlled conditions.
Research Question/Problem/ Need	What are some possible ways to measure behavior responses to stimuli in drosophila?
Important Figures	 Figure shows how to measure response to light - Flies start out in the vial and go to the light source
VOCAB: (w/definition)	**Phototaxis**: the bodily movement of a motile organism in response to light, either toward the source of light (*positive phototaxis*) or away from it (*negative phototaxis*). **Chemotaxis**: movement of a motile cell or organism in a direction corresponding to a gradient of increasing or decreasing concentration of a particular substance. **Hygrotaxis:** the directional movement of an organism or cell in response to the stimulus of water.
Cited references to follow up on	Herrero P. Fruit fly behavior in response to chemosensory signals. Peptides. 2012 Dec;38(2):228-37. doi: 10.1016/j.peptides.2012.09.019. Epub 2012 Sep 26. PMID: 23022590. Vosshall LB, Stocker RF. Molecular architecture of smell and taste in

	Drosophila. Annu Rev Neurosci. 2007;30:505-33. doi: 10.1146/annurev.neuro.30.051606.094306. PMID: 17506643.
Follow up Questions	Does the sex of the fly matter when conducting these tests, is it ideal that they be separated? What should be the limit of flies inside the test tube when conducting the behavioral tests?

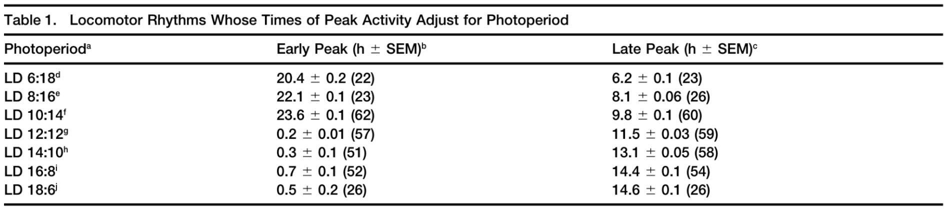
Article #13 Notes: Gut–Brain Axis: Role of Gut Microbiota on Neurological Disorders and How Probiotics/Prebiotics Beneficially Modulate Microbial and Immune Pathways to Improve Brain Functions

Source Title	Gut–Brain Axis: Role of Gut Microbiota on Neurological Disorders and How Probiotics/Prebiotics Beneficially Modulate Microbial and Immune Pathways to Improve Brain Functions
Source citation (APA Format)	Suganya, K.; Koo, B.-S. Gut–Brain Axis: Role of Gut Microbiota on Neurological Disorders and How Probiotics/Prebiotics Beneficially Modulate Microbial and Immune Pathways to Improve Brain Functions. *Int. J. Mol. Sci.* **2020**, *21*, 7551. https://doi.org/10.3390/ijms21207551
Original URL	https://www.mdpi.com/1422-0067/21/20/7551
Source type	Journal Article
Keywords	gut microbiota; gut–brain axis; neurological disorders; probiotics; antibiotics
#Tags	#biology, #microbiology, #bacteria, #neuroscience
Summary of key points + notes (include methodology)	The gut microbiome plays a crucial role in the gastrointestinal tract (GIT), acting as a significant interface for observing foods, nutrients, and environmental factors while distinguishing between commensals, pathogens, and others. - There's a strong and bidirectional connection between the gut and the central nervous system (CNS), influencing both health and disease. - A diverse and healthy gut microbiome is essential for normal brain functions and emotional behaviors. - Mechanisms such as endocrine, neuronal, toll-like receptor, and metabolite-dependent pathways contribute to this bidirectional relationship. Alterations in this relationship are associated with the development of gastrointestinal and neurological disorders → establishes the microbiota/gut-and-brain axis as a widely accepted concept. The review outlines recent findings supporting the role of the gut microbiota and the immune system in maintaining brain functions and influencing the development of neurological disorders. It also highlights advances in managing neurological diseases through probiotics, prebiotics, synbiotics, and fecal microbiota transplantation.
Research Question/Problem/ Need	How does the introduction of probiotics/prebiotics to the gut microbiome impact brain functions and what is the relationship between neurological disorders and

	gut microbiota?
Important Figures	 A schematic diagram showing the communication between the gut and brain. This is a bidirectional relationship that is strongly influenced by multiple pathways, including the autonomic nervous system (ANS), enteric nervous system (ENS), hypothalamic–pituitary–adrenal (HPA), immune pathways, endocrine pathways.
VOCAB: (w/definition)	**Enteric nervous system:** one of the main divisions of the peripheral nervous system, consists of neurons that govern the function of the gastrointestinal tract. **Intestinofugal neurons:** a unique subset of myenteric ganglion neurons that regulate normal gastrointestinal function.
Cited references to follow up on	Pellegrini C, Antonioli L, Colucci R, Blandizzi C, Fornai M. Interplay among gut microbiota, intestinal mucosal barrier and enteric neuro-immune system: a common path to neurodegenerative diseases? Acta Neuropathol. 2018 Sep;136(3):345-361. doi: 10.1007/s00401-018-1856-5. Epub 2018 May 24. PMID: 29797112.
Follow up Questions	What conditions may make the biome inhospitable to certain probiotic/prebiotic strains?

