Project Notes:

Project Title: Unraveling the Role of GABAergic Dysfunction in Catatonia: A GABAergic Investigation in Drosophila

Name: Varsha

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

Contents:

Knowledge Gaps:

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

Knowledge Gap	Resolved By	Information is located	Date resolved
Is there a connection between affective dysregulation and catatonia?	Read an article specifically talking about the relationship between dysregulation and catatonia	https://www.sciencedirect.com/science/article/pii/S0920996422003346	10/5/2024
Animal models that exhibit catatonic symptoms	Read a journal article about the rodent models of catatonia	https://www.sciencedirect.com/science/article/pii/S092099642300244X -Look more into the schizophrenic models of organisms --> Such as drosophila or c. elegans	10/11/2024 -Still look more into the schizophrenic models
Is there a therapeutic plant that can be used?	Reading an article about the different type therapeutic plants used in neuroscience	https://www.mdpi.com/1424-8247/17/10/1339#:~:text=Discussion%3A%20Numerous%20studies%20have%20highlighted,Withania%20somnifera	11/16/2024

		%2C%20and%20Curcuma%20longa.	
The different types of assays that can be completed with drosophila	Read an article about the different assays that can be used.	https://pmc.ncbi.nlm.nih.gov/articles/PMC3671839/	11/25/2024
Chemicals that can induce GABA dysfunction in drosophila	Read a journal article that consisted of information regarding chemicals used	https://pmc.ncbi.nlm.nih.gov/articles/PMC3988906/	11/27/2024

Literature Search Parameters:

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

Database/search engine	Keywords	Summary of search
IEEE Xplore	Functional Magnetic Resonance Imaging (fMRI), schizophrenia, depression, pearson correlation, effective connectivity, directed connectivity, brain nodes	People with schizophrenia and depression have differences in their brain connectivity compared to healthy individuals. To analyze the differences, researchers use fMRI data to analyze function connectivity, which measures the relationship between different brain regions, and effective connectivity, which investigates the flow of information between these regions. The results display that patients with schizophrenia and depression have disrupted functional connectivity with weaker relationships between brain regions, indicating that the flow of information within the brain is impaired compared to healthy individuals.
Nature Communication		MRI-based microthrombi detection in stroke with polydopamine iron oxide Acute ischemic stroke occurs when a blood clot blocks a brain artery, leading to significant brain damage. Even after doctors successfully reopen the blocked artery, smaller blood clots, called microthrombi, can persist in the tiny blood vessels and further damages the brain. The problem doctors are currently facing is that it is difficult to detect these microthrombi with current

		imaging techniques.

Tags:

Tag Name	

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: Comparative Analysis of Functional and Effective Connectivity in Mental Disorders

Article notes should be on separate sheets

Source Title	Comparative Analysis of Functional and Effective Connectivity in Mental Disorders
Source citation (APA Format)	Li, Y. Comparative analysis of functional and effective connectivity in mental disorders. (2023). IEEE Conference Publication | IEEE Xplore. https://ieeexplore.ieee.org/document/10565451/authors#authors
Original URL	https://ieeexplore.ieee.org/document/10565451/authors#authors
Source type	Journal
Keywords	Functional Magnetic Resonance Imaging (fMRI), schizophrenia, depression, Pearson correlation, effective connectivity, directed connectivity, brain nodes
#Tags	#fMRI #Brain Connectivity #Schizophrenia #Depression
Summary of key points + notes (include methodology)	People with schizophrenia and depression have differences in their brain connectivity compared to healthy individuals. To analyze the differences, researchers use fMRI data to analyze function connectivity, which measures the relationship between different brain regions, and effective connectivity, which investigates the flow of information between these regions. The results display that patients with schizophrenia and depression have disrupted functional connectivity with weaker relationships between brain regions, indicating that the flow of information within the brain is impaired compared to healthy individuals. Objective: Researchers wanted to analyze functional and effective connectivity differences in patients with schizophrenia and depression compared to healthy controls using fMRI data. - They used people with schizophrenia and depression as well as healthy individuals Functional Connectivity: - Researchers investigated using Pearson correlation to measure the strength of connectivity between brain regions - Looked for differences in this connectivity between patients Effective Connectivity: - Used Granger Causality Analysis to find the information influence between brain regions Conclusion: - Results found alterations in functional and effective connectivity in patients with schizophrenia and depression Notes:

	Introduction
	- FMRI looks into physiological mechanisms as well as pathways of mental illnesses
	  o Explores neural connectivity patterns in people with depression and schizophrenia
	Functional Connectivity
	- Looks into how the different brain regions interact with one another
	- Quantifying function connectivity
	  o Model driven and data driven
	  o Correlation analysis
	  ▪ Analyzes connection strengths between regions in the brain
	  ▪ Uses activity time series correlation

Research Question/Problem/ Need	How are brain connectivity patterns (both functional and effective) different between patients with schizophrenia and depression and healthy individuals?
Important Figures	 - Shows that the functional connectivity between individuals with depression and the healthy control group
VOCAB: (w/definition)	Function connectivity: A measure of how different regions of the brain interact and exchange information Activity time series correlation: A correlation between two time series functions
Cited references to follow up on	Danish M. Khan et al., "Effective connectivity in default mode network for alcoholism diagnosis", IEEE Transactions on Neural Systems and Rehabilitation Engineering, vol. 29, pp. 796-808, 2021. Kang-Min Choi et al., "Comparative analysis of default mode networks in major psychiatric disorders using resting-state EEG", Scientific reports, vol. 11.1, pp. 22007, 2021.

region_1	region_2	t_value	diff_value	p_value	p_fdr
Thalamus_R	Heschl_R	4.0075	0.1619	1.23E-04	1.17E-01
Paracentral_Lobule_L	Paracentral_Lobule_R	-3.9396	-0.0561	1.57E-04	1.19E-01
OFClat_R	SupraMarginal_L	-4.0679	-0.1646	9.86E-05	1.25E-01
Rectus_L	Angular_R	3.7983	0.1218	2.58E-04	1.63E-01
Thalamus_L	Heschl_R	4.0986	0.1793	8.82E-05	1.67E-01
Cingulate_Post_L	Angular_R	3.6345	0.1007	4.54E-04	2.16E-01
Rectus_R	Angular_R	3.6590	0.0986	4.18E-04	2.27E-01
OFClat_L	Hippocampus_R	-3.3923	-0.0997	1.02E-03	2.41E-01
Thalamus_L	Temporal_Pole_Sup_L	3.5350	0.1685	6.35E-04	2.41E-01
Thalamus_R	Temporal_Sup_L	3.3540	0.1563	1.15E-03	2.43E-01
OFClat_L	Insula_L	-3.3668	-0.1082	1.10E-03	2.46E-01
OFClat_L	Insula_R	-3.2923	-0.1057	1.40E-03	2.53E-01
Thalamus_R	Temporal_Mid_L	3.3950	0.1358	1.01E-03	2.55E-01
Frontal_Inf_Oper_R	Postcentral_R	3.2415	0.1337	1.65E-03	2.60E-01
Insula_L	Temporal_Pole_Mid_L	-3.2521	-0.1233	1.59E-03	2.63E-01
Thalamus_L	Temporal_Mid_L	3.5395	0.1428	6.25E-04	2.64E-01
Lingual_L	Angular_L	3.1760	0.1090	2.02E-03	2.65E-01
Thalamus_L	Temporal_Sup_R	3.1982	0.1433	1.89E-03	2.65E-01
Thalamus_R	Temporal_Sup_R	3.2933	0.1373	1.40E-03	2.65E-01
Thalamus_R	Temporal_Pole_Sup_L	3.2628	0.1523	1.54E-03	2.66E-01

	Aryutova Katrin et al., "Differential aberrant connectivity of precuneus and anterior insula may underpin the diagnosis of schizophrenia and mood disorders", World Journal of Psychiatry, vol. 11.12, pp. 1274, 2021.
Follow up Questions	- How do the differences in brain connectivity between patients with schizophrenia and depression affect their symptoms? - Can brain connectivity patterns be used to improve diagnosis and treatment for schizophrenia and depression? - Here are some follow-up questions that could stem from the research: - Are there any similarities in brain connectivity patterns between schizophrenia and depression patients?

Article #2 Notes: Navigating the evolving landscape of catatonia research

Article notes should be on separate sheets

Source Title	Navigating the evolving landscape of catatonia research
Source citation (APA Format)	Hirjak, D., & Northoff, G. (2023). Navigating the evolving landscape of catatonia research. *Schizophrenia Research, 263*, 1–5. https://doi.org/10.1016/j.schres.2023.10.014
Original URL	https://www.sciencedirect.com/science/article/pii/S0920996423003754#s0015
Source type	Journal
Keywords	Catatonia, diagnostic markers, neuroimaging, benzodiazepine, lorazepam, hypertonia, parkinsonism, GABAergic
#Tags	#Catatonia #Benzodiazepine #pathophysiology #MRI

Summary of key points + notes (include methodology)	So far, this past decade has seen an increase in Catatonia research leading it to its reclassification as a separate diagnosis. Catatonia is explored through various lenses such as genetics, neurobiology, and history causing researchers to investigate new diagnostic and treatment strategies. The historical origins of Catatonia state that there are several brain pathologies linked to catatonia, however there is currently a treatment known as Benzodiazepine. Additionally, movement disorders like hypertonia and parakinesia were discussed in the journal as it offered researchers fresh perspectives on motor symptoms in psychiatric conditions. They were then able to correlate these findings to the symptoms of Catatonia. Scientists have also discovered that rodent models can offer insights into catatonia's neural underpinnings, particularly within brain networks and neurotransmitter systems. Using these animal models and advanced imaging technology revealed abnormalities in brain structures like the hypothalamus and amygdala in catatonia patients. This research points to genetic factors and neuroinflammatory connections in catatonia, with implications for conditions like autism and schizophrenia.
	Notes:
	- Brain regions:
	  ○ Linked to brain regions including the anterior hypothalamus, amygdala, and motor cortex
	  ○ Smaller volumes in these regions have been observed in catatonia patients compared to those without catatonia
	- Neurodvelopment factors:
	  ○ Catatonia could be the result of early neurodevelopmental insults
	  ○ Involves abnormal growth or development of motor and premotor areas of the brain

	- Gyrification
	  o Folding of the brain's cortex
	  o Areas like the motor and parietal cortices indicates that structural changes in the brain's surface might contribute to catatonia symptoms
	- *Possibly investigate brain imaging data (such as MRIs) and compare catatonia patients to healthy controls to see if there are any patterns of abnormalities*
	- GABAergic system
	  o A rare genetic mutation in the GABRB2 gene, which is involved in GABA transmission, was recently linked to catatonia
	- Dopaminergic system
	  o Catatonia might also be linked to dopamine dysfunction
	  o Some motor symptoms overlap with conditions like Parkinsonism, which is characterized by dopamine deficiency
	- Glutamatergic System
	  o Catatonia is also associated with disruptions in the glutamate system
	  o Glutamate is a key neurotransmitter involved in brain signaling
	- Animal Models
	  o Rodent models of catatonia have shown similar brain abnormalities as human patients
	  ▪ Similarities are seen in the cortico-striatal-thalamocortical pathways
	  ▪ These models are good for studying neurotransmitter dynamics (GABA, dopamine, glutamate)
	  o Behavioral studies of rodents
	  ▪ Rodent behavior under different stimuli can mimic catatonic symptoms (immobility, rigidity)
	  ▪ By manipulating brain regions or neurotransmitter levels, scientists can observe catatonia-like behavior
	- Schizophrenia Spectrum Disorders (SSD)
	  o Two main catatonic phenotypes in SSD
	  ▪ Progressive Periodic Catatonia (PPC)
	  ▪ Chronic System Catatonia (CSC)
	  ▪ Differ in their presentation of psychotic and depressive symptoms, as well as cognitive function
	- Motor Symptom Patterns
	  o Patients display specific motor disturbances such as paratonia, hypertonia, and spontaneous parkinsonism
	  o Motor abnormalities are often linked to underlying brain circuits

Research Question/Problem/ Need	The problem is the lack of a comprehensive understanding of catatonia, including its diagnosis, neurobiology, and treatment, which limits

Important Figures	 - This figure highlights important points about progressing catatonia research and a summary of the disorder
VOCAB: (w/definition)	Vocab: Post-acute: Medical treatment that patients receive after an acute illness Distal: Sites located away from a specific area Proxies: Authority to represent someone else Aknetic: Without motion or unmoving
Cited references to follow up on	Brandt, G. A., Fritze, S., Krayem, M., Daub, J., Volkmer, S., Kukovic, J., Meyer-Lindenberg, A., Northoff, G., Kubera, K. M., Wolf, R. C., & Hirjak, D. (2024). Extension, translation and preliminary validation of the Northoff Scale for Subjective Experience in Catatonia (NSSC). Schizophrenia Research, 263, 282–288. https://doi.org/10.1016/j.schres.2023.06.002 Csihi, L., Ungvari, G. S., Caroff, S. N., Mann, S. C., & Gazdag, G. (2022). Catatonia during pregnancy and the postpartum period. Schizophrenia Research, 263, 257–264. https://doi.org/10.1016/j.schres.2022.08.003
Follow up Questions	-How do genetic and environmental factors contribute to the development of catatonia, and can this knowledge lead to personalized treatments?

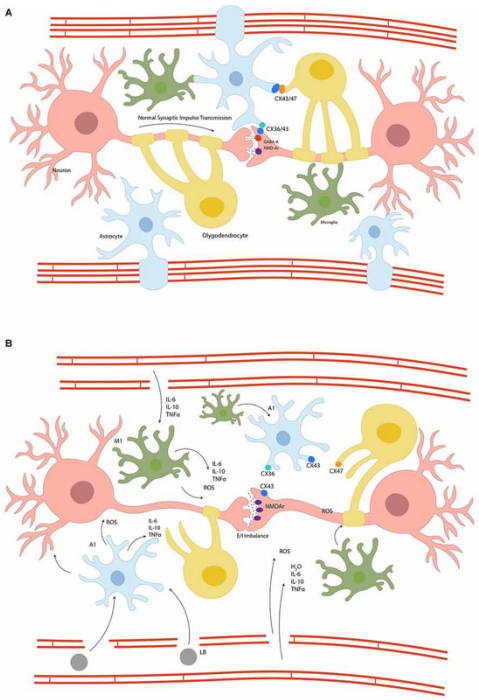
	- What challenges exist in differentiating catatonia from other psychiatric and neurological disorders, and how can they be addressed? - How can improved diagnostic tools for catatonia strengthen patient outcomes in psychiatric care? - What are the implications of neuroimaging findings for understanding the biological basis of catatonia?

