

Project Notes:

Project Title: The Effects of fucoidan on depression symptoms of a Drosophila model

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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.

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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
How do SSRIs and other antidepressants work	Doing research, and taking notes on articles	Article notes of #4 and 5	September 10, 2023
Why are Drosophila used in neuroscience studies	Reading articles	Article 12	October 23, 2023
What are assays to model Drosophila depression	Research	In Articles. Use tags to find.	December 1, 2023
What model of depression is best for testing fucoidan effects	Research	Articles 14, 16-19	December 1, 2023

Literature Search Parameters:

These searches were performed between (Start Date of reading) and August 2023.

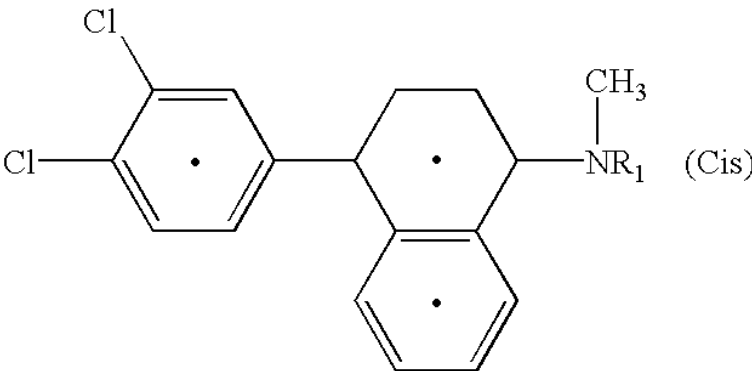
List of keywords and databases used during this project.

Database/search engine	Keywords	Summary of search
National Institute of Health	"depression" "gut"	Wide variety of articles. I added the keyword "serotonin" to further refine the search. I found a few papers that I looked into from this search including a very interesting study on <i>Hizikia fusiformis</i> .
National institute of Health	"Drosophila" "serotonin"	Brought up many studies on different neurological disorders using <i>Drosophila</i> . I looked and found a paper on the more general neurological structure for <i>Drosophila</i> and the reasoning for using the species in neuro-based studies.
PubMed (only used to find articles, summaries are of the full texts"	"Fucoidan" - Narrowed down search to articles released in the last 5 years	This gave 606 results I then sorted through the results by using command+F to search for words related to my project, this narrowed it down to 6 articles Then I skimmed these articles, taking notes on 2 because they were most relevant to my research question

Tags:

Tag Name	
#anxiety	#gut microbiome
#biomedical engineering	#cells
#depression	#neurotransmitters
#antidepressants	#neuron production
#SSRIs	#neuroimaging
#Tryptophan	#food ideas
#psychology	#serotonin
#brown seaweed	#dopamine
#overview	#neuron
#fucoidan	#Hizikia fusiformis
#components of Hizikia fusiformis	#omega-3
#gut-brain	#diet
#glutamate	#drosophila
#neurotransmitter transporters	#assays
#RING method	#CUMS
#aggression assay	#L-DOPA
#locomotive assay	#methods

Patent #1 Notes: Long Acting Antidepressant Microparticles

Source Title	Google Patents
Patent number	US6482440B2
Patent Office/location of patent application	United States
Source citation (APA Format)	Zemlan, F. P., & Mulchahey, J. (2002). <i>Long acting antidepressant microparticles</i> (Patent US6482440B2). https://patents.google.com/patent/US6482440B2/en
Original URL	https://patents.google.com/patent/US6482440B2/en
Keywords	Depression, antidepressant, treatment
#Tags	#depression #antidepressants
Summary of key points + notes (include methodology)	<p>It's an antidepressant treatment containing sertraline. Sertraline is made up of many tiny particles, this helps the medication release slower, henceforth resulting in longer lasting effects. The longer release time will also help sustain effects longer and regulate the medication more.</p> <p>Notes:</p> <ul style="list-style-type: none"> - Active chemical substance that is in the same grouping of fluoxetine - Microparticles of this substance are used - One method of implementing treatment is through injection
Research Question/Problem/Need	Treatment for depression
Important Figures	 <p>The antidepressant proposed</p>

Cited references to follow up on	Tice, T. R., & Lewis, D. H. (1983). <i>Microencapsulation process</i> (Patent US4389330A). https://patents.google.com/patent/US4389330A/en
Follow up Questions	Can fluoxetine and other similar chemicals be distributed as microparticles? What is the size difference between the particles of this medication and other commonly used medications?

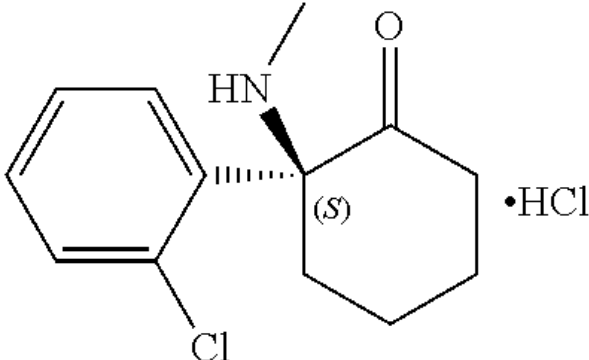
Patent #2 Notes: Fluoxetine Pill Formation Method

Source Title	Google Patents
Patent number/ application number	95304975.6
Patent Office/location of patent application	European Patent Office
Source citation (APA Format)	Mendizabal, F. A. (1996). <i>Fluoxetine Pharmaceutical formulations</i> (Patent EP0693281A2). https://patents.google.com/patent/EP0693281A2/en
Original URL	https://patents.google.com/patent/EP0693281A2/en
Keywords	Depression, antidepressant, treatment, Fluoxetine
#Tags	#depression #antidepressants
Summary of key points + notes (include methodology)	<p>This is a way to distribute antidepressants in pill forms. It uses fluoxetine as its base and developed formula to make fluoxetine pills easy to manufacture and distribute, while also being effective. The pills are claimed to be able to disintegrate in water in less than 3 minutes. This pill formation uses direct compression to create pills. The formula has other substances and possible add-ins to help with a variety of things, including but not limited to disintegration, lubrication, and flavoring.</p> <p>Notes:</p> <ul style="list-style-type: none"> - Water temperature for disintegration is 19°C to 21°C - Excipients - substance that serves as a vehicle for drug disposal - Coadjuvantes - component of a pill that is used for supportive qualities(disintegration, lubrication, etc.) - There are issues with current medications <ul style="list-style-type: none"> - Difficulty swallowing <ul style="list-style-type: none"> - Mainly with elder and child patients - Dosage adjustability
Research Question/Problem/ Need	Treatment for depression

Important Figures	<table border="1" data-bbox="553 226 1487 575"> <thead> <tr> <th>COMPONENTS</th> <th>WEIGHT (mg)</th> <th>% BY WEIGHT</th> </tr> </thead> <tbody> <tr> <td>FLUOXETINE HYDROCHLORIDE</td> <td>20</td> <td>6.7</td> </tr> <tr> <td>SODIUM STARCH GLYCOLATE</td> <td>50</td> <td>16.66</td> </tr> <tr> <td>LACTOSE</td> <td>123</td> <td>40.97</td> </tr> <tr> <td>L-HPC 21</td> <td>75</td> <td>25.00</td> </tr> <tr> <td>SODIUM SACCHARIN</td> <td>2</td> <td>0.67</td> </tr> <tr> <td>MINT AROMA</td> <td>30</td> <td>10.00</td> </tr> </tbody> </table> <p data-bbox="521 604 1211 636">This is Example one of possible formulations of the tablet.</p>	COMPONENTS	WEIGHT (mg)	% BY WEIGHT	FLUOXETINE HYDROCHLORIDE	20	6.7	SODIUM STARCH GLYCOLATE	50	16.66	LACTOSE	123	40.97	L-HPC 21	75	25.00	SODIUM SACCHARIN	2	0.67	MINT AROMA	30	10.00
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L-HPC 21	75	25.00																				
SODIUM SACCHARIN	2	0.67																				
MINT AROMA	30	10.00																				
Cited references to follow up on	<p data-bbox="521 667 1214 699"><i>Antidepressant composition</i> (Patent GB1498857A). (1978).</p> <p data-bbox="553 737 1175 768">https://patents.google.com/patent/GB1498857A/en</p> <p data-bbox="521 806 1430 837">Mckee, I. K., & William, H. (1962). <i>Tablet disintegrants</i> (Patent US3034911A).</p> <p data-bbox="553 875 1175 907">https://patents.google.com/patent/US3034911A/en</p>																					
Follow up Questions	<p data-bbox="521 976 1484 1045">How did you decide on specific qualities (disintegration, flavor, etc.) to prioritize? Which is more important?</p> <p data-bbox="521 1050 1484 1081">How much does dosage effect the formula, pill size, and manufacturing process?</p>																					

Patent #3 Notes: Methods for the Treatment of Depression

Source Title	Google Patents
Patent number/ application number	10,869,844B2
Patent Office/location of patent application	United States
Source citation (APA Format)	Caers, L. I., Singh, J., Zannikos, P. N., Drevets, W. C., Daly, E., Canuso, C. M., Fedgchin, M., & Wiegand, F. (2020). <i>Methods for the treatment of depression</i> (Patent US10869844B2). https://patents.google.com/patent/US10869844B2/en
Original URL	https://patents.google.com/patent/US10869844B2/en
Keywords	Depression, antidepressant, treatment, treatment methods
#Tags	#depression #antidepressants
Summary of key points + notes (include methodology)	<p>This patent is a method of specifying dosage for an antidepressant medication. It uses multiple factors, but mainly focuses on using a patient's genotype to determine their Val66Met rs6265 polymorphism in their BDNF. The system then will determine dosage and administer ketamine.</p> <p>Notes:</p> <ul style="list-style-type: none"> - Continuation of US patent 14/853,351 - Treatment through (S)-2-(2-chlorophenyl)-2-(methylamino) cyclohexanone starts with induction phase of 4 weeks <ul style="list-style-type: none"> - During this phase dosage ranges from about 28 to 84 mg - Also during this phase treatment is administered twice a week - After induction phase there is a maintenance phase <ul style="list-style-type: none"> - Administered once per week or once per every other week - Dosage of 56 to 84 mg
Research Question/Problem/Need	Treat depression → has a more specific focus of preventing suicide due to depression

<p>Important Figures</p>	<p style="text-align: right;">(I)</p>  <p>Esketamine referred to by patent</p> <ul style="list-style-type: none"> - This is one of the substances that could be administered after applying the patent method
<p>Cited references to follow up on</p>	<p>Caers, L. I., Salvatore, G., & Singh, J. (2016). <i>VAL66MET (SNP rs6265) GENOTYPE SPECIFIC DOSING REGIMENS AND METHODS FOR THE TREATMENT OF DEPRESSION</i> (Patent US20160074340A1).</p> <p>https://patents.google.com/patent/US20160074340A1/en?q=14%2f853%2c35</p> <p>1</p>
<p>Follow up Questions</p>	<p>What future work is planned to continue this method? Are there any issues with the method that is directly associated with looking at genotype?</p>

Article #1 Notes: Title

Article notes should be on separate sheets

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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: the connection between the gut microbiome and social anxiety

Source Title	The gut microbiome in social anxiety disorder: evidence of altered composition and function
Source citation (APA Format)	Butler, M. I., Bastiaanssen, T. F. S., Long-Smith, C., Morkl, S., Berding, K., Ritz, N. L., Strain, C., Patangia, D., Patel, S., Stanton, C., O'Mahony, S. M., Cryan, J. F., Clarke, G., & Dinan, T. G. (2023). The gut microbiome in social anxiety disorder: evidence of altered composition and function. <i>Translational Psychiatry</i> , 13(1), 1–12. https://doi.org/10.1038/s41398-023-02325-5
Original URL	https://www.nature.com/articles/s41398-023-02325-5
Source type	Scientific Journal
Keywords	Gut microbiome, SAD
#Tags	#anxiety, #gut microbiome
Summary of key points + notes (include methodology)	<p>A test showed that the gut microbiome of people with SAD compared to that of a person without SAD had many differences beta-diversity wise, but no differences were seen in alpha diversity. This proved that the gut microbiome of patients with SAD differed from that of the control group, further studies are being planned to look further into the differences and possible applications.</p> <ul style="list-style-type: none"> - Gut microbiome of people with SAD differed from that of a person without SAD - Further suggests gut-brain axis has an effect on anxiety and other mental health disorders
Research Question/Problem/Need	How does the gut microbiome differ in people with social Anxiety Disorder(SAD)?
Important Figures	“A total of 73 genera and 159 species were identified Of these, three genera and two species were found to show significant differences in relative abundance after false discovery rate (FDR) correction using the Benjamini-Hochberg procedure”
VOCAB: (w/definition)	Genera: ranks used for biological classification

Cited references to follow up on	Keller MB. The lifelong course of social anxiety disorder: a clinical perspective. <i>Acta Psychiatr Scand Suppl.</i> 2003;2003:85–94. Dinan TG, Cryan JF. Regulation of the stress response by the gut microbiota: implications for psychoneuroendocrinology. <i>Psychoneuroendocrinology.</i> 2012;37:1369–78.
Follow up Questions	Do any anxiety medications that are currently prescribed to patients affect these specific microorganisms? Can the microbiome be changed just by a specific diet or supplements? If the gut microbes can be altered from the SAD groups biome to the control groups, will it show a significant change in SAD symptoms?

Article #2 Notes: Tissue Engineers Hack Life's Code for 3-D Folded Shapes

Article notes should be on separate sheets

Source Title	Tissue Engineers Hack Life's Code for 3-D Folded Shapes
Source citation (APA Format)	<i>Tissue Engineers Hack Life's Code for 3-D Folded Shapes</i> <i>Quanta Magazine</i> . (2018, January 25). Quanta Magazine. https://www.quantamagazine.org/tissue-engineers-hack-lifes-code-for-3-d-folded-shapes-20180125/
Original URL	https://www.quantamagazine.org/tissue-engineers-hack-lifes-code-for-3-d-folded-shapes-20180125/
Source type	Science News Cite
Keywords	Synthetic tissue, scaffolding, cells
#Tags	#biomedical engineering, #cells,
Summary of key points + notes (include methodology)	Gartner, Hughes and their colleagues looked at clusters of mouse cells and examined how they pulled on their surrounding matrix. From what they found they were able to manipulate the process to get the cells to grow into a specific shape.
Research Question/Problem/Need	How can cells for synthetic tissue be shaped without using scaffolding?
Important Figures	The engineers were able to get the tissues to form in a variety of shapes
VOCAB: (w/definition)	Scaffolding - supports for cell attachment and tissue development
Cited references to follow up on	Popkin, G. (2016, August 16). <i>Jammed Cells Expose the Physics of Cancer</i> . Quanta Magazine. https://www.quantamagazine.org/jammed-cells-expose-the-physics-of-cancer-20160816/

Follow up Questions

Can this method be modified to be used for different types of cells?
How can these synthetic tissues be used in other fields?
Can these synthetic tissues safely be used inside a person?