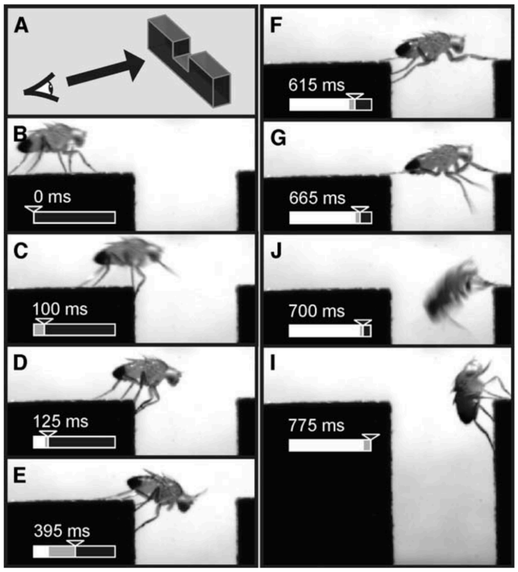
Article #14 Notes: Flies by Night: Effects of Changing Day Length on Drosophila's Circadian Clock

Source Title	Flies by Night: Effects of Changing Day Length on Drosophila's Circadian Clock
Source citation (APA Format)	Shafer OT, Levine JD, Truman JW, Hall JC. Flies by night: Effects of changing day length on Drosophila's circadian clock. Curr Biol. 2004 Mar 9;14(5):424-32. doi: 10.1016/j.cub.2004.02.038. PMID: 15028219.
Original URL	https://www.sciencedirect.com/science/article/pii/S0960982204001319
Source type	Journal Article
Keywords	Circadian rhythm, locomotion, drosophila
#Tags	#genetics, #protein, #gene-expression, #model-organism, #light-dark-cycle
Summary of key points + notes (include methodology)	In Drosophila, there is a self-regulating molecular mechanism involving two intersecting loops with a 24-hour oscillation period. The loops involve proteins PERIOD (PER) and TIMELESS (TIM), which repress the transcription of their respective genes by blocking positive transcription factors from the other loop. The interaction between these loops is marked by the entry of PER and TIM into the nucleus of a clock cell. Light pulses during the night affect the degradation of TIM and destabilize PER, leading to delayed or advanced clock time. While current models focus on the state of PER:TIM oscillation, this study investigates the effects of altered day length on PER and TIM dynamics in clock cells and locomotor rhythms, considering the influence of light-dark cycles mimicking seasonal changes on behavioral and gene expression adjustments. - Method: manipulated L/D cycles to assess the effects of altered day length on PER and TIM dynamics in central brain - Tracked locomotor activity peaks of Drosophila in different L/D cycles
Research Question/Problem/ Need	How can one deepen the understanding of the Drosophila Circadian Clock from a genetics angle?

<table>
<tr><td>Important Figures</td><td>
Table 1. Locomotor Rhythms Whose Times of Peak Activity Adjust for Photoperiod<table><tr><th>Photoperiod[a]</th><th>Early Peak (h ± SEM)[b]</th><th>Late Peak (h ± SEM)[c]</th></tr><tr><td>LD 6:18[d]</td><td>20.4 ± 0.2 (22)</td><td>6.2 ± 0.1 (23)</td></tr><tr><td>LD 8:16[e]</td><td>22.1 ± 0.1 (23)</td><td>8.1 ± 0.06 (26)</td></tr><tr><td>LD 10:14[f]</td><td>23.6 ± 0.1 (62)</td><td>9.8 ± 0.1 (60)</td></tr><tr><td>LD 12:12[g]</td><td>0.2 ± 0.01 (57)</td><td>11.5 ± 0.03 (59)</td></tr><tr><td>LD 14:10[h]</td><td>0.3 ± 0.1 (51)</td><td>13.1 ± 0.05 (58)</td></tr><tr><td>LD 16:8[i]</td><td>0.7 ± 0.1 (52)</td><td>14.4 ± 0.1 (54)</td></tr><tr><td>LD 18:6[j]</td><td>0.5 ± 0.2 (26)</td><td>14.6 ± 0.1 (26)</td></tr></table>Light-Dark conditions - the 24 hr day is broken up into hours of light on the left and hours of darkness on the right. The time of the activity peaks, such that “0” corresponds to lights-on. Numbers in parentheses designate the number of subjects that displayed an early peak in locomotor activity.</td></tr>
<tr><td>VOCAB: (w/definition)</td><td>Heterodimer: a protein composed of two polypeptide chains differing in composition in the order, number, or kind of their amino acid residues
Photoperiod: the period of time each day during which an organism receives illumination
Cytoplasm: the gelatinous liquid that fills the inside of a cell. It is composed of water, salts, and various organic molecules</td></tr>
<tr><td>Cited references to follow up on</td><td>Menegazzi P, Beer K, Grebler V, Schlichting M, Schubert FK, Helfrich-Förster C. A Functional Clock Within the Main Morning and Evening Neurons of <i>D. melanogaster</i> Is Not Sufficient for Wild-Type Locomotor Activity Under Changing Day Length. Front Physiol. 2020 Mar 26;11:229. doi: 10.3389/fphys.2020.00229. PMID: 32273848; PMCID: PMC7113387.</td></tr>
<tr><td>Follow up Questions</td><td>Considering the insights gained, are there potential therapeutic implications for understanding and manipulating circadian rhythms in other organisms?
What are the potential implications of these dynamics for seasonal adaptations in Drosophila?</td></tr>
</table>