Article #3 Notes: Molecular and cellular mechanisms leading to catatonia: an integrative approach from clinical and preclinical evidence

Source Title	Molecular and cellular mechanisms leading to catatonia: an integrative approach from clinical and preclinical evidence
Source citation (APA Format)	Ariza-Salamanca, D. F., Corrales-Hernández, M. G., Pachón-Londoño, M. J., & Hernández-Duarte, I. (2022). Molecular and cellular mechanisms leading to catatonia: an integrative approach from clinical and preclinical evidence. *Frontiers in Molecular Neuroscience, 15*. https://doi.org/10.3389/fnmol.2022.993671
Original URL	https://www.frontiersin.org/journals/molecular-neuroscience/articles/10.3389/fnmol.2022.993671/full
Source type	Research Article
Keywords	Microglia, gap junction, GABA allosteric modulators, antipsychotics, Electroconvulsive therapy,
#Tags	#Catatoni #D1R receptor #Dopamine #Neurotransmitters

Summary of key points + notes (include methodology)	Catatonia is a neuropsychiatric syndrome that involves both motor and behavioral abnormalities, and its pathology is connected to specific brain structures and neurotransmitters. The basal ganglia, specifically the striatum, globus pallidus, and substantia nigra, play important roles in controlling movement through direct and indirect pathways, which either initiate or inhibit motor activity. Dopamine controls these pathways through D1R and D2R receptors, affecting movement regulation. Abnormal dopamine signaling, particularly reduced activity, can disrupt this balance, leading to catatonic symptoms. Understanding the precise mechanisms of dopamine regulation and basal ganglia function is necessary for developing better treatments for catatonia.
	Notes:
	- Motor dysfunction
	  o Catatonia is linked to the dysfunction of the basal ganglia
	- Direct pathway
	  o GABAergic neurons inhibit movement-blocking structures (iGP, SNr) to allow thalamic activation of the cortex
	- Dopamine in Movement
	  o Dopamine has dual roles, depending on receptor type (D1R excites, D2R inhibits), affecting both movement initiation and inhibition
	- Psychosis

	o Overactivity of dopamine in the mesolimbic pathway contributes to psychosis o Heightened dopamine sensitivity seen in D2 receptors - Altered dopamine pathways contribute to catatonic symptoms, with abnormal dopamine signaling in basal ganglia and prefrontal areas - Affective Symptoms o Involves emotional dysregulation, mainly involving structures like the amygdala, prefrontal cortex (PFC), and orbital frontal cortex (OFC) - Amygdala Hyperactivation o Leads to heightened emotional responses (fear, anxiety), with reduced OFC function ▪ failing to inhibit this emotional output - Altered Brain Areas o Studies reveal changes in brain regions like the prefrontal cortex, primary motor cortex (M1), and cerebellum - Decreased Connectivity o Reduced GABA-A receptor binding and PFC activity correlate with movement suppression and emotional dysregulation - Catatonia is hypothesized to result from GABAergic dysfunction, exacerbated by excess glutamate activity - Serotonin o Controls dopamine release o Alterations in serotonin levels affect motor inhibition, playing a role in psychiatric disorders with catatonic features - NMDAR Encephalitis o Autoimmune cases of catatonia o Result from reduced NMDA receptor expression, disrupting glutamatergic signaling
Research Question/Problem/ Need	What is the role of astrocytes, neurons, and microglia in the pathophysiology of catatonia? How does dysregulated dopamine signaling in the basal ganglia contribute to the development of catatonia?

Important Figures	 - This image represents the glial syncytium and depicts a normal and abnormal synaptic impulse transmission
VOCAB: (w/definition)	Exacerbated: Make (a problem, bad situation, or negative feeling) worse Malignant: Very virulent or infectious Reticulum: Any fine network, especially one in the body composed of cells
Cited references to follow up on	Aandi Subramaniyam, B., Muliyala, K. P., Suchandra, H. H., and Reddi, V. S. K. (2020). Diagnosing catatonia and its dimensions: cluster analysis and factor solution using the Bush Francis Catatonia Rating Scale (BFCRS). Asian J. Psychiatr. 52:102002. doi: 10.1016/j.ajp.2020.102002 Babington, P. W., and Spiegel, D. R. (2007). Treatment of catatonia with olanzapine and amantadine. Psychosomatics 48, 534–536. doi: 10.1176/appi.psy.48.6.534 Belteczki, Z., Ujvari, J., and Dome, P. (2021). Clozapine withdrawal-induced malignant catatonia or neuroleptic malignant syndrome: a case report and a brief review of the literature. Clin. Neuropharmacol. 44, 148–153. doi: 10.1097/WNF.0000000000000462
Follow up Questions	- How do astrocytes and microglia contribute to the neuroinflammatory processes seen in catatonia? - What specific roles do oligodendrocytes play in the pathology of catatonia? - Are there clinical studies proving that there were involvements of specific cellular mechanisms in catatonia? - What are the areas for future research that could further determine

	the cellular and molecular mechanisms behind catatonia?

Article #4 Notes: GABA and Negative Affect—Catatonia as Model of RDoC-Based Investigation in Psychiatry

Source Title	GABA and Negative Affect—Catatonia as Model of RDoC-Based Investigation in Psychiatry
Source citation (APA Format)	Hirjak, D., Wolf, R. C., & Northoff, G. (2019). GABA and Negative Affect—Catatonia as model of RDOC-Based Investigation in Psychiatry. *Schizophrenia Bulletin, 45(6),* 1168–1169. https://doi.org/10.1093/schbul/sbz088
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6811819/ https://academic.oup.com/schizophreniabulletin/article/45/6/1168/5571188
Source type	Journal Article
Keywords	GABAergic, neurotransmission, neurotransmitter systems, motor symptoms,
#Tags	#GABA #GABA dynfunction #GABAergic #lorazepam

Summary of key points + notes (include methodology)	This text talks about the importance of studying the GABAergic system in understanding catatonia. Catatonia is a condition characterized by a mix of motor, affective, and behavioral symptoms. It highlights how catatonia is not limited to schizophrenia but can be linked to various mental disorders and emphasizes the need to investigate its role beyond current diagnostic categories. The text supports using catatonia as a model for studying GABA dysfunction, and states that therapies like GABA-targeting drugs and electroconvulsive therapy (ECT) show promise across multiple conditions. Animal models and multimodal MRI research are suggested as tools for exploring the neural circuits involved. Overall, this research could lead to more effective treatments for catatonia and a better understanding of how neurotransmitter imbalances affect the brain.
	Notes:
	- GABA Dysfunction
	  ○ Catatonia is linked to problems with the GABAergic system
	  ○ GABA is an important neurotransmitter in the brain
	  ○ This imbalance affects emotional regulation, motor functions, and behavior
	  ○ GABA-targeting treatments like lorazepam and electroconvulsive therapy have been effective in reducing symptoms
	- Catatonia is now being studied as a standalone condition in the ICD-11
	- researchers using tools like MRI scans and animal models

	- Clinical studies focus on how treatments affecting the GABA system, like lorazepam (a drug that enhances GABA activity) or electroconvulsive therapy, impact catatonia symptoms
	- The effectiveness of these treatments is measured through changes in motor, emotional, and behavioral symptoms
	- Researchers use a combination of behavioral tests, neuroimaging, and electrophysiological recordings to see how sensorimotor dysfunction is linked to GABAergic dysfunction in catatonia
	  o Allows for a deeper understanding of the pathways and circuits involved
	- Methodology
	  o Researchers used animal models (like mice) to study GABAergic dysfunction
	  ▪ These models display catatonic symptoms to understand how genes, molecules, and cells in the GABA system behave
	  o Multimodal MRI was used to observe brain circuits
	  ▪ Focused on how areas like the cortico-motor circuits and basal ganglia are affected by catatonia
	  o GABA-targeted treatments like lorazepam and ECT were tested on patients to observe how they improve catatonic symptoms

Research Question/Problem/ Need	What is the role of GABAergic dysfunction in the onset of catatonia?
Important Figures	There were no figures in this journal article
VOCAB: (w/definition)	Paradigmatic: Serving as a typical example of something Lorazepam: A drug that enhances GABA activity Phenomenological Approach: A method of research that focuses on patients' subjective experiences and perceptions Sensorimotor Dysfunction: Problems in the brain's ability to process sensory information and control motor functions
Cited references to follow up on	Taylor SF, Grove TB, Ellingrod VL, Tso IF. The fragile brain: stress vulnerability, negative affect and GABAergic neurocircuits in psychosis. [published online ahead of print May 31, 2019]. Schizophr Bull. doi: 10.1093/schbul/sbz046. Reed GM, First MB, Kogan CS, et al. Innovations and changes in the ICD-11 classification of mental, behavioural and neurodevelopmental disorders. World Psychiatry. 2019;18(1):3–19. Hirjak D, Kubera KM, Northoff G, et al. Cortical contributions to distinct symptom dimensions of catatonia. [published online ahead of print February 7, 2019]. Schizophr Bull. doi:10.1093/schbul/sby192.
Follow up Questions	- How do imbalances between GABA and other neurotransmitters lead to Catatonia?

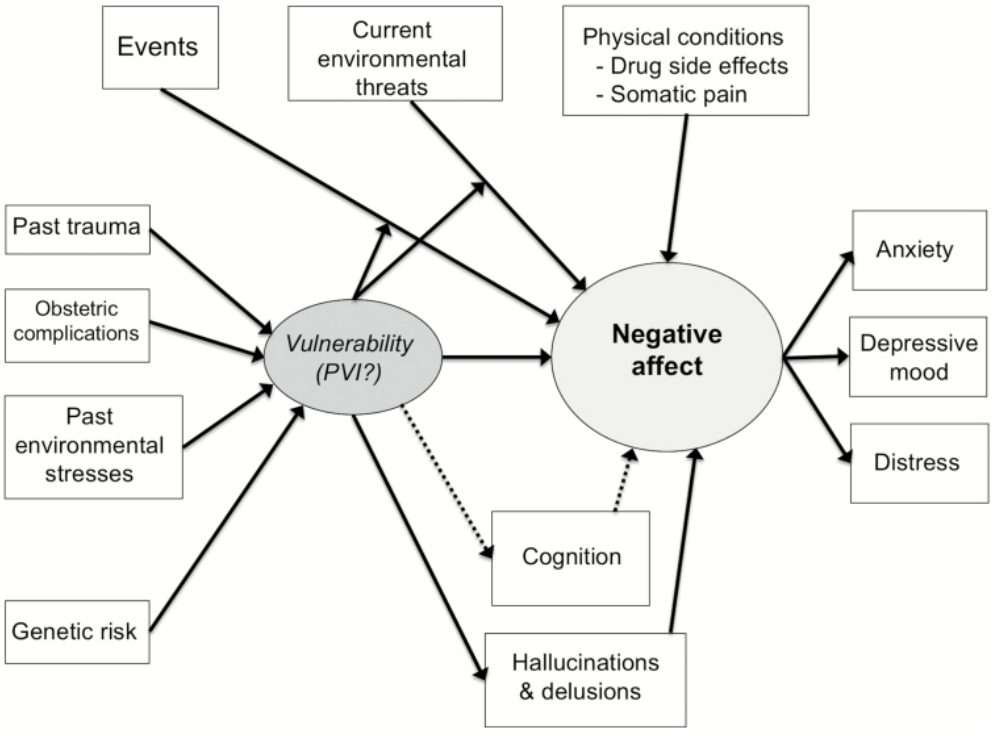
	- What specific brain circuits (such as the cortico-motor circuits) are involved in catatonia, and how do they malfunction? - How can current animal models of GABAergic dysfunction be improved to better simulate catatonic symptoms in humans? - What are the most promising GABA-targeted treatments (like lorazepam, ECT) for catatonia?

Article #5 Notes: The Fragile Brain: Stress Vulnerability, Negative Affect and GABAergic Neurocircuits in Psychosis

Source Title	The Fragile Brain: Stress Vulnerability, Negative Affect and GABAergic Neurocircuits in Psychosis
Source citation (APA Format)	Taylor, S. F., Grove, T. B., Ellingrod, V. L., & Tso, I. F. (2019). The fragile brain: stress vulnerability, negative affect and GABAergic neurocircuits in psychosis. *Schizophrenia Bulletin, 45(6)*, 1170–1183. https://doi.org/10.1093/schbul/sbz046
Original URL	https://academic.oup.com/schizophreniabulletin/article/45/6/1170/5509821?login=false
Source type	Journal Article
Keywords	Interneurons, GABAergic pathway, risk factors, schizophrenia, inhibition, immunoreactivity, PVI, GAD67 protein
#Tags	#Schizophrenia #GABA #Inhibition #Interneurons

Summary of key points + notes (include methodology)	Schizophrenia patients normally experience an increase in emotional sensitivity and negative feelings in response to stress. This sensitivity isn't just because of more stressful life events but a lower threshold for what they find stressful. Researchers believe this stress sensitivity is connected to problems in certain brain cells called GABAergic interneurons, particularly a type known as parvalbumin-positive interneurons (PVI), which play a role in controlling emotions and stress responses. Environmental factors like early trauma and genetic risks can also worsen this vulnerability. The inhibition in these brain cells also affects patients' ability to think clearly and handle emotions, leading to poorer social interactions and quality of life. Postmortem studies and animal models have shown reduced levels of important GABA-related proteins in these patients, and research continues to investigate how these changes lead to emotional and cognitive difficulties.
	Notes:
	- Emotional Sensitivity
	  - Schizophrenia patients show high emotional fragility, often experiencing negative affect in response to minor stresses
	  - Emotional deficits are typically associated with schizophrenia, but some patients display heightened sensitivity and overactive emotions

	- GABAergic Dysfunction
	  o GABA interneurons, specifically PVI, play an important role in regulating stress and emotional responses
	  o PVI abnormalities, such as reduced expression of GABA-related enzymes (like GAD67), have been observed in schizophrenia
	  ▪ Could lead to poor emotional regulation and heightened NA
	- NA is normally present in schizophrenia, alongside traditional positive (hallucinations, delusions) and negative (emotional flatness) symptoms
	- NA may contribute to poor functional outcomes in patients
	  o Affects social interactions and quality of life
	- Dysfunction in PVI has been linked to both emotional and cognitive deficits
	Methodology
	- Postmortem analysis of schizophrenia patients' brains revealed abnormalities in
	  o GABAergic interneurons (PVI), particularly reductions in GABA-related proteins
	  o Enzymes like GAD6
	- Animal models mimicking schizophrenia-like symptoms showed GABAergic deficits and PVI dysfunction
	  o Researchers can now explore the molecular mechanisms of emotional dysregulation
	- Genetic analyses have identified a strong link between GABAergic genes and schizophrenia