Article #3 Notes: Causes of Depression

Article notes should be on separate sheets

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Source Title	What Causes Depression
Source citation (APA Format)	<p>Harvard Health Publishing. (2022, January 10). <i>What causes depression?</i> Harvard Health; Harvard Health.</p> <p>https://www.health.harvard.edu/mind-and-mood/what-causes-depression</p>
Original URL	https://www.health.harvard.edu/mind-and-mood/what-causes-depression
Source type	General Article
Keywords	Depression, neurotransmitters, serotonin, antidepressants, neurons
#Tags	#depression #neurotransmitters #antidepressants #neuron production
Summary of key points + notes (include methodology)	<p>Depression can have a variety of causes. There have been proven differences in certain brain areas of people with depression. PET, SPECT, and fMRI scanners were used to see which brain regions had a larger effect on depression. Research is also being done to see the correlation between the production of new neurons in the hippocampus and depression. In the past researchers believed antidepressants worked by increasing the number of neurotransmitters, but because antidepressants take a few weeks to see the effects it is now being debated that they work by increasing neuron production.</p>
Research Question/Problem/Need	What causes depression?
Important Figures	In a study it was shown that on average, the hippocampus of people suffering from depression was 9% to 13% smaller than those who were not depressed
VOCAB: (w/definition)	Neurogenesis - the process in which new neurons are made
Cited references to follow up on	<p>https://www.health.harvard.edu/depression/depression-chemicals-and-communication</p> <p>https://www.health.harvard.edu/depression/how-genes-and-life-events-affect-mood-and-depression</p>

Follow up Questions

Can we improve and/or increase neurogenesis with diet?

How do antidepressants work?

How does depression affect the connections between brain regions?

What chemicals improve neurogenesis?

Article #4 Notes: How antidepressants work

Article notes should be on separate sheets

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Source Title	Antidepressants
Source citation (APA Format)	<i>Antidepressants</i> . (n.d.). Www.nhsinform.scot. https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/antidepressants#:~:text=It%27s%20thought%20that%20antidepressants%20work
Original URL	https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/antidepressants#:~:text=It%27s%20thought%20that%20antidepressants%20work,pain%20signals%20sent%20by%20nerves.
Source type	General Article
Keywords	Antidepressants, neuroimaging, depression, SSRIs
#Tags	#antidepressants #neuroimaging #depression #SSRIs
Summary of key points + notes (include methodology)	Antidepressants are a type of medication that can be used to treat a variety of diseases. Most commonly it is used to treat clinical depression but it can also be used to treat other mental illnesses. There are 4 main types of antidepressants, these are SSRIs, SNRIs, NASSAs, and TCAs. They mainly work by increasing levels of neurotransmitters, typically serotonin and noradrenaline. They are the most effective way to treat depression. Dosage, type, and effectiveness all depend on the particular patient. Consistency when taking the medicine is very important. Each type has different side effects.
Research Question/Problem/Need	Overall workings of and information on antidepressants
Important Figures	SSRIs are the most common type Dosages usually start off low Stopping causes side effects
VOCAB: (w/definition)	Serotonin reuptake - One serotonin is done carrying a message, nerve cells will reabsorb the serotonin

Cited references to follow up on	https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/antidepressants#cautions-and-interactions
Follow up Questions	Why does not taking the medicine consistently have such great side effects? How do antidepressants increase neurotransmitters? How does an increase in neurotransmitters help lessen depression symptoms? Why do different types of antidepressants work for different people? How is it decided what antidepressant is best for a specific patient?

Article #5 Notes: SSRIs

Article notes should be on separate sheets

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Source Title	Selective serotonin reuptake inhibitors (SSRIs)
Source citation (APA Format)	<p><i>Selective serotonin reuptake inhibitors (SSRIs)</i>. (2023). NHS Inform.</p> <p>Www.nhsinform.scot.https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/selective-serotonin-reuptake-inhibitors-ssris#:~:text=It%27s%20thought%20to%20have%20a</p>
Original URL	https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/selective-serotonin-reuptake-inhibitors-ssris#:~:text=It%27s%20thought%20to%20have%20a,messages%20between%20nearby%20nerve%20cells
Source type	General Article
Keywords	SSRIs, antidepressants
#Tags	#SSRIs #antidepressants
Summary of key points + notes (include methodology)	<p>Selective serotonin reuptake inhibitors (SSRIs) are a commonly used form of antidepressants, but they are prescribed for a variety of disorders. They work by preventing serotonin from being absorbed by nerve cells, therefore increasing the amount of serotonin available in the brain. It wouldn't be correct to say depression and other related disorders are caused by low serotonin levels, but it is shown that increasing serotonin levels can help depression and related disorders. The increased level of serotonin is believed to lessen the symptoms of depression. They are usually taken as a tablet. At first a low dose is prescribed. There are many side effects associated with SSRIs.</p>
Research Question/Problem/Need	What are SSRIs and how do they work?
Important Figures	SSRIs work by preventing serotonin from being absorbed by nerve cells, therefore

	increasing the amount of serotonin available in the brain
VOCAB: (w/definition)	Reuptake: nerve cells that reabsorb a neurotransmitter
Cited references to follow up on	Not a cited reference, but another website found while doing this research https://www.ocduk.org/overcoming-ocd/medication/how-ssri-work/
Follow up Questions	How do SSRIs block reuptake?

Article #6 Notes: Tryptophan

Article notes should be on separate sheets

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Source Title	Tryptophan
Source citation (APA Format)	<i>Tryptophan: MedlinePlus Medical Encyclopedia.</i> (2013). Medlineplus.gov. https://medlineplus.gov/ency/article/002332.htm
Original URL	https://medlineplus.gov/ency/article/002332.htm
Source type	Medical encyclopedia entry
Keywords	Tryptophan, depression, serotonin
#Tags	#Tryptophan #food ideas #depression #serotonin
Summary of key points + notes (include methodology)	Tryptophan is an amino acid. It is used by the human body to create proteins, muscle, enzymes, and neurotransmitters. Specifically, two things Tryptophan is used to make are serotonin and melatonin. It can be found in many food sources: poultry, milk, egg, certain seeds, fish, etc. The body cannot produce tryptophan so it must be ingested.
Research Question/Problem/Need	What is Tryptophan?
Important Figures	<ul style="list-style-type: none"> - Can't be made by the body - Helps production of serotonin and melatonin
Cited references to follow up on	United States Department of Health and Human Services; United States Department of Agriculture. <i>2015-2020 Dietary Guidelines for Americans</i> . 8th ed. health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines/guidelines/ . Updated December 2015. Accessed May 27, 2022.
Follow up Questions	Does increasing serotonin production in the brain have the same effect as preventing reuptake?

Article #7 Notes: Hizikia fusiformis extracts effect on brain

Article notes should be on separate sheets

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Source Title	Dopamine and serotonin alterations by Hizikia fusiformis extracts under in vitro cortical primary neuronal cell cultures
Source citation (APA Format)	Jung, J.-W., Kim, Y.-J., Choi, J. S., Goto, Y., & Lee, Y.-A. (2023). Dopamine and serotonin alterations by <i>Hizikia fusiformis</i> extracts under <i>in vitro</i> cortical primary neuronal cell cultures. <i>Nutrition Research and Practice</i> , 17(3), 408. https://doi.org/10.4162/nrp.2023.17.3.408
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10232209/
Source type	Research Paper
Keywords	Dopamine, serotonin, seaweed, neuronal outgrowth, psychiatric disorders
#Tags	#neurotransmitters #psychology #dopamine #serotonin #neuron #food ideas #brown seaweed
Summary of key points + notes (include methodology)	<p>Neural cell cultures were taken from mice. They were then treated with Hizikia fusiformis(HF) extract. Multiple antibodies for dopamine(DA) and serotonin (5HT) were monitored in the cell cultures. HF was shown to significantly affect the levels of DRD1 but not other DA receptors. The effect was shown to be dose dependent. It was also shown to potentially down regulate DAT. The effect on evidence of one molecule associated with 5HT transmission (5HT1B) also showed to be higher at the same dose. At this same dose, the expression levels of NF-L, a molecule associated with neuronal structure formation, increased. Although no differences were observed in the other 2 molecules measured. This suggests a possible association with the specific dosage and effect on neuronal structure formation. Results: increased specific DA and 5HT cell receptors and down regulated the levels of DA and 5HT transporters</p> <p>Notes</p> <ul style="list-style-type: none"> - Hizikia fusiformis is a type of brown seaweed - It is known to affect the nervous system but it is unsure how this

	<p>connection is made</p> <ul style="list-style-type: none"> - dopamine(DA) and serotonin(5HT) are two neurotransmitters that play important roles in psychiatric disorders and brain development - Cell cultures were monitored in virtue <ul style="list-style-type: none"> - Taken from the Cortical part of mice' brains - the non - control groups were treated with 0.1, 1.0, and 10. $\mu\text{g}/\text{mL}$ HF extract <ul style="list-style-type: none"> - The one with the most significant results was the 1.0 $\mu\text{g}/\text{mL}$ HF extract - DRD1, DRD2, DRD3, DRD5 were all measured <ul style="list-style-type: none"> - Only DRD1 showed a significant change - shown to potentially down regulate DAT - In the cells treated with 1.0 $\mu\text{g}/\text{mL}$ HF extract SERT expression appeared to increase compared to the control group <ul style="list-style-type: none"> - No increase of other 5HT related molecules <p>Results: increased specific DA and 5HT cell receptors and down regulated the levels of DA and 5HT transporters</p>
Research Question/Problem/Need	Does HR increase dopamine levels, serotonin levels, or neuronal structure formation.
Important Figures	The greatest expression of DRD1 was in the HR group with 1.0 $\mu\text{g}/\text{mL}$, compared to 0.1 $\mu\text{g}/\text{mL}$ and 10.0 $\mu\text{g}/\text{mL}$. The effect on evidence of 5HT transmission also showed to be higher at 1.0 $\mu\text{g}/\text{mL}$
VOCAB: (w/definition)	Embryonic - relating to an embryo Immunostaining - a way to detect amount of a protein using antibodies Neurofilament - filaments found in the cytoplasm of neurons Cortical - relating to the outer layer of the cerebrum
Cited references to follow up on	Gamo NJ, Arnsten AF. Molecular modulation of prefrontal cortex: rational development of treatments for psychiatric disorders. <i>Behav Neurosci.</i> 2011;125:282–296. [PMC free article] [PubMed] [Google Scholar] Spies M, Knudsen GM, Lanzenberger R, Kasper S. The serotonin transporter in psychiatric disorders: insights from PET imaging.

	<p><i>Lancet Psychiatry</i>. 2015;2:743–755. [PubMed] [Google Scholar]</p> <p>Meinita MD, Harwanto D, Sohn JH, Kim JS, Choi JS. <i>Hizikia fusiformis</i>: pharmacological and nutritional properties. <i>Foods</i>. 2021;10:1660. [PMC free article] [PubMed] [Google Scholar]</p> <p>Luo D, Zhang Q, Wang H, Cui Y, Sun Z, Yang J, Zheng Y, Jia J, Yu F, Wang X, et al. Fucoidan protects against dopaminergic neuron death <i>in vivo</i> and <i>in vitro</i>. <i>Eur J Pharmacol</i>. 2009;617:33–40. [PubMed] [Google Scholar]</p> <p>30. Paudel P, Seong SH, Jung HA, Choi JS. Characterizing fucoxanthin as a selective dopamine D3/D4 receptor agonist: relevance to Parkinson’s disease. <i>Chem Biol Interact</i>. 2019;310:108757. [PubMed] [Google Scholar]</p>
<p>Follow up Questions</p>	<p>Does only finding correlation between one of the molecules for neurotransmitter result from or correlate with a low amount of the neurotransmitter produced? Can the same results be made from digesting HF? What made the researchers choose hizikia fusiformis? What other foods can be tested in the family? Should similar food groups be looked into? Should algae?</p>