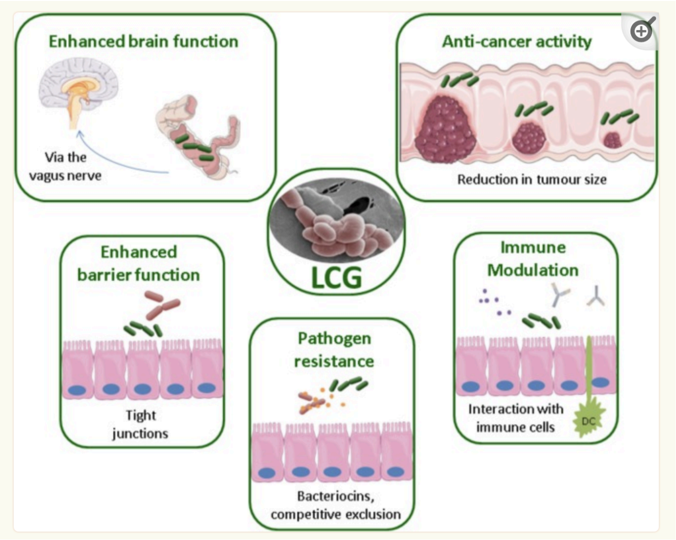
Article #15 Notes: Goal-Driven Behavioral Adaptations in Gap-Climbing Drosophila

Source Title	Goal-Driven Behavioral Adaptations in Gap-Climbing Drosophila
Source citation (APA Format)	Pick, S., & Strauss, R. (2005). Goal-Driven Behavioral Adaptations in Gap-Climbing Drosophila. *Current Biology*, *15*(16), 1473–1478. https://doi.org/10.1016/j.cub.2005.07.022
Original URL	https://www.sciencedirect.com/science/article/pii/S0960982205007633
Source type	Journal Article
Keywords	Drosophila, Behavior Assay, Locomotion
#Tags	#model-organism, #behavioral-study, #biology
Summary of key points + notes (include methodology)	A novel paradigm using neurogenetic tools in Drosophila was introduced to investigate reaching-task coordination. Freely walking flies encounter a gap obstacle and initiate gap-crossing behavior at all and how vigorously they try to reach the other side of the gap depends on a visual estimate of the gap width. By manipulating potential distance-measuring mechanisms, it was discovered that flies primarily use vertical edges on the target side to gauge gap width from parallax motion during approach. Flies exhibit three behavioral adaptations to maximize front-leg reach at surmountable gaps, with each leg pair contributing differently. - Mutant screening for climbing behaviors identified lines with defects in climbing initiation and specific impairments in distinct behavioral adaptations during climbing, highlighting these adaptations as separate subunits. - Method: varied the width of standardized chasm, flies were able to surmount gaps of up to 4.3 mm. At gaps up to 2.5 mm wide, approximately 80% of all approaches were successful
Research Question/Problem/ Need	How can we deepen our understanding of the role the CNS plays during goal-oriented muscle activity?

Important Figures	 Male Drosophila Crossing a 3.5-mm-Wide Gap in a video. Arrowheads indicate the time point of a given frame on a linear timescale. Remaining time is in black, time elapsed since the last-shown frame in gray.
VOCAB: (w/definition)	**Photoreceptors**: specialized neurons found in the retina that convert light into electrical signals that stimulate physiological processes. **Binocular disparity**: the difference in image location of an object seen by the left and right eyes, resulting from the eyes' horizontal separation (parallax)
Cited references to follow up on	Niven JE. Visuomotor control: Drosophila bridges the gap. Curr Biol. 2010 Apr 13;20(7):R309-11. doi: 10.1016/j.cub.2010.02.028. PMID: 20392418.
Follow up Questions	What specific neurogenetic tools were employed in the novel paradigm, and how did they contribute to the study's findings?

Article #16 Notes: The *Lactobacillus casei* Group: History and Health Related Applications

Source Title	The *Lactobacillus casei* Group: History and Health Related Applications
Source citation (APA Format)	Hill D, Sugrue I, Tobin C, Hill C, Stanton C, Ross RP. The *Lactobacillus casei* Group: History and Health Related Applications. Front Microbiol. 2018 Sep 10;9:2107. doi: 10.3389/fmicb.2018.02107. PMID: 30298055; PMCID: PMC6160870.
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6160870/
Source type	Review article
Keywords	lactobacillus, casei, paracasei, rhamnosus, health, stress, taxonomy
#Tags	#biology, #health, #education, #lactobacillus-group
Summary of key points + notes (include methodology)	The Lactobacillus casei group (LCG), consisting of Lactobacillus casei, Lactobacillus paracasei, and Lactobacillus rhamnosus, is one of the most extensively studied and widely applied probiotic species within the lactobacilli family. - Differentiation among these species is challenging using traditional phenotypic and genotypic methods, prompting ongoing development of new distinguishing techniques. - The health-promoting properties of these species have led to their classification and reclassification over time. As significant probiotics, they find widespread use in various industries. Recent research has primarily focused on their potential applications in promoting health, both in the treatment and prevention of various diseases and disorders, especially those linked to disturbances in the gut microbiota. Stress responses, critical for their survival and probiotic efficacy, have been a key area of investigation within the LCG. - Potential mechanisms of the bacteria include the production of antimicrobial substances such as bacteriocins, enhancing the epithelial barrier through attachment, competition for pathogenic binding sites, or modulation of the immune system.
Research Question/Problem/ Need	To educate the reader on the various health impacts involving the Lactobacillus group.