Research Question/Problem / Need	How do abnormalities in GABAergic interneurons, for example parvalbumin-positive interneurons, contribute to the susception to stress and the negative affect in individuals with schizophrenia?
Important Figures	

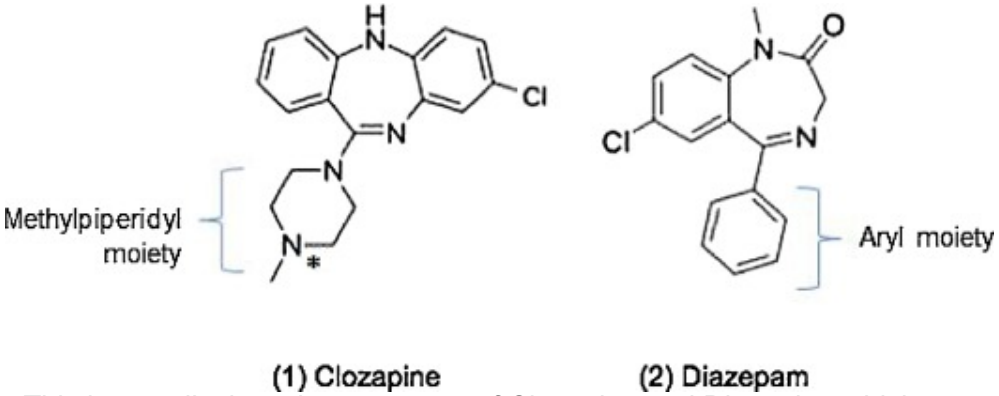
	- This figure displays the relationship between stress vulnerability and negative effects. This model includes factors that could be recognized as side effects of schizophrenia which could cause problems in GABAergic interneurons.
VOCAB: (w/definition)	Parvalbumin positive interneurons: The largest class of GABAergic inhibitory neurons in the central nervous system. Oxidative stress: A condition that occurs when the body has too many unstable molecules called free radicals, and not enough antioxidants to neutralize them Neurocognition: The brain's cognitive processes, including the ability to think, reason, learn, and remember Stress-Diathesis Model: A psychological theory that posits that mental disorders develop due to a combination of genetic vulnerability and environmental stress
Cited references to follow up on	https://pubmed.ncbi.nlm.nih.gov/3358462/ https://pubmed.ncbi.nlm.nih.gov/15803162/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4262918/
Follow up Questions	- How can interventions targeting GABAergic dysfunction reduce stress sensitivity in schizophrenia patients? - Could the role of PVI in emotional regulation be an important factor across other psychiatric disorders like bipolar disorder and depression?

Article #6 Notes: The role of the GABAergic system in catatonia—Insights from clozapine and benzodiazepines

Source Title	The role of the GABAergic system in catatonia—Insights from clozapine and benzodiazepines
Source citation (APA Format)	Plevin, D., Mohan, T., & Bastiampillai, T. (2017). The role of the GABAergic system in catatonia—Insights from clozapine and benzodiazepines. *Asian Journal of Psychiatry, 32,* 145–146. https://doi.org/10.1016/j.ajp.2017.12.008
Original URL	https://www.sciencedirect.com/science/article/pii/S1876201817308456
Source type	Journal article
Keywords	GABA receptors, anti-catatonic effect, GABAergic neurotransmission, negative feedback, threshold, clozapine, benzodiazepine
#Tags	#Catatonia #Benzodiazepine #GABA-B receptor #GABA

Summary of key points + notes (include methodology)	Catatonia is a severe motor disorder commonly treated with benzodiazepines, but clozapine is also showing promise as an effective treatment. The article talks about how clozapine and benzodiazepines are structurally different but share similar effects in treating catatonia. Benzodiazepines enhance GABA transmission through GABA-A receptors, while clozapine affects GABA-B receptors. The balance of GABAergic neurotransmission plays a significant role in catatonia, and the interaction between different GABA receptors may explain why clozapine works while other drugs do not. The authors propose that clozapine could be a preferred treatment for schizophrenia with catatonia and drug-resistant catatonia, and they suggest further research into the GABA system's role in these disorders.
	Notes:
	- Benzodiazepines are the first-line treatment
	- Clozapine, an antipsychotic, has shown potential in treating resistant cases of catatonia
	- Clozapine and benzodiazepines differ chemically.
	  ○ Clozapine has two benzene rings
	  ○ Benzodiazepines only have one
	  ○ But both have effects on GABA neurotransmission
	- Benzodiazepines work through GABAA receptors, increasing GABA's calming effects
	- Clozapine affects GABAB receptors, which are involved in more complex brain processes

	- GABA is crucial for regulating brain activity, and its dysfunction is linked to catatonia
	- GABAB receptors can either enhance or reduce GABA's effects depending on their location in the brain
	  o Can lead to varying impacts on catatonia
	- Clozapine may help by increasing GABA activity through GABAB receptors at postsynaptic sites
	  o Believed to reduce Catatonia symptoms
	
	- Excessive GABAB receptor activation can also cause catatonia in some cases
	  o Balance of GABA transmission is needed

Research Question/Problem/ Need	Why might clozapine be more effective than other drugs like benzodiazepines? How do the distinct properties of GABAA and GABAB receptors contribute to the pathophysiology of Catatonia?
Important Figures	 (1) Clozapine (2) Diazepam - This image displays the structures of Clozapine and Diazepine which are somewhat like benzodiazepines. The article wants to display their properties while also highlighting their similarities to benzodiazepines.,
VOCAB: (w/definition)	Pharmacological: Related to how drugs work in the body Neurotransmission: The process of sending signals between nerve cells in the brain GABAA and GABAB receptors: Types of sites in the brain where the chemical GABA works to either calm or regulate brain activity Antagonist: A substance that blocks or reduces the effect of something in the body Glutamate: A chemical in the brain that helps with learning and memory Neuroleptic Malignant Syndrome: A rare but serious reaction to certain medications that can affect the nervous system
Cited references to follow up on	Subramaniyam, B. A., Muliyala, K. P., Hara, S. H., & Reddi, V. S. K. (2019). Prevalence of catatonic signs and symptoms in an acute psychiatric unit from a tertiary psychiatric center in India. Asian Journal of Psychiatry, 44, 13–17. https://doi.org/10.1016/j.ajp.2019.07.003

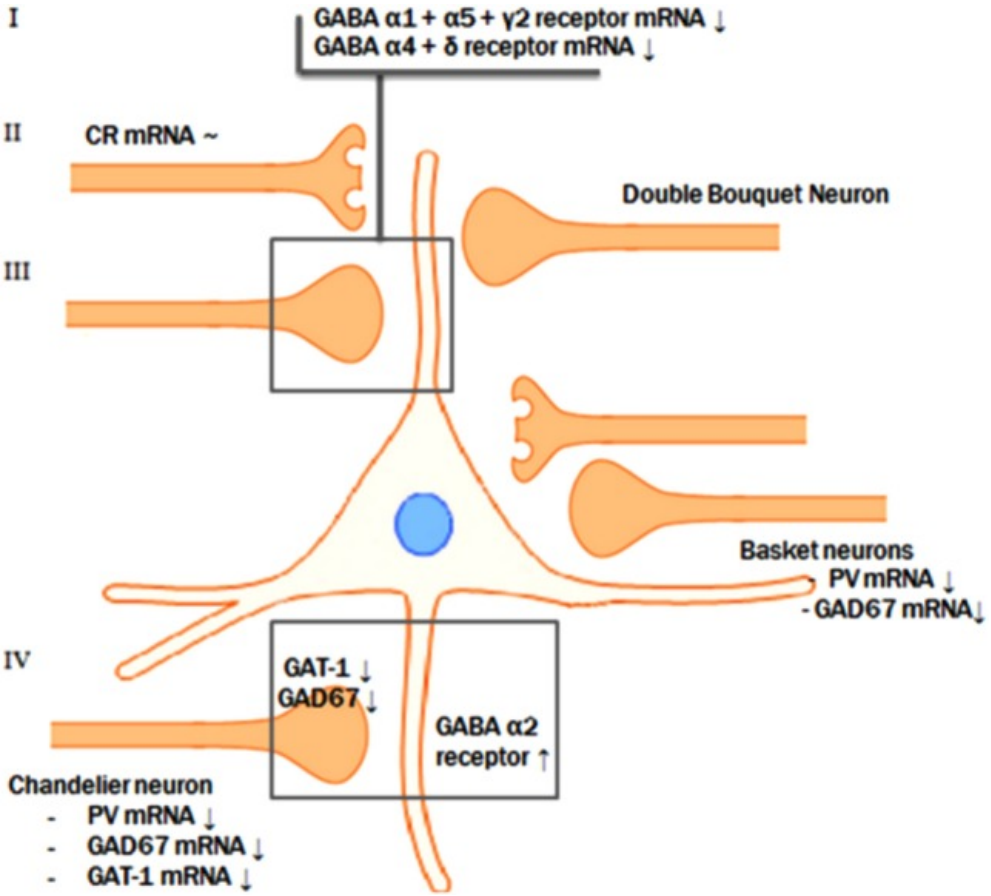
	Daskalakis, Z. J., & George, T. P. (2009). Clozapine, GABAB, and the treatment of resistant schizophrenia. Clinical Pharmacology & Therapeutics, 86(4), 442–446. https://doi.org/10.1038/clpt.2009.115
Follow up Questions	- How do GABA receptors differ in their role within the brain? - Why might clozapine be preferred over benzodiazepines for treating catatonia in some cases? - What role does GABA play in both the onset and treatment of catatonia? - What is the relationship between GABA transmission and other neurotransmitters like dopamine and acetylcholine in catatonia?

Article #7 Notes: GABAergic Mechanisms in Schizophrenia: Linking Postmortem and In Vivo Studies

Source Title	GABAergic Mechanisms in Schizophrenia: Linking Postmortem and In Vivo Studies
Source citation (APA Format)	De Jonge, J. C., Vinkers, C. H., Pol, H. E. H., & Marsman, A. (2017). GABAergic Mechanisms in schizophrenia: linking postmortem and in vivo studies. *Frontiers in Psychiatry, 8*. https://doi.org/10.3389/fpsyt.2017.00118
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5554536/
Source type	Journal article
Keywords	GABA, GABA synthesis, subunits, mRNA, pyramidal neurons, cingulate Cortex, neurotransmission, tonic inhibition
#Tags	#Schizophrenia #GABA #GAD65 #GAD67

Summary of key points + notes (include methodology)	Schizophrenia is a chronic mental disorder that affects about 1% of the population, causing hallucinations, delusions, disorganized thinking, and cognitive issues. Researchers believe that abnormalities in GABA, an important brain chemical that helps regulate activity, may play a role in the disorder. GABA is produced by an enzyme called GAD, which has two forms: GAD65 (used for quick production) and GAD67 (for maintaining steady levels). In people with schizophrenia, there is a large reduction in GAD67 in certain brain areas, especially in a type of neuron called parvalbumin-containing neurons. These changes may be linked to the cognitive deficits seen in patients. While some studies using brain imaging techniques have found reduced GABA levels, results are inconsistent. More advanced research methods are needed to understand GABA's role and its potential as a treatment target in schizophrenia.
	Notes:
	- There is evidence that abnormalities in GABAergic neurotransmission, especially in the cortical inhibitory neurons, play a role in schizophrenia
	- GABA is synthesized by two enzymes, GAD65 and GAD67. GAD67 is responsible for maintaining baseline GABA levels
	  ○ Its dysfunction is strongly linked to schizophrenia
	- These GABAergic neurons (a type of inhibitory neuron) show reduced activity in schizophrenia
	- Parvalbumin neurons are important for regulating brain rhythms and inhibiting excessive activity
	  ○ Disruption in these neurons could potentially be linked to catatonia, as they are involved in movement regulation
	- Magnetic Resonance Spectroscopy (MRS) studies on GABA levels in schizophrenia could be used for Catatonia

Research	What role do GABAergic neurotransmission abnormalities play in the onset and

Question/Problem/ Need	progression of catatonia?
Important Figures	 - This image depicts the pre and postsynaptic GABAergic alterations.
VOCAB: (w/definition)	Glutamate decarboxylase: The enzyme responsible for converting glutamate into GABA. Antipsychotic Medication: Drugs used to treat schizophrenia, potentially affecting GABA levels in the brain GAT-1: A transporter protein that recycles GABA in synapses Dorsolateral Prefrontal Cortex: A brain region involved in cognitive functions,
Cited references to follow up on	Mirnics K, Middleton FA, Marquez A, Lewis DA, Levitt P. Molecular characterization of schizophrenia viewed by microarray analysis of gene expression in prefrontal cortex. Neuron (2000) 28(1):53–67. 10.1016/S0896-6273(00)00085-4 Hashimoto T, Bergen SE, Nguyen QL, Xu B, Monteggia LM, Pierri JN, et al. Relationship of brain-derived neurotrophic factor and its receptor TrkB to altered inhibitory prefrontal circuitry in schizophrenia. J Neurosci (2005) 25(2):372–83. 10.1523/JNEUROSCI.4035-04.2005 Duncan CE, Webster MJ, Rothmond DA, Bahn S, Elashoff M, Shannon WC. Prefrontal GABA(A) receptor alpha-subunit expression in normal postnatal human

	development and schizophrenia. J Psychiatr Res (2010) 44(10):673–81. 10.1016/j.jpsychires.2009.12.007
Follow up Questions	- Can abnormalities in GABA synthesis be linked to the severity of cognitive impairments in schizophrenia patients? - What are the benefits of using GABAergic neurotransmission, specifically parvalbumin-containing neurons, in the development of new treatments for schizophrenia? - What factors contribute to the variations in GABA levels between medicated and unmedicated schizophrenia patients?