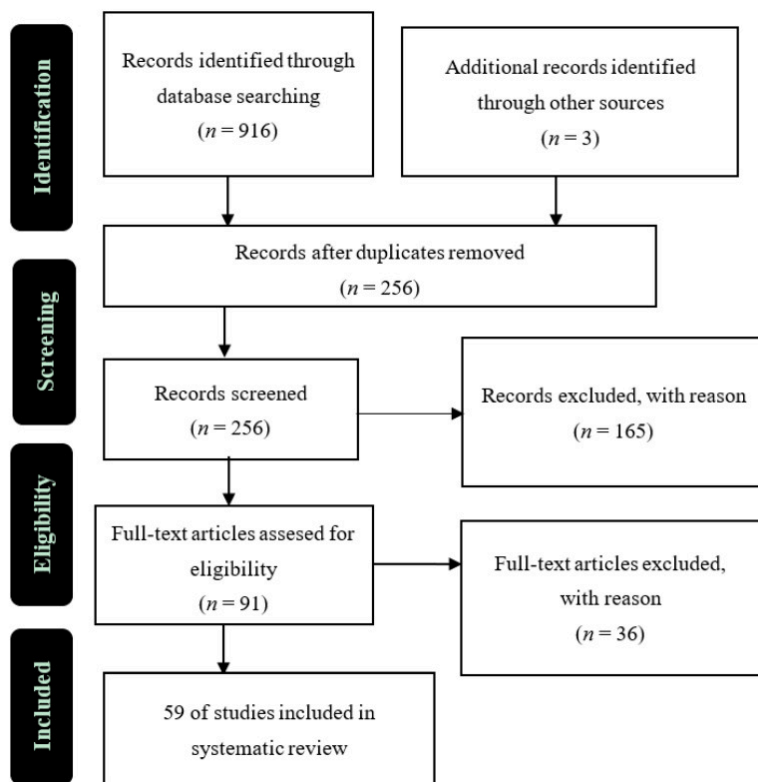
Article #8 Notes: Hizikia fusiformis

Article notes should be on separate sheets

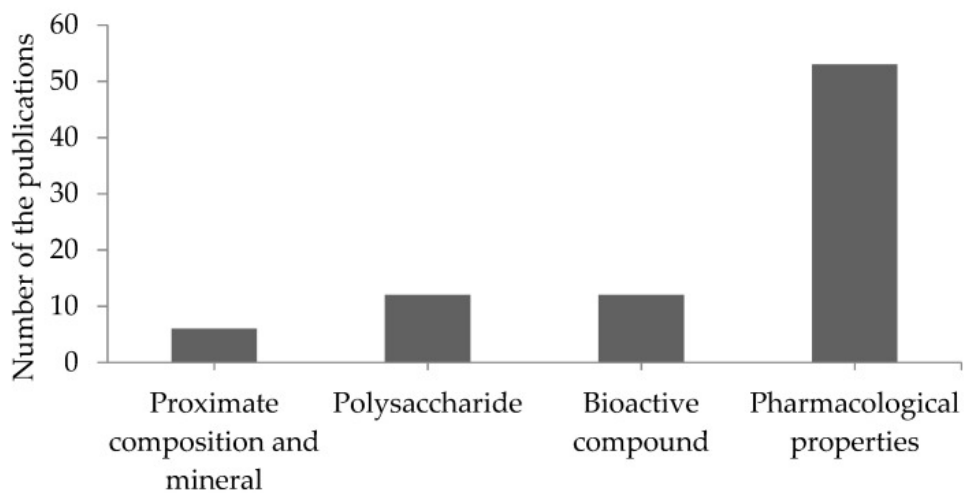
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Source Title	Hizikia fusiformis: Pharmacological and Nutritional Properties
Source citation (APA Format)	Meinita, M. D. N., Harwanto, D., Sohn, J.-H., Kim, J.-S., & Choi, J.-S. (2021). Hizikia fusiformis: Pharmacological and Nutritional Properties. <i>Foods</i> , 10(7), 1660. https://doi.org/10.3390/foods10071660
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8306711/
Source type	Journal article
Keywords	Hizikia fusiformis, Sargassum fusiforme, hijiki, nutritional properties, pharmacological properties, fucoidan
#Tags	#food ideas #brown seaweed #fucoidan #Hizikia fusiformis #components of Hizikia fusiformis
Summary of key points + notes (include methodology)	<p>Hizikia Fusiformis has been used by East Asian countries in traditional cuisine and medicine for centuries. This research paper provided a comprehensive overview of the research done on the pharmaceutical properties of Hizikia Fusiformis. They found 916 articles from 2010 to 2021 on the topic, they then further narrowed the number of articles down to 59.</p> <p>Findings</p> <ul style="list-style-type: none"> - Research into Hizikia Fusiformis has greatly increased over the last 10 years - Most articles focused on the pharmaceutical properties of hizikia fursiformis - Seaweeds contain higher of macro minerals - Fucoidans are a sulfated polysaccharide in brown seaweed <ul style="list-style-type: none"> - Known to have very good pharmaceutical properties - Hizikia forfumos has been found to have a multitude of pharmaceutical properties: antibacterial, antioxidant, anticancer, anti inflammatory, photoprotective, neuroprotective, antidiabetic, immunomodulatory, osteoprotective, and gastroprotective
Research Question/Problem/Need	What are the pharmacological and nutritional properties of Hizikia fusiformis?

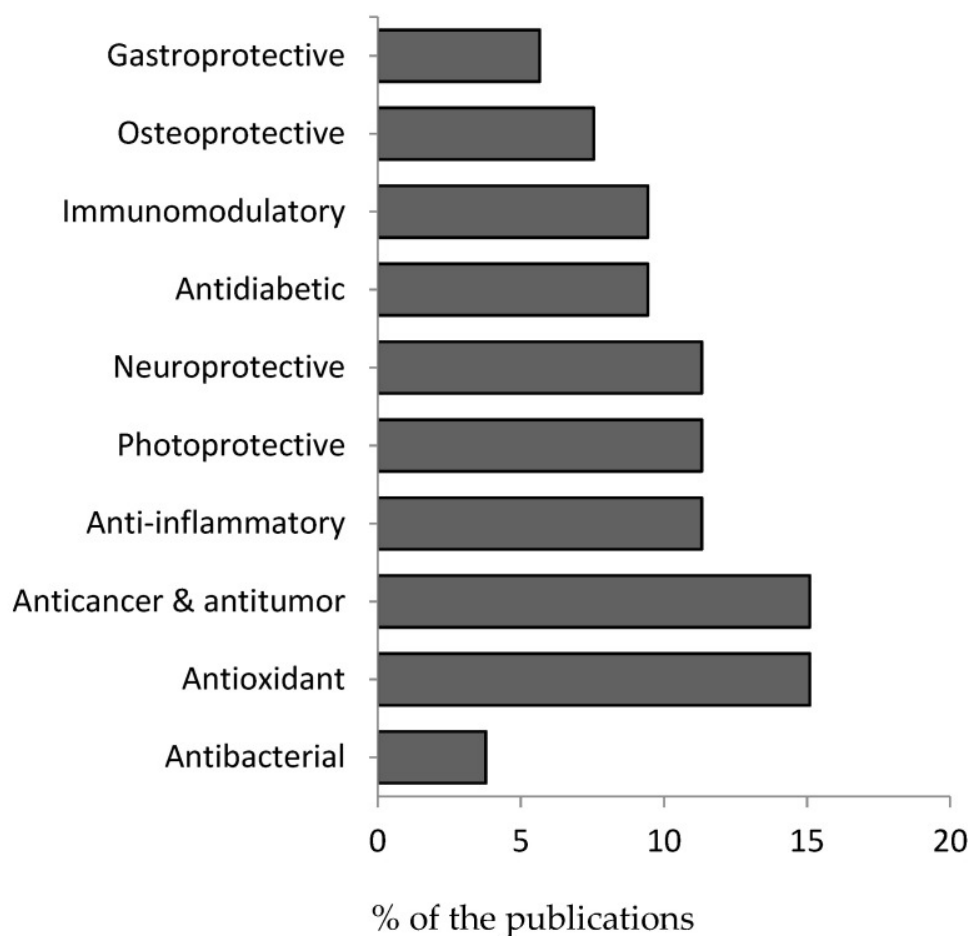
Important Figures



Graph of how the articles were chosen and how the selection process chose which articles to focus on



Bar graph of the main topics of the articles



This bar graph is of the percent of the articles(out of articles that focused on the pharmaceutical properties) by what their more specific focus was
 Most important to my research: 11.32% were focused on the neuroprotective effects of Hizikia Fusiformis

- "Polysaccharides account for 40–50% of the dry matter of seaweed cell walls"
- 2 main types of fucoidan

<p>VOCAB: (w/definition)</p>	<p>Alga - a group of aquatic plants including seaweeds and multiple single celled organisms Neuroprotective: working to protect nerve cells from any form of impairment Photoprotective: protection from UV damage</p>
<p>Cited references to follow up on</p>	<p>Cherry P., O’hara C., Magee P.J., Mcsorley E.M., Allsopp P.J. Risks and benefits of consuming edible seaweeds. <i>Nutr. Rev.</i> 2019;77:307–329. doi: 10.1093/nutrit/nuy066. [PMC free article] [PubMed] [CrossRef] [Google Scholar] Chen L., Chen P., Liu J., Hu C., Yang S., He D., Yu P., Wu M., Zhang</p>

	<p>X. <i>Sargassum fusiforme</i> polysaccharide SFP-F2 activates the NF-κB signaling pathway via CD14/IKK and p38 axes in RAW264.7 cells. <i>Mar. Drugs</i>. 2018;16:264. doi: 10.3390/md16080264. [PMC free article] [PubMed] [CrossRef] [Google Scholar]</p> <p>Cheng Y., Sibusiso L., Hou L., Jiang H., Chen P., Zhang X., Wu M., Tong H. <i>Sargassum fusiforme</i> fucoidan modifies the gut microbiota during alleviation of streptozotocin-induced hyperglycemia in mice. <i>Int. J. Biol. Macromol.</i> 2019;131:1162–1170. doi: 10.1016/j.ijbiomac.2019.04.040. [PubMed] [CrossRef] [Google Scholar]</p> <p>Wang Y., Xing M., Cao Q., Ji A., Liang H., Song S. Biological activities of fucoidan and the factors mediating its therapeutic effects, A review of recent studies. <i>Mar. Drugs</i>. 2019;17:183. doi: 10.3390/md17030183. [PMC free article][PubMed] [CrossRef] [Google Scholar]</p>
Follow up Questions	<p>What benefits does fucoidan have?</p> <p>What is the effect of fucoidan on depression?</p>

Article #9 Notes: Gut microbiome overview of effects on Mental disorders

Article notes should be on separate sheets

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Source Title	Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders
Source citation (APA Format)	Horn, J., Mayer, D. E., Chen, S., & Mayer, E. A. (2022). Role of diet and its effects on the gut microbiome in the pathophysiology of mental disorders. <i>Translational Psychiatry</i> , 12(1), 164. https://doi.org/10.1038/s41398-022-01922-0
Original URL	https://www.nature.com/articles/s41398-022-01922-0
Source type	Journal article
Keywords	Mental disorders, brain-gut axis, microbiome, brain
#Tags	#gut microbiome, #food ideas, #overview, #gut-brain axis
Summary of key points + notes (include methodology)	<p>The abstract highlights the growing evidence suggesting that diet significantly influences the interactions between the brain, gut, and microbiome, collectively known as the brain-gut-microbiome (BGM) system. This system involves various communication channels, including neuroendocrine, neural, and immune pathways, which establish bidirectional connections between the brain, gut, and their microbiota. Diet not only shapes the composition of the gut microbiome but also affects the brain's structure and function through these communication channels.</p> <p>The review discusses the available evidence from both preclinical and clinical studies regarding the impact of dietary habits and interventions on certain psychiatric and neurological disorders such as depression, cognitive decline, Parkinson's disease, autism spectrum disorder, and epilepsy. It specifically focuses on the role of diet-induced changes in the microbiome, which have been implicated in these disorders, and some of these effects are shared among various brain disorders.</p> <p>The majority of findings in this area have been demonstrated in preclinical</p>

and cross-sectional epidemiological studies, but there is currently insufficient mechanistic evidence from human studies to establish a causal relationship between a specific diet and microbiome-mediated brain function. Many of the observed dietary benefits on the microbiome and brain health are attributed to anti-inflammatory effects mediated by microbial metabolites of dietary fiber and polyphenols.

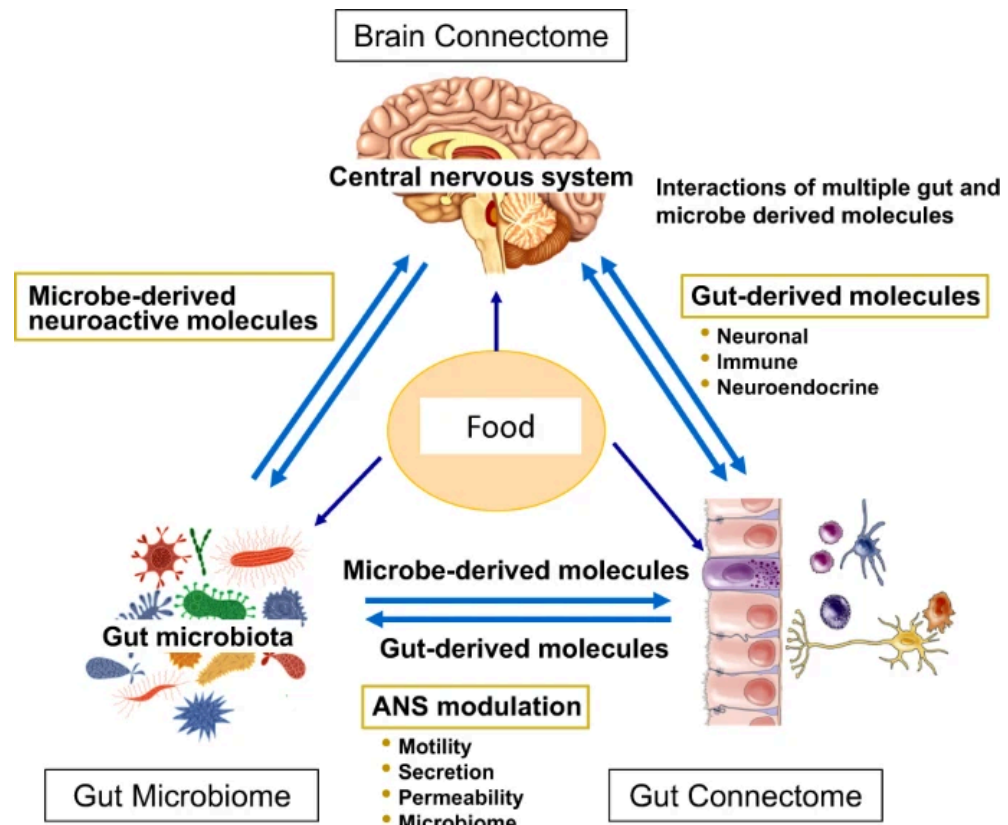
Overall, the increased attention to dietary factors in brain disorders has the potential to enhance the effectiveness of existing pharmacological and non-pharmacological treatments for these conditions.

Summary by ChatGPT

Research Question/Problem/Need

What is the effect of diet on gut microbiome on mental disorders?

Important Figures



- Graphic from article depicting the relationship between the gut, more specifically the gut microbiome, and the central nervous system.

VOCAB: (w/definition)

Pathophysiology - disordered changes in body functions caused by diseases
 Connectome- the comprehensive map of the elements and connections of a body system
 Connectome - A thorough overview of the connections throughout the nervous

	system
Cited references to follow up on	https://www.tandfonline.com/doi/full/10.1080/1028415X.2017.1411320?scroll=top&needAccess=true&role=tab
Follow up Questions	How do specific foods affect the gut microbiome? Which microbiota have the greatest effect on depression?

Article #10 Notes: Mediterranean Diet with fish oil effect on the Mental Health of people with depression

Source Title	A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED)
Source citation (APA Format)	Parletta, N., Zarnowiecki, D., Cho, J., Wilson, A., Bogomolova, S., Villani, A., Itsiopoulos, C., Niyonsenga, T., Blunden, S., Meyer, B., Segal, L., Baune, B. T., & O’Dea, K. (2019). A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: A randomized controlled trial (HELFIMED). <i>Nutritional Neuroscience</i> , 22(7), 474–487. https://doi.org/10.1080/1028415X.2017.1411320
Original URL	https://www.tandfonline.com/doi/full/10.1080/1028415X.2017.1411320?scroll=top&needAccess=true&role=tab
Source type	Journal article
Keywords	Mediterranean diet, depression, anxiety, fish oil
#Tags	#diet #depression #omega-3 #gut-brain #anxiety
Summary of key points + notes (include methodology)	Using randomized controlled trials the study tested the impact of a mediterranean diet on mental health. Trial was over 3 months with a follow up after 6. Participants were also given fish oil supplements for the 6th month because of the low levels of omega - 3 in people with mental illness. The participants were given cooking classes and ingredients to keep up the mediterranean diet. The other group was given socials fortnightly to control the social interaction aspect of the cooking classes. Both the Depression Anxiety Stress Scale (DASS-21) and the Assessment of Quality of Life (AQoL)-8D were the primary outcome measures. Dietary questionnaires were also monitored to confirm participants were staying on the diet. Fasted blood samples were also conducted to monitor the direct effect of the fish oil supplements. The MedDiet group showed significantly greater increase in consumption of vegetables, fruit, wholegrain foods, nuts and legumes, along with significantly lower consumption of unhealthy snacks and meat/chicken, and a greater diversity of vegetables. Results: Depression scores(DASS, PANAS and other subscales) improved by 45% in the MedDiet group and 26.8% in the control

group – equating to 1.68 times greater improvement in depressive symptoms in the MedDiet group. All changes were sustained for 6 months. With the mean of the med diet group decreasing to under the qualifying factor of extremely severe depression. Correlations were also made between reduced anxiety and increase in omega 3 due to fish oil.