Important Figures	 Probiotic action taken by the LCG
VOCAB: (w/definition)	***L.rhamnosus***: bacterium originally considered to be a subspecies of L. casei, but genetic research found it to be a separate species in the L. casei clade **Genotoxic agent**s: chemical or agent that can cause DNA or chromosomal damage.
Cited references to follow up on	Huang CH, Li SW, Huang L, Watanabe K. Identification and Classification for the *Lactobacillus casei* Group. Front Microbiol. 2018 Aug 22;9:1974. doi: 10.3389/fmicb.2018.01974. PMID: 30186277; PMCID: PMC6113361.
Follow up Questions	Are there other bacterial groups that perhaps address issues that Lactobacilli is limited to?

Article #17 Notes: Gut microbiome and human health: Exploring how the probiotic genus *Lactobacillus* modulate immune responses

Source Title	Gut microbiome and human health: Exploring how the probiotic genus *Lactobacillus* modulate immune responses
Source citation (APA Format)	Rastogi, S., & Singh, A. (2022). Gut microbiome and human health: Exploring how the probiotic genus Lactobacillus modulate immune responses. *Frontiers in Pharmacology*, *13*. https://doi.org/10.3389/fphar.2022.1042189
Original URL	https://doi.org/10.3389/fphar.2022.1042189
Source type	Review Article
Keywords	Lactobacillus, Probiotics, Immune System
#Tags	#biology, #immune-response, #bacteria
Summary of key points + notes (include methodology)	Lactobacillus species belonging to the phylum Firmicutes are crucial components of the gut microbiome and play a pivotal role in probiotic bacteria. The gut-residing Lactobacillus members engage in communication not only with each other but also with the gut epithelial lining. Their functions include maintaining the balance of gut barrier integrity, reinforcing mucosal barrier defense, and modulating host immune responses. Given their significant influence on the gut microbiome, these Lactobacillus species are implicated in addressing inflammatory diseases affecting various bodily tissues, including the gut, lungs, heart, bones, and neural tissues.
Research Question/Problem/ Need	To educate the reader on the impact that the probiotic genus Lactobacillus has on immune health.

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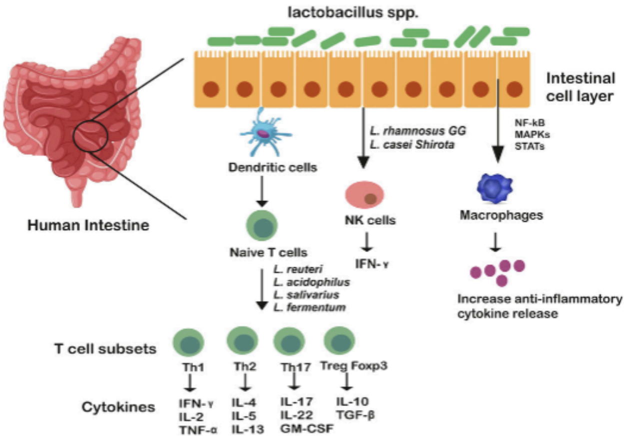
<tr><td>Important Figures</td><td>


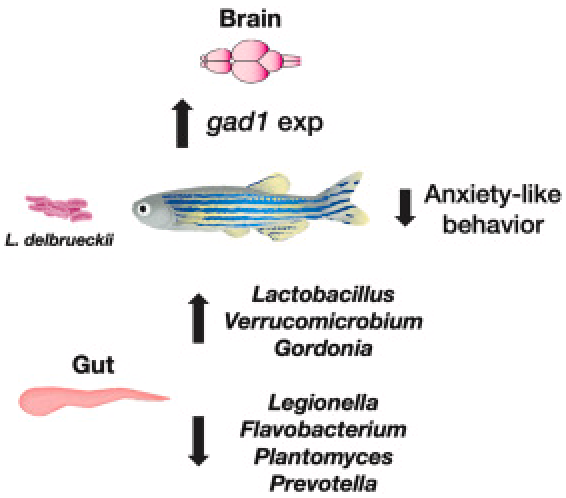
Lactobacillus mediated immune modulation in the gut. <i>Lactobacillus</i> as whole bacteria or their components communicate through membrane receptors TLR-6 and TLR-2, expressed on macrophages and dendritic cells.</td></tr>
<tr><td>VOCAB: (w/definition)</td><td>Macrophages: specialized cells involved in the detection, phagocytosis and destruction of bacteria and other harmful organisms

Immune modulation: regulation and modulation of immunity that might be achieved by reducing or enhancing the immune response

Dendritic cells: cells that inform the fight against invasive pathogens while enforcing tolerance to self and harmless environmental antigens</td></tr>
<tr><td>Cited references to follow up on</td><td>Ahsan, A., Mazhar, B., Khan, M. K., Mustafa, M., Hammad, M., and Ali, N. M. (2022). Bacteriocin-mediated inhibition of some common pathogens by wild and mutant Lactobacillus species and <i>in vitro</i> amplification of bacteriocin encoding genes. <i>ADMET DMPK</i> 10, 75–87. doi:10.5599/admet.1053</td></tr>
<tr><td>Follow up Questions</td><td>Have there been studies exploring the synergistic effects of Lactobacillus with other immune-modulating agents or therapies?</td></tr>
</table>

Article #18 Notes: *Lactobacillus delbrueckii* reduces anxiety-like behavior in zebrafish through a gut microbiome – brain crosstalk