Article #8 Notes: First known case of catatonia due to cyclosporine A-related neurotoxicity in a pediatric patient with steroid-resistant nephrotic syndrome

Source Title	First known case of catatonia due to cyclosporine A-related neurotoxicity in a pediatric patient with steroid-resistant nephrotic syndrome
Source citation (APA Format)	Heekin, R. D., Bradshaw, K., & Calarge, C. A. (2019). First known case of catatonia due to cyclosporine A-related neurotoxicity in a pediatric patient with steroid-resistant nephrotic syndrome. BMC Psychiatry, 19(1). https://doi.org/10.1186/s12888-019-2107-6
Original URL	https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-019-2107-6
Source type	Case Report
Keywords	ECT, toxicity, corticosteroid treatment, prednisolone, pharmaceuticals, psychomotor abnormalities
#Tags	#Catatoni #NMDA #Pharmaceutical agents

Summary of key points + notes (include methodology)	This case presents a 9-year-old boy with a 9-month history of steroid-resistant nephrotic syndrome (SRNS) who developed catatonia due to cyclosporine A (CsA)-related neurotoxicity. The child exhibited symptoms such as mutism, posturing, and somatic delusions, leading to his admission. Elevated CsA levels were found, and the drug was not used again. Initial treatment with lorazepam and later quetiapine helped resolve his symptoms. After a lengthy hospitalization, the boy was successfully tapered off both medications, with no recurrence of symptoms six months later. This is the first reported case of CsA-induced catatonia in SRNS.
	Notes:
	- Patient
	  ○ 9-year-old boy
	  ○ Boy with nephrotic syndrome due to focal segmental glomerulosclerosis
	- Symptoms
	  ○ Mutism
	  ○ Posturing
	  ○ Delusions
	- Cause
	  ○ CsA-related neurotoxicity
	  ○ CsA plasma levels elevated to 1224 ng/mL
	- Treatment
	  ○ Lorazepam and quetiapine

	○ This resolved the symptoms - Significance ○ First case of CsA-induced catatonia in a child with SRNS
Research Question/Problem/ Need	What is the role of cyclosporine A in catatonia in pediatric patients with nephrotic syndrome?
Important Figures	No figures were provided
VOCAB: (w/definition)	Steroid-resistant nephrotic syndrome: A kidney disorder that does not respond to steroid treatment Cyclosporine A: An immunosuppressive drug used to prevent organ rejection
Cited references to follow up on	Cornic F, Consoli A, Tanguy M, Bonnot O, Périsse D, Tordjman S, Laurent C, Cohen D. Association of adolescent catatonia with increased mortality and morbidity: evidence from a prospective follow-up study. Schizophr Res. 2009;113:233–40. Denysenko L, Freudenreich O, Philbrick K, Penders T, Zimbrean P, Nejad S, et al. Catatonia in medically ill patients: an evidence-based medicine (EBM) monograph for psychosomatic medicine practice. The guidelines and evidence-based medicine Subcommittee of the Academy of psychosomatic medicine (APM) and the European Association of Psychosomatic Medicine (EAPM). 2015. https://www.eapm.eu.com/wp-content/uploads/2018/06/Catatonia_APM-EAPM_2015-04-17.pdf.
Follow up Questions	- What are the long-term outcomes in pediatric patients who experience catatonia as a result of drug-related neurotoxicity? - How can treatment protocols for catatonia be improved for children who cannot receive electroconvulsive therapy?

Article #9 Notes: The metabolic effects of antipsychotics in the early stage of treatment in first-episode patients with schizophrenia: A real-world study in a naturalistic setting

Source Title	The metabolic effects of antipsychotics in the early stage of treatment in first-episode patients with schizophrenia: A real-world study in a naturalistic setting
Source citation (APA Format)	Cao, H., Meng, Y., Li, X., Ma, X., Deng, W., Guo, W., & Li, T. (2020). The metabolic effects of antipsychotics in the early stage of treatment in first-episode patients with schizophrenia: A real-world study in a naturalistic setting. *Journal of Psychiatric Research, 129*, 265–271. https://doi.org/10.1016/j.jpsychires.2020.07.038
Original URL	https://www.sciencedirect.com/science/article/pii/S0022395620309031
Source type	Journal article
Keywords	Antipsychotic treatment, metabolic, insulin, schizophrenia
#Tags	#schizophrenia #metabolism #antipsychotic treatment

Summary of key points + notes (include methodology)	This study investigates the early metabolic effects of antipsychotic treatment in first-episode, drug-naïve patients with schizophrenia. A analysis was conducted on metabolic profiles before and after 2 and 4 weeks of treatment. Results showed significant increases in insulin resistance and lipid metabolic abnormalities, including higher triglycerides and lower high-density lipoprotein cholesterol after two weeks. The findings display the need for monitoring metabolic health in patients starting antipsychotic treatment, as these effects come about early.
	Notes:
	- Retrospective real-world study in a naturalistic setting
	- Included in patients with first-episode schizophrenia
	- Patients
	  ○ Diagnosed with schizophrenia (ICD-10 criteria)
	  ○ Aged 16-45 years
	- Data collection
	  ○ Demographic and clinical data extracted from hospital records
	  ○ Metabolic parameters measured at baseline, 2 weeks, and 4 weeks after treatment
	- Research measured
	  ○ Fasting glucose, triglycerides, cholesterol
	  ○ Insulin resistance

<table>
<tr><td></td><td>

Body mass index

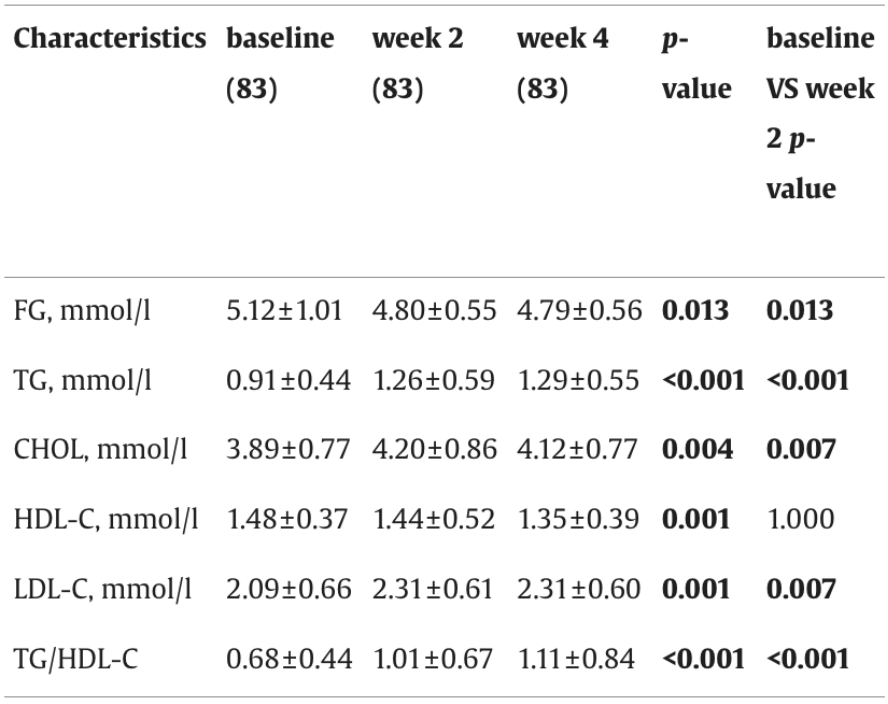
- Statistical Analysis

Analyzed using SPSS software
Group comparisons with t-tests, ANOVA, and chi-squared tests

- Insulin resistance significantly increased after 2 weeks
- TG and CHOL levels increased significantly after 2 weeks
- HDL-C decreased significantly after 4 weeks
</td></tr>
<tr><td>Research Question/Problem/ Need</td><td>How do different antipsychotic medications affect metabolic profiles in schizophrenia patients during the initial weeks of treatment?</td></tr>
<tr><td>Important Figures</td><td>
<table>
<tr><th>Characteristics</th><th>baseline (276)</th><th>week 2 (276)</th><th>p-value</th></tr>
<tr><td>FG, mmol/l</td><td>5.06±1.05</td><td>4.71±0.73</td><td><0.001</td></tr>
<tr><td>TG, mmol/l</td><td>0.96±0.52</td><td>1.31±0.78</td><td><0.001</td></tr>
<tr><td>CHOL, mmol/l</td><td>3.81±0.72</td><td>4.15±0.82</td><td><0.001</td></tr>
<tr><td>HDL-C, mmol/l</td><td>1.42±0.37</td><td>1.39±0.41</td><td>0.120</td></tr>
<tr><td>LDL-C, mmol/l</td><td>2.04±0.60</td><td>2.29±0.61</td><td><0.001</td></tr>
<tr><td>TG/HDL-C</td><td>0.74±0.51</td><td>1.06±0.81</td><td><0.001</td></tr>
</table>
Abbreviation: CHOL, cholesterol; FG, fasting glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; TG/HDL-C, ratio of triglycerides to high-density lipoprotein cholesterol.

This image displayed the comparison of the metabolic parameters between the baseline and 2 weeks of antipsychotic treatment in schizophrenia patients

</td></tr>
</table>

	 - The image displays the metabolic parameters at baselines and 2 to 4 weeks after the injection of antipsychotic treatment
VOCAB: (w/definition)	Insulin Resistance: A condition where the body's cells become less responsive to insulin which leads to higher blood sugar levels. Glucolipid Metabolism: The metabolic processes involving glucose and lipids that is used for maintaining energy balance and metabolic health. Lipid Metabolism: The process by which lipids (fats) are broken down and utilized for energy or stored in the body
Cited references to follow up on	De Hert, M., Vancampfort, D., Correll, C. U., Mercken, V., Peuskens, J., Sweers, K., Van Winkel, R., & Mitchell, A. J. (2011). Guidelines for screening and monitoring of cardiometabolic risk in schizophrenia: systematic evaluation. The British Journal of Psychiatry, 199(2), 99–105. https://doi.org/10.1192/bjp.bp.110.084665 Harris, L. W., Guest, P. C., Wayland, M. T., Umrania, Y., Krishnamurthy, D., Rahmoune, H., & Bahn, S. (2012). Schizophrenia: Metabolic aspects of aetiology, diagnosis and future treatment strategies. Psychoneuroendocrinology, 38(6), 752–766. https://doi.org/10.1016/j.psyneuen.2012.09.009

Follow up Questions	- How do lifestyle factors interact with antipsychotic treatment to affect metabolic outcomes? - Are certain antipsychotic medications more likely to cause metabolic side effects than others?

Article #10 Notes: Catatonia is associated with higher rates of negative affect amongst patients with schizophrenia and schizoaffective disorder

Source Title	Catatonia is associated with higher rates of negative affect amongst patients with schizophrenia and schizoaffective disorder
Source citation (APA Format)	Kline, C. L., Suzuki, T., Simmonite, M., & Taylor, S. F. (2022). Catatonia is associated with higher rates of negative affect amongst patients with schizophrenia and schizoaffective disorder. *Schizophrenia Research, 263*, 208–213. https://doi.org/10.1016/j.schres.2022.09.001
Original URL	https://www.sciencedirect.com/science/article/pii/S0920996422003346
Source type	Journal article
Keywords	Catatonia, schizophrenia, T-test, statistical analysis, motor symptoms, behavioral symptoms
#Tags	#catatonia #schizophrenia #statistical analysis

Summary of key points + notes (include methodology)	This study investigates the relationship between catatonia and affective dysregulation in patients with schizophrenia and schizoaffective disorders. Catatonia was viewed as a subtype of schizophrenia before but is now recognized as a syndrome that can occur across various psychiatric conditions. This study hypothesizes that individuals with schizophrenia exhibiting catatonia demonstrate higher levels of affective dysregulation, specifically anxiety and depression. By using an electronic medical record search tool, researchers were able to distribute the patients into different categories. The results reveal that patients with catatonia are more likely to have anxiety (1.71 times) and depression (1.8 times) compared to those without catatonia. This study overall shows the importance of recognizing affective dysregulation in schizophrenia patients presenting with catatonia.
	Notes:
	- Growing evidence to suggest affective dysregulation is a salient feature of both catatonia and schizophrenia
	- Catatonia is recognized as a syndrome, previously considered a subtype of schizophrenia
	  ○ Commonly associated with affective disorders
	- Retrospective review of patients diagnosed with schizophrenia or schizoaffective disorder
	  ○ Used the EMERSE tool
	  ○ Exclusion phrases used to minimize false positives
	- Statistical tests
	  ○ Chi-square analyses for associations between catatonia and

<table>
<tr><td></td><td>anxiety/depression
○ Odds ratios (OR) calculated for these associations
- Anxiety disorder prevalence
○ 43% in the cohort
○ Patients with catatonia were 1.71 times more likely to have anxiety
-</td></tr>
<tr><td>Research Question/Problem/ Need</td><td>How does the presence of catatonia influence the severity of affective dysregulation in schizophrenia patients?</td></tr>
<tr><td>Important Figures</td><td>Table 2. Crosstabs of relations of catatonia with anxiety and depression.
<table><tr><th>Variables</th><th></th><th>Catatonia</th><th></th><th>χ^2</th><th>OR</th></tr><tr><th></th><th></th><th>Absent</th><th>Present</th><th></th><th></th></tr><tr><td>Anxiety</td><td>Absent</td><td>54.3%</td><td>2.1%</td><td>118.9</td><td>1.71</td></tr><tr><td></td><td>Present</td><td>40.9%</td><td>2.7%</td><td></td><td></td></tr><tr><td>Anxiety given catatonia</td><td></td><td>43.0%</td><td>56.3%</td><td></td><td></td></tr><tr><td>Depression</td><td>Absent</td><td>57.2%</td><td>2.2%</td><td>145.4</td><td>1.80</td></tr><tr><td></td><td>Present</td><td>38.1%</td><td>2.6%</td><td></td><td></td></tr><tr><td>Depression given catatonia</td><td></td><td>39.9%</td><td>54.5%</td><td></td><td></td></tr></table>Note. χ^2=chi-square statistic, OR=odds ratio.
- This image displays a chi square test that indicated that catatonia was associated with both anxiety and depression</td></tr>
<tr><td>VOCAB: (w/definition)</td><td>Affective Dysregulation: Difficulty in regulating emotional responses
Global Assessment of Functioning (GAF) Scale: A numeric scale used to assess overall mental health
Odds Ratio (OR): A statistic that quantifies the odds of an outcome occurring in one group compared to another</td></tr>
<tr><td>Cited references to follow up on</td><td>Bjorkquist, O. A., Olsen, E. K., Nelson, B. D., & Herbener, E. S. (2016). Altered amygdala-prefrontal connectivity during emotion perception in schizophrenia. Schizophrenia Research, 175(1–3), 35–41. https://doi.org/10.1016/j.schres.2016.04.003</td></tr>
</table>