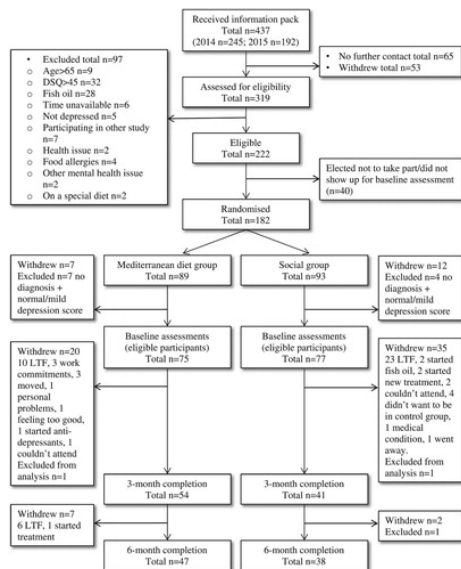
Notes:

- 2 groups one with changed diet one control
 - MedDiet group:
 - Got cooking classes every other week
 - Received ingredients
 - Also given fish oil supplements to increase omega 3
 - This was because people with mental illness were seen to have a low level of omega - 3
 - Control group
 - Had socials every other week to compensate for the social aspect of the cooking classes.
 - At these they were discouraged from discussing depression in a way therapeutic sense
 - Depression scores also improved
- Trial 3 months long with a 6 month double check

Research Question/Problem/Need

Can a mediterranean style diet improve the mental health of people suffering with depression?

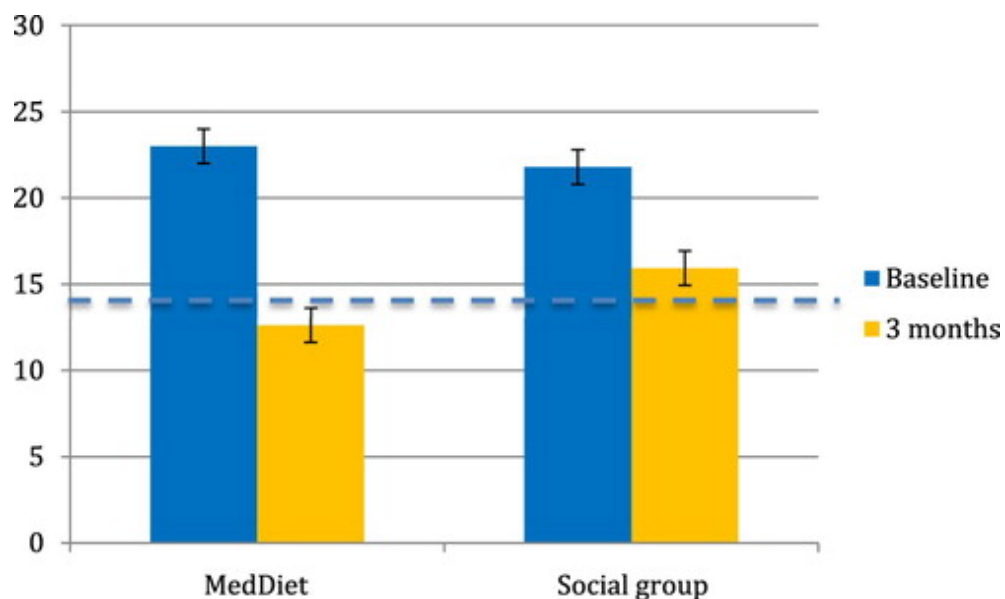
Important Figures



This is a flow chart for confirming eligibility in the study.

From the 152 eligible participants who commenced the study, 95 completed 3-month and 85 completed 6-month assessments

Increased omega-3 PUFA eicosapentaenoic acid (EPA) was significantly associated with reduced anxiety and stress at 3 months and 6 months



Dotted line is the cutoff for extremely severe depression
 Depression scores improved by 45% in the MedDiet group and 26.8% in the Social group – equating to 1.68 times greater improvement in depressive symptoms in the MedDiet group. All changes were sustained at 6 months

VOCAB: (w/definition)
 non-communicable diseases - chronic diseases not spread from infection or from person to person; they result in long term damage
 Meta-analyses - a statistical analysis designed to assess the research found by previous studies
 Obesogenic - tending to cause obesity
 GP - short for general practitioner(used in european countries)

Cited references to follow up on
 Frasure-Smith N, Lespérance F, Julien P. Major depression is associated with lower omega-3 fatty acid levels in patients with recent acute coronary syndromes. *Biol Psychiatry* 2004;55:891–6. doi: 10.1016/j.biopsych.2004.01.021 [Crossref], [PubMed], [Web of Science®], [Google Scholar]
 O’Neil A, Berk M, Itsiopoulos C, Castle D, Opie R, Pizzinga J, et al. A randomized, controlled trial of a dietary intervention for adults with major depression (the ‘SMILES’ trial): study protocol. *BMC Psychiatry* 2013;13. doi:10.1186/1471-244X-13-114):114. [Web of Science®], [Google Scholar]

Follow up Questions
 How much does a variety of vegetable and other food groups affect the gut microbiome?
 What gut micro - organisms are affected by omega - 3?

	<p>How great did the reduction of stress from meal planning and grocery shopping have an effect on the MedDiet group?</p> <p>How much of an error margin due to human unreliability on the surveys is there? If the study factored this in their data, how did they do so?</p>
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Article #11 Notes: Fucoidan antidepressant effects

Source Title	Science Direct Biochemical and Biophysical Research Communications Fucoidan exerts antidepressant-like effects in mice via regulating the stability of surface AMPARs
Source citation (APA Format)	Li, M., Sun, X., Li, Q., Li, Y., Luo, C., Huang, H., Chen, J., Gong, C., Li, Y., Zheng, Y., Zhang, S., Huang, X., & Chen, H. (2020). Fucoidan exerts antidepressant-like effects in mice via regulating the stability of surface AMPARs. <i>Biochemical and Biophysical Research Communications</i> , 521(2), 318–325. https://doi.org/10.1016/j.bbrc.2019.10.043
Original URL	https://www.sciencedirect.com/science/article/abs/pii/S0006291X19319321?via%3Dihub
Source type	Journal article
Keywords	Fucoidan, MDD, caspase-1, depression, hippocampus
#Tags	#depression, #gut-brain axis, #fucoidan, #diet
Summary of key points + notes (include methodology)	<p>Fucoidan is a polysaccharide found in brown seaweeds, including <i>Hizikia Fusiformis</i>.</p> <p>Results: Looking at the tail suspension test (TST) and the forced swim test (FST), acute administration showed no antidepressant effect. But, chronic fucoidan administration showed dose - dependent downregulation of depression symptoms in the TST, FST, <u>sucrose preference test (SPT)</u>, and novelty-suppressed feeding test (NSFT) and stabilizing surface AMPARs which lessens the increase of a caspase 1 pathway cause by stress and restores the stress induced lessening of the BDNF signaling pathway.</p> <ul style="list-style-type: none"> - downregulation of brain-derived neurotrophic factor dependent synaptic plasticity. Fucoidan prevents BDNF by mediating amounts of caspase-1 in the hippocampus, preventing inflammation. <p>Notes:</p> <ul style="list-style-type: none"> - “prevents stress-induced increase of caspase-1-IL-1β pathway and reverses stress-induced attenuation of BDNF signaling

pathway in the hippocampus of mice”

- Therefore, reducing depression symptoms by stabilizing surface AMPARs

Previously known before study:

- Proinflammatory cytokines like interleukin (IL)-1 β , IL-6 and tumor necrosis factor (TNF)- α are shown to be more prevalent in brains of people with depression. They also show an increased amount of caspase - 1.
- Fucoïdan contains L- fucose(a sugar with chemical composition C₆H₁₂O₅) and sulfate groups
- Fucoïdan has been shown to have anti-inflammatory and antioxidant properties.

Variables/what was monitored:

- tests for depression symptoms: TST, FST, SPT and NSFT.
- Expression of proinflammatory cytokines
- Expression of BDNF signaling pathway
- Expression of AMPARs
-

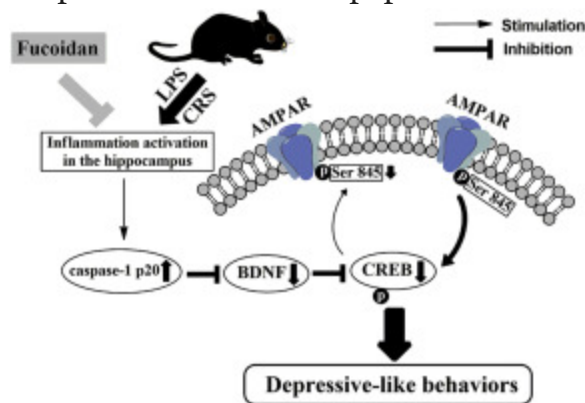
Method:

- Using two depressive mouse models , lipopolysaccharide (LPS) and chronic restraint stress (CRS)
- For comparison they also had a fluoxetine and control group that received a placebo
- Dosages of fucoïdan were 25 mg/kg, 50 mg/kg, and 100 mg/kg
 - First tested acute effect on both
 - Dosages were given 30 minutes before the tests
 - For the crs - fucoïdan group there was no change in depressive symptoms in the first dosage but increase in dosage did show a decrease on depressive symptoms
 - For the lps, depending on the does their was antidepressant effects
 - When used as chronic treatment both fucoïdan and fluoxetine where shown to fully reverse depression effects in the CRS mice group
 - Then tested for proinflammatory cytokines and BDNF in both the mPFC and hippocampus
 - Fucoïdan did not fully restore changes from LPS induced effects in the mPFC
 - Significantly prevented proinflammatory cytokines in hippocampus
 - In LPS groups fucoïdan significantly reduced caspase-1 level and increased BDNF expression

- The CRS group had similar results, except fucoidan fully restored increase of caspase-1 and prevented downregulation of BDNF in hippocampus
- Also was shown to increase the stability of surface level AMPARs in the hippocampus
 - In general stabilizing receptors helps regulate synaptic inhibition

Overall study found that fucoidan has antidepressant effects through decrease of proinflammatory cytokines and caspase-1

Graphical abstract from paper:



Research Question/Problem/Need Can fucoidan be used as a non-invasive treatment for depression?

Important Figures

- Dosages of fucoidan were 25 mg/kg, 50 mg/kg, and 100 mg/kg
- Results comparable to those of fluoxetine

VOCAB: (w/definition)

brain-derived neurotrophic factor: a protein with a great effect on neuronal survival and growth and works as a neurotransmitter modulator. It also has an effect on neuronal plasticity

Ameliorated: improved something

AMPA's: receptors that control glutamatergic signaling

Caspase-1: inflammatory caspase(protease enzyme)

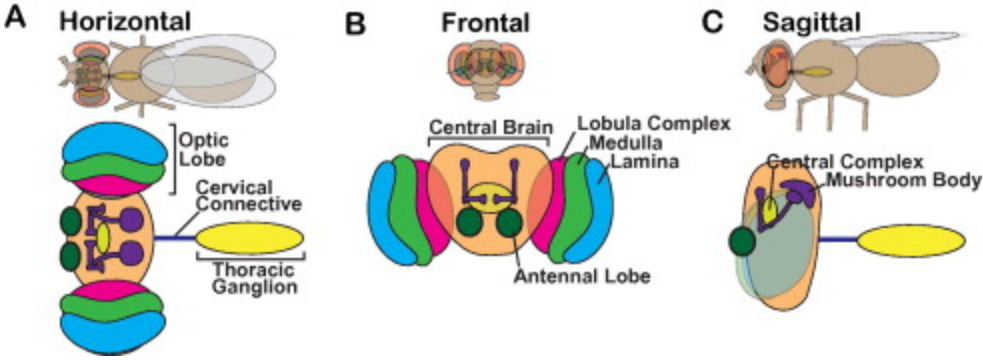
Glutamatergic: related to glutamate(an excitatory neurotransmitter)

Proinflammatory cytokines: signaling proteins that result in increased rate of inflammatory response

	<ul style="list-style-type: none"> - Two proinflammatory cytokines discussed in study are interleukin (IL)-1β, IL-6 and tumor necrosis factor (TNF)-α <p>Synaptic inhibition: downregulation of neural activity to prevent the brain from too many reactions</p> <p>Neuronal plasticity: the ability of the nervous system to respond to stimuli, whether it be internal or external, by changing structure, functions, or connections.</p>
Cited references to follow up on	<p>Miller, Andrew H., and Charles L. Raison. "The Role of Inflammation in Depression: From Evolutionary Imperative to Modern Treatment Target." <i>Nature Reviews Immunology</i>, vol. 16, no. 1, Jan. 2016, pp. 22–34, https://doi.org/10.1038/nri.2015.5.</p>
Follow up Questions	<p>What was the time period used with the chronic fucoidan treatment?</p> <p>When you described the effects of fucoidan on depression as "comparable" to those of fluoxetine, how great of a difference was there in the results of these treatments?</p> <p>What made the author choose to research fucoidan?</p> <p>Will the same results on depression symptoms be concluded if depression wasn't man-made(for lack of a better term)?</p> <p>Did the difference of results between the LPS induced mice and the CRS induced mice relate to what</p>

Article #12 Notes: Drosophila as a model system for neurotransmitter transporters