Source Title	*Lactobacillus delbrueckii* reduces anxiety-like behavior in zebrafish through a gut microbiome – brain crosstalk
Source citation (APA Format)	Olorocisimo, J. P., Diaz, L. A., Co, D. E., Carag, H. M., Ibana, J. A., & Velarde, M. C. (2023). Lactobacillus delbrueckii reduces anxiety-like behavior in zebrafish through a gut microbiome – brain crosstalk. *Neuropharmacology*, *225*, 109401–109401. https://doi.org/10.1016/j.neuropharm.2022.109401
Original URL	https://doi.org/10.1016/j.neuropharm.2022.109401.
Source type	Journal Article
Keywords	Psychobiotics, AnxiolyticGut-brain axis, *Danio rerio,* Lactic acid bacteria
#Tags	#zebrafish, #lactobacillus, #neuroscience, #gut-microbiome
Summary of key points + notes (include methodology)	Certain bacteria can alleviate anxiety and stress-related behaviors through the gut microbiome-brain axis, known as psychobiotics, enhancing mood and cognition. This study investigated three species within the Lactobacillacea family—Lactobacillus delbrueckii, Lacticaseibacillus casei, and Lacticaseibacillus paracasei—for potential psychobiotic activities. Treatment with L. delbrueckii in zebrafish reduced anxiety-like behavior, increased brain and gut glutamic acid decarboxylase (gad) gene expression, and influenced the gut microbial community. Unlike L. delbrueckii, L. paracasei and L. casei did not consistently improve anxiety-like behavior in zebrafish, suggesting L. delbrueckii's potential role as a psychobiotic for anxiety reduction. - Method: Bacteria were cultured in De Man, Rogosa and Sharpe (MRS) broth at a concentration of 3 × 109 CFU/ml using serial dilution and pour plate methods. Bacterial suspensions were pelleted at 4000×*g* and resuspended in 1 ml PBS, then inoculated twice a day into fish tanks containing ten 6-7 month-old female fish each, at a final concentration of 1.6 × 106 CFU/ml per aquarium for 2 weeks
Research Question/Problem/	What Lactobacillus strains are most effective as psychobiotics in zebrafish?

Need	
Important Figures	 Graphical Abstract of the study, details the beneficial and non-beneficial bacteria that impacts the zebra fish
VOCAB: (w/definition)	**Psychobacterium**: beneficial bacteria (probiotics) or support for such bacteria (prebiotics) that influence bacteria–brain relationships **Thigmotaxis**: the motion or orientation of an organism in response to a touch stimulus. **Anxiolytic**: something used to reduce anxiety.
Cited references to follow up on	Almeida, A., Mitchell, A. L., Boland, M., Forster, S. C., Gloor, G. B., Tarkowska, A., Lawley, T. D., & Finn, R. D. (2019). A new genomic blueprint of the human gut microbiota. *Nature*, *568*(7753), 499–504. https://doi.org/10.1038/s41586-019-0965-1
Follow up Questions	How were the fish tanks set up for the experiment, and were there any specific environmental conditions maintained during the treatment period? Could you elaborate on the rationale behind selecting a concentration of 1.6 × 106 CFU/ml per aquarium and the decision to inoculate twice a day for a duration of 2 weeks?

Article #19 Notes: A new genomic blueprint of the human gut microbiota

Source Title	A new genomic blueprint of the human gut microbiota
Source citation (APA Format)	Almeida, A., Mitchell, A. L., Boland, M., Forster, S. C., Gloor, G. B., Tarkowska, A., Lawley, T. D., & Finn, R. D. (2019). A new genomic blueprint of the human gut microbiota. *Nature*, *568*(7753), 499–504. https://doi.org/10.1038/s41586-019-0965-1
Original URL	https://www.scopus.com/record/display.uri?eid=2-s2.0-85062538500&origin=inward&txGid=d3a0d1dfbdd39ed8650ad3295303f74d
Source type	Journal Article
Keywords	Bacteria; Gastrointestinal Microbiome; Genome, Bacterial; Genomics;
#Tags	#bacterium; #digestive system; #genome; #microbial activity
Summary of key points + notes (include methodology)	Understanding the individual microbial species within the human gut microbiota is crucial for unraveling their roles in health and disease. - Despite extensive efforts in culturing and sequencing, the complete bacterial diversity in the human gut remains unknown. - This study addresses this gap by identifying 1,952 uncultured candidate bacterial species. By reconstructing metagenome-assembled genomes from a large number of human gut microbiomes, these uncultured genomes significantly increase the known species diversity by 281%. - While these new species are less common in well-studied populations, they substantially enhance the classification accuracy of understudied African and South American samples by more than 200%. Overall, this research contributes to an expanded understanding of uncultured gut bacteria diversity, offering unprecedented insights for characterizing the taxonomic and functional aspects of the intestinal microbiota.
Research Question/Problem/ Need	To broaden the incomplete understanding of the bacterial diversity within the human gut microbiota as a result of various uncultured and thus, unidentifiable bacteria.

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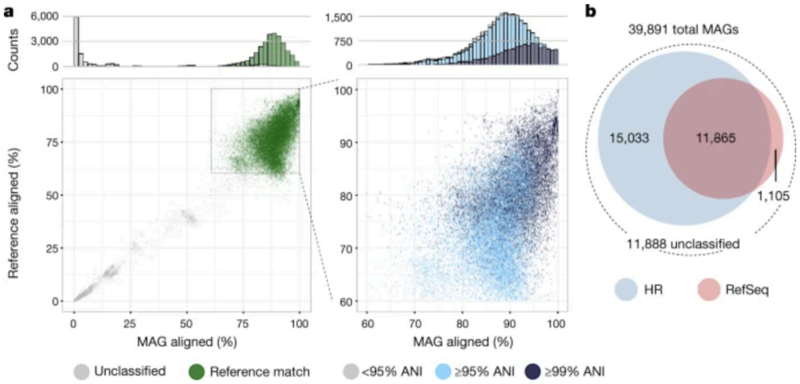
Fig. 1: Thousands of metagenome-assembled genomes do not match isolate genomes.