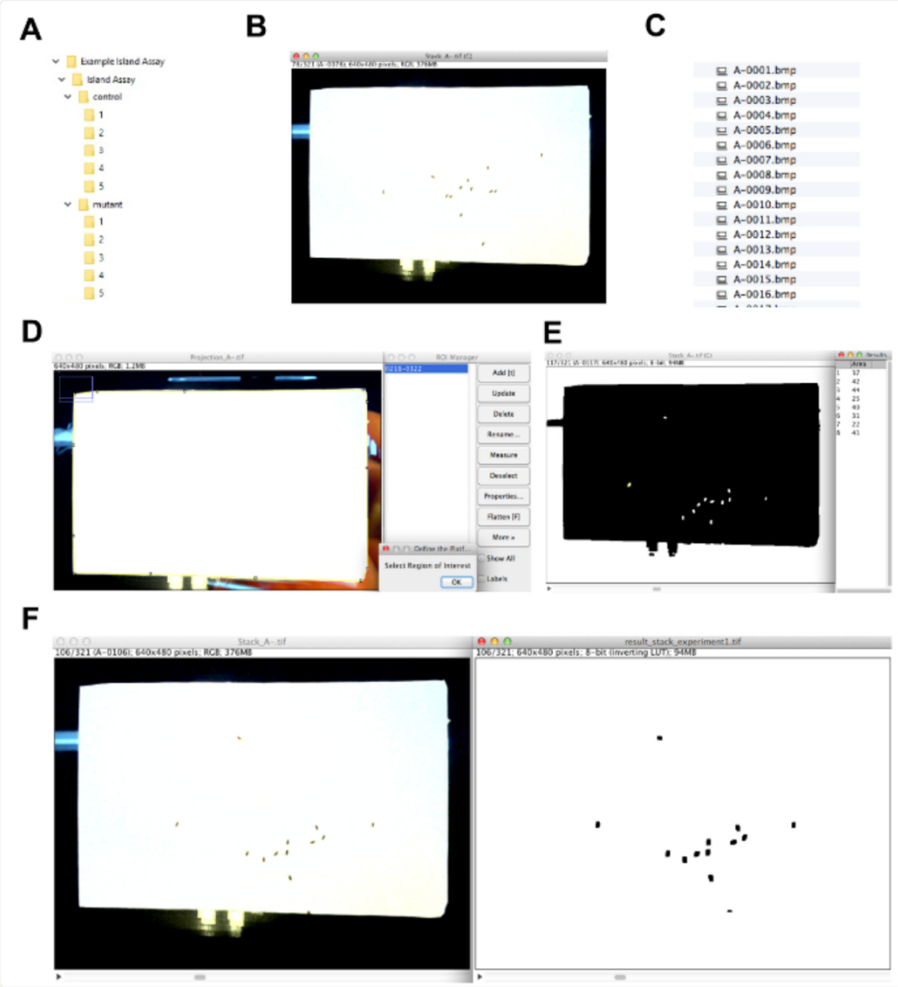
	Duman, R. S., Sanacora, G., & Krystal, J. H. (2019). Altered connectivity in depression: GABA and glutamate neurotransmitter deficits and reversal by novel treatments. Neuron, 102(1), 75–90. https://doi.org/10.1016/j.neuron.2019.03.013
Follow up Questions	- Could GABAergic dysfunction be further explored as a primary cause of catatonia in schizophrenia? - What other neurotransmitter systems might be involved in the relationship between catatonia and affective dysregulation? - Can early detection of anxiety and depression help prevent the onset of catatonia in schizophrenia?

Article #11 Notes: High-throughput Analysis of Locomotor Behavior in the Drosophila Island Assay

Source Title	High-throughput Analysis of Locomotor Behavior in the Drosophila Island Assay
Source citation (APA Format)	Eidhof, I., Fenckova, M., Elurbe, D. M., Van De Warrenburg, B., Nobau, A. C., & Schenck, A. (2017). High-throughput Analysis of Locomotor Behavior in the Drosophila Island Assay. *Journal of Visualized Experiments*, *129*. https://doi.org/10.3791/55892
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC5755321/
Source type	Journal Article
Keywords	Locomotor, behavior, drosophila, molecular mechanisms, recording
#Tags	#Locomotion #Behavior #Data

Summary of key points + notes (include methodology)	The article explains the Drosophila Island Assay, a cost-effective and efficient way to measure movement in fruit flies (Drosophila melanogaster). This method involves dropping flies onto a platform to test their ability to escape by flying, jumping, or walking. Normally, analyzing the results is done manually, which takes a lot of time. The researchers created a new automated system using a webcam and computer algorithms to make this process faster and more accurate. This system helps scientists study genes, drugs, and conditions that affect movement, especially for diseases like Ataxia Telangiectasia (AT).
	Notes:
	- What is the Island Assay?
	  ○ A test to measure how quickly flies escape from a platform
	  ○ Tests motor abilities
	  ▪ Flight
	  ▪ Jumping
	  ▪ Walking
	- Usage of drosophila
	  ○ Flies are easy to breed and study
	  ○ Their genetics and behavior are similar to humans in some ways
	- Problem with the old method
	  ○ Data analysis was done manually, making it slow and

	tedious
	- Solution to the problem
	  ○ Developed an automated system using a webcam and software (Fiji and R)
	  ○ Makes data collection and analysis faster and more reliable
	- What can it be used for
	  ○ Identifying genes involved in movement disorders
	  ○ Testing drugs for neurological diseases

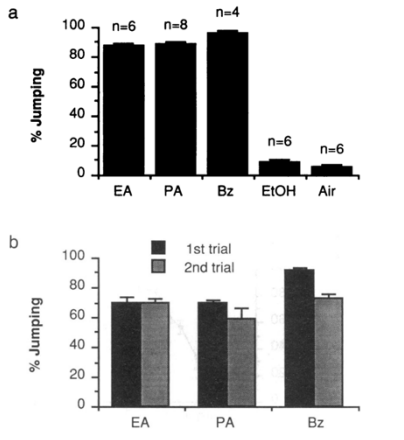
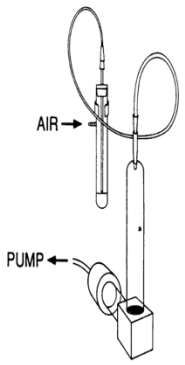
Research Question/Problem/ Need	How can we make the analysis of Drosophila locomotor behavior faster, more accurate, and suitable for large-scale genetic or drug screenings?
Important Figures	 - This image showed an example of what appears for when people use the video software to examine the flies
VOCAB: (w/definition)	Locomotor Behavior: Movements like walking, jumping, or flying High-throughput: A method that allows testing many samples quickly Drosophila melanogaster: A species of fruit fly used in scientific research ROI (Region of Interest): The specific area analyzed in an experiment

	Macro: A set of instructions that automates tasks in software ANOVA: A statistical test used to compare differences among multiple groups
Cited references to follow up on	He J, Mangelsdorf M, Fan D, Bartlett P, Brown MA. Amyotrophic Lateral Sclerosis Genetic Studies: From Genome-wide Association Mapping to Genome Sequencing. Neuroscientist. 2015;21:599–615. doi: 10.1177/1073858414555404. Hada B, et al. D-chiro-inositol and pinitol extend the life span of Drosophila melanogaster. J Gerontol A Biol Sci Med Sci. 2013;68:226–234. doi: 10.1093/gerona/gls156. Volkenhoff A, et al. Glial Glycolysis Is Essential for Neuronal Survival in Drosophila. Cell Metab. 2015;22:437–447. doi: 10.1016/j.cmet.2015.07.006.
Follow up Questions	- Why is the Island Assay better than traditional methods for studying movement in flies? - How does automated analysis improve efficiency compared to manual counting? - Can this system be adapted for other model organisms or behaviors?

Article #12 Notes: A simple chemosensory response in Drosophila and the isolation of acj mutants in which it is affected

Source Title	A simple chemosensory response in Drosophila and the isolation of acj mutants in which it is affected
Source citation (APA Format)	McKenna, M., Monte, P., Helfand, S. L., Woodard, C., & Carlson, J. (1989). A simple chemosensory response in Drosophila and the isolation of acj mutants in which it is affected. *Proceedings of the National Academy of Sciences*, *86*(20), 8118–8122. https://doi.org/10.1073/pnas.86.20.8118
Original URL	https://www.pnas.org/doi/10.1073/pnas.86.20.8118?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed
Source type	Journal Article
Keywords	Chemosensory, acj mutants, drosophila, jump response
#Tags	#chemosensory #Response #physiology
Summary of key points + notes (include methodology)	The article explores how the sense of smell (chemosensation) works in Drosophila melanogaster (fruit flies) and why it is important for their survival and behavior. While the visual system of fruit flies has been studied in detail, chemo sensation remains less understood. Smell plays a critical role in helping flies find food, choose places to lay eggs, and interact during mating, but studying it has been difficult because of limited tools to measure their responses to odors. To address this, the researchers developed a new method called the "jump assay." In this test, a single fly is placed in a tube, and when exposed to certain strong chemical smells, it reacts by jumping. This simple behavior provides a way to measure how well a fly's chemosensory system works. The jump assay is very precise and allows scientists to study individual flies instead of whole groups, making it easier to find and study genetic mutations that affect smell. Using this method, the researchers tested the

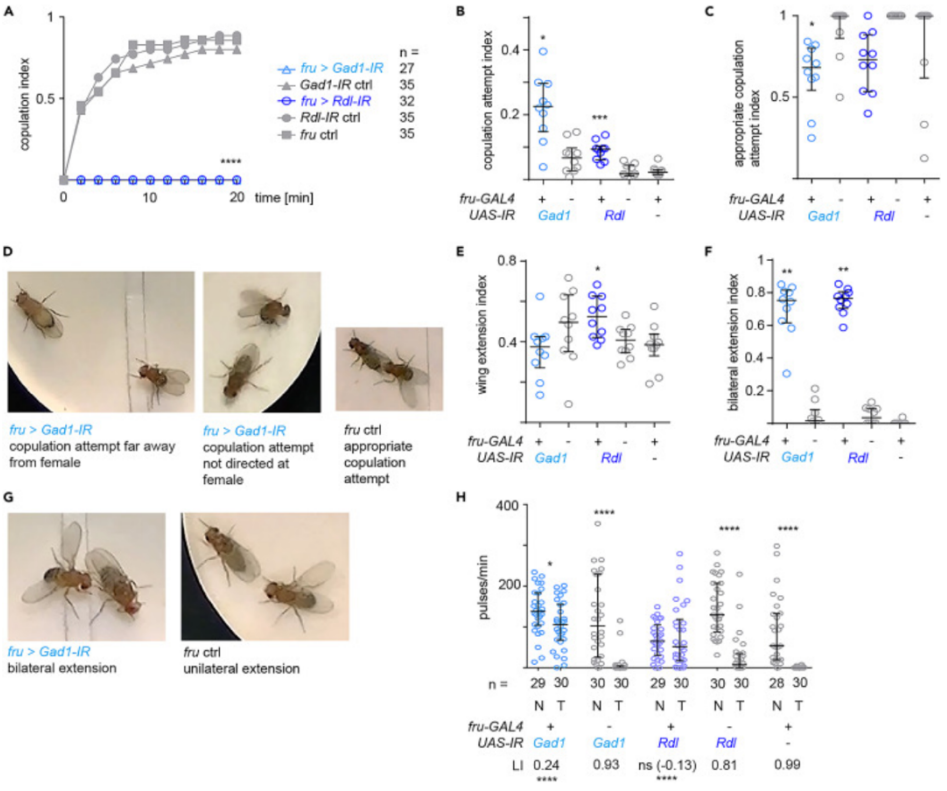
	responses of flies to different chemicals and identified genes and mutations that influence chemosensory behavior. This work opens new possibilities for understanding how flies' sense and respond to their environment and provides a foundation for future genetic studies on smell.
	Notes:
	- The jump assay offers significant advantages:
	  o Efficiency: It allows rapid testing of large numbers of flies, crucial for screening mutants
	  o Precision: Single-fly testing reduces variability due to genetic background effects
	  o Scalability: The assay supports advanced analyses like mosaic experiments and identification of rare mutations
	- Using a chemosensory-based assay could help:
	  o Identify genes critical for sensory processing and their behavioral consequences
	  o Establish connections between sensory deficits and broader neurological dysfunctions
	  o Develop pharmacological interventions by testing responses to chemical stimuli under drug treatments

Research Question/Problem/ Need	How can the "jump response" in Drosophila melanogaster be used to study the genetic basis of chemosensory (smell-related) behavior?
Important Figures	 FIG. 2. (*a*) Jump response to chemicals of different classes. All chemicals were undiluted. *n* indicates the number of experiments, each experiment consisting of 50 trials, one CS-5 fly per trial. Error bars indicate SEM. (*b*) Jump response to sequential stimuli. CS-5 flies were assayed with vapor of the indicated chemical, transferred to a vial, allowed to rest 1 min, and then assayed again. This procedure was repeated on each of 30 flies per experiment; five experiments were performed in the case of each chemical. Error bars indicate SEM. EA, ethyl acetate; PA, propionic acid; Bz, benzaldehyde, undiluted.  FIG. 1. Apparatus for testing jump response. A single fly is introduced into the tube with a mouth aspirator and is allowed to walk approximately one-third to one-half of the way up the side. Air is drawn through the system continuously by means of a pump. When the Teflon tubing from the sidearm vessel is inserted into the hole at the top of the tube, air is drawn over the surface of the chemical placed in the sidearm vessel and through the tube. The tubing is inserted into the tube for 3 s, giving the animal a 3-s exposure to chemical vapors. A jump event is scored if the fly lands on the screen at the base of the tube during this period.
VOCAB: (w/definition)	Chemosensory: The ability to sense chemicals, like smells or tastes Jump Assay: A test where flies are exposed to strong smells, and their jumping reaction is measured Mutation: A change in a gene that can affect how an organism behaves or functions

	Signal-to-Noise Ratio: A measure of how clear and reliable a result is compared to background activity or random responses Genetic Analysis: Studying an organism's DNA to understand how its genes work and affect its traits
Cited references to follow up on	Corrales, M., Cocanougher, B. T., Kohn, A. B., Wittenbach, J. D., Long, X. S., Lemire, A., Cardona, A., Singer, R. H., Moroz, L. L., & Zlatic, M. (2022). A single-cell transcriptomic atlas of complete insect nervous systems across multiple life stages. Neural Development, 17(1). https://doi.org/10.1186/s13064-022-00164-6
Follow up Questions	- What other behaviors in Drosophila could be studied to understand how their senses work? - Could this jump assay be adapted to study other sensory systems like touch or hearing in flies? - How do the identified genes in this study relate to similar genes in humans or other animals?