Source Title	ScienceDirect → Neurochemistry International
Source citation (APA Format)	Martin, C. A., & Krantz, D. E. (2014). Drosophila melanogaster as a genetic model system to study neurotransmitter transporters. <i>Neurochemistry International</i> , 73, 71–88. https://doi.org/10.1016/j.neuint.2014.03.015
Original URL	https://www.sciencedirect.com/science/article/abs/pii/S0197018614000709?via%3Dihub
Source type	Journal article
Keywords	Drosophila, fly, neuroscience, neurobiology, neurotransmitters.
#Tags	#glutamate #drosophila #neurotransmitter transporters
Summary of key points + notes (include methodology)	<p>The abstract emphasizes the resemblance between the fruit fly <i>Drosophila melanogaster</i> and mammals in terms of neurotransmitter utilization and transport mechanisms. <i>Drosophila</i> provides valuable molecular-genetic tools for investigating transporters, which can be challenging in mammalian models. The abstract reviews the progress achieved in understanding neurotransmitter transporters using <i>Drosophila</i> and considers future research directions in this field.</p> <p>SUMMARY BY CHATGPT INPUT: Summarize the following abstract in a few sentences: [abstract copied from paper]</p> <p><u>Notes:</u></p> <ul style="list-style-type: none"> - There are transporters responsible for the transportation of the biogenic amines(DA,5ht, etc.),acetylcholine, GABA, Glutamate, glycine - Two types of transporters: plasma membrane and vesicular transporters <ul style="list-style-type: none"> - Direct definition from text: “Plasma membrane neurotransmitter transporters are responsible for the

	<p>termination of synaptic transmission and recycling neurotransmitters after they are released”</p> <ul style="list-style-type: none"> - Vesicular transports neurotransmitters locally in a cell from storing it to bringing it to the cell membrane - Article itself goes more in depth about neurotransmitters - After hatching larvae mature over about 5 days and go through 3 separate stages - Reorganized of neural system before entering adulthood - Neurons and glia are both present in the larval and adult nervous system
Research Question/Problem/Need	Do <i>Drosophila melanogaster</i> work as a model for neurotransmitter studies? Why?
Important Figures	 <p>Nuero anatomy of a drosophila</p>
VOCAB: (w/definition)	Glia - connective tissues of the nervous system
Cited references to follow up on	<p>Alekseyenko et al., 2010 O.V. Alekseyenko, C. Lee, E.A. Kravitz Targeted manipulation of serotonergic neurotransmission affects the escalation of aggression in adult male <i>Drosophila melanogaster</i> PLoS ONE, 5 (2010), p. E10806 View article CrossRefView in ScopusGoogle Scholar</p> <p>Bauer et al., 2012 D.E. Bauer, J.G. Jackson, E.N. Genda, M.M. Montoya, M. Yudkoff, M.B. Robinson The glutamate transporter, GLAST, participates in a macromolecular complex that supports glutamate metabolism Neurochem. Int., 61 (2012), pp. 566-574 View PDFView articleView in ScopusGoogle Scholar</p>
Follow up Questions	<p>What differency are present between the neural transmitter of <i>Drosophila</i> and of humans?</p> <p>Are there any major differences in <i>drosophila</i> brains due to common genetic mutations?</p>

Article #13 Notes: Overview Methods to Assay *Drosophila* Behavior

Article notes should be on separate sheets

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Source Title	National Library of Medicine Methods to Assay <i>Drosophila</i> Behavior
Source citation (APA Format)	Nichols, C. D., Becnel, J., & Pandey, U. B. (2012). Methods to Assay <i>Drosophila</i> Behavior. <i>Journal of Visualized Experiments : JoVE</i> , 61, 3795. https://doi.org/10.3791/3795
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3671839/
Source type	Journal article
Keywords	Assays, <i>Drosophila</i> , behavior, neuroscience
#Tags	#assays #RING method #Drosophila
Summary of key points + notes (include methodology)	Some ways to measure fruit fly behaviors for neuroscience studies are the larval crawling assay/ locomotive assay, the RING protocol, and the courtship and mating assay. Larval crawling assay is a locomotive assay that measure how many centimeters a drosophila larva crawls in 1 minutes RING protocol is a locomotive assay, it forces drosophila to fall to the bottom of the test tube and measures how high they climb in 3 seconds Courtship mating assay measures social behaviors with other flies Article goes into depth about the process of each assay and results
Research Question/Problem/ Need	How can <i>Drosophila</i> behavior be tested for neuroscience studies?
Important Figures	RING assay <ul style="list-style-type: none"> - wild -type adult drosophila should have an average climbing height of 4-5 cm in a 3 second period - DO NOT use same test tubes for new groups of fly trials
VOCAB: (w/definition)	polystyrene vials - a type of vital used to store and test drosophila

Cited references to follow up on	Pandey UB, Nichols CD. Human disease models in <i>Drosophila melanogaster</i> and the role of the fly in therapeutic drug discovery. <i>Pharmacol. Rev.</i> 2011;63(2):411–436. [PMC free article] [PubMed] [Google Scholar] Johnson O, Becnel J, Nichols CD. Serotonin 5-HT(2) and 5-HT(1A)-like receptors differentially modulate aggressive behaviors in <i>Drosophila melanogaster</i> . <i>Neuroscience.</i> 2009;158(2):1292–1300. [PMC free article] [PubMed] [Google Scholar]
Follow up Questions	How significant is forcing drosophila to fall before measuring height climbed? What are other types of social assays that can be monitored to test for depression?

Article #14 Notes: L-DOPA

Article notes should be on separate sheets

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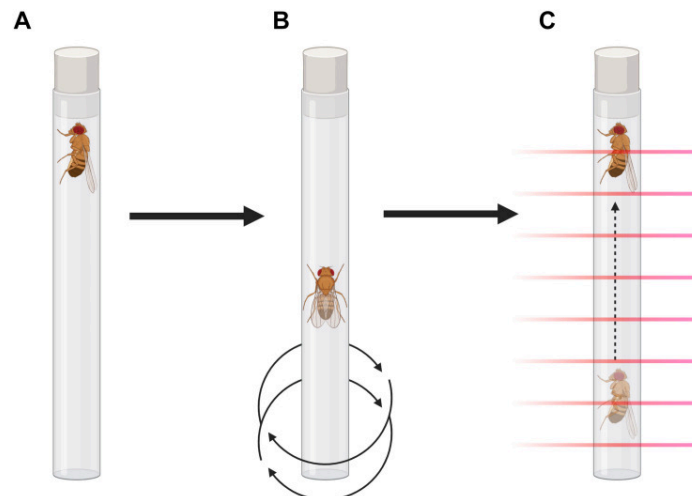
Source Title	National Library of Medicine The Drosophila melanogaster Levodopa-Induced Depression Model Exhibits Negative Geotaxis Deficits and Differential Gene Expression in Males and Females.
Source citation (APA Format)	Moulin, T. C., Ferro, F., Hoyer, A., Cheung, P., Williams, M. J., & Schiöth, H. B. (2021). The Drosophila melanogaster Levodopa-Induced Depression Model Exhibits Negative Geotaxis Deficits and Differential Gene Expression in Males and Females. <i>Frontiers in Neuroscience</i> , 15, 653470. https://doi.org/10.3389/fnins.2021.653470
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8165388/
Source type	Journal article
Keywords	Depression, L-Dopa, Drosophila, negative geotaxis
#Tags	#L-DOPA #locomotive assay #assays #drosophila
Summary of key points + notes (include methodology)	<p>Sex specific differences in depression prevalence are not understood or studied broadly. Depression affects males and females differently and males and females with present symptoms differently. This study measures the difference of gene expression and negative geotaxis between the sexes in its relation to depression. Used L-Dopa to model depression. L-Dopa decreased forced climbing rate in both male and female drosophila, but through different gene patterns. Overall this study proposed that L-Dopa induced depression can be used in future studies to learn more about the differences of depression in men and women.</p> <p>Notes:</p> <ul style="list-style-type: none"> - Methodology: <ul style="list-style-type: none"> - Exposed to food containing 1 mM L-Dopa for 2 days - Used automated machine for assay measuring negative geotaxis - Results: <ul style="list-style-type: none"> - L-Dopa had no effect on horizontal locomotion - L-dopa displayed a negative effect on forced climbing

- L-dopa affected gene expression
- Females showed a greater difference to their corresponding control group than males in the beginning of the forced climbing test
- In the discussion the article states the reduction of negative geotaxis over time may be due to “learned helplessness”

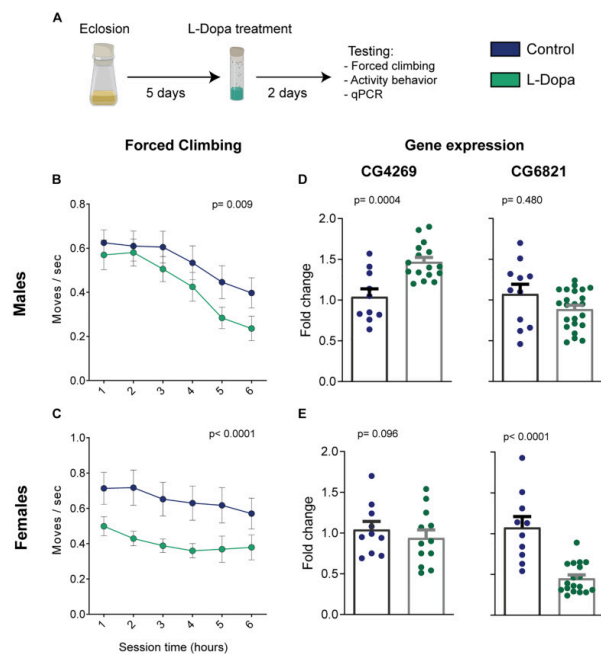
Research Question/Problem/Need

What is the effect of L-DOPA on negative geotaxis and sex specific gene expression in Drosophila?

Important Figures



Graphic depicting testing for negative geotaxis



Effect of L-Dopa on negative geotaxis

	<div style="display: flex; flex-direction: column; align-items: center;"> <div style="display: flex; justify-content: space-around; width: 100%;"> <div style="text-align: center;"> <p>General Activity (Initial hours)</p> <p>Mean activity counts / hour</p> <p>1h 2h 3h 4h 5h 6h 7h</p> </div> <div style="text-align: center;"> <p>General Activity (3 days)</p> <p>Activity counts / day</p> </div> </div> <div style="display: flex; justify-content: space-around; width: 100%; margin-top: 20px;"> <div style="text-align: center;"> <p>Females</p> <p>Mean activity counts / hour</p> <p>1h 2h 3h 4h 5h 6h 7h</p> </div> <div style="text-align: center;"> <p>General Activity (3 days)</p> <p>Activity counts / day</p> </div> </div> <p>Effect of <i>Drosophila</i> on horizontal locomotion Shows no significant difference between L-Dopa groups and control</p> </div>
<p>VOCAB: (w/definition)</p>	<p>Negative geotaxis - the escape response of <i>Drosophila</i> urging them to climb when they have fallen because of an external force. Also is commonly referred to as forced climbing.</p>
<p>Cited references to follow up on</p>	<p>Ellis L. L., Carney G. E. (2011). Socially-responsive gene expression in male <i>Drosophila melanogaster</i> is influenced by the sex of the interacting partner. <i>Genetics</i> 187 157–169. 10.1534/genetics.110.122754 [PMC free article] [PubMed] [CrossRef] [Google Scholar]</p>
<p>Follow up Questions</p>	<p>When both male and female <i>Drosophila</i> are used in a study are they stored in separate test tubes?</p>

Article #15 Aggression Assay

Source Title	Fighting Flies: Quantifying and Analyzing Drosophila Aggression
Source citation (APA Format)	Fernandez, M. P., Trannoy, S., & Certel, S. J. (2023). Fighting Flies: Quantifying and Analyzing Drosophila Aggression. <i>Cold Spring Harbor Protocols</i> , 2023(9), pdb.top107985. https://doi.org/10.1101/pdb.top107985
Original URL	https://cshprotocols.cshlp.org/content/2023/9/pdb.top107985.full
Source type	Journal article
Keywords	Aggression, assays, drosophila
#Tags	#drosophila, #aggression assay, #assays
Summary of key points + notes (include methodology)	<p>Scientists have noticed a clear relationship between neurological factors and aggression shown by drosophila. Both neurotransmitters that regulate depression and sex differences in the presentation of depression have been found. Aggression is a behavior based on interaction between individuals, not just a singular behavior unit. This means that the frequency and initiation of these behaviors can be affected by the method used to transport flies into the flight chamber, the chamber itself(size and composition), and the drosophila's previous social interactions with other drosophila. Aggression behavior in drosophila is considered sexually dimorphic. While both male and female drosophila display aggression to other drosophila of the same sex, the ways the aggression is displayed is different per male or female drosophila. Drosophila fights are broken up into brief encounters, in these encounters flies will come together, interact for a short period of time, then they will break apart signaling the end of one encounter. Many studies will solely look at the amount of physical attacks in a fixed time period. Aggression requires a lot of energy from drosophila. To participate in an aggressive encounter a drosophila will weigh the costs and benefits; internal and external factors also play a major role. One of these main external factors is pheromones displayed by the flies and the detection of these pheromones by the flie's opponent. Latency in time before aggression is an important parameter in measuring the aggression between two drosophila. Auditory signals are also very important, visual displays(wing flicking and wing threats) also have shown to be auditory signals of aggression. Motion being detected visually has been found to play a role in male flies initializing aggression through studies on blind male drosophila, although little difference has been found between aggression</p>

initialization in dark vs. light settings. Internal factors that affect initialization of aggression include hunger, mating state, the need for sleep, and more. The neurotransmitters that affect aggression in drosophila have been extensively studied. The intensity of an aggressive encounter between drosophila can be categorized into 3 different levels of intensity: low, medium, and high. Drosophila also need a resource to fight over to initialize aggression. Neurotransmitters and neuropeptides affect aggression through the interaction and release of monoamines, neuropeptides, and neurotransmitters.

Most of this is based on aggression between male drosophila as there has been much more research on male drosophila than on female drosophila.