On the left, a near-complete (>90% completeness, <5% contamination) MAGs that matched the HR database (green; ≥95% average nucleotide identity over at least 60% of the genome) and those that could not be classified (gray). On the right, an expanded view of MAGs with an alignment fraction of at least 60%, coloured on the basis of the ANI in relation to the best matching HR genome

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<td>VOCAB: (w/definition)</td>
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Phylum: a group of organisms with a certain degree of morphological or developmental similarity or as a group of organisms with an evolutionary relationship. “Phylum” is placed below “Kingdom” and above “Class”

Cultured vs uncultured bacteria: Cultured means it can be reproduced in a lab for further study, uncultured means that the bacteria is unable to grow in lab conditions.

Metagenome-assembled genomes (MAGS): a group of scaffolds with similar characteristics from a metagenome assembly that represent the microbial genome.

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<tr>
<td>Cited references to follow up on</td>
<td>

Kim, C.-S. (2024). Roles of diet-associated gut microbial metabolites on brain health: cell-to-cell interactions between gut bacteria and the central nervous system. *Advances in Nutrition*, *15*(1), 100136–100136. https://doi.org/10.1016/j.advnut.2023.10.008

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<tr>
<td>Follow up Questions</td>
<td>

What criteria was used for selecting the human gut microbiomes in the study?
How might this impact fields in medicine and nutrition?

</td>
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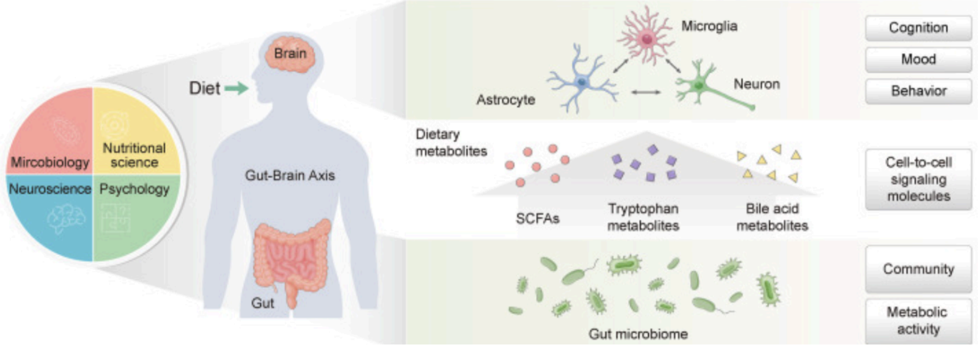
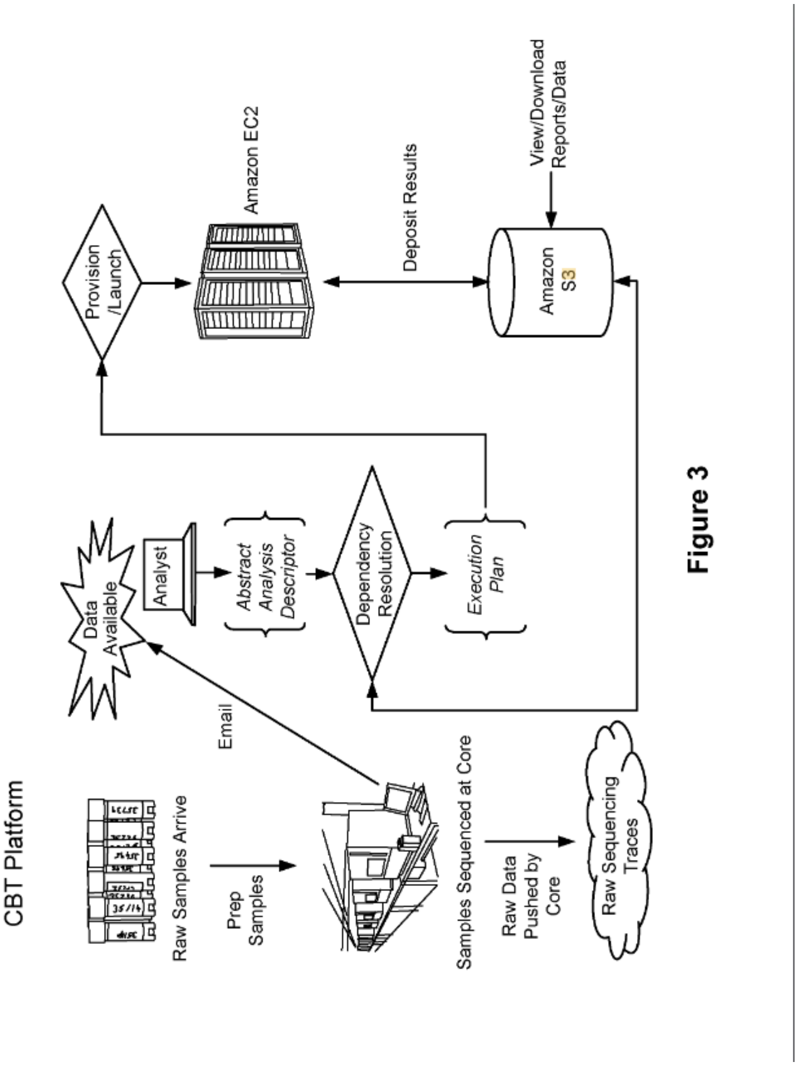
Article #20 Notes: Roles of Diet-Associated Gut Microbial Metabolites on Brain Health: Cell-to-Cell Interactions between Gut Bacteria and the Central Nervous System