Article #13 Notes: GABAergic signaling shapes multiple aspects of Drosophila courtship motor behavior

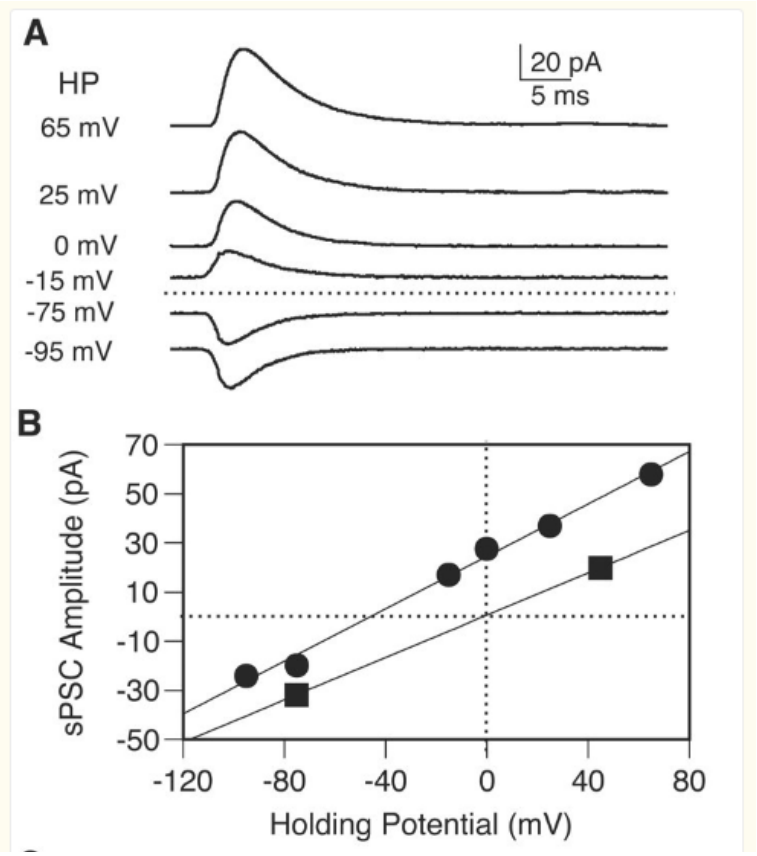
Source Title	GABAergic signaling shapes multiple aspects of Drosophila courtship motor behavior
Source citation (APA Format)	Amin, H., Nolte, S. S., Swain, B., & Von Philipsborn, A. C. (2023). GABAergic signaling shapes multiple aspects of Drosophila courtship motor behavior. *iScience*, *26*(11), 108069. https://doi.org/10.1016/j.isci.2023.108069
Original URL	https://www.sciencedirect.com/science/article/pii/S2589004223021466
Source type	Journal Article
Keywords	GABAergic, Drosophila, Motor Activity, Inhibition, Neurotransmitters
#Tags	#GABAergic #Motor #Behavior #Neurons
Summary of key points + notes (include methodology)	This study looks into how inhibitory neurons, which use a chemical called GABA, help male fruit flies (Drosophila melanogaster) coordinate their courtship behavior. Male courtship involves several steps, like chasing a female, tapping her with their legs, producing a courtship song by vibrating their wings, and attempting to mate. The researchers focused on neurons that produce GABA and express a male-specific factor called FruM, which controls courtship behaviors. By reducing GABA signaling in these neurons (using RNAi to knock down the genes GAD1 and Rdl), the researchers found that male flies showed uncoordinated behaviors, like trying to mate in the wrong position, using both wings instead of one to produce courtship songs, and failing to learn from past experiences with unreceptive females. These issues led to a lack of successful mating. The study highlights the importance of GABA in fine-tuning behaviors and ensuring they are done in the right sequence. Notes: - Key Observations:

	○ Male flies with reduced GABA signaling had trouble with coordination during mating attempts ○ Their courtship songs were abnormal, using two wings instead of one ○ They didn't learn to stop courting unreceptive females, unlike normal flies - Focus ○ How GABA neurons influence male fruit fly courtship behavior
Research Question/Problem/ Need	How do GABAergic (inhibitory) neurons influence male courtship behaviors in fruit flies?
Important Figures	 Download: Download high-res image (930KB) Download: Download full-size image Figure 1. Depletion of GABAergic inhibition affects the motor coordination of male courtship behavior
VOCAB: (w/definition)	GABA (Gamma-Aminobutyric Acid): A neurotransmitter that reduces neuron activity, helping to balance and control behaviors FruM (Fruitless Male): A male-specific protein in flies that controls behaviors like courtship RNAi (RNA Interference): A method used to reduce or "silence" the activity of

	specific genes GAD1: A gene that produces the enzyme needed to make GABA Rdl: A receptor on neurons that responds to GABA signals Courtship Song: A sound made by male flies vibrating one wing to attract females
Cited references to follow up on	Cossart, R., Bernard, C., & Ben-Ari, Y. (2004). Multiple facets of GABAergic neurons and synapses: multiple fates of GABA signalling in epilepsies. Trends in Neurosciences, 28(2), 108–115. https://doi.org/10.1016/j.tins.2004.11.011 Rentzsch, F., Juliano, C., & Galliot, B. (2019). Modern genomic tools reveal the structural and cellular diversity of cnidarian nervous systems. Current Opinion in Neurobiology, 56, 87–96. https://doi.org/10.1016/j.conb.2018.12.004
Follow up Questions	- How does GABA signaling influence behaviors other than courtship in fruit flies? - Can similar GABA-related mechanisms be found in the courtship behaviors of other animals? - How do GABAergic neurons interact with other sensory signals during male courtship?

Article #14 Notes: GABA Receptors Containing Rdl Subunits Mediate Fast Inhibitory Synaptic Transmission in Drosophila Neurons

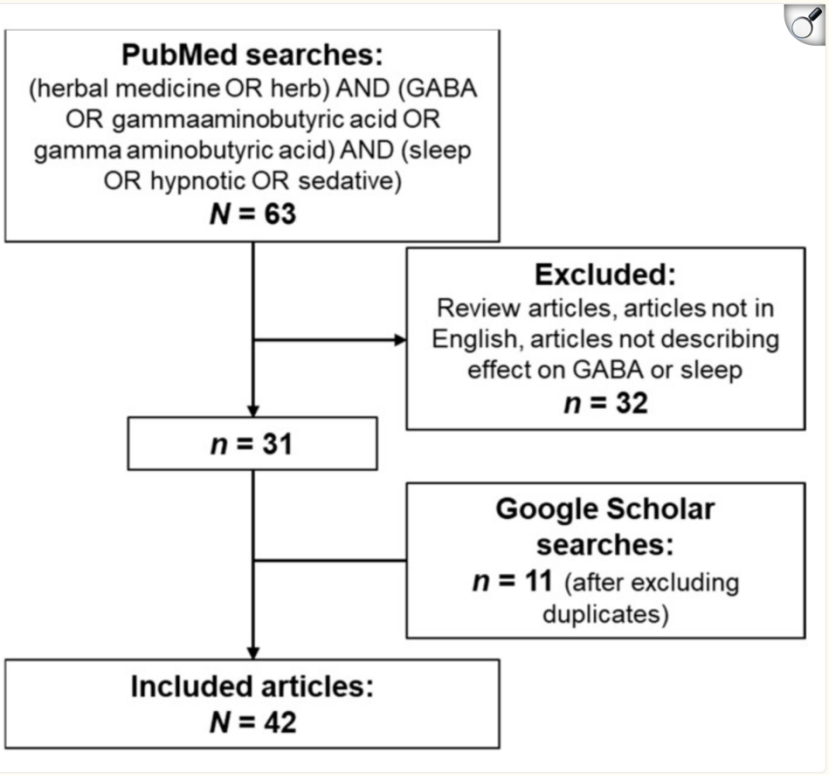
Source Title	GABA Receptors Containing Rdl Subunits Mediate Fast Inhibitory Synaptic Transmission in Drosophila Neurons
Source citation (APA Format)	Lee, D., Su, H., & O'Dowd, D. K. (2003). GABA receptors containing RDL subunits mediate fast inhibitory synaptic transmission inDrosophilaNeurons. *Journal of Neuroscience*, *23*(11), 4625–4634. https://doi.org/10.1523/jneurosci.23-11-04625.2003
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC6740792/
Source type	Journal Article
Keywords	GABA receptor, neurons, drosophila, inhibitory
#Tags	#drosophila #GABA receptors
Summary of key points + notes (include methodology)	This study investigates how GABAergic inhibition regulates neuronal activity in Drosophila (fruit flies) and highlights the role of the Rdl GABA receptor subunit. Researchers cultured Drosophila neurons and observed their spontaneous GABA signals. They found that GABA receptors inhibit neuronal activity by allowing chloride ions to flow into the neurons. When GABA inhibition was blocked using picrotoxin, neurons fired more frequently, showing the importance of GABA in controlling activity. Neurons with mutations in the Rdl gene were less sensitive to picrotoxin, proving that Rdl-containing GABA receptors play a direct role in this inhibition. Additionally, the properties of GABAergic

	synapses changed as the neurons matured in culture, showing that synaptic inhibition is dynamically regulated over time. By studying GABAergic inhibition in Drosophila, researchers can gain insights into how GABA functions in nervous systems across species. Overall, the author descriptively described the process of understanding the GABAergic inhibition's role in regulating neural activity in the drosophila.
Research Question/Problem/ Need	How do Rdl GABA receptors contribute to regulating neuronal activity in Drosophila?
Important Figures	
VOCAB: (w/definition)	GABA Receptors: Reduce neuronal activity by allowing chloride ions to flow into the neuron. Blocking GABA: Picrotoxin blocks GABA receptors, causing neurons to fire more frequently. Mutations in Rdl: Make neurons resistant to picrotoxin, proving that Rdl is essential for GABA inhibition. Neuronal Maturation: Over time, the strength and timing of GABA signals change as neurons develop. Synaptic Currents: Two types are studied which were sPSCs (spontaneous currents) and mIPSCs (miniature currents).
Cited references to follow up on	Etter A, Cully DF, Liu KK, Reiss B, Vassilatis DK, Schaeffer JM, Arena JP (1999) Picrotoxin blockade of invertebrate glutamate-gated chloride channels:

	subunit dependence and evidence for binding within the pore. J Neurochem 72: 318–326. Hodges DD, Lee D, Preston CF, Boswell K, Hall LM, O'Dowd DK (2002) tipE regulates Na +-dependent repetitive firing in Drosophila neurons. Mol Cell Neurosci 19: 402–416.
Follow up Questions	- What happens to neuron activity when GABA inhibition is blocked with picrotoxin? - How does the Rdl mutation affect the GABA receptor's response to picrotoxin? - Why is GABAergic inhibition important for neurons?

Article #15 Notes: Herbal Remedies and Their Possible Effect on the GABAergic System and Sleep

Source Title	Herbal Remedies and Their Possible Effect on the GABAergic System and Sleep
Source citation (APA Format)	Bruni, O., Ferini-Strambi, L., Giacomoni, E., & Pellegrino, P. (2021). Herbal remedies and their possible effect on the GABAergic system and sleep. *Nutrients*, *13*(2), 530. https://doi.org/10.3390/nu13020530
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC7914492/
Source type	Journal Article
Keywords	Herbal, GABAergic system, GABA receptors, phramacotherapy, GABA metabolism
#Tags	#Herbal #GABAergic #GABA receptors
Summary of key points + notes (include methodology)	Sleep is very important for both physical and emotional health. When people have trouble sleeping, it's called insomnia, which is a common problem. Many people prefer to use herbal medicines like valerian, passionflower, lemon balm, lavender, and Californian poppy to help with sleep. These herbs are considered safe and have been used for centuries to treat insomnia. Research has shown that these herbs may help people fall asleep faster and improve sleep quality by affecting a substance in the brain called GABA. GABA is a neurotransmitter, which is a chemical that helps control sleep by calming the brain's activity. Some medications for insomnia, like benzodiazepines, work by affecting the GABA system. Many herbal remedies are thought to work the same way, helping to calm the brain and promote sleep. However, we still don't fully understand how these herbal treatments work, and more research is needed.
Research Question/Problem/ Need	How do herbal medicines influence GABA receptors to help improve sleep in people with insomnia?

Important Figures	 Open in a new tab PRISMA flow diagram. GABA, gamma-aminobutyric acid; PRISMA, preferred reporting items for systematic reviews and meta-analyses.
VOCAB: (w/definition)	Insomnia: Difficulty falling asleep or staying asleep, leading to poor sleep quality. Herbal Medicines: Plant-based substances used for healing or health, often as an alternative to prescription medications. Neurotransmitter: A chemical in the brain that helps send messages between nerve cells. GABA: A neurotransmitter that helps calm brain activity and plays a key role in sleep regulation. Benzodiazepines: A class of medications often used to treat anxiety and insomnia by affecting GABA receptors. Sedative: A substance that has a calming or sleep-inducing effect. Hypnotic: A drug or substance that helps induce sleep.
Cited references to follow up on	Steiger A. Sleep and Its Modulation by Substances That Affect GABAA Receptor Function. In: Monti J.M., Pandi-Perumal S.R., Möhler H., editors. GABA and Sleep: Molecular, Functional and Clinical Aspects. Springer; Basel, Switzerland: 2010. pp. 121–146.

	Uusi-Oukari M., Korpi E.R. Regulation of GABAA Receptor Subunit Expression by Pharmacological Agents. Pharmacol. Rev. 2010;62:97–135. doi: 10.1124/pr.109.002063.
Follow up Questions	- What are some other natural ways to improve sleep without using medications? - Why is it important to study how herbal medicines work on GABA receptors? - What are the potential risks of using herbal medicines for insomnia, even though they are generally considered safe?