Notes/main points:

- The frequency and initiation of these behaviors can be affected by the method used to transport flies into the flight chamber, the chamber itself (size and composition), and the drosophila's previous social interactions with other drosophila.
- Three types of aggression assays:
 - Multiwell chamber
 - Sliding chamber
 - Divider chamber
- Which type of assay you use is dependent on the research question
- Encounters between males:
 - Early dyadic encounters involve orientation and approach in relation between the two flies, and fencing, touching of the forelegs and wing flick and wing flecks (more about these visual displays in article) to send chemosensory information
 - These fights usually intensify to physical interactions: the lunge (description of lunge in article)
 - As fights continue, a change in flight strategy is shown
 - "one chases and lunges at his opponent (often in defense of a territory), whereas the second male retreats from the resource or territory"
 - This leads to a dominance relationship
 - In formation or maintenance of a dominance relationship drosophila display wing threats and boxing
 - Fights may escalate to boxing, tussling, and holding
 - "Repetitive aggressive encounters in males can lead to wing damage or generate an internal state that displays persistence in aggression"
 - This can lead to issues in other behaviors of the fly
- Prior fighting experience will affect the outcomes of future fights
- Encounters between females:
 - First approach and fencing
 - Female drosophila present two true dimorphic behaviors: headbutts and shoves

- Headbutt: “a female snaps forward with a negligible change in leg position”
- Shove: “the female snaps forward with her forelegs in a level trajectory”
- Females will display behaviors of both competing for and sharing the resource
 - This is very different than males considering they do not present this.
 - There is less research on female aggression
- Aggression visual displays:
 - Wing threats in males
 - Wing flicking in females
- Low energy threat displays are used to discourage competitor
- High energy attack behaviors are needed to chase competitors from a valuable resource
- Many studies solely look at physical attacks shown in a fixed time period
- An external factor that is essential to a *Drosophila* entering an aggressive attack is smelling the pheromones released by their opponent.
- Pheromone detection
 - Volatile pheromones are detected from a far through smell
 - For males: *cis*-vaccenyl acetate promotes aggression
 - “activation of the Or67d-expressing olfactory neurons that detect *cis*-vaccenyl acetate also increases male aggression”
 - Non volatile cuticular hydrocarbon pheromones are detected through taste
 - Contact pheromonal information in the form of CHs
 - Both volatile and nonvolatile to create an aggressive response
 - *Drosophila* CH profiles are sexually dimorphic
 - Dienes are mainly produced by females to increase male attention
 - Males produce monoenes which inhibit male courtship
- The exchange of male CH information during fencing is enough to start an aggressive attack.
 - Wild type male flies will attack females that display male like pheromone profiles
 - Because of this males in larger attack chambers will take a longer time period to display lower lunge numbers and start fighting
 - This may cause two male flies fighting to take a longer time to realize the other fly is male
- Time it takes to display aggressive behavior or the “latency to initiate aggression” is a very important parameter as it could show deficits of the flies ability to identify the gender of a conspecific
 - Chamber size also affects latency
- Mechanosensory plays a role in either male or male and female aggression
- “the activity of neurons or gene expression can be manipulated by transactivators”
- Level of intensity

	<ul style="list-style-type: none"> - “<i>Drosophila</i> males, aggression intensity is defined by lunge number as well as the usage of boxing and tussling” - Higher levels of aggression may also be due to higher activity levels so locomotive assays should also be monitored and compared if intensity of aggression is looked at - Diet can affect aggression <ul style="list-style-type: none"> - Because of this other assays should be monitored
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Research Question/Problem/Need	What are the behavioral patterns shown in drosophila aggression and what affects these patterns?
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Important Figures	<p>table</p> <ul style="list-style-type: none"> - This link goes to a table from the article - This table shows different behavioral patterns of aggression presented by drosophila - Displays descriptions of the patterns/behaviors and what gender drosophila presents these behaviors. <p>The diagram illustrates various aggression patterns in <i>Drosophila</i>, categorized by gender. It is organized into three horizontal sections from top to bottom: <ul style="list-style-type: none"> Mixed patterns: Includes 'Fencing', shown as two flies facing each other with their front legs raised. True female patterns: Includes 'Headbutts' (flies with heads touching) and 'Shoving' (flies pushing against each other). True male patterns: Includes 'Tussling' (flies with heads touching and legs raised), 'Holding' (flies with one leg raised and head touching), 'Lunging' (one fly lunging towards another), and 'Boxing' (flies with legs raised and heads touching). </p> <ul style="list-style-type: none"> - Mixed patterns are shown at the top, female specific behavior patterns in the middle, and male specific behavior patterns on the bottom - Boxing is rarely shown in wild-type flights <ul style="list-style-type: none"> - Do not confuse boxing with high-posture fencing -
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VOCAB: (w/definition)	<p>Phenotypically- relating to the physical characteristics of a living organism</p> <p>Plastic (adj.) - capable of being shaped or molded</p> <p>Connectomics - the study of the individual connections of neurons that make functional networks</p> <p>dimorphic- occurring or representing in two forms</p> <p>True dimorphic behaviors - completely different behaviors are shown in male and</p>
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	<p>females</p> <p>Mixed dimorphic behaviors - drosophila share some behavioral actions, these behaviors are displayed by both the sexes of a species</p> <p>Conspecifics - members of the same sex</p> <p>Dienes - an unsaturated hydrocarbon containing two double bonds between carbon atoms</p>
<p>Cited references to follow up on</p>	<p>Alekseyenko OV, Chan YB, Okaty BW, Chang Y, Dymecki SM, Kravitz EA. 2019. Serotonergic modulation of aggression in <i>Drosophila</i> involves GABAergic and cholinergic opposing pathways. <i>Curr Biol</i> 29: 2145–2156. doi:10.1016/j.cub.2019.05.070 CrossRef Medline Google Scholar</p> <p>Certel SJ, Kravitz EA. 2012. Scoring and analyzing aggression in <i>Drosophila</i>. <i>Cold Spring Harb Protoc</i> doi:10.1101/pdb.prot068130 FREE Full Text</p> <p>Chowdhury B, Wang M, Gnerer JP, Dierick HA. 2021. The Divider Assay is a high-throughput pipeline for aggression analysis in <i>Drosophila</i>. <i>Com</i></p> <p>Ferveur JF. 1997. The pheromonal role of cuticular hydrocarbons in <i>Drosophila melanogaster</i>. <i>Bioessays</i> 19: 353–358. doi:10.1002/bies.950190413 CrossRef Medline Google Scholar</p> <p>Hoopfer ED. 2016. Neural control of aggression in <i>Drosophila</i>. <i>Curr Opin Neurobiol</i> 38: 109–118. doi:10.1016/j.conb.2016.04.007 CrossRef Medline Google Scholar</p> <p>Pandolfi M, Scaia MF, Fernandez MP. 2021. Sexual dimorphism in aggression: sex-specific fighting strategies across species. <i>Front Behav Neurosci</i> 15: 659615. doi:10.3389/fnbeh.2021.659615 CrossRef Google Scholar</p> <p>Schretter CE, Vielmetter J, Bartos I, Marka Z, Marka S, Argade S, Mazmanian SK. 2018. A gut microbial factor modulates locomotor behaviour in <i>Drosophila</i>. <i>Nature</i> 563: 402–406. doi:10.1038/s41586-018-0634-9 CrossRef Medline Google Scholar</p> <p>Trannoy S, Fernandez MP, Certel SJ. 2023. Comparing methods for quantifying and analyzing <i>Drosophila</i> aggression. <i>Cold Spring Harb Protoc</i> doi:10.1101/pdb.prot108144 FREE Full Text</p> <p>vermeiren Y, Van Dam D, Aerts T, Engelborghs S, De Deyn PP. 2014. Monoaminergic neurotransmitter alterations in postmortem brain regions of depressed and aggressive patients with Alzheimer's disease. <i>Neurobiol Aging</i> 35: 2691–2700. doi:10.1016/j.neurobiolaging.2014.05.031 CrossRef Medline Google Scholar</p>
<p>Follow up Questions</p>	<p>What is the best way to measure aggression when testing for depression?</p> <p>How should level of intensity be compared to the results of the locomotive assays?</p>

Article #16 Notes: A study monitoring depression in *Drosophila* with CUMS

Source Title	The International Journal on the Biology of Stress <i>γ</i> -Oryzanol produces an antidepressant-like effect in a chronic unpredictable mild stress model of depression in <i>Drosophila melanogaster</i>
Source citation (APA Format)	Araujo, S. M., Bortolotto, V. C., Poetini, M. R., Dahleh, M. M. M., Couto, S. D. F., Pinheiro, F. C., Meichtry, L. B., Musachio, E. A. S., Ramborger, B. P., Roehrs, R., Guerra, G. P., & Prigol, M. (2021). <i>γ</i> -Oryzanol produces an antidepressant-like effect in a chronic unpredictable mild stress model of depression in <i>Drosophila melanogaster</i> . <i>Stress</i> , 24(3), 282–293. https://doi.org/10.1080/10253890.2020.1790519
Original URL	https://www.tandfonline.com/doi/pdf/10.1080/10253890.2020.1790519
Source type	Journal Article
Keywords	Drosophila, depression, neuroscience, CUMS
#Tags	#assays #drosophila #CUMS #methods
Summary of key points + notes (include methodology)	<p>The study explores the potential antidepressant effect of <i>c</i>-oryzanol (ORY) in male fruit flies subjected to chronic unpredictable mild stress (CUMS), a model for inducing depression-like symptoms. The researchers conducted various behavioral tests and chemical analyses on the flies treated with ORY and exposed to CUMS. The results showed that ORY-treated flies did not exhibit depressive-like behaviors, such as immobility, increased aggression, or reduced mating and virility. ORY also did not affect sucrose preference and body weight. Importantly, ORY prevented the reduction of serotonin (5HT) and octopamine (OCT) levels and partially protected against the reduction of dopamine (DA). The findings suggest that ORY has potential as an antidepressant compound.</p> <p>ABOVE SUMMARY BY CHAT GPT</p> <p>Results:</p>

ORY treatment and CUMS exposure showed:

- No effect on locomotion
 - Specifically looked at exploratory behavior
- Prevents immobility if forced swim test
- Treat showed decrease in aggression when compared to non-ORY but CUMS exposed groups
- Prevents differences in mating behaviors and and virility
- Did not prevent anhedonia
- Treatment did not affect body weight
- Treatment prevents anxiogenic behavior
- Treatment prevents the reduction of monoamine levels

Conclusion:

- May have antidepressant effects but data was not very conclusive so further research needs to be done

Notes:

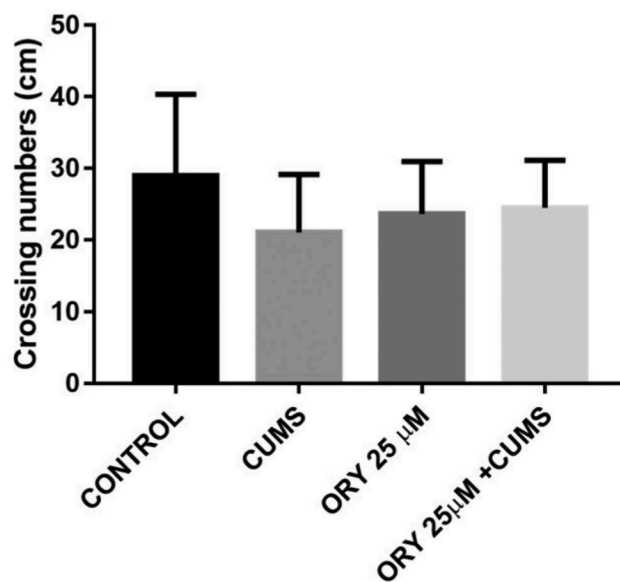
- The study only looked at male drosophila
- This article is really helpful because it goes in depth into the methodology of treating drosophila and each assay
 - Assays used in this article:
 - Locomotion
 - Specifically looked at exploratory behavior
 - Measure how much a fly walked around a petri dish in set time period
 - Acclimated 5 minutes
 - Measured amount moved in 1 minute
 - Forced Swim Test
 - 5 minute long tests
 - No adjustment period
 - Measured variables:
 - Time to first immobility
 - Time fly was actively swimming
 - Time spent immobile
 - Number bout of each fly
 - 1 fly per experiment
 - This is inconvenient and may not be doable for personal project because of time constraints
 - Flies were tested after for ability to walk and climb, if the flies were unable to climb they were excluded from final data analysis.
 - Aggressiveness Test
 - Used circular combat chamber
 - Acclimated 2 minutes
 - Monitored 5 minutes
 - Variables:

- Number of aggressive encounters (leg extensions resulting in contact, chase, fast loading approach, wing raising, high box of flies' front legs)
 - 10 pairs per experiment
 - 5 experiments
- Courtship and mating behaviors in males
 - random male matched with random virgin control female
 - Circular dish
 - Acclimated 2 minutes
 - 10 minute test period
 - Variables:
 - Time till first physical contact
 - Total copulation time
 - Total mating time
 - 5 pairs tested per experiment
 - 4 experiments
- Sucrose preference index (PI)
 - Starved 90 minutes before assay
 - Transferred without anesthesia
 - Left for 6 hours
 - Preference index(PI) is calculated for each liquid by dividing the amount of a single liquid consumed by the total amount consumed.
- Body weight
 - In article this is include in the Sucrose Preference section
 - Flies were anesthetized and weighed
- Light/dark test
 - 10 flies from each group
 - Box with two compartments: one light, one dark
 - Acclimate for 5 minutes
 - Tested for 3 minutes
 - Variable: average amount of time spent in light compartment
- Measured neurotransmitters in brain
 - Measured serotonin, dopamine, and octopamine
- Article separately explains statistical analysis for each assay

**Research Question/Problem/
Need**

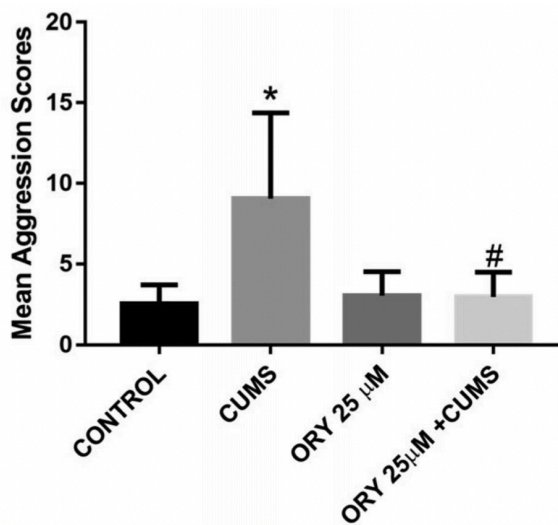
What is the effect of γ -Oryzanol on depression?