Source Title	Roles of Diet-Associated Gut Microbial Metabolites on Brain Health: Cell-to-Cell Interactions between Gut Bacteria and the Central Nervous System
Source citation (APA Format)	Kim, C.-S. (2024). Roles of diet-associated gut microbial metabolites on brain health: cell-to-cell interactions between gut bacteria and the central nervous system. *Advances in Nutrition*, *15*(1), 100136–100136. https://doi.org/10.1016/j.advnut.2023.10.008
Original URL	https://www.sciencedirect.com/science/article/pii/S2161831323013972?pes=vor
Source type	Review Article
Keywords	dietary metabolites; gut microbiota; gut–brain axis;astrocytes; microglia;cell-to-cell interaction;mental health
#Tags	#nutrition, #biology, #gut-microbiome
Summary of key points + notes (include methodology)	The gut microbiota has a significant influence on brain function through the gut–brain axis. Emerging evidence indicates that this interaction is facilitated by signaling molecules originating from dietary components metabolized by the intestinal microbiota. While recent studies have provided valuable insights into the cell-specific effects of these microbial molecules in gut microbiome brain research, additional validation is required. - Review consolidates recent findings on gut microbiota-derived dietary metabolites that enter the systemic circulation, impacting cell-to-cell interactions between gut microbes and central nervous system (CNS) cells, including microglia, astrocytes, and neuronal cells. - Specifically, the review emphasizes the roles of metabolites, such as short-chain fatty acids, tryptophan metabolites, and bile acid metabolites, produced by the gut microbiota through the transformation of dietary components. These metabolites promote the function and maturation of brain cells while suppressing inflammatory signals in the CNS.

	The review also outlines future directions for gut microbiome–brain research, with a focus on potential diet-induced microbial metabolite-based therapies as novel approaches to mental health treatment.
Research Question/Problem/ Need	To educate the reader on the relationship between diet and gut bacteria.
Important Figures	 Role of diet-associated metabolites as signaling molecules in cell-to-cell interactions between the gut bacteria and CNS.
VOCAB: (w/definition)	**Metabolite**: a substance produced during metabolism, helps with energy conversion, signaling, and epigenetic influence **Bile**: a bitter greenish-brown alkaline fluid that aids digestion and is secreted by the liver and stored in the gallbladder.
Cited references to follow up on	Fan, Y., & Pedersen, O. (2020). Gut microbiota in human metabolic health and disease. *Nature Reviews Microbiology*, *19*. https://doi.org/10.1038/s41579-020-0433-9
Follow up Questions	What are the specific roles of specific metabolites like short-chain fatty acids, tryptophan metabolites, and bile acid metabolites especially in regards to its relationship to the gut microbiome?

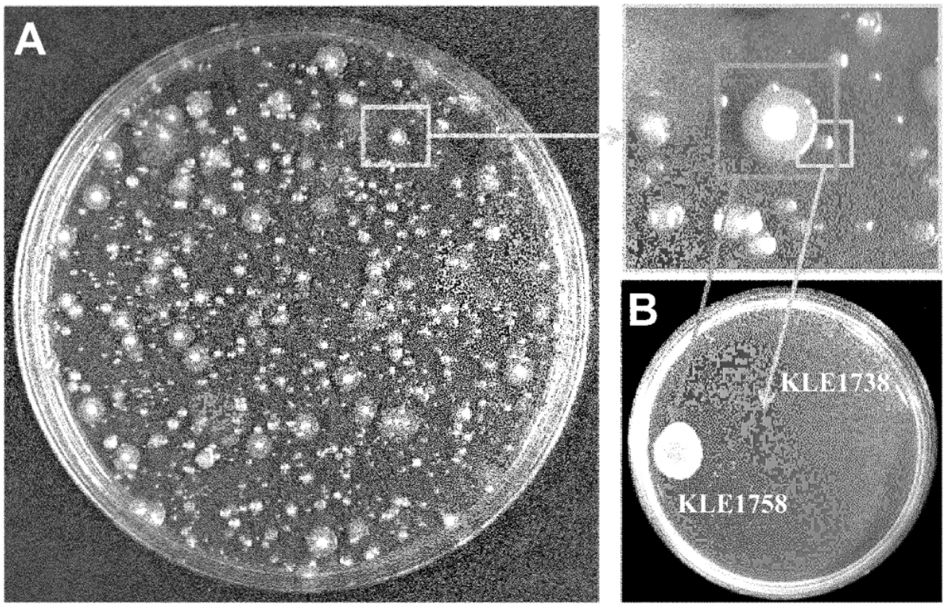
Patent #1: METHODS AND COMPOSITIONS RELATING TO MICROBIAL TREATMENT AND DIAGNOSIS OF DISORDERS

Source Title	METHODS AND COMPOSITIONS RELATING TO MICROBIAL TREATMENT AND DIAGNOSIS OF DISORDERS
Source citation (APA Format)	Cutcliffe, C. (2016). *Methods and compositions relating to microbial treatment and diagnosis of disorders* (Pendulum Therapeutics Patent). https://patents.google.com/patent/US20160228476A1/fi
Original URL	https://patents.google.com/patent/US20160228476A1/fi
Source type	Patent
Summary of key points + notes (include methodology)	Patent provides methods, systems, compositions, and kits to address the need for microbiome-related treatment of health conditions and disease, along with treatment of metabolic conditions using microbial compositions.
Research Question/Problem/ Need	Despite the interrelation between microbiomes and health, the complexity of the various microbiomes, as well as difficulties in characterizing, categorizing, and analyzing microbiome constituents makes understanding microbiomes challenging. These challenges present hurdles in the development of diagnostic and therapeutic applications for microbiome-related health conditions and diseases.