Article #16 Notes: Herbal Insomnia Medications that Target GABAergic Systems: A Review of the Psychopharmacological Evidence

Source Title	Herbal Insomnia Medications that Target GABAergic Systems: A Review of the Psychopharmacological Evidence
Source citation (APA Format)	Shi, Y., Dong, J., Zhao, J., Tang, L., & Zhang, J. (2014). Herbal Insomnia Medications that Target GABAergic Systems: A Review of the Psychopharmacological Evidence. *Current Neuropharmacology*, *12*(3), 289–302. https://doi.org/10.2174/1570159x11666131227001243
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC4023459/
Source type	Journal Article
Keywords	Insomnia, GABAergic, Therapeutic, Natural, Hypotonic, natural products, sedatives, γ-aminobutyric acid
#Tags	#GABAergic #Therapeutic plants #Hypotonic
Summary of key points + notes (include methodology)	Insomnia is a common sleep disorder, especially among women and older adults. It is often treated with drugs that target neurotransmitters like GABA, melatonin, histamine, orexin, and serotonin. Among these, GABAA receptor modulators are commonly used, but they can cause problems such as dependency and tolerance. To find safer treatments, many studies have focused on GABA and herbal medicines. Herbs like Piper methysticum and Zizyphus jujuba have been used for centuries in traditional medicine to improve sleep and treat anxiety. These herbs are generally considered effective and safe, though they can cause side effects such as liver damage in the case of Kava. Despite their popularity and historical use, there is not enough research to fully confirm the safety of many herbal remedies. This review looks at the current knowledge about herbal medicines that help with insomnia and highlights the need for further research into their safety and effectiveness.
Research Question/Problem/ Need	How do herbal medicines like Piper methysticum and Zizyphus jujuba affect GABA receptors to improve sleep in people with insomnia?

Important Figures

Herbal Medicine	Common Names	Medicinal Parts	Mechanisms of Action	Type of Evidence*
Piper methysticum L.f. (Piperaceae)	Kava, Kava Kava, Kava Pepper, Kava Shrub, Kava-Kava, Kawa Pepper, Yangona Pepper	Root	Modifies the GABAA receptor [23]	1, 2, 3
Zizyphus jujuba Mill var. *spinosa* (Rhamnaceae)	Plants, Chinese Date, Common Jujube	Seed	Modifies the GABAA receptor; Activates the GABAA receptor; Increases GABA synthesis by GAD activation [25]	1, 2, 3

VOCAB: (w/definition)

Herbal Medicines: Natural remedies derived from plants, often used to treat various health conditions, including insomnia.
Sedative: A substance that calms the body and induces sleep.
Anxiolytic: A substance used to reduce anxiety.
Kava (Piper methysticum): A plant from the Pacific Islands known for its calming effects, commonly used to treat anxiety and insomnia.
Lactones: Chemical compounds found in Kava that are believed to contribute to its calming effects.

Cited references to follow up on

Chen FP, Jong MS, Chen YC, Kung YY, Chen TJ, Chen FJ, Hwang SJ. Prescriptions of Chinese herbal medicines for insomnia in Taiwan during 2002. Evid-Based. Complement. Altern. Med. 2011;2011(236341) doi: 10.1093/ecam/nep018.

Olsen RW, Sieghart W. GABAA receptors: subtypes provide diversity of function and pharmacology. Neuropharmacology. 2009;56:141–148. doi: 10.1016/j.neuropharm.2008.07.045.

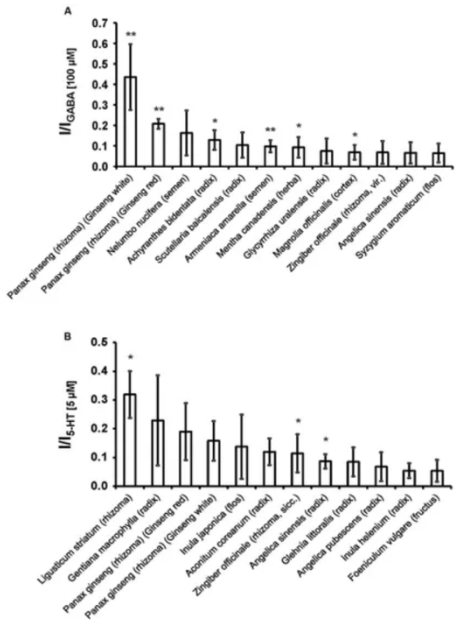
Follow up Questions

- What are the potential side effects of using herbal remedies like Kava for insomnia?

	- How do GABA receptors work in regulating sleep, and why are they important in treating insomnia? - What additional research is needed to fully understand the safety and effectiveness of herbal medicines for insomnia?

Article #17 Notes: Kampo Medicine: Evaluation of the Pharmacological Activity of 121 Herbal Drugs on GABAA and 5-HT3A Receptors

Source Title	Kampo Medicine: Evaluation of the Pharmacological Activity of 121 Herbal Drugs on GABAA and 5-HT3A Receptors
Source citation (APA Format)	Hoffmann, K. M., Herbrechter, R., Ziemba, P. M., Lepke, P., Beltrán, L., Hatt, H., Werner, M., & Gisselmann, G. (2016). Kampo Medicine: Evaluation of the pharmacological activity of 121 herbal drugs on GABAA and 5-HT3A receptors. *Frontiers in Pharmacology*, *7*. https://doi.org/10.3389/fphar.2016.00219
Original URL	https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2016.00219/full
Source type	Journal Article
Keywords	Herbal, GABA A receptors, Pharmacology
#Tags	#GABA #Therapeutic #Activation
Summary of key points + notes (include methodology)	Kampo medicine, a form of Japanese traditional medicine rooted in Chinese practices, uses a variety of herbal remedies to treat symptoms such as nausea, gastrointestinal issues, anxiety, restlessness, and insomnia. This study looked to investigate the pharmacological effects of 121 Kampo herbal tinctures on two important receptors: 5-HT3A and GABAA receptors, which are involved in various physiological processes, including mood regulation, sleep, and gastrointestinal motility.The study found that several tinctures, such as those derived from Lindera aggregata and Leonurus japonicus, were particularly effective at inhibiting the 5-HT3A receptor, which is involved in nausea and vomiting. Additionally, tinctures from plants like Panax ginseng, Syzygium aromaticum, and Magnolia officinalis were found to potentiate the GABAA receptor, which plays a role in anxiety and sleep regulation. Leonurine, a compound from Leonurus japonicus, was identified as a new antagonist of the 5-HT3A receptor. These findings offer new insights into the mechanisms of Kampo remedies and their potential therapeutic applications in modern medicine, especially for treating insomnia and anxiety
Research Question/Problem / Need	How do Kampo herbal tinctures interact with 5-HT3A and GABAA receptors to treat symptoms like insomnia and anxiety?

Important Figures	Figure 1  **FIGURE 1. The strongest 12 direct activating tinctures for the 5-HT_{3A} (A) and $GABA_A$ receptors (B).** The 121 tinctures were made from Kampo remedies via ethanol extraction (see section Tinctures and substances). A 1:1,000-dilution was applied to the oocytes and compared with agonist induced currents (5 μM 5-HT, 100 μM GABA). Error bars represent the SEM. Statistical significance was calculated based on the current evoked by ethanol (0.1 Vol.-%; $^*p < 0.05$, $^{**}p < 0.005$; $n = 3–5$).
VOCAB: (w/definition)	Kampo Medicine: Traditional Japanese medicine based on Chinese herbal practices, often used to treat gastrointestinal, anxiety, and sleep-related issues. 5-HT3A Receptor: A serotonin receptor involved in nausea, vomiting, and gastrointestinal motility. It is a target for certain anti-nausea medications. GABAA Receptor: A receptor for gamma-aminobutyric acid (GABA), involved in inhibiting neuronal activity and inducing sedative effects. It is a major target for drugs used to treat anxiety and insomnia. Tincture: A liquid extract of plant material, typically dissolved in ethanol, used in herbal medicine. Leonurine: A compound isolated from Leonurus japonicus, identified as a new antagonist of the 5-HT3A receptor. Panax Ginseng: A plant used in Kampo medicine for its sedative and anxiolytic (anxiety-reducing) effects, known to potentiate GABAA receptors. Syzygium Aromaticum: Also known as clove, used in Kampo for its anxiolytic and sedative effects. Magnolia Officinalis: A plant traditionally used in Kampo medicine to treat anxiety and sleep disorders by potentiating GABAA receptor activity.
Cited references to follow up on	Guenette, S. A., Beaudry, F., Marier, J. F., and Vachon, P. (2006). Pharmacokinetics and anesthetic activity of eugenol in male Sprague-Dawley rats. J. Vet. Pharmacol. Ther. 29, 265–270. doi: 10.1111/j.1365-2885.2006.00740.x Gyermek, L. (1995). 5-HT3 receptors: pharmacologic and therapeutic aspects. J. Clin. Pharmacol. 35, 845–855. doi: 10.1002/j.1552-4604.1995.tb04129.x Haniadka, R., Rajeev, A. G., Palatty, P. L., Arora, R., and Baliga, M. S. (2012). (Ginger) as an anti-emetic in cancer chemotherapy: a review. J. Altern. Complement. Med. 18, 440–444.

	doi: 10.1089/acm.2010.073
Follow up Questions	- What are the specific benefits and risks of using Kampo remedies for insomnia, especially in combination with modern treatments? - How does the interaction between Leonurine and the 5-HT3A receptor contribute to its potential in treating nausea and insomnia? - Could the findings from this study lead to the development of new pharmacological agents targeting GABAA and 5-HT3A receptors for insomnia and anxiety disorders?

Article #18 Notes: Dietary and botanical anxiolytics

Source Title	Dietary and botanical anxiolytics
Source citation (APA Format)	Alramadhan, E., Hanna, M. S., Hanna, M. S., Goldstein, T. G., Avila, S. M., & Weeks, B. S. (2012). Dietary and botanical anxiolytics. *Medical Science Monitor*, *18*(4), RA40–RA48. https://doi.org/10.12659/msm.882608
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC3560823/#:~:text=Valerian%20is%20a%20temperate%20root%20and%20has,involved%20in%20the%20synthesis%20of%20GABA%20[95].
Source type	Journal Article
Keywords	Anxiety, Benzodiazepines, Genetics, GABA, GAD
#Tags	#Benzodiazpine #GABA #Therapy
Summary of key points + notes (include methodology)	This article talks about different ways to treat anxiety, focusing on natural methods instead of drugs. Anxiety is when you feel worried, scared, or uneasy, even when there isn't a real danger. Many people use medicine to help with anxiety, but those medicines can cause problems like addiction, depression, or bad side effects. The article suggests that there are better, natural treatments using vitamins, minerals, herbs, and amino acids. These things can help balance the chemicals in your brain and reduce anxiety without the harsh side effects of medicines. Some important nutrients, like L-tryptophan (which helps make serotonin) and L-tyrosine (which helps make dopamine), can help improve mood. There are also herbs like Kava Kava and St. John's Wort that are known to reduce anxiety. These natural treatments focus on fixing the real causes of anxiety, rather than just hiding the symptoms.
Research Question/ Problem/ Need	How do natural supplements like amino acids and herbs help reduce anxiety compared to prescription medications?
Important Figures	
VOCAB: (w/definition)	Anxiety: A feeling of worry, fear, or uneasiness, often without a clear cause. Neurotransmitters: Chemicals in the brain that help transmit signals between nerve cells and affect mood and emotions. Amino Acids: Building blocks of protein that also help make neurotransmitters in the brain. Herbs: Plants used for their medicinal properties, such as reducing anxiety or improving mood. Supplements: Additional vitamins, minerals, or other nutrients taken to improve health. HPA Axis: A system in the body that helps control the stress response, involving the brain and adrenal glands.

Cited references to follow up on	Hood SD, Hince DA, Davies SJ, et al. Effects of acute tryptophan depletion in serotonin reuptake inhibitor-remitted patients with generalized anxiety disorder. Psychopharmacology (Berl) 2010;208(2):223–32. doi: 10.1007/s00213-009-1722-1. Ruhe HG, Mason NS, Schene AH. Mood is indirectly related to serotonin, norepinephrine and dopamine levels in humans: a meta-analysis of monoamine depletion studies. Mol Psychiatry. 2007;12:331–59. doi: 10.1038/sj.mp.4001949.
Follow up Questions	- What are some common symptoms of anxiety? - How can supplements like L-tryptophan and L-tyrosine help with anxiety? - What are the benefits of using herbs like Kava Kava instead of prescription drugs for anxiety?

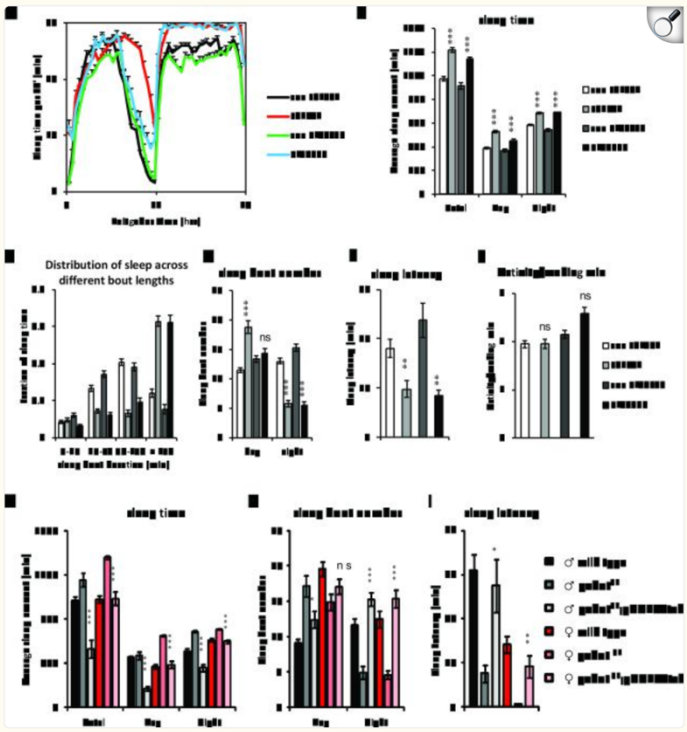
Article #19 Notes: PCR-Based homology probing reveals a family of GABA receptor-like genes in Drosophila melanogaster

Source Title	PCR-Based homology probing reveals a family of GABA receptor-like genes in Drosophila melanogaster
Source citation (APA Format)	Henderson, J. E., Knipple, D. C., & Soderlund, D. M. (1994). PCR-Based homology probing reveals a family of GABA receptor-like genes in Drosophila melanogaster. *Insect Biochemistry and Molecular Biology*, *24*(4), 363–371. https://doi.org/10.1016/0965-1748(94)90029-9
Original URL	https://www.sciencedirect.com/science/article/pii/0965174894900299
Source type	Journal Article
Keywords	Drosophila melanogaster, GABA receptor, Chloride channel, Gene family
#Tags	#Drosophila #GABA recptor
Summary of key points + notes (include methodology)	This article describes a study that used a technique called Polymerase Chain Reaction (PCR) to search for genes in Drosophila melanogaster (fruit flies) that are similar to genes found in vertebrates, specifically genes for GABA receptors and glycine receptors. These receptors are important for brain function because they help control the flow of chloride ions, which are essential for nerve signaling. The researchers found three regions in the fruit fly DNA, named LCCH1, LCCH2, and LCCH3, that had genes encoding proteins with more than 40% similarity to similar proteins found in vertebrates. They isolated these genes and sequenced them to study their structure. The researchers also found that these genes did not have all the typical parts that are present in vertebrate genes. This study provides evidence that Drosophila melanogaster has a diverse set of genes that are structurally related to the chloride channel family, like those found in vertebrates.
Research Question/Problem/ Need	How do the genes in Drosophila melanogaster that are related to vertebrate chloride channels function, and what are their roles in fruit fly biology?
Important Figures	
VOCAB: (w/definition)	Polymerase Chain Reaction (PCR): A laboratory technique used to amplify (make many copies of) specific DNA sequences. Ligand-Gated Chloride Channel: A type of receptor in the cell membrane that opens in response to a chemical signal, allowing chloride ions to enter the cell.