Important Figures



Data of locomotive assay on exploratory locomotion

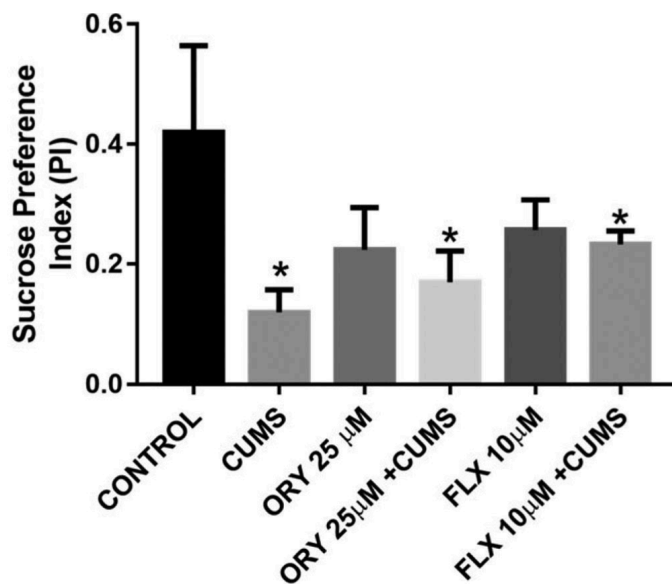
- Notice data was not significant



Results of the aggression assay

*- represents significance tested between CUMS and ORY

- means significance tested against control



Results if the sucrose preference test

VOCAB: (w/definition)

Virility - quality of having strength, energy, and sex drive. Specifically used for males
Anxiogenic - anxiety inducing

Cited references to follow up on

Araujo, S. M., Poetini, M. R., Bortolotto, V. C., de Freitas Couto, S., Pinheiro, F. C., Meichtry, L. B., de Almeida, F. P., Santos Musachio, E. A., de Paula, M. T., & Prigol, M. (2018). Chronic unpredictable mild stress-induced depressive-like behavior and dysregulation of brain levels of biogenic amines in *Drosophila melanogaster*. *Behavioural Brain Research*, 351, 104–113. <https://doi.org/10.1016/j.bbr.2018.05.016>

Denno, M. E., Privman, E., & Venton, B. J. (2015). Analysis of neurotransmitter tissue content of *Drosophila melanogaster* in different life stages. *ACS Chemical Neuroscience*, 6(1), 117–123. <https://doi.org/10.1021/cn500261e>

Helfrich-Forster, C. (2000). Differential control of morning and evening components in the activity rhythm of *Drosophila melanogaster*-sex-specific differences suggest a different quality of activity. *Journal of Biological Rhythms*, 15(2), 135–154. <https://doi.org/10.1177/074873040001500208>

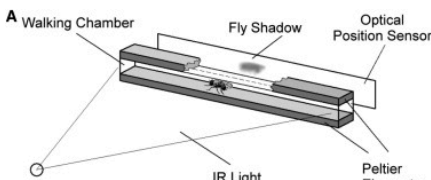
Follow up Questions

How much does only having significant data on some of the assays affect the validity of the data?

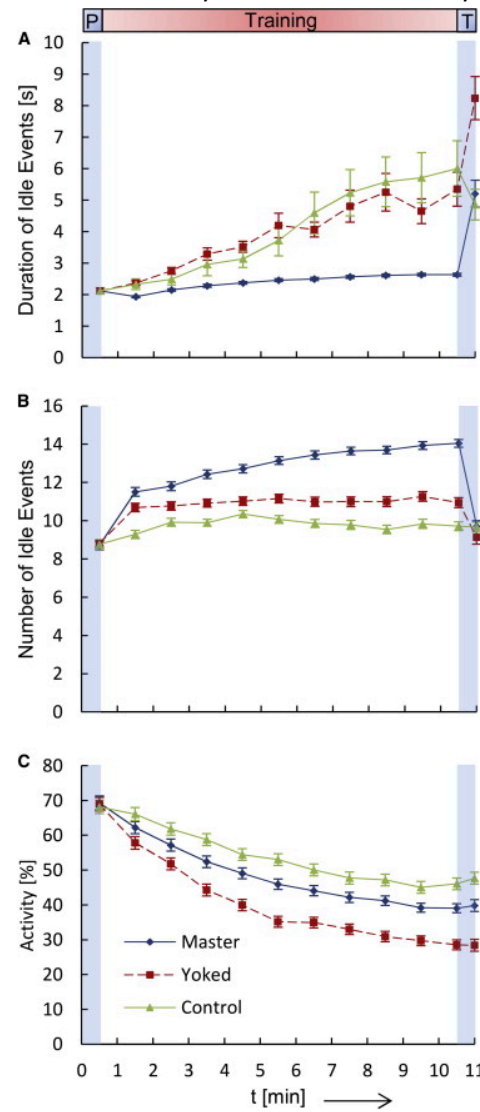
Was not getting significant data for these amounts of results expected? Was it unusual compared to other studies?

What caused the high error bar on the mean aggressiveness data on the CUMS group.

Article #17 Notes: Uncontrollable stress effect on drosophila

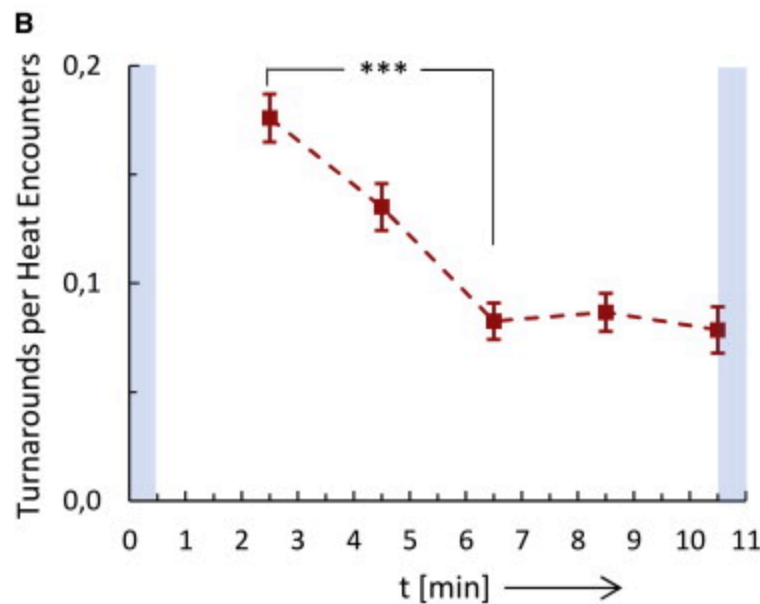
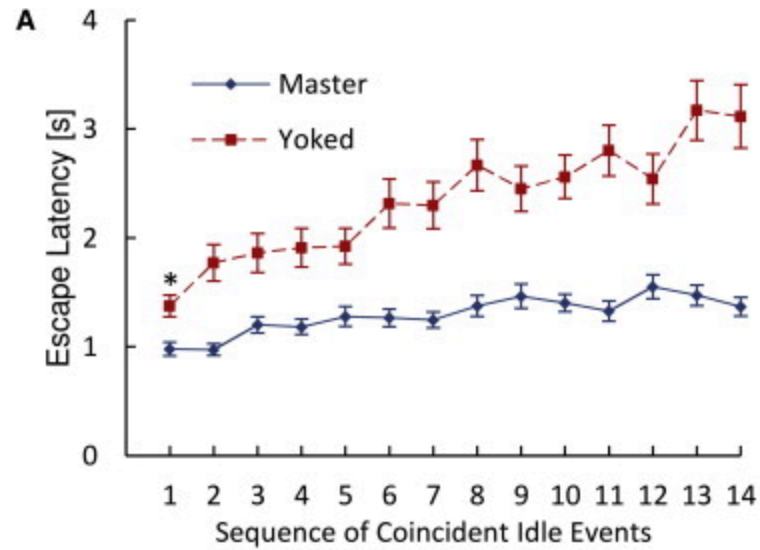
Source Title	Flies Cope with Uncontrollable Stress by Learned Helplessness
Source citation (APA Format)	Yang, Z., Bertolucci, F., Wolf, R., & Heisenberg, M. (2013). Flies Cope with Uncontrollable Stress by Learned Helplessness. <i>Current Biology</i> , 23(9), 799–803. https://doi.org/10.1016/j.cub.2013.03.054
Original URL	https://www.cell.com/current-biology/fulltext/S0960-9822(13)00356-4?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0960982213003564%3Fshowall%3Dtrue
Source type	Journal article
Keywords	Drosophila, unpredictable stress, learned helplessness, neuroscience
#Tags	#drosophila #CUMS
Summary of key points + notes (include methodology)	<p>Exposing animals to uncontrollable stressful events causes “learned helplessness” in the animals; this is used as a model of depression in scientific research. In experimentation of uncontrollable stress three groups were viewed, control, “master”, and “yoked”. The “master” groups would receive the same stressful events as the yoked but there was based on their behavior. While animals can remember when they were. When animals are continually exposed to negative stimuli they will remember it in the specific type of memory called “learned uncontrollability”. This is a pretty basic memory type in all animals, but drosophila can have a more specific memory type called “learned helplessness” Looking at these three groups. After a few heat pulses it was shown the yoked flies realized there was no correlation</p> <ul style="list-style-type: none"> - “Escape latencies have a very small variance throughout the conditioning period, showing the high reliability of the response” - For heat stressor 10 minute intervals - 24°C–37°C for heat test
Research Question/Problem/Need	What is the effect of uncontrollable stressors on Drosophila?
Important Figures	 <p>In this graph you can see the immediate effects in the difference of a master and yoked group of drosophila. The heat turned on after the master group had stopped moving for 1s and it</p>

was immediately turned off when they started moving again



Master group had shorter idle periods than the control group but they actually have a higher overall rest time because they take breaks more frequently

- Long escape latencies of yoked flies
- Control experiments show that in master flies, a longer idle allowance does not lead to a longer response latency
- In the experiment yoked



Another way the flies would respond to the negative stimuli is by changing directions while moving, after the time continued the fly would realize it makes no affect and in simple terms give up
 A 2 sample t test compared idle breaks mean time and variance of the yoked group vs the control with $p > 0.05$ the null hypothesis was proven true, that the mean duration and variance of the breaks was the same, although the yoked group took a lot more breaks

VOCAB: (w/definition)

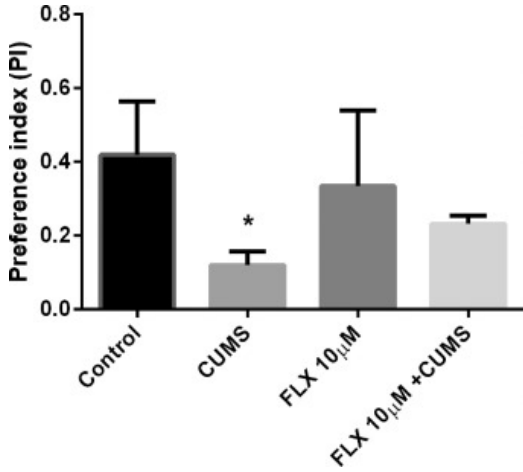
Idle allowency - the amount of time the fly would spend at rest before harsh heat conditions kicked in
 Response latency - time after heat is turned on until a fly starts moving again
 Escape latency - response latency

Cited references to follow up on	<p>Brown, Gary E., et al. "Learned Helplessness in Drosophila Melanogaster?" <i>Psychological Reports</i>, vol. 78, no. 3, 1996, pp. 962–962, https://doi.org/10.2466/pr0.1996.78.3.962.</p> <p>Wustmann, G., et al. "A New Paradigm for Operant Conditioning of Drosophila Melanogaster." <i>Journal of Comparative Physiology A</i>, vol. 179, no. 3, 1996, https://doi.org/10.1007/BF00194996.</p>
Follow up Questions	<p>Do you think learned helplessness will affect using aggression as a depression assay?</p> <p>How did you decide on the α values for each significance test?</p> <p>Would the master group show any neurological symptoms from their exposure to trauma? Would this resemble ptsd like behaviors?</p>

Article #18 Notes: Chronic unpredictable mild stressors

Source Title	<p>ScienceDirect</p> <p>Behavioral Brain Research Volume 531</p> <p>Chronic unpredictable mild stress-induced depressive-like behavior and dysregulation of brain levels of biogenic amines in <i>Drosophila melanogaster</i></p>
Source citation (APA Format)	<p>Araujo, S. M., Poetini, M. R., Bortolotto, V. C., de Freitas Couto, S., Pinheiro, F. C., Meichtry, L. B., de Almeida, F. P., Santos Musachio, E. A., de Paula, M. T., & Prigol, M. (2018). Chronic unpredictable mild stress-induced depressive-like behavior and dysregulation of brain levels of biogenic amines in <i>Drosophila melanogaster</i>. <i>Behavioural Brain Research</i>, 351, 104–113.</p> <p>https://doi.org/10.1016/j.bbr.2018.05.016</p>
Original URL	<p>https://www.sciencedirect.com/science/article/pii/S0166432818301232?via=ihub#sec0010</p>
Source type	Journal Article
Keywords	CUMS, drosophila, depression, learned helplessness
#Tags	#methods #drosophila #CUMS #assays
Summary of key points + notes (include methodology)	<p>The study wanted to prove the effectiveness of CUMS as a depressive model in <i>Drosophila</i>. It exposed <i>drosophila</i> to multiple chronic unpredictable mild stressors and monitored their behaviors and monitored serotonin and dopamine levels of <i>ex vivo</i> <i>Drosophila</i>. The chronic unpredictable mild stressors the flies were exposed to were cold conditioning, heat conditioning, starvation, and sleep deprivation. They tested control, CUMS, CUMS + FLX, and FLX groups. CUMS was shown to decrease biogenic amines. It was also shown to have data leaning the same way as other depressive models in the FST, aggression test, male mating and fertility, and the light dark preference test.</p> <p>Notes:</p> <ul style="list-style-type: none"> - Shows validity of CUMS as depressive model - Showed no significant difference in horizontal locomotive data <ul style="list-style-type: none"> - This is very different from forced climbing locomotive data assays - Tested exploratory locomotion, FST, aggression, male mating, male fertility, sucrose preference, body weight, light-dark preference and levels of