Important Figures	 Figure 3 Flowchart describing patented data extraction and analysis procedure
VOCAB: (w/definition)	**Sequencing**: used in molecular biology to study genomes and the proteins they encode. **Pure bacteria**: A pure bacteria culture that only contains one single type
Follow up Questions	What were the specific challenges associated with characterizing and categorizing microbiome constituents? What are the key obstacles in this process?

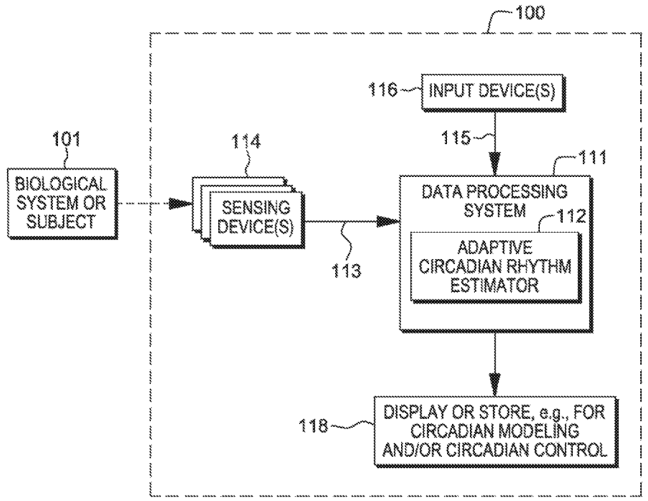
Patent #2 Notes: Modulation of the gut microbiome to treat mental disorders or diseases of the central nervous system

Source Title	Modulation of the gut microbiome to treat mental disorders or diseases of the central nervous system
Source citation (APA Format)	Strandwitz, P. (2021). *Modulation of the gut microbiome to treat mental disorders or diseases of the central nervous system* (Holobiome Inc Patent). https://patents.google.com/patent/US20190070225A1/en
Original URL	https://patents.google.com/patent/US20190070225A1/en
Source type	Patent
Summary of key points + notes (include methodology)	Patent discloses methods of treating at least one symptom of a mental disorder or disease of the central nervous system in a subject by modulating the amount of GABA produced in the subject's gut. The present disclosure also relates to methods of culturing the bacterial strain and new bacterial strains. Also disclosed are methods of identifying bacterial strains capable of producing GABA, and engineering strains to produce GABA.
Research Question/Problem/ Need	Microbiological studies have been limited by the necessity to focus on cultivable microorganisms. It is estimated that, particularly in external environments, around 99% of bacteria remain uncultured. The advancement of novel culturing techniques for previously uncultured or deemed unculturable bacteria presents an opportunity to broaden the scope of microbiology research.
Important Figures	

	 shows a co-culture assay to grow and identify previously unculturable bacteria.
VOCAB: (w/definition)	**GABA**: inhibitory neurotransmitter, principal role is reducing neuronal excitability throughout the nervous system **Glutamate**: an excitatory neurotransmitter with several types of receptors found throughout the CNS, functions include learning and memory
Follow up Questions	In what specific ways does the ability to culture previously uncultured bacteria expand the scope of microbiology research? What challenges are commonly encountered when attempting to culture previously uncultured bacteria?

Patent #3 Notes: Circadian phase estimation, modeling and control

Source Title	Circadian phase estimation, modeling and control
Source citation (APA Format)	Zhang, J. (2021). *Circadian phase estimation, modeling and control* (Rensselaer Polytechnic Institute Patent). https://patents.google.com/patent/US10896739B2/en?q=(drosophila+circadian)&oq=drosophila+circadian+
Original URL	https://patents.google.com/patent/US10896739B2/en?q=(drosophila+circadian)&oq=drosophila+circadian+
Source type	Patent
Summary of key points + notes (include methodology)	A method, system, and computer program product was designed for estimating the circadian phase of a subject. - Process involves obtaining a sensed biological signal for the subject and utilizing adaptive frequency tracking by one or more processors to dynamically estimate the circadian phase from the sensed signal. - Accelerated circadian phase estimation is achieved through a feedback loop for adaptive frequency tracking, incorporating a circadian phase model to automatically determine a phase correction. - The estimated circadian phase is further utilized to automatically construct a light-based circadian rhythm model for the subject using a linear parameter-varying (LPV) formulation. Once constructed, the circadian rhythm model is employed for light-based circadian rhythm regulation.
Research Question/Problem/ Need	Biological markers for circadian rhythm may be masked by other factors, (ex. Light stimulation may affect body temperature and heart rate as well), which may affect research outcome.

Important Figures	 FIG. 1 A Flow Chart illustrating an embodiment of a system for facilitating estimating circadian phase and generating a circadian rhythm model from the input
VOCAB: (w/definition)	**Retinal ganglion cell**: a type of neuron located near the inner surface of the retina of the eye, receives visual information from photoreceptors **Electronic oscillator**: electronic circuit that produces a periodic, oscillating or alternating current signal
Follow up Questions	What types of biological signals are typically sensed in this method? Is the method adaptable to different individuals with varying circadian patterns, and how does it account for individual differences in circadian phase?