	GABA (Gamma-Aminobutyric Acid): A neurotransmitter that inhibits brain activity and helps regulate nervous system function. Glycine Receptor: A type of receptor that also regulates nervous system function by allowing chloride ions to flow into the cell. Open Reading Frame (ORF): A part of a gene that can be translated into a protein.
Cited references to follow up on	Benton, W. D., & Davis, R. W. (1977). Screening λgt Recombinant Clones by Hybridization to Single Plaques in Situ. Science, 196(4286), 180–182. https://doi.org/10.1126/science.322279
Follow up Questions	- What is the function of the GABA and glycine receptors in the nervous system? - How do the new genes (LCCH2 and LCCH3) found in Drosophila melanogaster differ from known genes in other species? - What is the importance of finding a diverse family of chloride channel genes in Drosophila melanogaster?

Article #20 Notes: A neuron-glia interaction involving GABA Transaminase contributes to sleep loss in sleepless mutants

Source Title	A neuron-glia interaction involving GABA Transaminase contributes to sleep loss in sleepless mutants
Source citation (APA Format)	Chen, W., Maguire, S., Sowcik, M., Luo, W., Koh, K., & Sehgal, A. (2014). A neuron–glia interaction involving GABA transaminase contributes to sleep loss in sleepless mutants. *Molecular Psychiatry*, *20*(2), 240–251. https://doi.org/10.1038/mp.2014.11
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC4168011/
Source type	Journal Article
Keywords	Sleep, GABA transaminase, Glia, Mitochondria, Quiver/sleepless, Drosophila
#Tags	#Drosophila #GABA #Glia
Summary of key points + notes (include methodology)	This study looks at how sleep is controlled in Drosophila (fruit flies), using a gene called sleepless (sss) as a model. The sss gene is important for sleep regulation, and when it is lost, flies sleep less and their neurons become more excitable. To understand why this happens, the researchers looked at the proteins in the brains of flies with the sss mutation. They found that a protein called CG7433 was increased in the brains of sss flies. This protein is linked to GABA, a chemical in the brain that helps with sleep and wakefulness. In sss flies, the increase in CG7433 led to lower levels of GABA, which was associated with less sleep. When the researchers removed CG7433 from the flies, their sleep returned to normal, suggesting that CG7433 plays a role in reducing sleep. Interestingly, CG7433 acts in the glial cells (cells that support neurons) rather than neurons themselves to influence sleep.
Research Question/Problem/ Need	How does the protein CG7433, found in glial cells, affect sleep regulation in Drosophila flies?

Important Figures	Figure 2.  Open in a new tal Loss of *GABAT* promotes sleep. (**A-F**) Male *GABAT* mutants and control flies from outcrossing were monitored for sleep behavior in 12hr light:12hr dark cycles (12:12LD) at 25°C. Daily sleep profiles (**A**) and parameters of sleep behavior (**B-F**) were compared between each of the two *GABAT*
VOCAB: (w/definition)	Neuronal excitability: The ability of neurons to be easily activated, which can lead to increased brain activity and less sleep. Proteomic approach: A method used to study the proteins in a cell or organism, especially their functions and interactions. CG7433: A protein found to be increased in the brains of sss mutant flies, which plays a role in regulating sleep. GABA (gamma-aminobutyric acid): A neurotransmitter that inhibits brain activity, playing a key role in promoting sleep and relaxation. Glia: Supportive cells in the brain that help neurons function. They don't carry signals like neurons but are crucial for brain health. Transgene: A gene that has been transferred into an organism, often used in genetic experiments to study gene function. Two-dimensional differential gel electrophoresis (2D-DIGE): A technique used to compare the protein content of different samples to identify changes in protein expression.
Cited references to follow up on	Chung BY, Kilman VL, Keath JR, Pitman JL, Allada R. The GABA(A) receptor RDL acts in peptidergic PDF neurons to promote sleep in Drosophila. Curr Biol. 2009 Mar 10;19(5):386–390. doi: 10.1016/j.cub.2009.01.040.

	Fei H, Chow DM, Chen A, Romero-Calderon R, Ong WS, Ackerson LC, et al. Mutation of the Drosophila vesicular GABA transporter disrupts visual figure detection. J Exp Biol. 2010 May;213:1717–1730. doi: 10.1242/jeb.036053. Pt 10.
Follow up Questions	- What is the exact role of GABA in sleep regulation in flies and other animals? - How do neurons and glial cells communicate to regulate sleep and wakefulness? - Could manipulating the levels of CG7433 be a way to treat sleep disorders in humans?

Patent #1 Notes: System for early detection and risk prediction of schizophrenia

Source Title	System for early detection and risk prediction of schizophrenia
Source citation (APA Format)	吴凯, 刘亚, 韩俊南. (2020). *Autonomic nerve function data processing method and device for high-risk schizophrenic people* (China CN112057087B).

	https://patents.google.com/patent/CN112057087B/en?q=(schizophrenia)&oq=schizophrenia
Original URL	https://patents.google.com/patent/CN110063732B/en?q=(schizophrenia)&oq=schizophrenia
Source type	Patent
Keywords	Schizophrenia, classification, detection, MRI
#Tags	#Schizophrenia #Detection #Algorithm

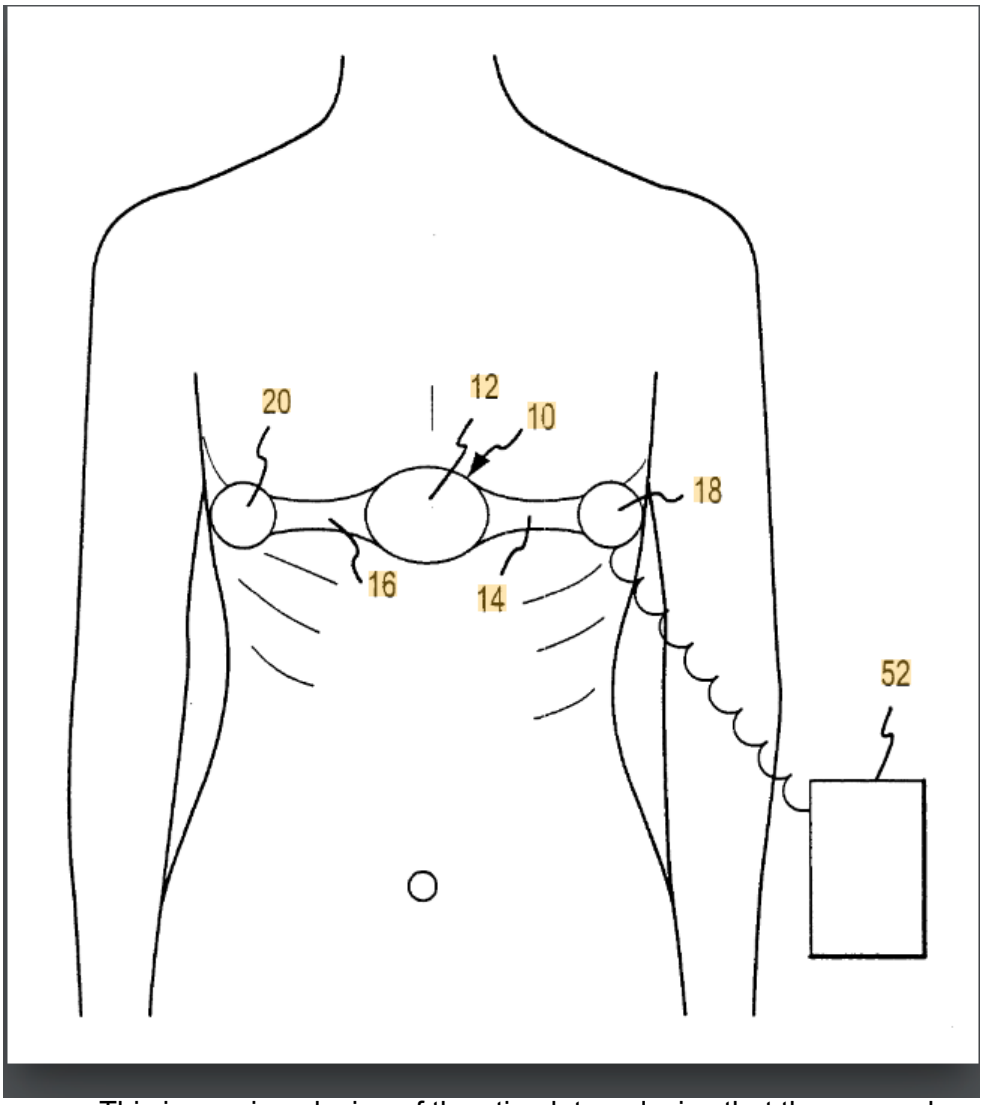
Summary of key points + notes (include methodology)	Schizophrenia is a serious mental disorder with an unknown cause. It normally occurs in patients who suffer from cognitive, social, and functional disorders and affects about 1 percent of the population all over the world. Currently, there are no systems for doctors to detect the early onset of schizophrenia, and by the time they detect the disease, there are no ways to cure it. In this patent, the device can accurately detect schizophrenia early and also determine a risk prediction for four different groups of people.
	
	Notes:
	- The device is used for the early detection and risk prediction of schizophrenia
	  ○ Can accurately and objectively detect
	- The test model can carry out examinations on 4 different groups of people
	  ○ First-onset
	  ○ High-risk
	  ○ Ultrahigh risk
	  ○ Normal control group
	- There are different modules that are mentioned in the model
	  ○ Acquisition and preprocessing module
	  ▪ It acquires encephalograms of the four groups
	  ○ Data analysis module
	  ▪ Carries out event-related potential analysis
	  ▪ Source positioning analysis
	  ▪ Brain network analysis
	  ○ Learning classification module
	  ▪ Used for taking cognitive characteristics and electrophysiological characteristics

Research Question/Problem / Need	Problem: Currently, about 1% of the world is diagnosed with Schizophrenia and the issue is that there is no way to detect the early onset of it.
Important Figures	

	$$ERP_{S_i} = \frac{1}{n}\sum_{j=1}^{n} ERP_{P_j,S_i}$$ - This image displays the method of superposition used in the device to detect and analyze the stored data from the patients.
VOCAB: (w/definition)	Parameter: A measurable factor forming one of a set that the conditions of its operation Resonance: The quality in a sound of being deep or full Acquisition: The learning or developing of a skill Embodiments: A tangible or visible form of an idea
Cited references to follow up on	CN112568912B - Depression biomarker identification method based on non-invasive brain electric signal - Google Patents. (n.d.). https://patents.google.com/patent/CN112568912B/en?q=(schizophrenia)&oq=schizophrenia CN112057087B - Autonomic nerve function data processing method and device for high-risk schizophrenic people - Google Patents. (n.d.). https://patents.google.com/patent/CN112057087B/en?q=(schizophrenia)&oq=schizophrenia
Follow up Questions	- What patterns in EEG signals contribute to this improvement? - Why was the XGBoost machine learning algorithm specifically chosen for classification? - What role does the P50 sensory gating task play in identifying early neural abnormalities in schizophrenia?

Patent #2 Notes: Non-invasive nerve stimulation to treat or prevent autism spectrum disorders and other disorders of psychological development

Source Title	Non-invasive nerve stimulation to treat or prevent autism spectrum disorders and other disorders of psychological development
Source citation (APA Format)	Simon, B.,Errico, J., Raffle, J. (2013). *Non-invasive nerve stimulation to treat or prevent autism spectrum disorders and other disorders of psychological development* (United States US11534600B2). https://patents.google.com/patent/US11534600B2/en?q=(GABA+dysfunction)&oq=GABA+dysfunction
Original URL	https://patents.google.com/patent/US11534600B2/en?q=(GABA+dysfunction)&oq=GABA+dysfunction
Source type	Patent
Keywords	Schizophrenia, EEG, phenotypes, diagnosis, brain connect, neuro electrophysiological
#Tags	#schizophrenia #EEG #Diagnosis
Summary of key points + notes (include methodology)	This patent describes a method for enhancing blood flow to the thorax in patients by periodically stimulating the phrenic nerve to induce diaphragm contractions. The design creates increased negative intrathoracic pressure. The technique also involves occluding airflow to the lungs using a valve during diaphragm contractions to amplify this negative pressure effect. The methodology involves applying electrical current to the phrenic nerve using electrodes strategically placed over the cervical vertebrae (C3 to C7) and adjusting the stimulation parameters based on measured intrathoracic pressure. The method can be used in various clinical scenarios, including hemorrhagic shock, hypovolemic shock, etc.
Research Question/Problem/ Need	How does phrenic nerve stimulation affect hemodynamics in patients with different types of shock or cardiac arrest?

Important Figures	 - This image is a design of the stimulatory device that the researchers created to stimulate the nerves in the body
VOCAB: (w/definition)	T-test: A statistical tool that measures the difference between the means of two groups Acquisition: The learning or developing of a skill Dysfunction: Abnormality or impairment in the function
Cited references to follow up on	Simon, B. J., Errico, J. P., Raffle, J. T., & Inc, E. (n.d.). US6463327B1 - Stimulatory device and methods to electrically stimulate the phrenic nerve - Google Patents. https://patents.google.com/patent/US6463327B1/en?q=(GABA+dysfunction)&oq=GABA+dysfunction Lurie, K. G., Zielinski, T. M., Voelckel, W., Patterson, R., Samniah, N., McKnite, S., Lindner, K., & Llc, C. (n.d.). US6463327B1 - Stimulatory device and methods to electrically stimulate the phrenic nerve - Google Patents. https://patents.google.com/patent/US6463327B1/en?q=(GABA+dysfunction)&oq=GABA+dysfunction

Follow up Questions	- What are the long-term effects of repeated phrenic nerve stimulation in patients with chronic conditions? - What are the potential risks or complications associated with this method?