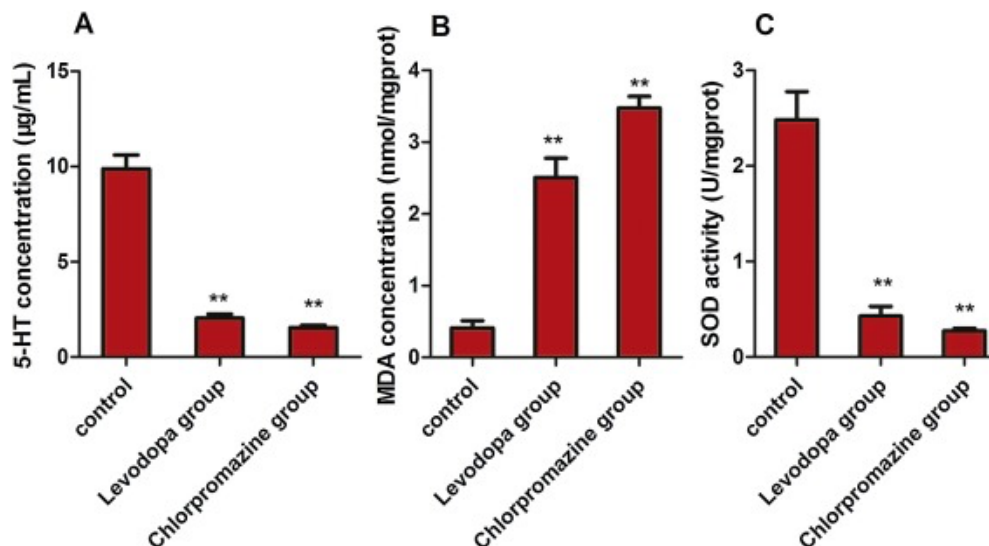
	biogenic amines																																																		
Research Question/Problem/Need	What changes do Chronic Unpredictable Mild Stressors(CUMS) cause in Drosophila? Is CUMS a usable and valid model of depression?																																																		
Important Figures	<div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <p>A) Latency of immobility</p> <table border="1"> <caption>Latency to first bout of immobility</caption> <thead> <tr> <th>Group</th> <th>Latency (approx. seconds)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>28</td> </tr> <tr> <td>CUMS</td> <td>14*</td> </tr> <tr> <td>FLX 10μM</td> <td>23</td> </tr> <tr> <td>FLX 10μM + CUMS</td> <td>23#</td> </tr> </tbody> </table> </div> <div style="width: 50%;"> <p>B) Immobility time</p> <table border="1"> <caption>Immobility time</caption> <thead> <tr> <th>Group</th> <th>Immobility time (approx. seconds)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>60</td> </tr> <tr> <td>CUMS</td> <td>140*</td> </tr> <tr> <td>FLX 10μM</td> <td>50</td> </tr> <tr> <td>FLX 10μM + CUMS</td> <td>60#</td> </tr> </tbody> </table> </div> <div style="width: 50%;"> <p>C) Bout duration</p> <table border="1"> <caption>Bout duration</caption> <thead> <tr> <th>Group</th> <th>Bout duration (approx. seconds)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>85</td> </tr> <tr> <td>CUMS</td> <td>25*</td> </tr> <tr> <td>FLX 10μM</td> <td>105</td> </tr> <tr> <td>FLX 10μM + CUMS</td> <td>100#</td> </tr> </tbody> </table> </div> <div style="width: 50%;"> <p>D) Number of Bouts</p> <table border="1"> <caption>Number of Bouts</caption> <thead> <tr> <th>Group</th> <th>Number of bouts (approx.)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>1.15</td> </tr> <tr> <td>CUMS</td> <td>1.05</td> </tr> <tr> <td>FLX 10μM</td> <td>1.5</td> </tr> <tr> <td>FLX 10μM + CUMS</td> <td>0.95</td> </tr> </tbody> </table> </div> </div> <p>FST results</p> <ul style="list-style-type: none"> - CUMS decreased latency of mobility, increased immobility time, and decreased bout duration - Notice number of bouts is not statistically significant <div style="display: flex;"> <div style="flex: 1;"> <p>Mean Aggression Scores</p> <table border="1"> <caption>Mean Aggression Scores</caption> <thead> <tr> <th>Group</th> <th>Mean Aggression Score (approx.)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>3</td> </tr> <tr> <td>CUMS</td> <td>12*</td> </tr> <tr> <td>FLX 10μM</td> <td>3.5</td> </tr> <tr> <td>FLX 10μM + CUMS</td> <td>5#</td> </tr> </tbody> </table> </div> <div style="flex: 1; padding-left: 20px;"> <p>Aggression Assay results</p> <ul style="list-style-type: none"> - CUMS increased aggression - Aggression score encounters that exhibited aggressive behaviors </div> </div>	Group	Latency (approx. seconds)	Control	28	CUMS	14*	FLX 10 μ M	23	FLX 10 μ M + CUMS	23#	Group	Immobility time (approx. seconds)	Control	60	CUMS	140*	FLX 10 μ M	50	FLX 10 μ M + CUMS	60#	Group	Bout duration (approx. seconds)	Control	85	CUMS	25*	FLX 10 μ M	105	FLX 10 μ M + CUMS	100#	Group	Number of bouts (approx.)	Control	1.15	CUMS	1.05	FLX 10 μ M	1.5	FLX 10 μ M + CUMS	0.95	Group	Mean Aggression Score (approx.)	Control	3	CUMS	12*	FLX 10 μ M	3.5	FLX 10 μ M + CUMS	5#
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	 <p>Sucrose Preference assay - Statistically significantly decreased sucrose preference</p>
VOCAB: (w/definition)	Neurogenesis - the formation of new neurons from the neural stem Autoreceptor - a type of receptor found in nerve cell membranes
Cited references to follow up on	Klepsatel, P., Gálíková, M., Xu, Y., & Kühnlein, R. P. (2016). Thermal stress depletes energy reserves in <i>Drosophila</i> . <i>Scientific Reports</i> , 6(1), 33667. https://doi.org/10.1038/srep33667
Follow up Questions	Why did the study choose to not measure negative geotaxis? How were stressors randomly selected and assigned to the schedule?

Article #19 Notes: L-dopa and chlorpromazine

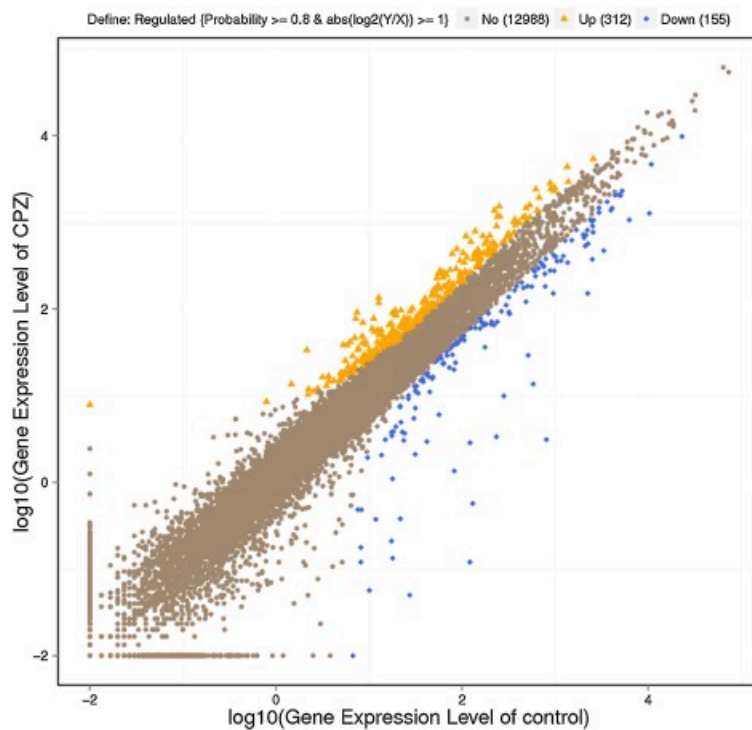
Source Title	ScienceDirect Brain research Bulletin volume 132 Drug induces depression-like phenotypes and alters gene expression profiles in <i>Drosophila</i>
Source citation (APA Format)	Jiang, M.-D., Zheng, Y., Wang, J.-L., & Wang, Y.-F. (2017). Drug induces depression-like phenotypes and alters gene expression profiles in <i>Drosophila</i> . <i>Brain Research Bulletin</i> , 132, 222–231. https://doi.org/10.1016/j.brainresbull.2017.06.009
Original URL	https://www.sciencedirect.com/science/article/pii/S0361923017302046?via%3Dihub
Source type	Journal article
Keywords	<i>Drosophila</i> , depression, L-dopa, genes
#Tags	#L-Dopa #Drosophila
Summary of key points + notes (include methodology)	<p>This study centers around the molecular mechanisms of depression. Even though depression is very common, its molecular mechanisms remain widely unknown. The study uses L-Dopa induced <i>Drosophila</i> to model depression. The study measures behavioral assays, biochemical assays, RNA sequencing, and Quantitative reverse transcriptase PCR (qRT-PCR). L-dopa and chlorpromazine showed depression linked behavioral symptoms, a decrease in serotonin, increase in malondialdehyde, a reduced activity of superoxide dismutase. Looking at the RNA of the <i>Drosophila</i> that consumed chlorpromazine 467 genes were expressed differently when compared to control flies</p> <p>Notes:</p> <ul style="list-style-type: none"> - Quantitative reverse transcriptase PCR (qRT-PCR) is used to measure and quantify RNA - Chlorpromazine is another food that can induce depression in <i>Drosophila</i>
Research Question/Problem/Need	What are the molecular mechanisms of depression?

Important Figures



Results from the serotonin concentration of 5HT

- ** represents p<0.01



- Gene expression of control drosophila
- Volcano plot
- Gray area shows similar expression levels
- Chlorpromazine vs. control drosophila

VOCAB: (w/definition)

Quantitative reverse transcriptase PCR (qRT-PCR) - a method to measure RNA expressions and quantify RNA

Cited references to follow up on	<p>van Alphen, B., & van Swinderen, B. (2013). Drosophila strategies to study psychiatric disorders. <i>Brain Research Bulletin</i>, 92, 1–11. https://doi.org/10.1016/j.brainresbull.2011.09.007</p> <p>Xu, Y., Wang, C., Klabnik, J. J., & O'Donnell, J. M. (n.d.). Novel Therapeutic Targets in Depression and Anxiety: Antioxidants as a Candidate Treatment. <i>Current Neuropharmacology</i>, 12(2), 108–119. Retrieved December 15, 2023, from https://www.eurekaselect.com/article/57565</p>
Follow up Questions	<p>Why is L-Dopa more expansively used when chlorpromazine? Was the RNA data for the L-Dopa groups in-significant?</p>

Article #20 Notes: Serotonin and dopamines effect on aggression

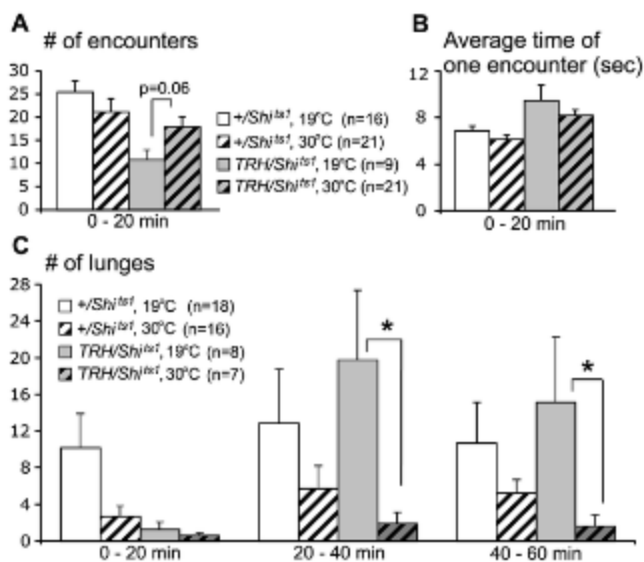
Source Title	Targeted Manipulation of Serotonergic Neurotransmission Affects the Escalation of Aggression in Adult Male <i>Drosophila melanogaster</i>
Source citation (APA Format)	Alekseyenko, O. V., Lee, C., & Kravitz, E. A. (2010). Targeted Manipulation of Serotonergic Neurotransmission Affects the Escalation of Aggression in Adult Male <i>Drosophila melanogaster</i> . <i>PLOS ONE</i> , 5(5), e10806. https://doi.org/10.1371/journal.pone.0010806
Original URL	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0010806
Source type	Journal article
Keywords	Serotonin, dopamine, depression
#Tags	#depression #neurotransmitters #aggression assay #serotonin
Summary of key points + notes (include methodology)	<p>In this study, the researchers investigated the roles of dopamine (DA) and serotonin (5HT) in aggression in <i>Drosophila</i> (fruit flies). They created a transgenic line allowing selective manipulation of serotonergic neurons and examined whether DA and 5HT have distinct effects on aggression. Using this newly generated line, they selectively disrupted 5 HT neurotransmission and found that it directly contributes to the escalation of aggression in fruit flies. In contrast, manipulation of DA neurotransmission did not replicate the same aggression phenotype. The study suggests a specific role for serotonin in the escalation of aggression in <i>Drosophila</i>.</p> <p>Summary written by Chat GPT</p> <p>Notes:</p> <ul style="list-style-type: none"> - Serotonin manipulation affected aggression in <i>Drosophila</i>

- Dopamine manipulation did not affect aggression
- Helps prove assays and using L-Dopa in my project because L-dopa decreases serotonin in drosophila

Research Question/Problem/Need

What is the effect of dopamine and serotonin on aggression in Drosophila?

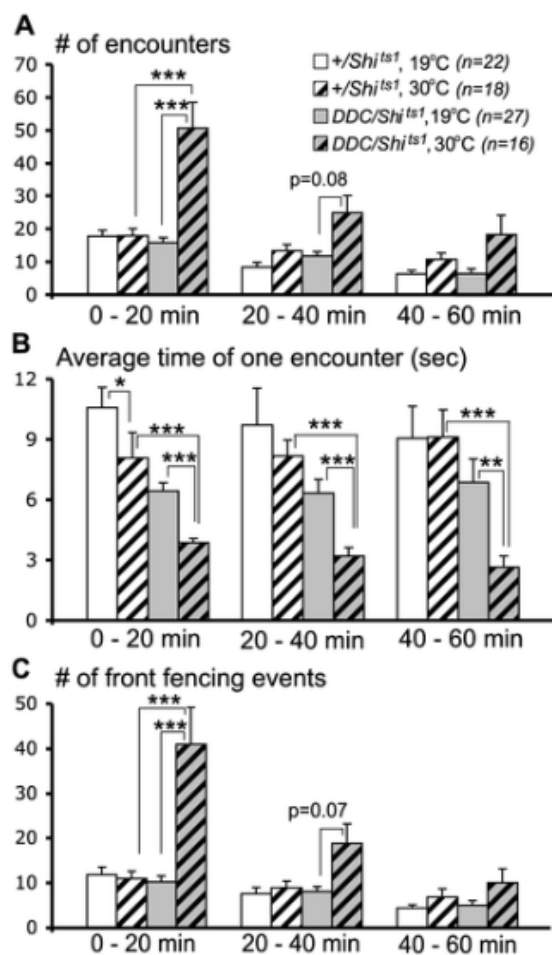
Important Figures



Aggression assay of serotonin

*p<0.05

Shows serotonin has a statistically significant effect on aggression



Effect of serotonin and dopamine on aggression

VOCAB: (w/definition)

Phototaxis - effect of light on movement/ movement in response to light

Cited references to follow up on

Alekseyenko, O. V., Lee, C., & Kravitz, E. A. (2010). Targeted Manipulation of Serotonergic Neurotransmission Affects the Escalation of Aggression in Adult Male *Drosophila melanogaster*. *PLOS ONE*, 5(5), e10806.

<https://doi.org/10.1371/journal.pone.0010806>

Ng, K. Y., Chase, T. N., Colburn, R. W., & Kopin, I. J. (1970). L-Dopa-Induced Release of Cerebral Monoamines. *Science*, 170(3953), 76–77.

<https://doi.org/10.1126/science.170.3953.76>

Follow up Questions

What prevents dopamine from having an effect on aggression?